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Ultrasound variations of diaphragm activity between prone position versus supine position in ventilated patients: a cross-sectional comparative study

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Abstract

Purpose To evaluate the effect of the positioning from the supine position (SP) to the prone position (PP) on the diaphragm activity in ventilated patients; using the ultrasound (US) imaging.

Methods A cross-sectional comparative study before/after PP was conducted on 40 ICU patients over 18 years who received invasive ventilation (IV) for at least 48 h. The considered ventilator modes were: assisted control volume with a low trigger flow (between −2 and 2 L/mn) and pressure support mode. US diaphragmatic assessments were performed at SP and at 60 min of PP. Both End-inspiratory and End-expiratory diameters (EID/EED) were taken at 3 levels of axillary lines and determined by the average values of multiple measures. Diaphragmatic thickening fraction (DTF) was calculated as: DTF = (EID − EED/EED) × 100. Pairing and ANOVA tests were used for comparisons.

Results Forty ventilated patients (42 years of median age) at 4 days [2–7] of median duration of ventilation were examined during the two positions: SP versus PP. EID decreased from the SP to the PP (2.8 mm in SP vs. 2.4 mm in PP, $p = 0.001$). No difference was showed regarding the expiratory thickness. Overall, DTF didn't change in PP (37.4 vs. 42.05%, $p = 0.36$). When the patient was placed in PP, the best DTF value was showed at the posterior part of diaphragm (posterior: 45%, median: 31% and anterior: 38%, $p = 0.049$).

Conclusion The ventral placement in ventilated patients reduced end-inspiratory diameter and tended to decrease DTF. In PP, the best contractile activity was detected at the posterior region of diaphragm.

Keywords Invasive ventilation · Prone position · Diaphragm · Ultrasound

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Abbreviations

ARDS	Acute respiratory distress syndrome
ACV	Assisted control volume
BMI	Body mass index
CRF	Chronic respiratory failure
DTF	Diaphragmatic thickening fraction
EID	End-inspiratory diameter
EED	End-expiratory diameter
IQR	Inter quartile range
ICU	Intensive care unit
IV	Invasive ventilation
med	Median
PP	Prone position
PSV	Pressure support ventilation
SP	Supine position
SAPS	Simplified acute physiology score
SOFA	Sequential organ failure assessment
US	Ultrasound
VIDD	Ventilator-induced diaphragmatic dysfunction

Background

Prone position (PP) is a simple and effective measure to manage severe hypoxemia regardless of the cause [1, 2]. In fact, PP induces a redistribution of ventilation to the dorsal zones; owing to an improvement of matching lung size with the chest cavity and as a result; a more uniform ventilation and perfusion [3, 4]. In addition, PP promotes drainage of the bronchial secretions, which reduces the risk of nosocomial pneumonia.

The diaphragm is the major inspiratory/pump muscle and its contractile function plays a pivotal role in the ribcage and lung compliance. Its anterior part (horizontal and convex upward) serves as a septum separating the thoracic (pleural) and abdominal (peritoneal) compartments of the body. The posterior part, vertical, is annexed to the vertebral column and to the last ribs forming its pillars [5–7]. During inspiration, the excursion of the muscular fibres of the diaphragm causes a piston-like action, dragging the lungs downwards and forcing the lower chest wall outwards.

In ventilated patients, PP improves thoraco-pulmonary compliance resulting from the release of the posterior regions. The opposite happens in the anterior chest wall where the compliance will be reduced. The effect of PP on diaphragm activity remains unclear and the focus here would be on this question.

Transthoracic ultrasound (US) has become a widely used tool, capable of providing a non-invasive bedside evaluation of diaphragmatic function. In ICU patients, this modality has raised great interest for the measuring of diaphragm thickening during invasive ventilation (IV) [8, 9].

At the present time and to the best of our knowledge, no study has evaluated the changes in diaphragmatic activity, caused by PP, in ventilated adult patients.

Herein, we aimed to describe the diaphragm thickening changes "potentially caused" by the ventral positioning in ventilated patients; using the ultrasound imaging. We have focused on the two-dimensional (B-mode) on the zone of apposition to measure end-inspiratory and end-expiratory diameters (EID/EED) and to calculate the diaphragm thickening fraction (DTF). Thus, DTFs were compared between the 2 positions SP versus PP.

Patients and methods

Study design

A cross-sectional comparative study on matched series; conducted in a medical intensive care unit (ICU) over a 6 months period (March–August 2019). Person responsible for making decision for the participant or patient were informed and consented for participation in the study. Approval was obtained by the local ethics committee of our hospital. Our study protocol was conforming to the Declaration of Helsinki.

Study population

We included 40 ICU patients over 18 years requiring invasive ventilation (IV) regardless of the underlying aetiology. The considered ventilator modes were assisted control volume with a low trigger flow (between -2 and 2 L/mn) in order to ensure a comfortable synchrony between patient and ventilator and pressure support ventilation (PSV) mode. Thus, we obtained 2 groups to compare by pairing: a group of ventilated patients in supine position (SP, $n=40$) versus the same patients positioned in prone position (PP, $n=40$). We excluded patients who presented an incident during the PP procedure requiring the return to SP, patients receiving deep sedation and/or neuromuscular blockers and those with a poor echogenicity.

Study protocol

For all the 40 studied patients, US assessment was performed in 2 stages: 1st stage: in SP with a minimum of 48 h of IV and 2nd stage: after a timing of at least 60 min of PP positioning.

Ultrasound examination was undertaken by two operators trained in diaphragmatic ultrasound. We used an ultrasonic device [*Model: Aloka-ARIETTA V60, manufacturing Year: 2014, Company: Hitachi, Ltd, manufacturing country Chiyoda, Tokyo, Japan],* equipped with a piezoelectric probe with linear array of high frequency (10 MHz) and providing incidences in B (two-dimensional) mode, in TM (time/movement) mode and TDI (Tissue Doppler Imaging) mode. Referring to the previously described diaphragm exploration techniques [9–11], the Diaphragmatic Thickening Fraction (DTF)'s assessment can be obtained in the zone of apposition of the diaphragm (7th–9th intercostals spaces). At both positions (SP and PP), the measurements were taken at 3 levels of axillary lines (posterior, median and anterior) according to the direction of probe pointer (supplementary material) and their means were recorded as EID and EED. To note that in obese patients (BMI > 30) the measurements were assisted by a low-resolution probe (dedicated to the abdominal organs).

Sonographic features of the diaphragm movements and measurements

The obtained image is observed as a structure made of three distinct layers: 2 echogenic lines, the interfaces to pleura and

peritoneum, sandwiching a hypoechogenic line, which represents the diaphragm muscle. With the B-mode, we recognize the variation of the diaphragmatic thickness, reflecting the inspiratory and expiratory excursions of the diaphragm. The 2 D video was frozen and moved to measure the end-inspiratory diameter (EID) and end-expiratory diameter (EED).

In order to avoid errors in the US measurements of the variations of such a small thickness, we ensured the following rules for all measurements:
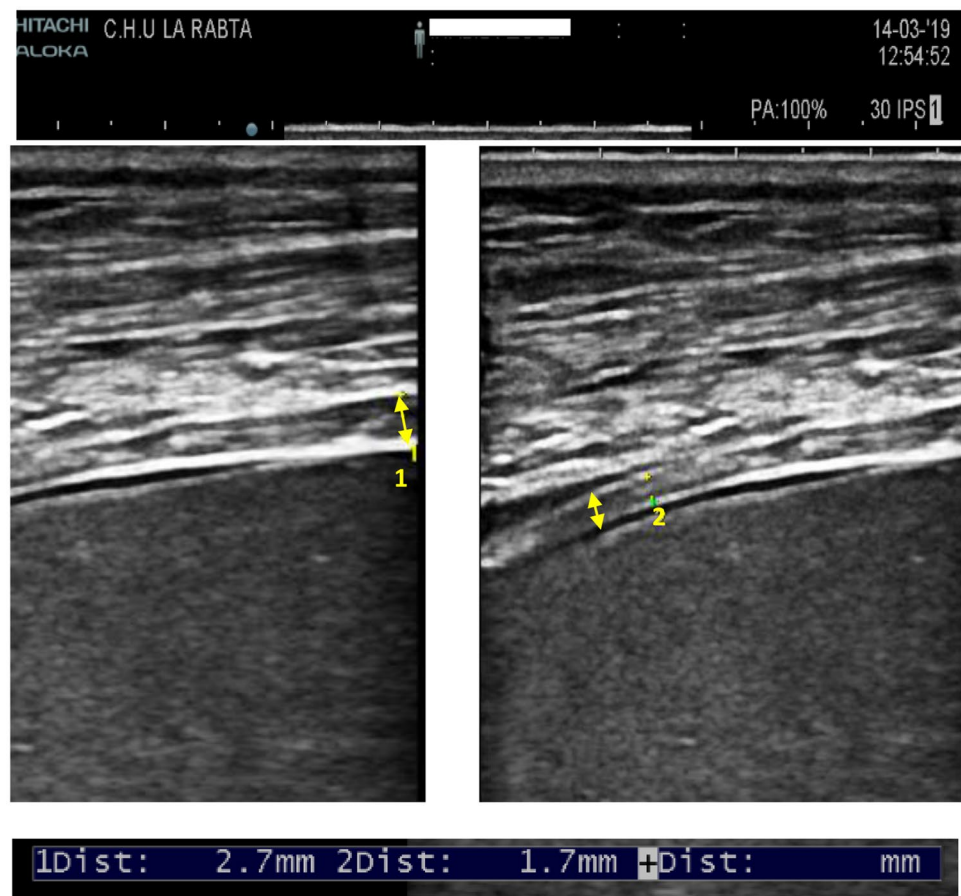
- The measurements were taken in B mode by positioning the calipers between the lower edge of the pleural line and the upper edge of the peritoneal line delimiting the hypoechogenic zone which is the diaphragmatic muscle (Fig. 1).
- We took the average value of 5 measurements for each diameter.

Diaphragmatic thickening fraction (DTF) was used as an index of diaphragmatic contractility and it was calculated as follows: $DTF = (EID - EED/EED) \times 100$.

Statistical analyses

Both clinical data and US measurements were saved and coded in a computerized data mask. Quantitative variables were expressed on mean $\pm$ standard deviation or median (IQR 25th–75th) as appropriate and qualitative variables were expressed in percentages. Ultrasound variables before/after the positioning in PP were compared using Wilcoxon's non-parametric paired series test. Comparison between the repeated measures at inspiration and expiration times of diaphragm diameters and DTF (3 measures in each position and all 6 measures in the two positions) were made using Analysis of Variance (ANOVA).

Fig. 1 Ultrasound Measurements of EID and EED of the diaphragm at the zone of apposition. *EID* end-inspiratory diameter, *EED* end-expiratory diameter

Measures 1 and 2 correspond to EID (maximum) and EED (minimum).
The measurements were taken in B mode (video moved and frozen) by positioning the calipers between the lower edge of the pleural line and the upper edge of the peritoneal line delimiting the hypoechogenic zone which is the diaphragmatic muscle.

The analysis was performed with SPSS software version 20. The level of significance was fixed at $p < 0.05$ and all tests were bilateral.

Results

Baseline characteristics

Table 1 displays all clinical characteristics.

Circumstances of ultrasound practice

US diaphragmatic evaluation was performed at a median delay from the beginning of IV at 4 [2–7] days. Vital constants are showed in Table 2. No major incident was detected during the patients turning.

Table 1 Baseline characteristics

Clinical data	Studied patients ($n = 40$)
Age, years (median [IQR])	42 [30–60]
Male/female (sex-ratio)	27/13 (2.07)
BMI, kg/m^2 (median [IQR])	23.6 [22–28]
Obesity (BMI > 30)	6 (15%)
Tobacco, n (%)	20 (50%)
Origin, n (%)	
Emergency department	28 (70%)
Medical services	7 (17.5%)
Surgical services	2 (5%)
Other hospital	3 (7.5%)
Co morbidities, n (%)	
CRF	11 (27.5%)
Hypertension	11 (27.5%)
Diabetes	7 (17.5%)
Cardiac failure	3 (7.5%)
Arrhythmia	2 (5%)
Renal insufficiency	3 (7.5%)
Alzheimer/psychological disorder	3 (7.5%)
Reason of admission in ICU, n (%)	
Respiratory distress	19 (47.5%)
Coma	18 (45%)
Shock	1 (2.5%)
Severe infection	2 (5%)
Severity scores (median [IQR])	
SAPS II	42 [29–51]
APACHE II	15 [12–21]
SOFA	5 [3–8]

APACHE II acute physiology and chronic health evaluation, *BMI* body mass index, *CRF* chronic respiratory failure, *ICU* intensive care unit, *SAPS II* simplified acute physiology score, *SOFA* sequential organ failure assessment

Table 2 Circumstances of US diaphragmatic exploration

| Circumstances	Studied patients ($n = 40$)	
Timing (days) of US exploration from IV, n (%)		
2–4	21 (52.5%)	
5–7	11 (27.5%)	
8–10	1 (2.5%)	
10–13	3 (7.5%)	
≥ 14	4 (10%)	
Nature of endotracheal device, n (%)		
Endotracheal probe	33 (82.5%)	
Cannula of tracheostomy	7 (17.5%)	
Respiratory context, n (%)		
Pneumonia of the Right lung	17 (42.5%)	
Pleurisy of the Right lung	5 (12.5%)	
Chest tube	2 (5%)	
Ventilator mode/settings		
ACV, n (%)	35 (87.5%)	
PSV, n (%)	5 (12.5%)	
Use of norepinephrine, n (%)	13 (32.5%)	
Hemodynamic constants:	In SP	In PP
SBP, mm Hg (med [IQR])	125 [113–140]	120 [110–133]
DBP, mm Hg (med [IQR])	70.5 [60–85]	70 [60–83]
HR, bpm (med [IQR])	90 [81–111]	98 [85–114]
	98 [96–100]	98.5 [97–100]
Pulsed saturation O$_2$	96%	96%

ACV assisted control volume, *DBP* diastolic blood pressure, *HR* heart rate, *IV* invasive ventilation, *PP* prone position, *PEEP* positive end expiratory pressure, *PSV* pressure support ventilation, *SBP* systolic blood pressure, *SP* supineposition, *US* ultrasound

US measurements

- End inspiratory diameters changes: by pairing, the 3 EIDs were significantly lower in PP than in SP. Similarly, the mean EID decreased (2.8 mm [2.4–3.19] in SP vs. 2.45 mm [2.24–2.95] in PP, $p = 0.001$). This significant difference was also observed by comparing all measurements by ANOVA ($p = 0.05$). Diameters by level in every position did not differ (Fig. 2).

- End expiratory diameters changes: by pairing, only the anterior value of EED decreased from SP to PP. The posterior and median levels were similar (Fig. 3). The mean EED decreased significantly (1.87 mm [1.64–2.18] in SP vs. 1.84 mm [1.47–2.05] in PP, $p = 0.037$). No difference was found when all values were compared by ANOVA ($p = 0.37$).

- Diaphragmatic thickening fraction: by pairing, DTF did not change by axillary line level nor by average value (37.4 [30–50] in PP vs. 42.05% in SP [33.5–52.7], $p = 0.36$). By ANOVA: In ventral position, the best DTF was showed with the posterior level (posterior: 45%,
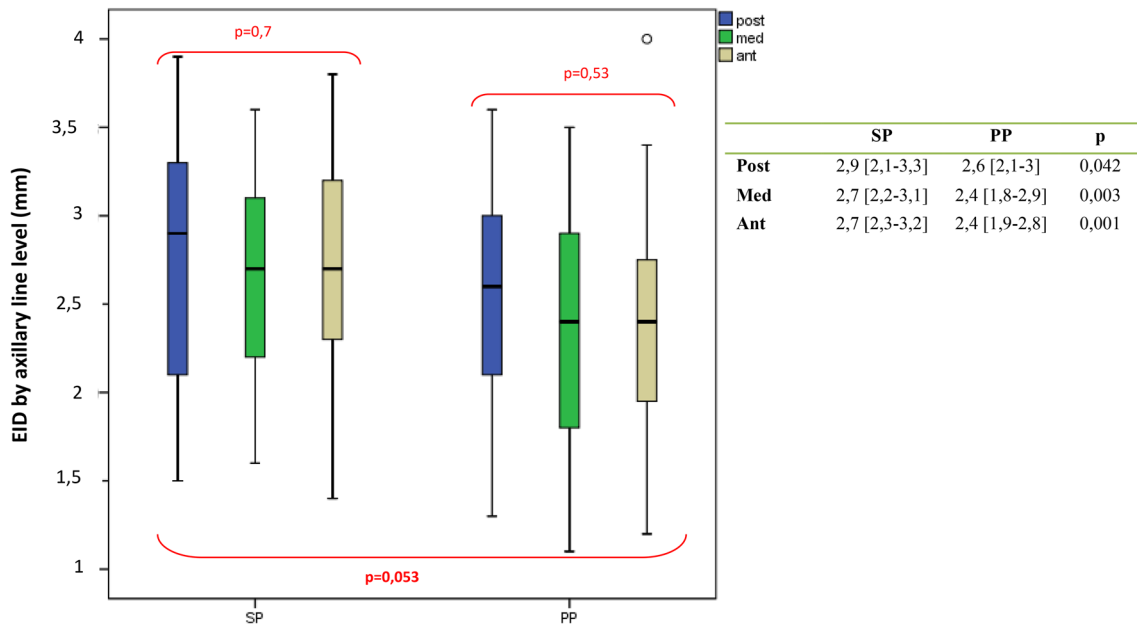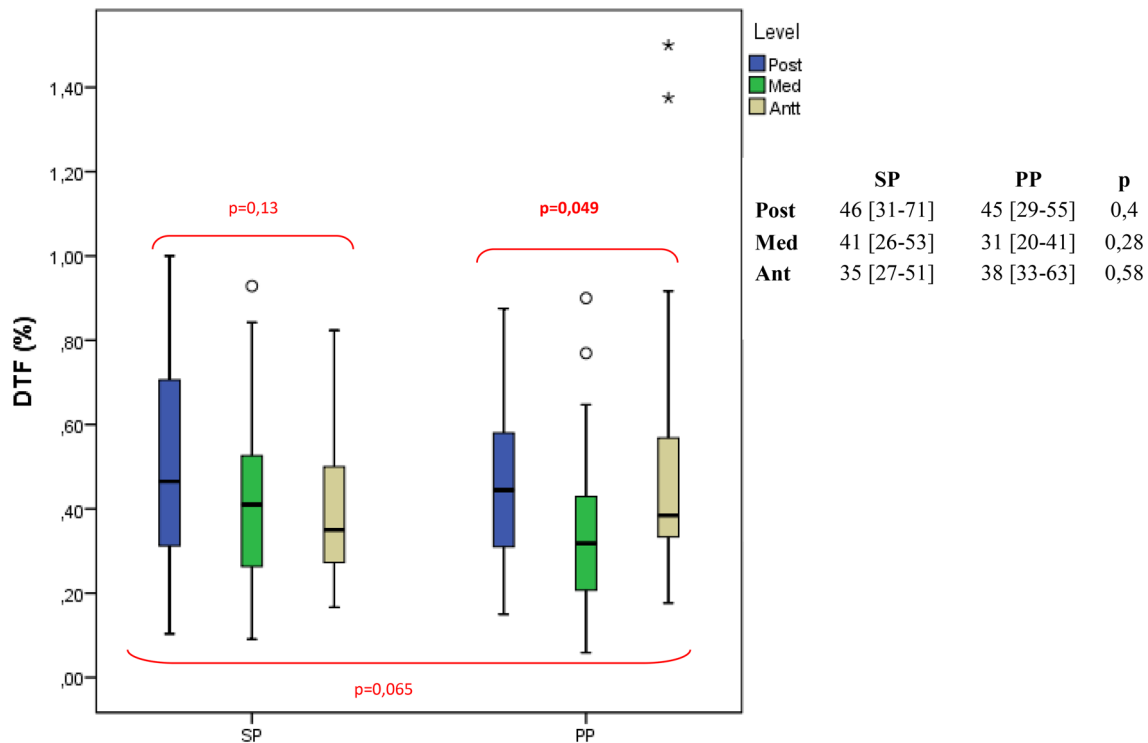
Fig. 2 Comparison between the values of EID: by pairing SP versus PP (table on the right) and by ANOVA (red colour). *ANT* anterior, *EID* end inspiratory diameter, *MED* median, *POST* posterior, *PP* prone position, *SP* supine position
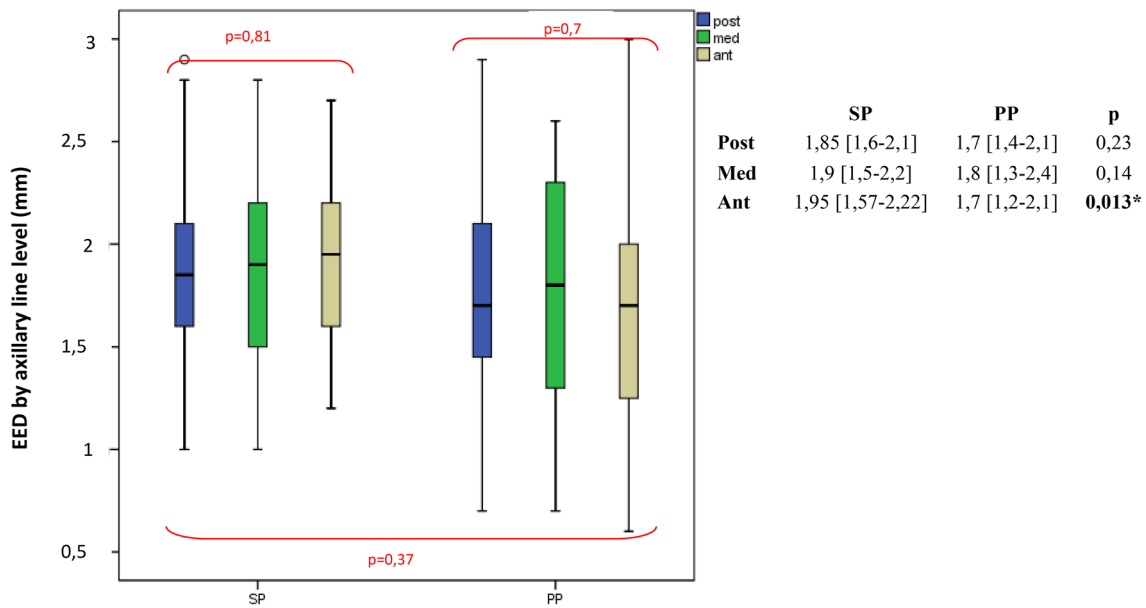
Fig. 3 Comparison between the values of EED: by pairing SP versus PP (table on the right) and by ANOVA (red colour). *ANT* anterior, *EID* end inspiratory diameter, *MED* median, *POST* posterior, *PP* prone position

median: 31% and anterior: 38%, $p = 0.049$). Overall, the difference between the 6 DTF value's was close to significance ($p = 0.065$) (Fig. 4).

Discussion

We showed that in ventilated patients, PP tended to decrease the global diaphragm thickening fraction. Nevertheless, when the patient was placed in PP, the thickening fraction

Fig. 4 Comparison between the values of DTF: by pairing SP versus PP on the right and by ANOVA in the figure. *ANT* anterior, *DTF* diaphragm thickening fraction, *MED* median, *POST* posterior, *PP* prone position, *SP* supine position

was better at the posterior part of the diaphragm than median and anterior zones.

The previous clinical trials showed that prone position improves oxygenation in patients with ARDS, without benefits in terms of survival [12–14]. Regarding the improvement of chest wall mechanics, it remains hypothetical. Physiologically, it is pretended that the total respiratory system mechanics are not modified during prone position [15]. Since a long time, it has been shown that respiratory mechanics improve after returning, suggesting the potential beneficial effects of prone positioning [12, 16, 17]. Despite the decrease in the chest wall compliance, PP does not affect the total respiratory system compliance [17]. The only exception may be the patients with non-pulmonary ARDS, when we showed an increase in respiratory system compliance [18–20].

As the diaphragm is the major muscle of breathing and plays a pivotal role in chest wall compliance, we hypothesized that the turning in PP induced change in diaphragm function. So why, we carried out this study using the ultrasound technique.

Although sonography has become a routinely used tool of diaphragmatic function, a significant limitation lies in its intrinsic operator dependency. In a recent study, Cappellini I et al. [21] focused on the B-mode and M-mode analysis of the zone of apposition to determine the reliability

of diaphragm US in the clinical environment. The authors enrolled 10 healthy volunteers examined by 3 operators with different skills in ultrasonography. They demonstrated that both B-mode and M-mode were sufficiently repeatable to assess DTF [Interclass correlation coefficient (ICC) = 0.16–0.26 and 0.10–0.15, respectively] [21]. In the case of B-mode for the less experienced operator, ICC was not significant [21]. In our study, we referred to the B-mode estimating that the operators are trained and experienced.

For the choice of the right side in our series, it was based on the previous data such as that of Goligher EC, et al. [9] reporting that in the right side, thickness was obtained on 95% of attempts and left hemidiaphragm measurements could not be obtained consistently. Moreover, right hemi diaphragm thickness measurements were highly reproducible (mean ± SD: 2.4 ± 0.8 mm, repeatability coefficient = 0.2 mm, reproducibility coefficient 0.4 mm) particularly after marking the location of the probe [9].

We found that the diaphragm was significantly thinner at end inspiration when the ventilated patient is placed in prone position. It is important to note that these changes have appeared after only 1 h of prone position in our series. As the zone of apposition is controlled by the abdominal muscles, the ventral position may be able to modify the pressure regime on both sides of this zone explaining the changes that we found.

These findings indicate that the ventral positioning hinders the expansion of the diaphragmatic muscle coupled to the chest wall. The most likely explanation is that when the ventilated patient is prone, the diaphragm descends, and it raises intra-abdominal pressure in the area of apposition which, in turn, blocks the diaphragmatic muscle inflation in the lower rib cage. A concomitant phrenic electromyogram (unfortunately not available in our study) could possibly illustrate this disordered diaphragm motion and thus strengthen our ultrasonographic findings.

Moreover, we marked that in PP, the diaphragm motility was better at its posterior zone (dependant in SP became non dependant in PP). Krayer et al. [22] studied 6 healthy volunteers first while awake and breathing spontaneously and again while anesthetized-paralyzed and their lungs ventilated mechanically. High-speed, three-dimensional X-ray computed tomography was the technique of measures. They showed that in five of the six subjects, dorsal diaphragm movement exceeded ventral movement regardless of body position [22]. In the supine position, the pattern of diaphragm motion during mechanical inflation was nearly uniform. By contrast, in the prone position, the motion was non-uniform, with most motion occurring in the dorsal (non-dependent) regions. Authors concluded that the dominant influence on diaphragm motion may be some anatomical difference between the crural and costal diaphragm regions rather than the abdominal hydrostatic pressure gradient [22].

It is possible that the difference of diaphragmatic excursions may occur after several hours of PP. In our series, there was no control of diaphragmatic thickness changes of measurements after prolonged duration of PP (12–16 h) as in ARDS, which is understandable considering the nature and the objective of our transversal study in a heterogeneous group of ventilated patients and not exclusively for ARDS.

A different result was showed in a paediatric study performed on 16 healthy term infants placed in prone position that found a significant increase in end expiratory, end inspiratory lung volumes, diaphragm thickness in the prone position [23]. A result was cited as an indication and not for comparative purposes. In fact, the physiognomy and mechanical properties of the rib cage and diaphragm have nothing to compare with those of an adult patient even more under ventilator.

In adults, Tomita et al. [24] analyzed the differences in diaphragmatic motion between supine and prone positioning during resting breathing in 11 healthy male volunteers using dynamic Magnetic Resonance Imaging. They defined the total diaphragmatic motion (TDM) as total excursion of the anterior (ANT), central (CNT), and posterior (PST) diaphragm. They found that motion tended to be the greatest in the posterior diaphragm. However, relative changes in CNT and ANT were less with prone. These findings suggest that ventilation in the posterior lung fields is decreased to a greater extent with prone rather than with supine positioning [24]. The result that we found concerning the best DTF in PP was at the posterior level which consolidates the suggestions of the above-mentioned study using MRI measurements in healthy subjects [24].

The literature review on this subject finds that the interests are somewhat focused on the ventilator-induced diaphragm dysfunction (VIDD). The VIDD is related with a difficult and prolonged weaning, [25–36] but the real impact of the ventilator on the diaphragm in ICU patient is not established due to the multiple undercurrent factors (sepsis, electrolyte disturbances, hyperinflation, and critical illness polyneuropathy and/or myopathy). While diaphragm atrophy is widely described in the recent literature, the reversal of this process is still poorly studied. Nevertheless, Grassi et al. [37] in a prospective multicentre study demonstrated that pressure support mode can lead to partial restoration of Diaphragm thickness.

In a large series of 107 patients, the authors described the daily evolution of US diaphragm thickness during mechanical ventilation and indirectly assessed the influence of inspiratory effort on it [34]. Over the first week of ventilation, diaphragm thickness decreased more than 10% in 47 patients (44%), remained unchanged in 47 (44%), and increased more than 10% in 13 (12%). Low diaphragm contractile activity was associated with rapid decreases in diaphragm thickness whereas high contractile activity was associated with increases in diaphragm thickness [34]. Contractile activity decreased with increasing ventilator driving pressure ($p = 0.01$) and controlled ventilator modes ($p = 0.02$) [34].

Regarding the level of contractile activity, a stable diaphragm thickness corresponds to normal levels during breathing in healthy subjects (thickening fraction of 25–40%) [9, 36, 38]. Our levels were taken at a median interval of 4-days from ventilation which appeared relatively high (42% in SP and 37% in PP). It was not an unexpected result since certain authors have found that diaphragm contractile activity varied widely between and within patients over the first week of ventilation and tended to increase over time [9, 34, 38]. DTF levels of less than 20% indicate a paralyzed diaphragm [36]. Several studies have used DTF as a predictor of extubating outcome and various cut-off values were reported: for DiNino et al. [38], a DTF ≥ 30% and for Farghaly and Hasan [39], a DTF of 34.2% was predicted as successful extubating. Dubé et al. [29] found an association between an increased ventilator day and a DTF ≤ 29% or less.

Recently, a novel technique using Doppler US has been developed to measure the movement of the liver as a proxy of diaphragm movement and to provide continuous measurement of diaphragm excursion and continuous monitoring of respiratory frequency (DiaMon device) [40]. This device detected a readable signal in 83–100% of the position/

posture-combinations [40]. As a consequence, it is thinkable to redesign the study using this device once obtained.

Conclusion

In summary, we have measured the changes of diaphragmatic muscle thickness induced by the prone positioning in ventilated patients. We ended up with a decrease of inspiratory diameter and a tendency to decrease thickening fraction and a contractile activity, which was better at the posterior region of diaphragm. In addition, a regular evaluation of the diaphragmatic motility must be part of the ordinary surveillance of a ventilated patient placed in PP for a hypoxemia beside blood gases, X Ray chest etc.,

As clinical implications, we propose certain measures to avoid the disruption of diaphragmatic activity during PP: Optimize the treatment of concomitant factors causing or aggravating ventilator-induced diaphragmatic dysfunction (malnutrition, sepsis, phosphorus and magnesium deficits, etc.), promote stimulation of the phrenic nerve by spontaneous ventilatory cycles even in PP and consider antioxidant agents (such vit E analogos) for patients requiring PP in order to minimize the harmful effect of PP on the diaphragm by reducing oxidative stress. Finally, for each patient requiring PP, we should analyze the benefit/risk ratio of positioning in PP, particularly for patients with already low DTF ($< 30\%$) testifying to diaphragmatic weakness.

Compliance with ethical standards

Consent for publication A consent for publication was obtained from parents of ventilated patients.

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval and consent to participate Patients or their parents were informed and consented for participation and approval was obtained by the local ethics committee of our Hospital. Our study protocol was conforming to the Declaration of Helsinki.

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