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Sonographic assessment of the diaphragm in COVID 19 and non-COVID ICU patients

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Abstract

Background Sonographic evaluation of the diaphragm has gained popularity in the ICU due to the necessity of assessing diaphragmatic function in a variety of clinical situations. The sonographic examination of diaphragmatic dynamics in ICU patients by measuring diaphragmatic thickness and excursion in connection to various modalities of mechanical ventilation (MV) and patient outcomes was the objective of this study.

Methods This prospective observational study was carried out on 50 patients in respiratory ICU in Kafr Elsheikh and Benha University Hospitals. Patients were classified into 2 equal groups: COVID-19 group and non-COVID group. All patients underwent ultrasound assessment included the diaphragm thickness fraction and excursion in ICU patients on admission and on weaning.

Results Successful weaning (SW) was higher in group I compared to group II. In group I (COVID), diaphragm excursion, thickness at end inspiration and at end expiration in NIV at weaning were significantly higher in patients with SW but thickness at end expiration on admission was significantly lower. In group II (non-COVID) MV patients, excursion at weaning was significantly higher in patients with SW, also were thickness at end inspiration and end expiration on admission, thickness at end inspiration and end expiration at weaning in NIV patients but thickness at end inspiration in MV on admission was significantly lower.

Conclusion Weaning success and mortality were significantly predicted by excursion in NIV at weaning, thickness at end inspiration in MV at weaning, thickness at end inspiration in NIV at weaning, and thickness at end expiration in MV at weaning.

Keywords Sonographic, Diaphragm, COVID-19, ICU

Introduction

In the management of patients in intensive care units (ICUs), bedside ultrasonography has become an invaluable tool. In emergency situations, a proper imaging approach is usually impeded by a variety of obstacles, such as the difficulty of bringing the patient to the radiology department because of their acute illness. Ultrasonography has shown to be an accurate, safe, and user-friendly imaging modality at the bedside that overcomes a number of constraints associated with conventional imaging methods [1, 2].

The diaphragm is the major respiratory muscle, and its dysfunction increases the likelihood of respiratory issues and the duration of MV. Sonographic examination of the diaphragm has lately gained popularity in the ICU due to the necessity of evaluating diaphragmatic function in a range of clinical circumstances [3, 4].

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The evidence for ventilator-induced diaphragmatic dysfunction in critically sick patients is now overwhelming, and the ideal ventilator setting should theoretically strive for a level of breathing effort that is clinically tolerable [5, 6]. Most assisted breathing methods have been investigated for their potential to reduce respiratory effort, especially while weaning off mechanical or non-invasive ventilation (NIV) [7, 8].

This emphasizes the need for precise and trustworthy methods of assessing diaphragmatic function in the ICU. In the context of clinical research, several methods have been employed to assess diaphragmatic function and derived variables in critically sick patients [9]. Ultrasonographic assessment of diaphragm excursions during weaning from artificial breathing may assist identify patients with diaphragmatic dysfunction [10, 11].

The aim of this work was diaphragmatic kinetics sonographic evaluation in ICU critically ill patients by determining diaphragmatic thickness and excursion and its relation to different modalities of MV and with different patient outcomes. The hypothesis was the question: Will abnormalities in diaphragmatic thickness or excursion affect the success of weaning from mechanical ventilation in both invasive and non-invasive modalities of mechanical ventilation?

The primary outcome was weaning success or failure. Secondary outcome was ventilator parameters and diaphragmatic excursion and thickness parameters in both successful and failed weaning to observe if there is a difference between successful and weaning groups in the secondary parameters.

Methods

This prospective observational study was carried out on 50 patients in respiratory ICU on non-invasive and invasive MV in Kafr El-Sheikh and Benha University Hospitals. We assumed similar conditions of the study as regards material technique and staff as it was done in university hospitals.

Informed signed consent was obtained from the patient or relatives of the patients. The study was done after being approved by the institutional Ethical Committee, Benha University. The study design and the time frame of the study (1 year) were planned by community medicine staff.

Exclusion criteria were abnormal diaphragmatic motion observed in conditions such as neuromuscular diseases [5], phrenic nerve injury, chest wall deformity and after abdominal [10] or cardiothoracic surgery, patients with neuromuscular diseases or chest wall deformity as spinal cord injury, brachial plexus neuritis, patients with systemic diseases affecting diaphragmatic muscles function as myasthenia gravis and multiple sclerosis, and patients with any cause of increased intra-abdominal pressure.

Patients were further classified into two groups: group I: (COVID-19) included twenty-five patients with COVID-19 respiratory disease admitted to Kafr Elsheikh University Hospital ICU and diagnosed by positive polymerase reaction (PCR), nasopharyngeal swab, or trans-tracheal aspirate for SARS-CoV-2 and group II (non-COVID): included twenty-five patients admitted to Benha University Hospital ICU with diagnosis other than SARS-CoV-2.

The question was whether COVID will affect diaphragmatic parameters which in turn will affect weaning success.

All patients were subjected to detailed history taking including personal, present and past medical history, clinical examination including vital signs (blood pressure, heart rate, respiratory rate, and temperature), anthropometric measure, and system examination. Laboratory investigations [complete blood count (CBC), random blood sugar, renal function tests as serum urea, creatinine, liver enzymes as serum alanine aminotransferase (ALT) and serum aspartate aminotransferase (AST), C-reactive protein, nasopharyngeal swab for detection of corona virus, reverse transcription polymerase chain reaction (RT-PCR)] and radiological investigations [chest X-ray, chest computed tomography (CT) scan, and ultrasound assessment] [12–14] included the diaphragm thickness fraction and excursion in ICU patients in two situations (on admission and on weaning) and their relation to the vent. Variables that were measured were thickness at end inspiration, thickness at end expiration, thickness fraction (TFDi) [thickness at end inspiration − thickness at end expiration/thickness at end expiration], and diaphragm excursion. The measurement was done by a lecturer of diagnostic radiology with a good experience and longtime of work in ultrasound assessments.

Measurements were done in mm with SD for thickness but for excursion it was measured in cm with SD.

Diaphragm thickness fraction method

A linear array transducer (10–15 MHz) was positioned cranio-caudally and perpendicular to the skin in the 8th to 11th intercostal area for the intercostal approach. We advise measuring the thickness of the diaphragm perpendicular to its fiber direction and leaving out the pleural and peritoneal membranes. In B-mode or M-mode, the thickening fraction of the diaphragm (TFdi) was calculated as the increase in diaphragm thickness relative to end-expiratory thickness during tidal breathing (TFdi) (Figs. 1, 2, and 3).

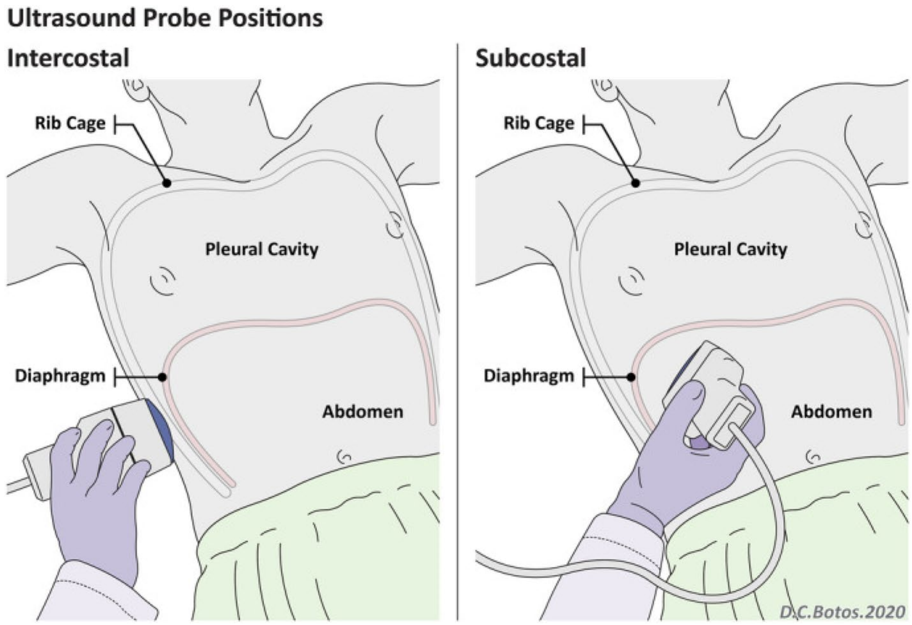

Fig. 1 Illustration of ultrasound probe positioning for evaluation of the diaphragm utilizing intercostal and subcostal windows. Adapted from Patel et al. [15]

Diaphragm excursion method

A low frequency phased curved-array ("abdominal") probe (2–5 MHz) was positioned slightly below the costal arch at the midclavicular line, with the patient in a semi-seated position, while angling the ultrasound beam as cranially and perpendicularly as possible to the diaphragmatic dome. Due to the narrow acoustic window of the spleen, obtaining a clear image of the left hemidiaphragm was difficult. A sweep speed of 10 mm/s was sufficient for capturing at least three respiration cycles in a single picture when recording motion in M-mode with the M-line perpendicular to the motion direction. To establish the maximum excursion of the patient, a maximal inspiratory effort was performed. During tidal breathing, the success rate for visualizing excursion exceeds 95%; however, it is more difficult during maximal breathing.

Statistical analysis

SPSS version v26 was used for statistical analysis (IBM Inc., Chicago, IL, USA). Using an unpaired Student's *t*-test, mean and standard deviation (SD) statistics for the two groups were produced. When applicable, qualitative variables were reported in terms of frequency and percentage (%) and analyzed using the chi-square or Fisher's exact test. Pearson correlation was done to estimate the degree of correlation between two quantitative variables. Evaluation of diagnostic performance uses ROC-curve analysis. A two tailed p value < 0.05 was considered statistically significant.

Results

This prospective observational study was carried out on 50 patients in respiratory ICU on non-invasive and invasive MV in Kafr El-Sheikh and Benha University Hospitals.

There was insignificant difference in age, sex, and ABG data on admission (pH, $PaCO_2$, and HCO_3) except for SO_2 which was considerably lower in group I compared to group II ($p = 0.002$). Patients diagnoses were as follows: three patients bronchial asthma exacerbation, 4 patients lung mass, 6 patients ILD, 2 patients ACOS, 1 breast cancer with lung metastases, 1 patient post COVID PHT, 1 obesity hypoventilation syndrome, 1 septic shock IV addict, 4 pneumonia, 2 COPD exacerbation, and 25 cases COVID-19.

Fourteen (45.2%) and 17 (54.8%) patients in group I and group II respectively were on NIV. PEEP and FiO_2 were substantially higher in NIV patients in group I compared to group II ($p < 0.001$). But SO_2 was substantially lower in group I compared to group II. There was insignificant difference in pressure support (PS) and respiratory rate (RR) between both groups. Eleven (57.9%) and 8 (42.1%) patients in group I and group II respectively were on MV. PEEP and RR were considerably higher in MV patients in group I compared to group II ($p < 0.001$ and =0.012 respectively). There was insignificant difference

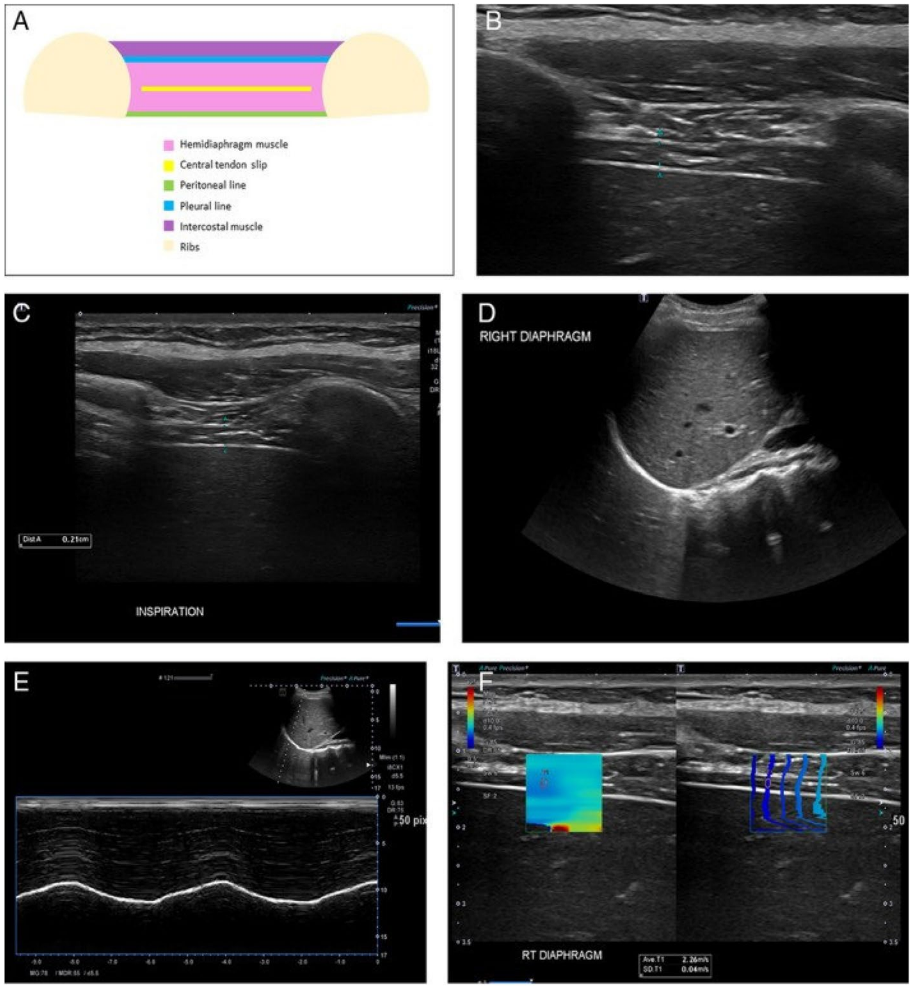

Fig. 2 Normal diaphragm ultrasound in a healthy volunteer. **A** Illustration depicts diaphragm anatomy as seen on ultrasound with an intercostal window. **B** Ultrasound of the right hemidiaphragm utilizing an intercostal window at expiration demonstrates normal muscle size with no evidence of atrophy (thickness > 0.15). The diaphragm (calipers) is identified as the muscle between the hyperechoic pleural and peritoneal lines, with a characteristic central tendon slip. **C** Ultrasound of the right hemidiaphragm utilizing an intercostal window at inspiration demonstrates intact contractility function with appropriate increase in size of the muscle compared to the expiration image (thickening ratio > 1.2). **D** Ultrasound of the right hemidiaphragm utilizing a subcostal window is performed to assess excursion. Cine clips during breathing can demonstrate intact versus decreased motility of the hemidiaphragm. Direct observation by the radiologist is helpful for determining paradoxical movement. Any pertinent findings such as pleural effusion or hepatomegaly should be noted in this view. **E** M-mode ultrasound of the right hemidiaphragm utilizing a subcostal window demonstrates normal excursion. **F** Sheer wave elastography of the hemidiaphragm can be performed utilizing the intercostal probe position, by placing the region of interest (pink oval) within the diaphragm muscle. Patel et al. [15]

in FiO_2, SO_2, PS, VT, and I:E ratio between both groups. There was insignificant difference in baseline diaphragm parameters between both groups.

Regarding ABG at weaning, there was no significant difference (pH, $PaCO_2$, and HCO_3) except for SO_2 which was considerably lower in group I compared to group II ($p < 0.001$).

Regarding ventilation data at weaning, PEEP and FiO_2 were considerably higher in group I compared to group II ($p < 0.001$). There was insignificant difference in RR and VT between both studied groups.

Successful weaning (SW) was considerably higher in group I compared to group II ($p = 0.022$). Regarding baseline characteristics of patients with successful and failed weaning, there was insignificant difference in age, gender, and ABG on admission (pH, $PaCO_2$, and HCO_3) except for SO_2 which was considerably higher in patients with SW ($p = 0.009$). Regarding ventilation data of patients with successful and failed weaning, PEEP was considerably higher in patients who failed weaning ($p = 0.05$) but SO_2 was significantly lower ($p = 0.001$). There was no significant difference in FiO_2, PS, RR, TV, and I:E

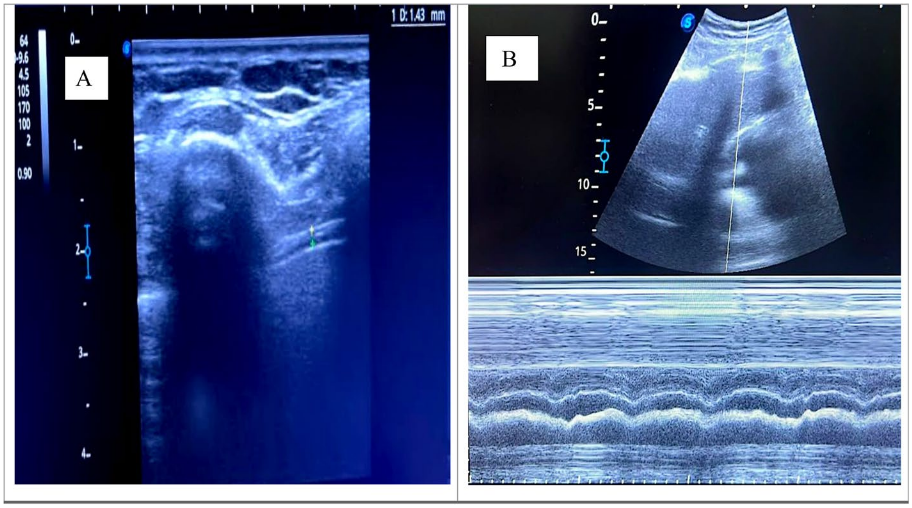

Fig. 3 Diaphragm ultrasound in MV patient, adapted from our patient records. **A** Ultrasound of the right hemidiaphragm utilizing an intercostal window at inspiration demonstrates intact contractility function with appropriate thickness (1.43 mm). **B** M-mode ultrasound of the right hemidiaphragm utilizing a subcostal window demonstrates decreased excursion

ratio between patients with successful and failed weaning. The number of patients who used sedation and muscle relaxants was considerably higher in patients who failed weaning compared with patients who succeeded weaning ($p = 0.002$ and 0.007 respectively) (Table 1).

In group I (COVID patients), diaphragm excursion, thickness at end inspiration, and thickness at end expiration in NIV at weaning were significantly higher in patients who had SW ($p = 0.007$, 0.004, and 0.004 respectively) but thickness at end expiration on admission was significantly lower ($p = 0.017$). There was no significant difference in the rest of diaphragm parameters between patients who had SW and patients who failed weaning.

In group II (non-COVID) mechanically ventilated patients, excursion at weaning was significantly higher in patients who had SW ($p = 0.036$), also were thickness at end inspiration and end expiration on admission, thickness at end inspiration and end expiration at weaning in NIV patients ($p = 0.029$, 0.015, 0.029 and 0.029 respectively) but thickness at end inspiration in MV on admission were significantly lower ($p = 0.036$). There was no significant difference in the rest of diaphragm parameters between patients who had SW and patients who failed weaning.

In MV patients, excursion, thickness at end inspiration, thickness at end expiration, and thickness fraction on admission together with thickness at end expiration at weaning were considerably lower in group I compared to group II ($p = 0.033$, 0.002, 0.009, 0.033, and 0.041 respectively). There was no significant difference in the rest of diaphragm parameters between COVID and non-COVID cases.

By comparing MV versus NIV patients, we found that in group I all diaphragmatic parameters on admission were significantly lower in MV patients ($p = <0.001$, <0.001, 0.001, 0.08) at weaning, and all diaphragmatic parameters except thickness fraction were significantly lower in MV patients. In group II, excursion at weaning was significantly lower in MV patients while thickness fraction on admission was significantly higher ($p = 0.027$, 0.21) (Table 2).

There was a significant positive correlation between excursion and SO_2 ($r = 0.523$, $p = 0.003$) and pH ($r = 0.506$, $p = 0.004$) but there was significant negative correlation between excursion and PEEP ($r = -0.49$, $p = 0.005$) and FiO_2 ($r = -0.533$, $p = 0.002$). There was a significant negative correlation between thickness at inspiration and $PaCO_2$ ($r = -0.396$, $p = 0.027$). There was a significant positive correlation between thickness at end expiration and SO_2 ($r = 0.41$, $p = 0.002$) but there was significant negative correlation between thickness at end expiration and FiO_2 ($r = -0.411$, $p = 0.022$) and $PaCO_2$ ($r = -0.36$, $p = 0.047$). There was a significant negative correlation between thickness fraction and SO_2 ($r = -0.414$, $p = 0.021$).

In group I, there was a significant negative correlation between total leucocytic count (TLC) and excursion in NIV at weaning ($r = -0.716$, $p = 0.005$), thickness at end inspiration in MV on admission ($r = -0.624$, $p = 0.043$), and thickness at end expiration in MV at weaning ($r = -0.614$, p 0.048). There was a significant negative correlation between IL6 and excursion in NIV on admission ($r = -0.744$, $p = 0.003$), and at weaning ($r = -0.871$, $p < 0.001$) but there was a significant positive correlation

Table 1 Baseline characteristics, type of ventilatory support, diaphragmatic assessment, patient and ventilator data at attempts of weaning, and baseline characteristics of patients of successful and failed weaning

			Group I	Group II	*p* value
Age (years)			62.2 ± 7.66	62.36 ± 12.53	0.768
Sex	**Male**		12 (48%)	15 (60%)	0.571
	Female		13 (52%)	10 (40%)	
ABG on admission	**pH**		7.34 ± 0.1	7.3 ± 0.13	0.503
	$PaCO_2$ (mmHg)		52.56 ± 16.17	57.54 ± 18.9	0.313
	HCO_3 (mEq/L)		23.36 ± 3.68	24.38 ± 6.44	0.784
	SO_2 (%)		80 ± 7	86 ± 4	**0.002***
Patients on NIV			14 (45.2%)	17 (54.8%)	0.561
PEEP (mmHg)			6.8 ± 1.3	5.3 ± 0.6	**<0.001***
FiO_2 (%)			71 ± 15	54 ± 6.1	**<0.001***
SO_2 (%)			95.7 ± 1.2	97 ± 0.7	**0.003***
PS (mmHg)			14.1 ± 1.4	14.2 ± 1.7	0.984
RR (breath/minute)			19.57 ± 1.2	18.8 ± 1.7	0.2
Patients on MV			11 (57.9%)	8 (42.1%)	0.561
PEEP (mmHg)			8.54 ± 1.6	4.87 ± 0.35	**<0.001***
FiO_2 (%)			65 ± 11	57.5 ± 4.6	0.062
SO_2 (%)			95.7 ± 1.2	96.2 ± 1.4	0.238
PS (mmHg)			19 ± 2.23	–	–
RR (breath/minute)			18.8 ± 2.18	16.75 ± 1.3	**0.012***
VT (mL)			440 ± 43	431 ± 70	0.904
I:E	**1:1**		1 (9.1%)	0 (0%)	0.418
	1:2		2 (18.2%)	3 (37.5%)	
	1:3		7 (63.6%)	5 (62.5%)	
	1:4		1 (9.1%)	0 (0%)	
Diaphragmatic assessment					
Excursion (cm)			0.92 ± 0.44	0.91 ± 0.27	0.767
Thickness at end inspiration (mm)			1.02 ± 0.43	1.09 ± 0.47	0.597
Thickness at end expiration (mm)			0.76 ± 0.34	0.83 ± 0.37	0.514
Thickness fraction (TFDi)			0.35 ±0.18	0.33 ± 0.18	0.606
ABG at weaning	**pH**		7.34 ± 0.08	7.36 ± 0.05	0.566
	$PaCO_2$ (mmHg)		47.82 ± 14.39	44.24 ± 11.28	0.382
	HCO_3 (mEq/L)		27.18 ± 13.54	23.78 ± 2.91	0.527
	SO_2 (%)		88 ± 7	95 ± 3	**<0.001***
Ventilation data at weaning	**PEEP (mmHg)**		8.8 ± 2.6	5.8 ± 1.6	**<0.001***
	FiO_2 (%)		77 ± 26	47 ± 25	**<0.001***
	RR (breath/minute)		19 ± 3.8	17 ± 1.1	0.135
	VT (mL)		432 ± 40	431 ± 65	0.717
	Weaning outcomes	**Successful**	9 (36%)	18 (72%)	**0.022***
		Failed	16 (64%)	7 (28%)	
Baseline characteristics of patients of successful and failed weaning					
			Successful weaning (*n* = 27)	**Failed weaning (*n* = 23)**	
Age (years)			61.7 ± 11.77	62 ± 8.4	0.785
Sex		**Male**	18 (66.7%)	9 (39.1%)	0.052
		Female	9 (33.3%)	14 (60.9%)	
ABG on admission		**pH**	7.29 ± 0.11	7.34 ± 0.11	0.316
		$PaCO_2$ (mmHg)	57.27 ± 18.67	52.45 ± 16.25	0.402
		HCO_3 (mEq/L)	23.6 ± 5.6	24.1 ± 4.8	0.748
		SO_2 (%)	85 ± 3.8	80 ± 7.8	**0.009***

Table 1 (continued)

			Group I	Group II	*p* value
Ventilation data on admission	**PEEP**		5.9 ± 1.5	6.9 ± 1.9	**0.05***
	FiO_2 (%)		60 ± 12.5	64 ± 12	0.139
	SO_2 (%)		97 ± 1	96 ± 1.3	**0.001***
	PS (mmHg)		14.5 ± 1.44	15.4 ± 3.4	0.742
	RR (breath/minute)		21 ± 6.9	17.8 ± 2.3	0.153
	VT (mL)		460 ± 55	428 ± 55	0.343
	I:E	**1:1**	0 (0%)	1 (7.1%)	0.08
		1:2	0 (%)	5 (35.7%)	
		1:3	4 (80%)	8 (57.1%)	
		1:4	1 (20%)	0 (0%)	

SO_2 oxygen saturation, *PEEP* positive end-expiratory pressure, *$PaCO_2$* partial pressure of carbon dioxide, *HCO_3* bicarbonate, *FiO_2* fraction of inspired oxygen, *PS* pressure support, *RR* respiratory rate, *VT* tidal volume, *I:E* inspiration to expiration ratio

Data are presented as mean ± SD or frequency (%)

[*] Statistically significant as *p* value ≤0.05

with thickness fraction in NIV at weaning (r = 0.559, p = 0.04), and there was a significant positive correlation between serum ferritin and thickness at end inspiration in NIV on admission (r = 0.678, p = 0.009), and thickness at end expiration in NIV on admission (r = 0.637, p = 0.016). There was a significant negative correlation between DD and excursion in NIV at weaning (r = −0.545, p = 0.046) but there was a significant positive correlation with thickness fraction in NIV at weaning (r = 0.576, p = 0.033) (Table 3).

Weaning success and mortality were significantly predicted by excursion and thickness at end inspiration in NIV at weaning, thickness at end inspiration, and thickness at end expiration in MV at weaning (Table 4).

Duration of ICU stay and mortality were significantly higher in group I compared to group II (p < 0.001 and 0.022 respectively) (Table 5).

Discussion

As a result of the global COVID-19 epidemic, interest in lung and diaphragm sonography for the examination of respiratory symptoms has increased. Diaphragm ultrasonography can be used to diagnose diaphragm dysfunction, measure the degree of dysfunction, and track disease development; came in line with our findings, Saad et al. found that the number of patients who successfully weaned from MV was 48 out of 60 (80%), while the number of patients who failed to successfully wean from MV was 12 (20%) [16].

Regarding the baseline characteristics of patients with successful and failed weaning, Vetrugno et al. reported comparable results to ours when they discovered that there was no significant difference between the two groups in terms of age, sex, ABGs, and SpO_2 or PaO_2 [17]. Vetrugno et al. [17] however, reported that the following parameters were statistically different between groups (weaning failure and weaning success): inspiratory oxygen fraction and PaO_2/FiO_2 ratio. In the research by Zhao et al., initial Pplat and DP were greater in the unsuccessful weaning (USW) group, and compliance was poorer than in the successful weaning (SW) group, but there was no change in PEEP, PCO_2, and P/F ratio [18]. Comparing the two groups' worst respiratory mechanical metrics, the findings for Pplat, DP, compliance, and PEEP were identical to the baseline data. PCO_2 was greater in the USW group, whereas P/F was lower.

In the current study, number of patients who used sedation and muscle relaxants was significantly higher in patients who failed weaning compared with patients who succeeded weaning (p = 0.002 and 0.007 respectively). This was in agreement with Yu et al. [19], who observed that higher doses of sedatives and fentanyl were associated with higher risk of extubation failure.

Regarding diaphragm parameters in patients who had SW and patients who failed weaning in COVID patients, in line with our study, Vetrugno et al. [17] observed that there was no statistical difference between MV patients with successful and failed weaning regarding initial ultrasound diaphragmatic parameters as expiratory diaphragmatic diameter, inspiratory diaphragmatic diameter, or diaphragmatic thickening fraction. However, Helmy et al. found that diaphragmatic excursion (DE) is an excellent indicator

Table 2 Diaphragm parameters in patients who had successful weaning and patients who failed weaning in groups I and II, US diaphragm parameters, diaphragm parameters in patients who were on MV and those who were on NIV in COVID patients and in non-COVID patients

			Group I		***p* value**
			Successful weaning ($n = 9$)	**Failed weaning ($n = 16$)**	
Excursion (cm)	**MV**	**On admission**	0.7 ± 0.42	0.58 ± 0.15	0.909
		At weaning	0.75 ± 0.63	0.45 ± 0.15	0.727
	NIV	**On admission**	1.41 ± 0.33	0.93 ± 0.37	0.165
		At weaning	1.68 ± 0.69	0.68 ± 0.37	**0.007***
Thickness at end inspiration (mm)	**MV**	**On admission**	1.05 ± 0.64	0.59 ± 0.25	0.436
		At weaning	1.05 ± 0.92	0.37 ± 0.2	0.218
	NIV	**On admission**	1.18 ± 0.23	1.41 ± 0.23	0.073
		At weaning	1.6 ± 0.29	1.03 ± 0.33	**0.004***
Thickness at end expiration (mm)	**MV**	**On admission**	0.82 ± 0.54	0.46 ± 0.19	0.582
		At weaning	0.93 ± 0.87	0.26 ± 0.14	0.145
	NIV	**On admission**	0.8 ± 0.16	1.1 ± 0.24	**0.017***
		At weaning	1.34 ± 0.31	0.74 ± 0.29	**0.004***
TFDi	**MV**	**On admission**	0.31 ± 0.08	0.27 ± 0.1	0.582
		At weaning	0.19 ± 0.14	0.43 ± 0.17	0.073
	NIV	**On admission**	0.49 ± 0.21	0.31 ± 0.19	0.097
		At weaning	0.24 ± 0.12	0.41 ± 0.17	0.073
			Group II		***p* value**
			Successful weaning ($n = 18$)	**Failed weaning ($n = 7$)**	
Excursion (cm)	**MV**	**On admission**	0.83 ± 0.15	0.8 ± 0.19	0.786
		At weaning	1.27 ± 0.23	0.46 ± 0.11	**0.036***
	NIV	**On admission**	0.95 ± 0.32	1 ± 0.28	0.824
		At weaning	1.33 ± 0.47	0.65 ± 0.21	0.059
Thickness at end inspiration (mm)	**MV**	**On admission**	0.93 ± 0.15	1.52 ± 0.19	**0.036***
		At weaning	1.13 ± 0.29	0.69 ± 0.41	0.143
	NIV	**On admission**	1.1 ± 0.43	0.17 ± 0.04	**0.029***
		At weaning	1.23 ± 0.75	0.08 ± 0.014	**0.015***
Thickness at end expiration (mm)	**MV**	**On admission**	0.68 ± 0.18	1.03 ± 0.17	0.071
		At weaning	0.85 ± 0.14	0.52 ± 0.31	0.143
	NIV	**On admission**	0.89 ± 0.37	0.13 ± 0.02	**0.029***
		At weaning	0.98 ± 0.58	0.07 ± 0.014	**0.029***
TFDi	**MV**	**On admission**	0.39 ± 0.21	0.49 ± 0.15	0.786
		At weaning	0.32 ± 0.15	0.32 ± 0.25	0.786
	NIV	**On admission**	0.28 ± 0.16	0.25 ± 0.12	1.000
		At weaning	0.27 ± 0.18	0.15 ± 0.03	0.618
US diaphragm parameters					
			Group I ($n = 25$)	**Group II ($n = 25$)**	***p* value**
Excursion (cm)	**MV**	**On admission**	0.61 ± 0.19	0.81 ± 0.16	**0.033***
		At weaning	0.51 ± 0.27	0.76 ± 0.44	0.206
	NIV	**On admission**	1.17 ± 0.42	0.95 ± 0.31	0.1
		At weaning	1.18 ± 0.74	1.25 ± 0.49	0.739
Thickness at end inspiration (mm)	**MV**	**On admission**	0.67 ± 0.35	1.3 ± 0.35	**0.002***
		At weaning	0.49 ± 0.43	0.86 ± 0.42	0.062
	NIV	**On admission**	1.3 ± 0.25	0.99 ± 0.51	0.1
		At weaning	1.33 ± 0.44	1.09 ± 0.8	0.336

Table 2 (continued)

			Group I		*p* value
			Successful weaning ($n = 9$)	**Failed weaning ($n = 16$)**	
Thickness at end expiration (mm)	**MV**	**On admission**	0.53 ± 0.28	0.9 ± 0.24	**0.009***
		At weaning	0.38 ± 0.41	0.64 ± 0.29	**0.041***
	NIV	**On admission**	0.95 ± 0.25	0.79 ± 0.43	0.493
		At weaning	1.04 ± 0.42	0.87 ± 0.63	0.493
TFDi	**MV**	**On admission**	0.28 ± 0.09	0.45 ± 0.17	**0.033***
		At weaning	0.38 ± 0.19	0.32 ± 0.2	0.442
	NIV	**On admission**	0.4 ± 0.22	0.27 ± 0.15	0.1
		At weaning	0.32 ± 0.17	0.26 ± 0.18	0.2
COVID patients			**MV ($n = 11$)**	**NIV ($n = 14$)**	
Excursion (cm)		**On admission**	0.61 ± 0.19	1.2 ± 0.42	**<0.001***
		At weaning	0.51 ± 0.27	1.19 ± 0.74	**0.018***
Thickness at end inspiration (mm)		**On admission**	0.67 ± 0.35	1.3 ± 0.25	**<0.001***
		At weaning	0.49 ± 0.43	1.34 ± 0.44	**<0.001***
Thickness at end expiration (mm)		**On admission**	0.53 ± 0.28	0.95 ± 0.25	**0.001***
		At weaning	0.38 ± 0.41	1.04 ± 0.42	**<0.001***
TFDi		**On admission**	0.28 ± 0.09	0.4 ± 0.22	0.08
		At weaning	0.38 ± 0.19	0.32 ± 0.16	0.4
Non-COVID patients			**MV ($n = 8$)**	**NIV ($n = 17$)**	***p* value**
Excursion (cm)		**On admission**	0.81 ± 0.16	0.95 ± 0.31	0.136
		At weaning	0.76 ± 0.44	1.25 ± 0.49	**0.027***
Thickness at end inspiration (mm)		**On admission**	1.3 ± 0.35	0.99 ± 0.51	0.096
		At weaning	0.86 ± 0.42	1.09 ± 0.8	0.343
Thickness at end expiration (mm)		**On admission**	0.9 ± 0.24	0.79 ± 0.43	0.459
		At weaning	0.64 ± 0.29	0.87 ± 0.63	0.218
TFDi		**On admission**	0.46 ± 0.17	0.27 ± 0.16	**0.021***
		At weaning	0.32 ± 0.20	0.26 ± 0.18	0.256

NIV non-invasive ventilation, *MV* mechanical ventilation

* Statistically significant as *p* value ≤0.05

of weaning success in COVID-19 patients [20]. The likelihood of re-intubating a patient with DE more than 12 mm during the SBT is low.

Concerning diaphragm parameters in patients who had SW and patients who failed weaning in non-COVID cases, our results were consistent with those of Ali and Mohamad, who reported a statistically significant decrease in the MDT (mean diaphragmatic thickness) among patients who failed weaning compared to those who had SW. Both the diaphragmatic thickness % and DE (mean DE) were statistically substantially lower in the group of patients whose weaning had failed compared to those whose weaning had been successful [21].

Regarding diaphragm parameters in COVID versus non-COVID cases, Farr et al. discovered that the mean diaphragm muscle thickness at end-expiration for COVID-19 patients was significantly less than for non-COVID-19 patients. Our results were consistent with their findings [22]. Compared to non-COVID-19 patients, the mean thickening ratio (diaphragm thickness at end-inspiration/end-expiration) had dropped significantly in COVID-19 patients. Overall, 16 of 21 COVID-19 patients (76%) and 5 of 11 non-COVID patients (45%) exhibited at least one structural or functional abnormalities on diaphragm ultrasonography.

Regarding diaphragm parameters in patients who were on MV and those who were on NIV in COVID patients, our findings were in agreement with Helmy et al. [20] who evaluated the DE during the first 12 h of admission and found that DE had an excellent ability to predict the need for ventilatory support, which was the highest among respiratory rate, SpO_2, and CT score.

The correlation coefficients between diaphragmatic and standard measures were assessed by Theerawit et al. The TPIAdia discovered a positive relationship between television and the TPIAdia and a negative relationship

Table 3 Correlation between diaphragm parameters and different patients' parameters at weaning

	Study participants ($n = 50$)							
	Excursion		**Thickness at inspiration**		**Thickness at expiration**		**TFDi**	
	r	***p* value**	***r***	***p* value**	***r***	***p* value**	***r***	***p* value**
pH	0.506	**0.004***	0.291	0.113	0.341	0.06	−0.259	0.159
$PaCo_2$ (mmHg)	−0.292	0.110	−0.396	**0.027***	−0.36	**0.047***	0.024	0.899
SO_2	0.523	**0.003***	0.344	0.058	0.410	**0.002***	−0.414	**0.021***
PEEP	−0.49	**0.005***	−0.25	0.175	−0.291	0.112	0.208	0.261
FiO_2 (%)	−0.533	**0.002***	−0.351	0.053	−0.411	**0.022***	0.278	0.13
ICU days	−0.149	0.425	0.094	0.617	0.029	0.877	0.210	0.256
Group I ($n = 25$)								
			TLC		**CRP**		**IL6**	
			r	***p* value**	***r***	***p* value**	***r***	***p* value**
Excursion	**MV**	**On admission**	−0.231	0.487	0.332	0.314	−0.199	0.551
		At weaning	−0.166	0.618	0.481	0.135	−0.166	0.617
	NIV	**On admission**	−0.716	**0.005***	−0.08	0.776	−0.744	**0.003***
		At weaning	−0.495	0.074	−0.2	0.488	−0.871	**<0.001***
Thickness at end inspiration	**MV**	**On admission**	−0.624	**0.043***	0.303	0.361	0.417	0.2
		At weaning	−0.539	0.089	0.155	0.646	0.333	0.314
	NIV	**On admission**	−0.152	0.599	−0.017	0.954	0.450	0.107
		At weaning	0.032	0.914	−0.167	0.564	−0.319	0.263
Thickness at end expiration	**MV**	**On admission**	−0.465	0.151	0.382	0.248	0.264	0.429
		At weaning	−0.614	**0.048***	0.155	0.647	0.399	0.221
	NIV	**On admission**	−0.013	0.965	0.175	0.545	0.403	0.152
		At weaning	−0.025	0.932	−0.187	0.517	−0.393	0.164
TFDi	**MV**	**On admission**	−0.328	0.319	−0.414	0.205	0.292	0.378
		At weaning	0.260	0.434	−0.244	0.468	−0.104	0.759
	NIV	**On admission**	−0.062	0.832	−0.176	0.543	−0.048	0.868
		At weaning	0.119	0.684	0.292	0.31	0.559	**0.040***
			Serum ferritin		**Lymphocytes**		**DD**	
			r	***p* value**	***r***	***p* value**	***r***	***p* value**
Excursion	**MV**	**On admission**	0.231	0.487	−0.083	0.806	−0.292	0.378
		At weaning	0.251	0.45	−0.067	0.841	−0.105	0.752
	NIV	**On admission**	−0.016	0.959	−0.099	0.733	−0.352	0.215
		At weaning	−0.234	0.418	−0.276	0.335	−0.545	**0.046***
Thickness at end inspiration	**MV**	**On admission**	0.029	0.931	−0.311	0.347	−0.154	0.646
		At weaning	−0.112	0.740	−0.438	0.177	−0.167	0.619
	NIV	**On admission**	0.678	**0.009***	−0.03	0.919	0.461	0.098
		At weaning	−0.24	0.405	−0.465	0.095	−0.192	0.507
Thickness at end expiration	**MV**	**On admission**	−0.045	0.896	−0.355	0.281	−0.082	0.811
		At weaning	−0.021	0.953	−0.431	0.184	−0.126	0.709
	NIV	**On admission**	0.637	**0.016***	0.001	1.000	0.219	0.447
		At weaning	−0.229	0.426	−0.497	0.072	−0.286	0.317
TFDi	**MV**	**On admission**	0.168	0.616	0.265	0.427	−0.598	0.056
		At weaning	−0.334	0.311	0.136	0.686	−0.233	0.486
	NIV	**On admission**	−0.194	0.503	0.124	0.669	0.208	0.472
		At weaning	0.138	0.637	0.489	0.078	0.576	**0.033***

$PaCO_2$ partial pressure of carbon dioxide, *SO_2* oxygen saturation, *PEEP* positive end-expiratory pressure, *FiO_2* fraction of inspired oxygen, *ICU* intensive care unit, *MV* mechanical ventilation, *NIV* non-invasive ventilation, *TLC* total leucocytic count, *CRP* C-reactive protein, *IL* interleukin

* Statistically significant as *p* value $\leq$0.05

Table 4 Sensitivity, specificity, positive and negative predictive value, and accuracy of diaphragmatic parameters in predicting weaning success and mortality

In predicting weaning success			Study participants ($n = 50$)						
			Cut-off	Sen.	Spc.	PPV	NPV	AUC	*p* value
Excursion	**MV**	**On admission**	>0.8	40	92.86	66.7	81.2	0.657	0.363
		At weaning	>0.7	80	100	100	93.3	0.829	0.056
	NIV	**On admission**	>0.8	72.7	44.4	76.2	40	0.563	0.607
		At weaning	>0.8	81.8	55.5	81.8	55.6	0.876	**<0.001***
Thickness at end inspiration	**MV**	**On admission**	>0.8	60	57.1	33.3	80	0.571	0.603
		At weaning	>0.8	60	85.7	60	85.7	0.864	**<0.001***
	NIV	**On admission**	≤0.9	36.4	77.8	80	33.3	0.586	0.522
		At weaning	>0.8	81.8	55.6	81.8	55.6	0.765	**0.002***
Thickness at end expiration	**MV**	**On admission**	>0.8	40	71.4	33.3	76.9	0.557	0.715
		At weaning	>0.9	40	92.8	66.7	81.2	0.879	**<0.001***
	NIV	**On admission**	≤0.9	59	55.5	76.5	35.7	0.568	0.597
		At weaning	>0.9	68.18	88.9	93.7	53.3	0.795	**<0.001***
TFDi	**MV**	**On admission**	>0.24	80	28.57	28.6	80	0.529	0.857
		At weaning	≤0.29	60	64.29	37.5	81.8	0.643	0.383
	NIV	**On admission**	>0.23	68.18	44.4	75	36	0.576	0.531
		At weaning	≤0.43	86.3	44.4	79.2	57.1	0.649	0.187
In predicting mortality									
Excursion	**MV**	**On admission**	≤0.8	92.8	40	81.2	66.7	0.657	0.363
		At weaning	≤0.7	100	80	93.3	100	0.829	0.056
	NIV	**On admission**	≤0.8	44	72.7	40	76.2	0.563	0.607
		At weaning	≤0.8	55.5	81.8	55.6	81.8	0.876	**<0.001***
Thickness at end inspiration	**MV**	**On admission**	≤0.8	57.14	60	80	33.3	0.571	0.603
		At weaning	≤0.8	85.7	60	85.7	60	0.864	**<0.001***
	NIV	**On admission**	>1.2	55.5	54.5	33.3	75	0.586	0.522
		At weaning	≤0.8	55.5	81.8	55.6	81.8	0.765	**0.002***
Thickness at end expiration	**MV**	**On admission**	≤0.8	71.4	40	76.9	33.3	0.557	0.715
		At weaning	≤0.9	92.8	40	81.2	66.7	0.879	**<0.001***
	NIV	**On admission**	>1.2	22.2	90	50	74.1	0.568	0.597
		At weaning	≤0.8	77.7	77.2	58.3	89.5	0.795	**<0.001***
TFDi	**MV**	**On admission**	≤0.35	57	40	72	25	0.529	0.857
		At weaning	>0.33	42.8	60	75	27.3	0.643	0.383
	NIV	**On admission**	≤0.36	77.7	36.3	33.3	80	0.576	0.531
		At weaning	>0.33	55.5	72.7	45.5	80	0.649	0.187

MV mechanical ventilation, *NIV* non-invasive ventilation, *Sen.* sensitivity, *Spc.* specificity, *PPV* positive predictive value, *NPV* negative predictive value, *AUC* area under the curve

[*] Statistically significant as *p* value ≤0.05

Table 5 Patients outcome in the studied groups

	Group I ($n = 25$)	Group II ($n = 25$)	*p* value
Duration of ICU stay (days)	7.44 ± 1.94	5.2 ± 1.2	**<0.001***
Mortality	16 (64%)	7 (28%)	**0.022***

ICU intensive care unit

[*] Statistically significant as *p* value ≤0.05

between television and the RSBI. Weak correlations were seen between TPIAdia and VC, diaphragmatic inspiratory excursion and RSBI, and diaphragmatic inspiratory excursion and TV. The RSBI had a negative relationship with all ultrasonographic diaphragm values. For instance, when the TPIAdia increases, the RSBI lowers. No correlation was discovered between PIMAX and any ultrasonographic diaphragm parameter [23].

In the current study, excursion in NIV at weaning, thickness at end inspiration in MV at weaning, thickness at end inspiration in NIV at weaning, thickness at end expiration in MV at weaning, and thickness at end expiration in NIV at weaning were significant predictors of weaning success. Matamis et al. [24] also did not revealed that the DE was a useful parameter in predicting weaning outcome. However, in the study by Thabet et al. [25], the RSBI performed as the best parameter in predicting weaning success. Nevertheless, the diaphragmatic indices Tdi, Tdexe, TF, and DE did not appear to have a major role in predicting SW, since their AUCs were all less than 0.56.

In line with the current work, Helmy et al. [20] observed that the right DE also had the highest AUC for predicting mortality in relation to respiratory rate, CT score, SpO2. Multivariable research revealed that low DE was an independent predictor of mortality. In the present investigation, group I had significantly longer ICU stays and higher mortality rates than group II. Guidet et al. showed that the ICU duration of stay was greater in COVID patients compared to non-COVID patients in both survivors and non-survivors. Our findings corroborated this finding. And the overall survival rate among COVID patients was lower [26]. The high mortality in COVID-19 group may be related to severity status of COVID-19 patients included from the start in the study and interestingly, increased fibrosis of the diaphragm muscle and a unique myopathic phenotype compared to control-ICU patients as proofed by a Shi et al. autopsy study found ACE2 expression in the human diaphragm and SARS-CoV-2 viral RNA in a subset of COVID-19 patients, with increased fibrosis and myopathy [27].

Conclusions

The thickness at the end of inspiration and the thickness at the end of expiration were significant indicators of successful weaning off MV. The thickness at the end of inspiration, the thickness at the end of expiration, and the excursion during weaning were all significant predictors of successful weaning off NIV. Significant predictors of mortality were thickness at end inspiration and thickness at end expiration in MV at weaning, excursion, and thickness at end inspiration and thickness at end expiration in NIV at weaning.

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