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Diaphragmatic impairment as a predictor of invasive ventilation in acute exacerbation of chronic obstructive pulmonary disease patients

Amr Abdalla Elsayed, Eman Hashem Mohamed Neanaa and Bassem Nashaat Beshey

Critical Care Medicine Department, Faculty of Medicine, Alexandria University, Alexandria, Egypt

ABSTRACT

Objective: Study the impact of ultrasound-assessed diaphragmatic impairment (DI) on predicting need for invasive mechanical ventilation (IMV) in acute exacerbation of chronic obstructive pulmonary disease (AECOPD) patients treated by non-invasive ventilation (NIV).

Design: A prospective observational study.

Setting: Critical Care Units of Alexandria Main University Hospital.

Patients: 75 adult AECOPD patients of both sexes according to sample size calculation.

Methods: Ultrasound was used to measure diaphragmatic thickness (DT), diaphragmatic thickness fraction (DTF) was calculated, and DI was diagnosed when fraction was less than 20%. Patients were treated by NIV. Switching to IMV was done after NIV failure. Primary outcome was value of DI to predict need for IMV after NIV failure. Secondary outcome was impact of DI on fate of patients.

Results: According to fate of NIV, patients were categorized into successful and failed NIV groups. DTF in both groups were ≥33–38% and ≤16–18%. DTF with a cut-off value of <26–29% on both sides was able to predict NIV failure with 96.67% sensitivity and 80–82.22% specificity. Days of MV and ICU stay were significantly lower in the successful NIV group, $p < 0.001$. 28-day mortality was significantly less encountered in successful NIV group, $p = 0.018$.

Conclusion: DTF was a good indicator of DI that could predict need for IMV after NIV failure in AECOPD patients with good sensitivity and moderate specificity. MV Days, ICU stay, and 28-day mortality were significantly higher in patients with DI who needed IMV.

1. Introduction

According to the Global Burden of Disease (GBD), chronic obstructive pulmonary disease (COPD) is the third leading cause of death worldwide [1,2]. Acute exacerbations of COPD (AECOPD) can be precipitated by infectious or noninfectious causes. However, up to 30% is of unknown etiology [3]. Indications for intensive care unit (ICU) admission in COPD patients include severe dyspnea that responds inadequately to initial emergency therapy, changes in mental status, persistent or worsening hypoxemia and/or severe worsening respiratory acidosis despite supplemental oxygen, need for invasive mechanical ventilation, hemodynamic instability, or need for vasopressors [4,5].

Treatment options include medical treatment and respiratory support. In case of respiratory failure, ventilator treatment is necessary either in the form of non-invasive ventilation (NIV) or invasive mechanical ventilation (IMV) through endotracheal intubation. Early use of NIV in patients with AECOPD is preferable due to its positive effects in recruitment of collapsed alveoli, improvement of ventilation-perfusion matching, with consecutive improved oxygenation and respiratory acidosis, and in decreasing the work of breathing with reduction of intubation risk. Despite its important role, there are many contraindications that necessitate immediate intubation and IMV [6–8].

The criteria for intubation include no improvement or worsening of pH and/or $PaCO_2$, emerging need for endotracheal intubation like cardiac arrest, hemodynamic instability, agitation, Glasgow coma score (GCS) deterioration, convulsive seizures, copious tracheal secretions, and severe NIV mask intolerance. The decision to institute IMV should be based on clinical judgment that integrates many clinical variables. The use of invasive ventilation in severe COPD patients is influenced by the likely reversibility of the precipitating event. Major hazards include the risk of ventilator associated pneumonia, barotrauma, and failure to wean to spontaneous ventilation [8–11].

Ultrasonography became an extension of the physical examination and is increasingly used by intensivists to guide a lot of procedures. It has been considered a non-invasive tool for quantification of diaphragmatic contractility through measuring its thickness (DT) or the variation of diaphragmatic thickness fraction (DTF) between end-inspiration and end-expiration [12–16]. AECOPD patients have a risk of

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CONTACT Bassem Nashaat Beshey ✉ basemnashaat@gmail.com

diaphragmatic dysfunction/impairment (DD/DI), which may affect ventilatory management. This makes ultrasound diaphragmatic assessment a reasonable tool during management plan [17–19]. Aim of this work was to study impact of ultrasound-assessed diaphragmatic impairment (DI) on predicting need for IMV in AECOPD patients treated by NIV. Primary outcome was value of DI to predict need for IMV after NIV failure. Secondary outcome was impact of DI on MV days, ICU stay, and 28-day mortality.

2. Patients and methods

This prospective observational study was carried out on 75 adult AECOPD patients of both sexes according to sample size calculation. A minimal total sample size of 56 patients with AECOPD (28 patients improved with non-invasive ventilation and another 28 patients were intubated) was needed to detect an AUC of 0.84 for using diaphragmatic ultrasonography to predict need for immediate invasive mechanical ventilation in AECOPD patients through assessment of diaphragmatic function during AECOPD using ROC curve analysis with a significance level (alpha) of 0.05 and power of 90% [20]. Sample size was calculated using MedCalc Statistical Software version 16.4.3.

Patients were admitted to Critical Care Medicine Department in Alexandria Main University Hospital. Approval of the Medical Ethics Committee of Alexandria Faculty of Medicine was obtained. An informed consent was taken from the patients' next of kin before their enrollment in the study. Inclusion criteria were adult (≥18 years) patients with AECOPD and eligible for NIV. Exclusion criteria were pregnant females and contraindications of NIV (unconscious uncooperative patients, shock, severe hemodynamic instability, neuromuscular disease, chest wall deformities, diaphragmatic palsy, or intra-abdominal hypertension).

All patients were subjected on admission to collection of demographic data (age and sex), patients' comorbidities, possible causes of AECOPD, Acute Physiologic Assessment and Chronic Health Evaluation II (APACHE II) score, level of consciousness by Glasgow Coma Scale (GCS), non-invasive blood pressure (mmHg), pulse rate (beats per minute), respiratory rate (breaths per minute), oxygen saturation (%) using pulse oximeter, routine laboratory tests, and radiological investigations as needed. Arterial blood gases (ABGs) were performed on admission and then hourly or earlier until stabilization or worsening clinical parameters.

U/S assessment of the diaphragm was performed on admission and before starting NIV by a physician experienced in lung/chest US assessment who was blinded to the study. Motility of the diaphragm was assessed using a Sonosite Mindray DP10 2015–08 (China) with a 3–5-MHz linear probe to assess the diaphragm at the zone of apposition, between the 8th and 10th intercostal space in the mid-axillary or anterior axillary line, 0.5–2 cm below the costophrenic sinus. Measurements were performed with the patient in supine position at an average inclination of 45 degrees. Two parallel echogenic layers could be identified at a depth of 1.5–3 cm, the nearest was the parietal pleura and the deeper was the peritoneum. The diaphragm is the less echogenic structure in between these two lines (Figure 1a) [18,21].

This approach was utilized to assess diaphragmatic thickness (DT) and thickening with inspiration, in B-mode (Figure 1b). In the subcostal area, between the mid-clavicular and anterior axillary lines, using liver or spleen as acoustic windows, diaphragm was identified as a hyperechoic line (produced by the pleura tightly adherent to the muscle) that approaches the probe during inspiration (Figure 1c). The thickness of the diaphragm was measured bilaterally at end-inspiration and end-expiration. Measurements were performed three times on both sides of the diaphragm, and the best value was recorded [18,21].

In healthy, spontaneously breathing subjects the normal thickness of the diaphragm at the zone of apposition is 1.7 ± 0.2 mm while relaxing, increasing to 4.5 ± 0.9 mm on deep inspiration [18,19]. The change in diaphragmatic thickness (ΔTdi) during spontaneous breathing from functional residual capacity

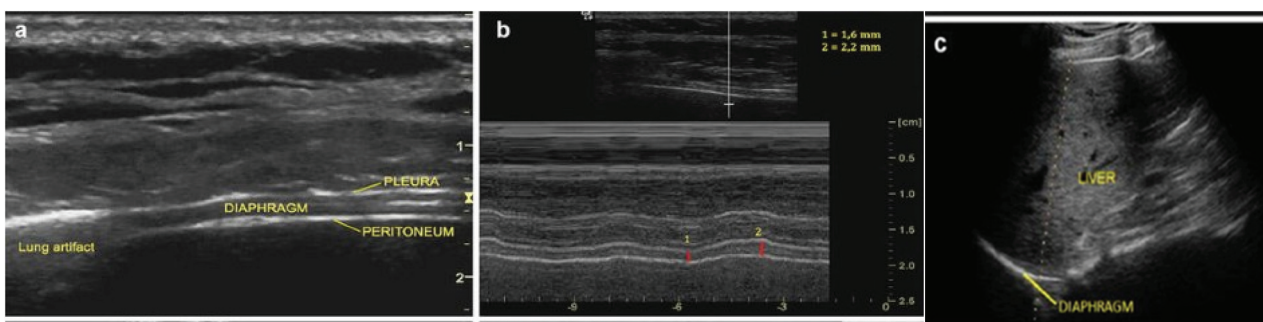**Figure 1.** Diaphragmatic Ultrasonography for measuring DT [21]. Diaphragmatic Thickness (DT) at zone of apposition in a B-mode, b M-mode. 1 Thickness at end-expiration, 2 thickness at end-inspiration. Right subcostal view in c B-mode [21].

(FRC) to tidal volume (Vt) is called diaphragmatic thickness fraction (DTF) [22]. It was calculated using the formula: (end-inspiratory DT – end expiratory DT)/end expiratory DT $\times$ 100. Diaphragmatic impairment (DI) was diagnosed when bilateral DTF was less than 20% [17,23,24].

Non-invasive mechanical ventilation (NIV) was started and set by an ICU physician who was blinded to the study, with specific software for NIV to display pressure and flow curves. Fitting face mask with proper size was used to allow using proper pressures without patient discomfort or any air leaks. Used mode was pressure support ventilation (PSV) with backup apnea ventilation. Continuous positive airway pressure (CPAP) was started at 4–6 cmH$_2$O to be adjusted according to clinical parameters and ventilator waveforms. Pressure support (PS) was set at 10 cmH$_2$O and gradually increased to reach tidal volume of 6–8 ml/kg (ideal body weight) and respiratory rate less than 25/minute. Inspired oxygen fraction (FiO$_2$) was adjusted to achieve oxygen saturation of 88–92% [20].

NIV was delivered as long as needed over next days and was then discontinued based on fulfillment of weaning criteria and clinical judgment. Patients were monitored and NIV was gradually discontinued when there was a general improvement in the patient's condition with RR < 25/minute, pH > 7.35, SpO$_2$ > 90%, and FiO$_2$ < 0.35. This was considered as successful NIV [20].

Switching to IMV was performed at any time by the attending physician who was blinded to diaphragmatic assessment of these patients according to these indications: respiratory arrest, persistent or severe respiratory distress (respiratory pauses or gasping for air, massive aspiration, or life-threatening hypoxemia), deterioration of pH, persistent respiratory acidosis despite NIV, worsening neurologic status (deteriorating GCS or agitation), intolerance to NIV, and hemodynamic instability (without response to fluids and vasoactive drugs or severe ventricular arrhythmias). This was considered as failed NIV [20].

All enrolled patients were managed and followed up according to local policies and guidelines for managing AECOPD patients all through their ICU stay. Primary outcome was value of diaphragmatic impairment to predict need for IMV after NIV failure. Secondary outcome was impact of DI on MV days, ICU stay, and 28-day mortality.

2.1. Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0 (Armonk, NY: IBM Corp). Qualitative data were described using number and percent. Quantitative data were described using range (minimum and maximum), mean, and standard deviation. Significance of the obtained results was judged at the 5% level. Chi-square test was used for categorical variables, to compare between different groups. Fisher's exact test was used for correction of chi-square. Student t-test was used for normally distributed quantitative variables. Paired t-test and Mann–Whitney test were used for normally and abnormally distributed quantitative variables, respectively. Receiver operating characteristic curve (ROC) was generated. Area under the ROC curve more than 50% gave acceptable performance, and area near 100% was best performance for the test.

3. Results

Figure 1 shows diaphragmatic thickness (DT) at zone of apposition in a: B-mode, b: M-mode. 1: Thickness at end-expiration, 2: thickness at end-inspiration, c: right subcostal view in B-mode.

Figure 2 draws patients' flow chart. Current study was carried out on 75 adult AECOPD patients. According to fate of NIV, they were categorized into successful NIV group; 45 patients (60%) and failed NIV group; 30 patients (40%).
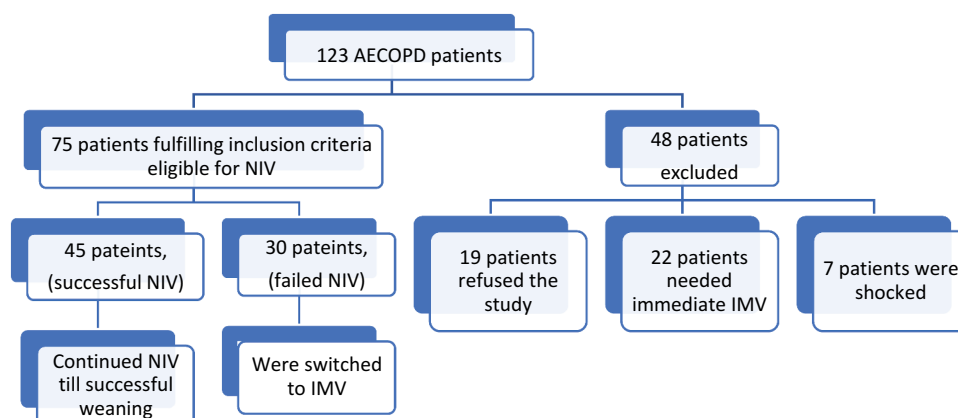

Figure 2. Patients' flow chart.

Table 1. Comparison between both groups according to baseline patient's criteria on admission.

AECOPD	Successful NIV (n = 45)	Failed NIV (n = 30)	Test of sign.	p
Sex				
Male	40 (88.9%)	24 (80%)	$\chi^2 = 1.136$	$^{FE}p = 0.33$
Female	5 (11.1%)	6 (20%)		0.136
Age (years)				
Range	42.0–80.0	48.0–79.0		
Mean ± SD.	59.27 ± 10.05	62.77 ± 9.57	$t = 1.506$	
Comorbidities				
DM	16 (35.6)	13 (43.3%)	$\chi^2 = 0.459$	0.498
HTN	11 (24.4%)	8 (26.7%)	$\chi^2 = 0.047$	0.828
IHD	10 (22.2%)	7 (23.3%)	$\chi^2 = 0.013$	0.910
CKD	6 (13.3%)	6 (20%)	$\chi^2 = 0.595$	$^{FE}p = 0.53$
Precipitating cause				
Pneumonia	29 (64.4%)	13 (43.3%)	$\chi^2 = 3.256$	0.071
DHF	10 (22.2%)	5 (17.9%)	$\chi^2 = 0.201$	0.654
Rx non-compliance	16 (35.6%)	12 (40%)	$\chi^2 = 0.152$	0.697
Irritant exposure	6 (13.3%)	5 (16.7%)	$\chi^2 = 0.160$	$^{FE}p = 0.75$
ACS	7 (15.6%)	4 (13.3%)	$\chi^2 = 0.071$	$^{FE}p = 1.00$
GCS				
Range	13.0–15.0	13.0–15.0		
Mean ± SD.	14.42 ± 0.69	14.40 ± 0.67	$t = 0.138$	0.891
APPACHE II				
Range	12.0–26.0	13.0–27.0		
Mean ± SD.	16.29 ± 2.81	18.20 ± 2.77	$t = 2.902*$	0.005*
Resp. Rate/minute				
Range	25.0–35.0	26.0–35.0		
Mean ± SD.	29.49 ± 3.25	30.57 ± 3.01	$t = 1.447$	0.152

NIV: non-invasive mechanical ventilation. AECOPD: acute exacerbation of chronic obstructive pulmonary disease. n: number of patients. Test of sign.: test of significance. DM: diabetes mellitus. HTN: hypertension. IHD: ischemic heart disease. CKD: chronic kidney disease. DHF: diastolic heart failure. Rx non-compliance: non-compliance to treatment. ACS: acute coronary syndrome. GCS: Glasgow coma scale. APACHE II: Acute Physiologic Assessment and Chronic Health Evaluation II score. Resp. Rate: respiratory rate per minute. Values are presented as mean ± standard deviation (SD), range, number, and percentage (%). t: student t-test. χ^2: Chi square test. FE: Fisher Exact test. p: probability for comparing between both groups. *: significant differences from baseline $p \leq 0.05$.

Table 2. Comparison between both groups according to ABG on admission and after NIV.

	ABG:	Successful NIV (n = 45)	Failed NIV (n = 30)	t	p
pH	On admission				
	Range	7.25–7.35	7.25–7.32		
	Mean ± SD.	7.29 ± 0.02	7.28 ± 0.02	1.517	0.133
	After NIV				
	Range	7.34–7.44	7.05–7.25		
	Mean ± SD.	7.38 ± 0.02	7.18 ± 0.04	24.863*	<0.001*
	$t_1(p_1)$	21.379*(<0.001*)	14.506*(<0.001*)		
$PaCO_2$ (mmHg)	On admission				
	Range	50.0–82.0	53.0–85.0		
	Mean ± SD.	68.38 ± 9.08	72.63 ± 5.85	2.468*	0.016*
	After NIV				
	Range	43.0–70.0	78.0–111.0		
	Mean ± SD.	56.78 ± 7.72	93.70 ± 7.57	20.453*	<0.001*
	$t_1(p_1)$	14.883*(<0.001*)	19.912*(<0.001*)		
PaO_2 (mmHg)	On admission				
	Range	40.0–80.0	45.0–65.0		
	Mean ± SD.	56.0 ± 9.39	53.53 ± 5.22	1.457	0.150
	After NIV				
	Range	55.0–80.0	45.0–65.0		
	Mean ± SD.	68.07 ± 5.99	52.70 ± 5.57	11.192*	<0.001*
	$t_1(p_1)$	21.175*(<0.001*)	0.847(0.404)		
HCO_3 (mEq/L)	On admission				
	Range	24.0–39.0	24.0–39.0		
	Mean ± SD.	32.0 ± 4.56	33.20 ± 2.98	1.379	0.172
	After NIV				
	Range	24.0–38.0	26.0–42.0		
	Mean ± SD.	32.6 ± 3.9	33.6 ± 3.7	1.147	0.255
	$t_1(p_1)$	1.402(0.168)	0.613(0.545)		
SaO_2 (%)	On admission				
	Range	75.0–90.0	70.0–88.0		
	Mean ± SD.	82.40 ± 4.11	79.67 ± 3.68	2.938*	0.004*
	After NIV				
	Range	82.0–94.0	75.0–85.0		
	Mean ± SD.	87.93 ± 3.05	78.63 ± 2.75	13.455*	<0.001*
	$t_1(p_1)$	12.054*(<0.001*)	1.549(0.132)		

NIV: non-invasive mechanical ventilation. ABG: arterial blood gases. n: number of patients. Values are presented as mean ± standard deviation (SD), and range. t: student t-test. t_1: Paired t-test. p: probability for comparing between both groups. p_1: probability for comparing between on admission and after NIV. *: significant differences from baseline $p \leq 0.05$.

Table 1 refers to baseline patients' criteria on admission in both groups. No statistically significant difference was found between both groups regarding mean values of age, sex, comorbidities, possible causes of AECOPD, GCS, or respiratory rate/minute ($p > 0.05$). There was statistically significant difference between both groups in their mean APACHE II score ($p = 0.005$); however, its values in both groups were abnormally high (16.29 ± 2.81 and 18.20 ± 2.77, respectively).

Table 2 illustrates mean ABG parameters on admission and after NIV in both groups. Admitting individual ABG readings were comparable without statistical significance between both groups ($p > 0.05$). $PaCO_2$ and SaO_2 despite showed statistically significant difference between both groups on admission ($p = 0.016$ and 0.004, respectively); however, this difference was of no clinical importance. After NIV, all ABG parameters (except HCO_3; $p = 0.255$) showed statistically significant improvement in their measured values regarding the successful NIV group when compared to failed NIV group ($p < 0.001$). When comparing before and after NIV trial in both groups, all ABG parameters (except HCO_3; $p_1 = 0.168$) showed statistically significant improvement in the successful NIV group ($p_1 < 0.001$), while only pH and $PaCO_2$ values showed statistically significant deterioration in the failed NIV group ($p_1 < 0.001$).

Table 3 demonstrates impact of DI on need for IMV after NIV failure as our primary outcome. Regarding successful NIV group, mean right and left DTF% were 0.38 ± 0.10 and 0.33 ± 0.09, respectively. DI was evident in failed NIV group (DTF <20%), mean right and left readings were 0.18 ± 0.05 and 0.16 ± 0.05, respectively. Such bilateral DTF difference between both groups was statistically significant ($p < 0.001$).

Table 3. Comparison between both groups according to DTF on admission.

DTF	Successful NIV (n = 45)	Failed NIV (n = 30)	U	p
Right				
Range	0.16–0.56	0.11–0.30		
Mean ± SD.	0.38 ± 0.10	0.18 ± 0.05	65.50*	<0.001*
Left				
Range	0.16–0.52	0.10–0.29		
Mean ± SD.	0.33 ± 0.09	0.16 ± 0.05	56.50*	<0.001*

NIV: non-invasive mechanical ventilation. DTF: Diaphragmatic Thickness Fraction. n: number of patients. Values are presented as mean ± standard deviation (SD), and range. U: Mann–Whitney test. p: probability for comparing between both groups. *: significant differences from baseline $p \leq 0.05$.

Table 4. Comparison between both groups according to secondary outcome.

	Successful NIV (n = 45)	Failed NIV (n = 30)	Test of sig.	p
MV days				
Range	4.0–13.0	7.0–19.0		
Mean ± SD.	6.38 ± 1.90	14.25 ± 2.80	t = 4.972*	<0.001*
ICU Stay (days)				
Range	7.0–16.0	10.0–21.0		
Mean ± SD.	10.98 ± 2.67	15.80 ± 3.10	t = 7.186*	<0.001*
28-days mortality				
Non survivors	4 (8.9%)	9 (30%)	χ^2 = 5.599*	0.018*

NIV: non-invasive mechanical ventilation. MV: mechanical ventilation. n: number of patients. Values are presented as mean ± standard deviation (SD), and range. t: student t-test. χ2: Chi square test. p: probability for comparing between both groups. *: significant differences from baseline $p \leq 0.05$.

Table 4 compares between both groups according to secondary outcome (MV days, ICU stay, and 28-day mortality). Mean MV days (6.38 ± 1.90 days) in successful NIV group were significantly less than failed NIV group (14.25 ± 2.80 days) ($p < 0.001$). Mean ICU stay (10.98 ± 2.67 days) in successful NIV group was significantly less than failed NIV group (15.80 ± 3.10 days) ($p < 0.001$). Regarding 28-day mortality, non-survivors in successful NIV group (4 patients) were less than in failed NIV group (9 patients). This was statistically significant ($p = 0.018$).

Table 5 and Figure 3 show agreement (sensitivity and specificity) data after plotting receiver operating characteristics (ROC) curve for DTF to predict need for IMV after NIV failure in all patients. Cut-off value of DTF % (<29%) at the right side was associated with NIV failure with 96.67% sensitivity, 82.22% specificity, 78.4 positive predictive value (PPV), and 97.4 negative predictive value (NPV). On the left side, cut-off value of DTF% (<26%) was associated with NIV failure with 96.67% sensitivity, 80% specificity, 76.3 PPV, and 97.3 NPV.

4. Discussion

Baseline patients' criteria on admission including age, sex, associated comorbidities, precipitating cause (s) of AECOPD, GCS, and respiratory rate per minute were homogenous without statistical significance in both studied groups. APACHE II score was the only statistically significant variable; however, its mean values in both groups were nearly fitting within the same category with approximated in-hospital mortality rates of
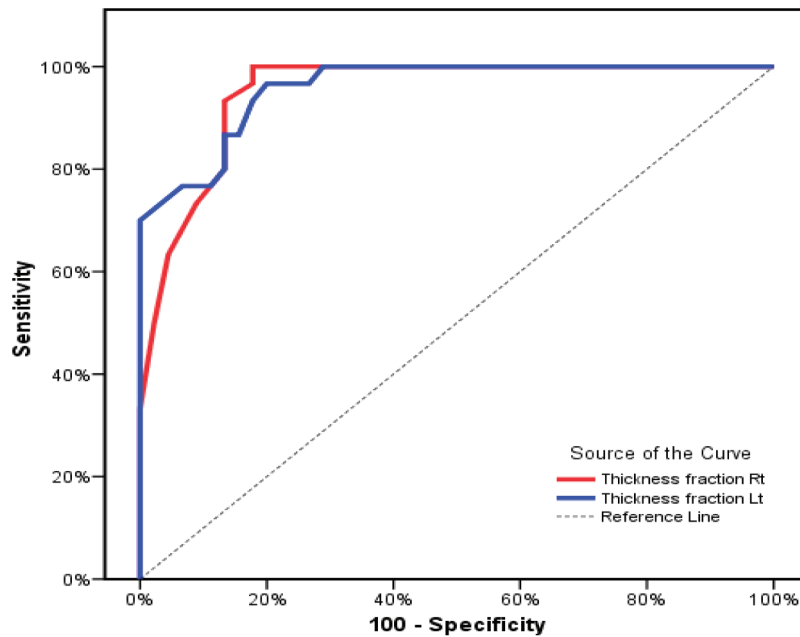
Table 5. Validity (AUC, sensitivity, specificity) of DTF to predict need for IMV after NIV failure.

DTF	AUC	p	95% C.I.	Cut-off	Sensitivity	Specificity	PPV	NPV
Right	0.951	<0.001*	0.907–0.994	≤0.29	96.67	82.22	78.4	97.4
Left	0.958	<0.001*	0.920–0.996	≤0.26	96.67	80.0	76.3	97.3

DTF: Diaphragmatic Thickness Fraction. IMV: invasive mechanical ventilation. NIV: non-invasive mechanical ventilation. AUC: Area Under the Curve. p: probability for comparing between both groups. *: significant differences from baseline $p \leq 0.05$ probability value. CI.: Confidence Intervals. NPV: Negative predictive value. PPV: Positive predictive value.

Figure 3. Receiver operating characteristic (ROC) curve for diaphragmatic thickness fraction (DTF) to predict need for invasive mechanical ventilation (IMV) after non-invasive ventilation (NIV) failure.

25%. D. Christopher et al. [25] in their review about scoring systems in critically ill patients reported that APACHE II score when calculated during the first 24 hours of ICU admission, a score of 25 represents a predicted mortality of 50%.

ABG parameters on admission in the current study were comparable. In both groups, they nearly showed uncompensated acute on top of chronic respiratory acidosis with relative hypoxia. After NIV, ABG parameters improved significantly toward normalization in the successful group, while they showed significant deterioration in the failed group. Confalonieri et al. [26] suggested a chart for failure risk of NIV in AECOPD patients. They reported that patients with a GCS < 11, APACHE II ≥ 29, RR ≥ 30 breaths/min, and pH on admission < 7.25 have a predicted risk of failure > 70%. A pH < 7.25 after 2 hours greatly increased the risk of failure of NIV > 90%.

Pejkovska et al. [27], in their study about predictive factors for the effect of NIV in AECOPD patients, concluded that measuring certain parameters like, pH, PaCO2, RR, and GCS may be valuable in predicting success of NIV treatment if these parameters improved within 2 hours. Fan et al. [28] examined semiquantitative cough strength score (SCSS) and associated outcomes in NIV for AECOPD. They concluded that sum of SCSS, APACHE II score, and total proteins had increased power to predict NIV failure. Meanwhile, they found no statistical significance of pH, PaCO2, or PaO2 to predict NIV failure. Of note was that they enrolled ABG only on admission without follow-up after NIV treatment.

DTF in our study was measured and calculated bilaterally in both groups. Diaphragmatic dysfunction (diaphragmatic impairment) was diagnosed when DTF

was < 20%. Readings in the successful NIV group were ≥ 33–38% while failed NIV readings were ≤ 16–18% indicating significant diaphragmatic impairment. Cut-off value of DTF < 26–29% on both sides was associated with NIV failure with 96.67% sensitivity and 80–82.22% specificity.

Qian et al. [29] reviewed ultrasound assessment of diaphragmatic dysfunction (DD) as a predictor of weaning outcome from MV. They concluded that both diaphragmatic excursion and DTF showed good diagnostic performance to predict weaning outcomes. They defined DD to be a predictor of weaning failure in critically ill patients.

Antenora et al. [30] underwent a pilot study on the prevalence and clinical consequences of diaphragmatic dysfunction (DD) diagnosed by ultrasonography during AECOPD. They considered DTF < 20% as diaphragmatic impairment (DD). They reported that NIV failure was found to be strongly associated with DD. Kocyigit et al. [31] in their prospective cohort study about diaphragmatic impairment detected by ultrasound to predict NIV failure concluded that DD has high sensitivity and specificity in predicting NIV failure in patients admitted to the emergency department with AECOPD.

Marchioni et al. [20] in their prospective observational study investigated ultrasound-assessed diaphragmatic impairment as a predictor of outcome in AECOPD patients on NIV. Also, they investigated the correlation between US-assessed DD and the trans-diaphragmatic pressure (Pdi) assessed using invasive sniff maneuver. They found that DTF < 20% demonstrated the same accuracy as Pdi sniff in identifying

diaphragmatic dysfunction. They concluded that AECOPD patients admitted for NIV treatment have a high risk of NIV failure and mortality if they had DD as assessed by US.

Mercurio et al. [32] performed a preliminary physiological study to evaluate DTF and RR/DTF ratio as predictors of NIV outcome in 18 acute respiratory failure (ARF) patients. They found that the cut-off value of DTF < 36.3% significantly predicted NIV failure with sensitivity of 71.7% and specificity of 94.3%. They concluded that DTF and RR/DTF ratio may both represent valid, feasible, and non-invasive tools to predict NIV outcome in patients with de-novo ARF.

Days of MV and ICU stay in the current study were significantly lower in the successful NIV group when compared to the failed NIV group of patients. This may be attributed to major hazards of invasive mechanical ventilation including the risk of ventilator associated pneumonia, barotrauma, and failure to wean to spontaneous ventilation, all such complications could prolong duration of MV, and ICU stay [11]. Such increased morbidity may have added to the increased 28-day mortality that was significantly less encountered in successful NIV group (4 patients) when compared to the failed NIV group (9 patients) who were intubated and mechanically ventilated.

Stefan et al. [33] in their retrospective study of prospectively collected data compared between NIV and IMV in critically ill patients with AECOPD as regards their outcomes. More than three thousand patients were enrolled into the study. They found that NIV failure was associated with the worst outcomes. They concluded that promoting NIV was associated with a lower risk of in-hospital mortality compared with that of IMV.

Ansari et al. [34] conducted a study on 104 AECOPD patients to assess frequency, predictors, and outcome of NIV failure after switching to IMV. showed statistical significance between success and failed group according to ICU stay. They found that tachycardia, hypotension, hypoxia, and respiratory acidosis when corrected by NIV within first 24 hours can predict successful NIV. They concluded also that failed NIV within first 24 hours carries poor outcome and higher mortality.

Lindenauer et al. [35] conducted a retrospective study on 25,628 AECOPD patients to compare patients' outcomes when treated with NIV or IMV. They concluded that COPD patients treated by immediate NIV had lower mortality, less morbidity, shorter ICU stay, and lower costs compared to those who failed NIV and were treated with IMV.

This study had some limitations. First, we didn't perform comparison with other methods that are considered gold standard in the diaphragmatic function assessment like transdiaphragmatic pressure, phrenic nerve stimulation, and electromyography. These methods are expensive, invasive, require special equipment,

and specialized team. Another point is that ultrasonography is an operator dependent technique that needs a lot of training.

5. Conclusion

Based on the results of this prospective observational study, DTF was a good indicator of DI that could predict need for IMV after NIV failure in AECOPD patients with 96.67% sensitivity and 80–82.22% specificity. Days of MV, ICU stay, and 28-day mortality were significantly higher in patients with DI who needed IMV after NIV failure.

Disclosure statement

ORCID

Bassem Nashaat Beshey http://orcid.org/0000-0001-8965-143X

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