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Original Article

Ultrasound-based evaluation of inspiratory muscle effort in patients with type 2 respiratory failure secondary to exacerbation of chronic obstructive pulmonary disease

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ABSTRACT

Background: Exacerbations of chronic obstructive pulmonary disease (ECOPD) are a major cause of acute hypercapnic respiratory failure. Diaphragmatic dysfunction is common, often accompanied by compensatory recruitment of parasternal intercostal (IC) and sternocleidomastoid (SCM) muscles. While diaphragm ultrasound (US) is established, evidence on extra-diaphragmatic and accessory muscle activity in this context is limited.
Methods: We conducted a single-center prospective exploratory proof-of-concept study in the Respiratory Intermediate Care Unit of the University Hospital of Modena This study aimed to characterize inspiratory muscle performance by bedside US in patients with ECOPD undergoing high-flow nasal cannula (HFNC), to explore its relationship with inspiratory effort and gas exchange, and to assess its potential prognostic value for HFNC outcome. Consecutive ECOPD patients with PaO_2/FiO_2 <300 mmHg underwent a 2-hour high-flow nasal cannula (HFNC) trial. US at initiation (T0) and 2 h later (T1) measured thickening fraction (TF) of diaphragm (TFdi), IC (TFic), and SCM (TFscm). Inspiratory effort was assessed by nasal pressure swings (ΔPnose). Associations with gas exchange and HFNC outcome were analysed.
Results: Thirty patients were enrolled (median age 75.5 years, 73 % male); 9 (30 %) failed HFNC. At baseline, TFdi was 27 % [16–38], and accessory activation (TFic >0 % or TFscm >0 %) occurred in 63 % ($n = 19$). Failures had higher TFic (33 % vs 5 %; $p = 0.01$) and TFscm (27 % vs 0 %; $p < 0.0001$). TFdi correlated inversely with TFic (r=–0.55), TFscm (r=–0.54), ΔPnose (r=–0.62), and $PaCO_2$ (r=–0.39), and positively with PaO_2/FiO_2 (r = 0.54) (all $p \leq 0.002$). TFic and TFscm correlated directly with ΔPnose ($r = 0.70$; $r = 0.77$) and $PaCO_2$, and

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; BE, Base excess; BMI, Body mass index; COPD, Chronic obstructive pulmonary disease; ECOPD, Exacerbation of chronic obstructive pulmonary disease; FiO_2, Fraction of inspired oxygen; HFNC, High-flow nasal cannula; HR, Heart rate; IC, Parasternal intercostal muscle; IQR, Interquartile range; MAP, Mean arterial pressure; NIV, Non-invasive ventilation; $PaCO_2$, Arterial carbon dioxide tension; PaO_2, Arterial oxygen tension; PaO_2/FiO_2, Ratio of arterial oxygen tension to fraction of inspired oxygen; PEEPi, Intrinsic positive end-expiratory pressure; ΔPnose, Nasal pressure swing; RICU, Respiratory intermediate care unit; RR, Respiratory rate; SCM, Sternocleidomastoid muscle; SOFA, Sequential Organ Failure Assessment; SpO2, Peripheral oxygen saturation; Tdi, Diaphragm thickness; Tic, Parasternal intercostal thickening; Tscm, Sternocleidomastoid thickening; TF, Thickening fraction; TFdi, Diaphragm thickening fraction; TFic, Parasternal intercostal thickening fraction; US, Ultrasound; Vt, Tidal volume.

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inversely with oxygenation and pH. At T1, responders showed increased TFdi, while failures had reduced TFdi with a trend toward progressive IC and SCM recruitment.
Conclusions: In ECOPD, impaired diaphragmatic function is frequently offset by accessory muscle activation. US-based assessment of inspiratory muscles may provide early prognostic information and guide HFNC management.

Introduction

Acute exacerbations of chronic obstructive pulmonary disease (ECOPD) impose a substantial mechanical workload on the respiratory system, driven by a combination of airflow limitation, dynamic hyperinflation, and intrinsic positive end-expiratory pressure [1,2]. These factors increase the elastic and resistive loads on the inspiratory muscles while placing the diaphragm at a mechanical disadvantage due to shortening and loss of optimal length–tension relationship [3–5]. As a result, neuromechanical coupling deteriorates, and sustaining adequate ventilation often requires compensatory recruitment of extra diaphragmatic inspiratory muscles, including the parasternal intercostals (IC) and sternocleidomastoid (SCM) muscles [6]. When the load–capacity balance becomes critically impaired, the risk of ventilatory failure and need for escalation of respiratory support increase significantly [7,8].

To date, assessment of inspiratory muscle performance in ECOPD has traditionally focused on the diaphragm, with ultrasound (US)-derived thickening fraction (TFdi) widely used as a surrogate marker of the contractile activity [9,10]. However, the diaphragm is only one component of the inspiratory pump and research into inspiratory extra-diaphragmatic muscles by US assessment has grown exponentially in recent years [11]. The parasternal IC, together with accessory muscle like scalene and SCM muscles, contribute significantly to tidal volume (Vt) generation, particularly under high load or when diaphragmatic function is impaired [12–17]. Experimental and clinical studies in COPD have shown that IC activity increases with rising inspiratory effort, as demonstrated by electromyographic recordings during both stable condition and exercise [18,19].

US imaging of the parasternal IC muscle has been validated in mechanically ventilated patients, and provides a feasible, reproducible, and non-invasive method to quantify extra-diaphragmatic inspiratory muscle recruitment through its thickening fraction (TFic), which has been explored as a predictor of weaning [20–22]. Further, the TFic/TFdi ratio has recently been proposed as an index of compensatory activation in stable COPD patients [23].

Similarly, US assessment of SCM has revealed structural adaptations in COPD: at end-expiration the muscle is often thinner than in controls, consistent with chronic remodelling and possible atrophy, yet during tidal breathing its thickening fraction increases when diaphragmatic function is impaired or inspiratory load is high [24]. Electromyographic studies confirm that SCM activation rises with inspiratory load, being particularly significant during exacerbations [12,25].

Notwithstanding, to our knowledge no study has yet comprehensively characterised diaphragmatic and extra diaphragmatic US indices in non-intubated ECOPD patients and correlated them with objective measures of inspiratory effort and clinical outcomes.

In this prospective study, we therefore sought to: (1) early assess by US the inspiratory muscle performance in patients with severe ECOPD under high-flow nasal cannula (HFNC) therapy, (2) examine its relationship with inspiratory effort as quantified by nasal pressure swing (ΔPnose), (3) explore associations with the key clinical outcomes.

Materials and methods

Study design and cohort

The study is a prospective, single-center, observational trial conducted at the Respiratory Intermediate Care Unit (RICU) of the University Hospital of Modena. The investigation represents a prespecified sub-analysis of the ongoing CORALINE study (ClinicalTrials.gov NCT06989385; SIRER code 7354; protocol number 165/2024/SPER/AOUMO), a prospective observational project designed to evaluate physiological predictors of noninvasive respiratory support failure in acute respiratory failure. The study was approved by the local Ethics Committee (Comitato Etico Area Vasta Emilia Nord).

Between November 2024 and May 2025, all adult patients admitted for ECOPD with a PaO_2/FiO_2 ratio <300 mmHg were screened for eligibility and consecutively enrolled. Those included were admitted to a 2-hour trial of HFNC as initial respiratory support, based on institutional criteria and in the absence of immediate indications for non-invasive ventilation (NIV) and/or mechanical ventilation (see below). Exclusion criteria were intolerance to non-invasive respiratory support, already documented either neuromuscular disease or diaphragmatic impairment of different origin (e.g., hemidiaphragm paralysis or surgical phrenic nerve injury), age <18 years, pregnancy, or inability/refusal to provide informed consent.

Data collection

For each patient, comprehensive clinical and physiological data were prospectively collected at predefined timepoints. Upon admission, demographic characteristics and comorbidities, were recorded. Arterial blood gases were obtained at baseline (T0) and after 2-hour of HFNC (T1) to assess the early response to treatment. Respiratory rate was determined by direct observation of chest wall movements over one minute, using the same standardized approach at both T0 and T1. Subjectively reported dyspnea by BORG scale and inspiratory effort by means of ΔPnose measurement were also recorded. Nasal pressure was measured by a custom-made, soft, self-expanding foam plug with an embedded 16-gauge cannula, inserted in one nostril and connected to a transducer, while the contralateral nostril remained open to allow HFNO delivery [26–28].

Ultrasound assessment of inspiratory muscle function

Ultrasound examination was performed within 30 min following admission and conducted sequentially on the diaphragm, parasternal IC, and SCM muscles to ensure standardized acquisition and minimize variability. Image acquisition and analysis were performed by three trained investigators (LT, JM, and SB), blinded to the patient outcomes, who followed a standardized protocol to minimize potential bias.

US assessment of the diaphragm activity was performed using a high-frequency linear probe (7.5–15 MHz) in B-mode, following standardized protocols and operator-dependent optimization. All measurements were conducted at T0 and T1 with patients positioned semi-recumbently (30° head elevation) and breathing spontaneously. The diaphragm was assessed at the zone of apposition of the right hemidiaphragm, with the transducer placed between the 8th and 10th IC space along the mid-axillary line, using the liver as an acoustic window. The diaphragm was identified as a trilaminar structure and thickness was measured at end-expiration and end-inspiration to calculate the TF as an index of contractile activity. The parasternal IC muscles were evaluated at the second IC space, 3–6 cm lateral to the sternal edge in a sagittal orientation. M-mode was used to quantify dynamic changes in thickness during tidal breathing, consistently with Formenti et al. [22]. The probe was adjusted to visualize the IC muscle belly between the superficial and

deep fascial layers, and TF was assessed during tidal breathing, again at end-expiration and end-inspiration. Similarly, activity of the SCM muscle was assessed in M-mode by placing the probe transversely at mid-belly, between the mastoid process and clavicle, lateral to the carotid sheath. The SCM was visualized between the superficial and prevertebral fasciae, and its TF (TFscm) was derived from measurements at end-expiration and peak inspiratory contraction.

For all the muscle groups, three consecutive respiratory cycles were recorded and averaged to reduce intra-observer variability. Measurements were consistently acquired during tidal breathing, avoiding voluntary deep breaths or sighs. To ensure temporal consistency, probe position and settings were maintained throughout each session. Each measure was completed within an approximate 10-minute time window.

HFNC trial and failure definition

All patients received standard treatment for ECOPD in accordance with current international guidelines, including systemic corticosteroids, antibiotics when indicated, and optimized bronchodilation [29]. In accordance with our institutional protocol, patients admitted to RICU with ECOPD and moderate hypercapnic respiratory failure—defined by an arterial pH greater than 7.25, a Glasgow Coma Scale score of 15, and absence of severe respiratory distress—and not requiring immediate criteria for NIV or endotracheal intubation were initially managed with a 2-hour HFNC [30]. HFNC was delivered using a heated humidifier system (Airvo™ 2, Fisher & Paykel Healthcare, Auckland, New Zealand) with flow set at 50 L/min, FiO_2 titrated to maintain SpO_2 ≥92 %, and temperature at 37 °C. Over this trial, patients were continuously monitored and predefined clinical thresholds were used to identify failure of HFNC. Within the 2-hour trial, failure has been defned by the occurrence of any of the following: persistent or worsening hypoxemia (PaO_2/FiO_2 <100 mmHg despite FiO_2 optimization) and respiratory acidosis, respiratory rate >25 breaths/min, progressive or unrelieved dyspnea (by Borg scale), rise in $PaCO_2$, clinical signs of increased work of breathing, escalation to NIV, or death.

Analysis plan

This study represents an exploratory, proof-of-concept analysis; therefore, no formal sample size calculation was performed. The distribution of continuous variables was assessed through visual inspection of quantile–quantile plots. Data are reported as median and interquartile range (IQR), unless otherwise specified. Comparisons between paired timepoints (T0 vs. T1) were conducted using either the Wilcoxon signed-rank test or Student's paired *t*-test, depending on data distribution. Three inspiratory activation patterns were reported according to the relative contribution of the diaphragm and the accessory muscles: (1) isolated diaphragmatic activation, i.e. TFdi ≥ 20 % without any thickening of the accessory muscle; (2) mixed activation, i.e. TFdi ≥ 20 % with US-detectable accessory muscles' activity; (3) predominant parasternal IC/SCM activation, i.e. TFdi < 20 % with US-detectable parasternal IC and/or SCM recruitment.

Between-group comparisons (i.e., HFNC failure vs. success) were performed using the Mann–Whitney U test. Correlations between inspiratory muscle TF and clinical and physiological variables were analysed using Pearson's or Spearman's correlation coefficients, as appropriate. Correlation coefficients are reported with 95 % confidence intervals (95 %CI) and p-values. To assess whether the temporal evolution of muscle thickening differed according to HFNC outcome, a two-way repeated measures ANOVA was applied, with interaction p-values reported.

Analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA) and GraphPad Prism version 8.0 (GraphPad Software, La Jolla, CA, USA). A two-sided p-value < 0.05 was considered as statistically significant.

Results

Patient characteristics

Thirty patients with ECOPD (median age 75.5 years, 73 % male) were studied (Table 1 and eFig. 1, Supplement). Hypertension was present in 70 %, chronic heart disease in 53 %, and diabetes in 33 %. At HFNC initiation (T0), the median PaO_2/FiO_2 ratio was 156 mmHg, while $PaCO_2$ and pH were 54.5 mmHg and 7.30 respectively. At admission, the main causes were infections (including viral-40 %, bacterial-23.3 %, or mixed-16.7 %), while non-infectious exacerbations accounted by 20 % of total cases. Nine patients (30 %) experienced HFNC failure at the end of the trial, all requiring escalation to NIV. Compared with those who succeeded (S), patients who failed (F) showed higher $PaCO_2$ (59.6 vs 51.6 mmHg, $p = 0.03$) and inspiratory effort (ΔPnose 6.0 vs 3.6 cmH_2O, $p = 0.001$) at baseline. At T1, ΔPnose (6.3 vs 2.6 cmH_2O, $p < 0.0001$), $PaCO_2$ (72.2 vs 49.3 mmHg, $p = 0.03$), and Borg scores (6.0 vs 4.0, $p = 0.04$) were higher, whereas PaO_2/FiO_2 was lower (120 vs 199 mmHg, $p < 0.0001$), in F compared with S (Table 1).

Inspiratory muscle performance and relationship with inspiratory effort

At T0, median TFdi was 27 % [15.5–38], TFic 6 % [0–31.5], and TFscm 7 % [0–23.3] (Table 2), with a detectable accessory muscle activation (TFic >0 % or TFscm >0 %) observed in 63 % ($n = 19$) of patients for both muscle groups.

Overall, TFdi inversely correlated with both TFic (r=–0.55, $p < 0.0001$) and TFscm (r=–0.54, $p < 0.0001$) (Fig. 1, panel A and B respectively), while TFic and TFscm correlated each other ($r = 0.59$, $p < 0.0001$) (Fig. 1, panel C). No sequential recruitment pattern of IC and SCM was observed.

TFdi inversely correlated (r=–0.62, $p < 0.0001$) (Fig. 2, panel A), whereas TFic ($r = 0.70$, $p < 0.0001$) and TFscm ($r = 0.77$, $p < 0.0001$) directly correlated (Fig. 2, panel B and panel C) with ΔPnose.

Higher $PaCO_2$ values were associated with lower TFdi ($r = –0.39$, $p = 0.002$) but higher TFic ($r = 0.41$, $p = 0.001$) and TFscm ($r = 0.47$, $p = 0.0001$) (Fig. 3). In contrast, higher PaO_2/FiO_2 ratios were associated with higher TFdi ($r = 0.54$, $p < 0.0001$) and with lower TFic ($r = –0.43$, $p = 0.001$) and TFscm ($r = –0.46$, $p = 0.0003$) (eFig. 2, Supplement); pH values correlated positively with TFdi ($r = 0.33$, $p = 0.01$) but inversely with TFic ($r = –0.24$, $p = 0.04$) and TFscm ($r = –0.38$, $p = 0.003$) (eFig. 3, Supplement).

Inspiratory muscle performance and HFNC outcome

As shown in Table 2, when stratified by outcome (F or S), patients who later failed HFNC already showed higher TFic (33 % vs 5 %, $p = 0.01$) and TFscm (27 % vs 0 %, $p < 0.0001$) at T0 together with significantly more frequent SCM muscle activation (TFscm >0 %: 100 % vs 48 %, $p = 0.01$), at difference with S. They also showed a not significant trend to lower baseline TFdi (19 % vs 28 %, $p = 0.06$). TFic/TFdi and TFscm/TFdi ratios were also higher in F than in S (202 % vs 14.1 %, $p = 0.01$; 182 % vs 0 %, $p = 0.0002$). Mixed activation was the most frequent (53 %), followed by predominant parasternal IC/SCM (30 %) and isolated diaphragmatic activation (17 %). Although not statistically significant, predominant IC/SCM activation was more common in F group.

At T1, F had lower TFdi (17 % vs 35.9 %, $p = 0.0003$) and higher TFic (33 % vs 0 %, $p < 0.0001$) and TFscm (28 % vs 0 %, $p < 0.0001$) with nearly universal accessory muscle recruitment (TFic >0 %: 89 % vs 38 %, $p = 0.02$; TFscm >0 %: 100 % vs 29 %, $p = 0.001$, Table 2). Ratios of TFic/TFdi and TFscm/TFdi were still also higher in F than in S (200 % vs 0 %, $p < 0.0001$; 100 % vs 0 %, $p < 0.0001$). Isolated diaphragmatic activation was seen only in S (30 % vs 0 %, $p = 0.03$), whereas predominant parasternal IC/SCM activation was observed exclusively in F group (44.4 % vs 0 %, $p = 0.005$).

Table 1
Demographic, clinical, and respiratory features by HFNC outcome.

Variable	Overall (*N* = 30)	HFNC success (*N* = 21)	HFNC failure (*N* = 9)	p value
Demographics and clinical scores				
Age, years	75.5 (66.5 – 81.3)	76 (66.0 – 84.0)	74.0 (68.0 – 78.5)	0.58
Male sex, n	22 (73)	16 (76)	6 (67)	0.67
BMI, kg/m^2	25.2 (22.9 – 26.6)	25.3 (22.7 – 27.2)	26.2 (23.4 – 27.2)	0.81
Comorbidities				
Hypertension, n	21 (70)	15 (71)	6 (67)	0.99
Diabetes, n	10 (33)	5 (47)	5 (56)	0.12
Cardiovascular disease, n	16 (53)	12 (57)	4 (44)	0.69
Chronic liver disease, n	1 (3.3)	1 (4.7)	0 (0)	0.99
Chronic kidney disease, n	3 (9.9)	2 (9.5)	1 (11)	0.99
ECOPD etiology				
Infectious-viral %	12 (40)	9 (42.9)	3 (33.3)	0.7
Infectious-bacterial, %	6 (23.3)	3 (9.5)	3 (33.3)	0.32
Infectious-mixed, %	5 (16.7)	4 (19)	1 (11.1)	0.99
Non-infectious, %	7 (20)	5 (23.8)	2 (22.1)	0.99
Steroid exposure *, %	5 (16.7)	3 (9.5)	2 (22.1)	0.62
Smoking habit				
Active, %	10 (33.3)	7 (33.3)	3 (33.3)	0.99
Former, %	20 (66.3)	14 (66.6)	6 (66.6)	0.99
SOFA, score	2 (2 – 3)	2 (2 – 3)	2 (2 – 3)	0.87
APACHE II, score	12 (8 – 18)	12 (8 – 16)	13 (10 – 18)	0.18
Baseline measurements at the initiation of HFNC (T0 time)				
Borg, score	6.0 (4.0 – 8.0)	6.0 (4.0 – 7.0)	6.0 (4.5 – 8.0)	0.21
MAP, mmHg	95.0 (83.0 – 107.0)	97.0 (84.0 – 110)	93.0 (80.0 – 104.0)	0.48
HR, bpm	81.5 (70.0 – 90.0)	83.0 (70.0 – 92.5)	78.0 (66.0– 88.0)	0.11
RR, bpm	25.0 (20.0 – 28.0)	25.0 (19.0 – 27.5)	25.0 (20 – 28)	0.78
PaO_2/FiO_2, mmHg	156 (116 – 204)	191 (123 – 233)	146 (112 – 158)	0.09
FiO_2, %	40.0 (35.0 – 60.0)	40.0 (30.0 – 60.0)	50 (40 – 60)	0.74
SpO_2, %	90.5 (89.0 – 92.3)	92.0 (88.5 – 94.5)	90.0 (89.5 – 91.5)	0.47
pH, value	7.30 (7.27 – 7.33)	7.31 (7.27 – 7.33)	7.29 (7.27 – 7.33)	0.92
PaO_2, mmHg	65.1 (58.1 – 72.1)	65 (58.9 – 76.7)	63.0 (57.9 – 65.9)	0.26
$PaCO_2$, mmHg	54.5 (49.0 – 63.8)	51.6 (47.5 – 56.1)	59.6 (57.0 – 66.5)	0.03
BE, mmol/L	1.6 (−2.4 – 4.0)	1.7 (−2.4 – 4.2)	3.6 (−0.4 – 5.3)	0.06
HCO_3-, mmol/L	27.2 (22.7 – 30)	26.8 (22.7 – 29.8)	28.0 (25.2 – 30.2)	0.06
Lactate, mmol/L	1.0 (0.7 – 1.2)	0.9 (0.6 – 1.2)	1.1 (1 – 1.2)	0.08
ΔPnose, cmH_2O	4.3 (3.3 – 6.5)	3.6 (2.5 – 5.3)	6.0 (5.2 – 8.3)	0.001
Measurements 2 h after HFNC initiation (T1 time)				
Borg, score	5.0 (3.0 – 7.0)	4.0 (3.0 – 6.0)	6.0 (4.5 – 8)	0.04
MAP, mmHg	93.5 (87.0 – 107.8)	94.0 (87.5 – 106.5)	90.0 (85.0 – 110.0)	0.90
HR, bpm	86.5 (75.0 – 92.3)	85.0 (75.6 – 95.0)	90.0 (74.5 – 97.5)	0.17
RR, bpm	23.0 (18.0 – 26.0)	24.0 (18.0 – 26.0)	26.0 (19.0 – 27.5)	0.08
PaO_2/FiO_2, mmHg	174 (122.5 – 207)	198.9 (157.9 – 221.3)	119.6 (102.6 – 135.4)	<0.0001
FiO_2, %	35.5 (30.0 – 51.3)	30.0 (30.0 – 40.0)	50.0 (33.0 – 65.0)	0.05
SpO_2, %	91.0 (89.0 – 93.3)	91.0 (89.0 – 93.0)	91 (90 – 95)	0.61
pH, value	7.34 (7.30 – 7.36)	7.35 (7.32 – 7.38)	7.33 (7.26 – 7.35)	0.27
PaO_2, mmHg	59.0 (55.1 – 67.1)	55.8 (54.8 – 65.7)	62.1 (58.6 – 72)	0.16
$PaCO_2$, mmHg	50.2 (46.4 – 61.1)	49.3 (46.4 – 52.8)	72.2 (48 – 75.7)	0.03
BE, mmol/L	2.8 (−1.8 – 6.6)	2.1 (−2.4 – 7.1)	3.7 (1.1 – 6.8)	0.02
HCO_3-, mmol/L	27.1 (23.9 – 32.0)	26.5 (22.1 – 32.8)	29.1 (27.1 – 32.4)	0.03
Lactate, mmol/L	1.2 (0.8 – 1.8)	1.0 (0.6 – 1.4)	1.8 (1.1 – 2.2)	0.01
ΔPnose, cmH_2O	3.1 (2.5 – 5.6)	2.6 (2.4 – 3.2)	6.3 (5.7 – 6.7)	<0.0001

Table 1. Baseline characteristics and physiological measurements of patients with acute exacerbation of COPD (ECOPD) according to HFNC outcome. Measurements were collected at the time of HFNC start (T0) and after 2 h of treatment (T1). Data are presented as number (n) and percentage (%) for dichotomous values or median and interquartile range (IQR) for continuous values. Statistical significance was set for $p < 0.05$.

ECOPD, acute exacerbation of chronic obstructive pulmonary disease; APACHE II, Acute Physiology Assessment and Chronic Health Evaluation II; BE, base excess; BMI, body mass index; FiO_2, fraction of inspired oxygen; HFNC, high-flow nasal cannula; HR, heart rate; MAP, mean arterial pressure; $PaCO_2$, arterial carbon dioxide tension; PaO_2, arterial oxygen tension; PaO_2/FiO_2, ratio of arterial oxygen tension to inspired oxygen fraction; ΔPnose, nasal pressure swing; RR, respiratory rate; SOFA, Sequential Organ Failure Assessment; SpO_2, peripheral oxygen saturation; TF, thickening fraction.

* Steroid exposure is intended as systemic corticosteroid treatment lasting >2 consecutive weeks within the previous 6 months.

The longitudinal analysis confirmed a divergent temporal evolution of TFdi, with a decrease in F and an increase in S (interaction $p = 0.04$) (Fig. 4). Although not significant the interaction for TFic ($p = 0.10$) or TFscm ($p = 0.60$) (eFig. 4 and 5, Supplement, respectively), both these muscle groups displayed a consistent trend toward increased recruitment among the patients who failed.

Discussion

The present exploratory and proof-of-concept study aimed at describing the inspiratory muscle activity, as assessed not invasively by US at the bedside, in patients admitted for ECOPD and undergoing 2-hour HFNC trial. To our knowledge, this is the first investigation reporting US assessment of IC and SCM activation in this clinical setting and to correlate these measures with inspiratory effort.

We have observed that: 1) IC and SCM muscle activation was frequent, being detectable in nearly two-thirds of patients at HFNC initiation, while TFdi was often reduced, 2) divergent patterns of muscle recruitment were tightly linked to inspiratory effort and gas exchange, and 3) diaphragmatic activity increased in patients who succeeded HFNC but declined in those who failed, whereas accessory muscle progressively intensified their activity in the latter. These trajectories indicate that early patterns of inspiratory muscle recruitment could provide useful prognostic information.

The inverse relationship we observed between diaphragmatic and accessory muscle TFs is consistent with the well-described physiological disadvantage of the diaphragm in COPD patients during incremental load, where hyperinflation flattens its dome and impairs its length–tension efficiency, thereby promoting reliance on extra-diaphragmatic muscles [6,31]. In our study, US method was able to reveal that when TFdi was blunted, both parasternal IC and the SCM muscle were increasingly recruited. This pattern reflects a redistribution of

Table 2
Respiratory muscle US measurements by HFNC outcome.

Variable	Overall (*N* = 30)	HFNC success (*N* = 21)	HFNC failure (*N* = 9)	p value
Baseline measurements at the initiation of HFNC (T0 time)				
Diaphragm US				
Tdi at end-expiration, mm	2.7 (1.9 – 3.1)	2.7 (1.9 – 3.2)	2.7 (1.7 – 3.1)	0.45
Tdi at end-inspiration, mm	3.5 (2.4 – 4.2)	3.8 (2.5 – 4.4)	3.3 (2.2 – 3.7)	0.13
TFdi, %	27.0 (15.5 – 38)	28.0 (20.0 – 41.5)	19.0 (11.5 – 31.0)	0.06
Parasternal IC muscle US				
Tic at end-expiration, mm	1.3 (1.1 – 1.7)	1.4 (1.3 – 1.9)	1.1 (1.0 – 1.3)	0.25
Tic at end-inspiration, mm	1.6 (1.3 – 2.0)	1.6 (1.3 – 2.1)	1.4 (1.3 – 1.8)	0.08
TFic, %	6.0 (0.0 – 31.5)	5.0 (0.0 – 14.0)	33.0 (9.0 – 41.0)	0.01
IC muscle activation, %	19 (63)	12 (57)	7 (78)	0.42
SCM muscle US	19 (63)	10 (48)	9 (100)	
Tscm at end-expiration, mm	1.7 (1.5 – 1.9)	1.7 (1.5 – 2.2)	1.7 (1.3 – 1.9)	0.88
Tscm at end-inspiration, mm	1.9 (1.6 – 2.3)	1.8 (1.6 – 2.4)	2.1 (1.9 – 2.5)	0.20
TFscm, %	7.0 (0.0 – 23.3)	0.0 (0.0 – 9.5)	27.0 (21.5 – 39.5)	<0.0001
SCM activation, %	19 (63)	10 (48)	9 (100)	0.01
TFic/TFdi ratio, %	17.0 (0.0 – 209)	14.1 (0.0 – 70.0)	202 (35 – 435)	0.01
TFscm/TFdi ratio, %	26.5 (0.0 – 162)	0.0 (0.0 – 53.0)	182 (87.5 – 258)	0.0002
Isolated diaphragmatic activation, %	5 (16.7)	5 (23.8)	0 (0)	0.29
Predominant parasternal IC/SCM activation, %	9 (30)	4 (19)	5 (55.5)	0.08
Mixed activation, %	16 (53.3)	12 (57.1)	4 (44.4)	0.69
Measurements 2 h after HFNC initiation (T1 time)				
Diaphragm US				
Tdi at end-expiration, mm	2.7 (1.9 – 3.1)	2.7 (1.9 – 3.2)	2.7 (1.7 – 3.1)	0.79
Tdi at end-inspiration, mm	3.4 (2.4 – 3.8)	3.7 (2.7 – 4.2)	3.3. (2.1 – 3.2)	0.16
TFdi, %	28.1 (22.9 – 42.3)	35.9 (26.7 – 50.0)	17.3 (13.1 – 24.0)	0.0003
Parasternal intercostal muscle US				
Tic at end-expiration, mm	1.3 (1.1 – 1.9)	1.4 (1.3 – 1.9)	1.1 (1 – 1.4)	0.15
Tic at end-inspiration, mm	1.5 (1.3 – 2.0)	1.5 (1.3 – 2)	1.6 (1.3 – 1.9)	0.73
TFic, %	5.3 (0.0 – 27.5)	0.0 (0.0 – 7.0)	33 (29 – 48)	<0.0001
IC muscle activation, %	16 (53)	8 (38)	8 (89)	0.02
SCM muscle US				
Tscm at end-expiration, mm	1.8 (1.6 – 2.0)	1.5 (1.7 – 2.1)	1.9 (1.7 – 2.1)	0.91
Tscm at end-inspiration, mm	1.9 (1.6 – 2.6)	1.8 (1.5 – 2.1)	2.4 (2.0 – 3)	0.08
TFscm, %	1.8 (0.0 – 18.8)	0 (0 – 4.6)	28 (17 – 41)	<0.0001
SCM activation, %	15 (50)	6 (29)	9 (100)	0.001
TFic/TFdi ratio, %	8.9 (0 – 129)	0 (0 – 17.6)	200 (100 – 350)	<0.0001
TFscm/TFdi ratio, %	5.7 (0 – 74.7)	0 (0 – 12.2)	100 (100 – 350)	<0.0001
Isolated diaphragmatic activation, %	9 (30)	9 (30)	0 (0)	0.03
Predominant parasternal IC/SCM activation, %	4 (13.3)	0 (0)	4 (44.4)	0.005
Mixed activation, %	17 (56.7)	12 (57.1)	5 (55.4)	0.99

Table 2. Ultrasound-derived respiratory muscle measurements according to HFNC outcome. Patients were stratified into three activation patterns based on TFdi and accessory muscle activity: isolated diaphragm (TFdi $\geq$ 20 %, no accessory recruitment), mixed (TFdi $\geq$ 20 % with accessory activation), and accessory-dominant (TFdi $<$ 20 % with accessory recruitment). Data are presented as median (IQR). Measurements were collected at the time of HFNC initiation (T0) and after 2 h of treatment (T1).

HFNC, high-flow nasal cannula; US, ultrasound; Tdi, diaphragm thickness; Tic, parasternal intercostal muscle thickness; Tscm, sternocleidomastoid thickness; TF, thickening fraction; TFdi, diaphragm thickening fraction; TFic, parasternal intercostal thickening fraction; TFscm, sternocleidomastoid thickening fraction; Tdi, diaphragm thickness; Tic, parasternal intercostal muscle thickness; Tscm, sternocleidomastoid thickness; IC, intercostal; SCM sternocleidomastoid.

ventilatory efficiency away from the diaphragm, which instead showed reduced TFdi and inverse correlation with effort and $PaCO_2$. Electrophysiological studies have demonstrated increased motor unit discharge frequencies in parasternal IC muscle and scalene muscle of COPD patients, consistent with heightened recruitment to sustain rib cage expansion when the diaphragm is mechanically disadvantaged [4,12]. Physiological studies also showed that during resistive loading, patients with COPD progressively shift their inspiratory activity toward extra-diaphragmatic muscles [32], which generate higher energy expenditure but translate effort less efficiently into the tidal ventilation [33].

US studies have recently showed that parasternal IC activity increases as diaphragmatic pressure-generating capacity declines, showing an inverse correlation with diaphragm output in stable COPD [23]. In our study, The TFic/TFdi and TFscm/TFdi ratios were used as an exploratory index to describe the relative contribution of accessory versus diaphragmatic activation, as no validated reference values still exist in acute settings. Previous studies in stabilized COPD under mechanical ventilation [23,34] have shown higher TFic/TFdi ratio in the presence of compensatory IC recruitment. In this line, our findings extend these physiological concepts during the acute phase and to other extra-diaphragmatic muscle group by documenting that SCM recruitment follows a similar pattern, thus supporting its role as an additional marker of neuromechanical load. In our population, the shift toward accessory muscle activation was associated to the worsening of gas exchange, consistent with a lower efficiency in converting inspiratory effort into alveolar ventilation. This imbalance appears to become indeed clinically critical in the acute setting, where progressive reliance on accessory muscles may forecast a less efficient ventilatory adaptation.

During ECOPD, a large fraction of inspiratory effort is dissipated against airway resistance and intrinsic positive end-expiratory pressure, rather than being translated into tidal expansion [35]. Dynamic hyperinflation progressively shortens diaphragmatic fibers, impairing their length–tension efficiency and reducing pressure-generating capacity [36]. The relationship between effort and diaphragmatic function is therefore nonlinear. In patients with lower respiratory system elastance, even modest increases in effort can initially generate large swings in volume [37]. However, as hyperinflation develops, further escalation of effort fails to proportionally augment tidal volume: the diaphragm flattens, its contractile efficiency deteriorates, and a growing fraction of the load is borne by accessory muscles [38]. Beyond a critical threshold, additional effort not only ceases to enhance diaphragmatic thickening but may paradoxically reduce it, reflecting early neuromechanical dissociation [31,39]. Consistent with these concepts, Umbrello et al. demonstrated that in critically ill patients, increases in inspiratory effort as assessed by esophageal manometry were often accompanied by a paradoxical reduction in TFdi, while IC activation became proportionally greater, thereby mirroring the redistribution of ventilatory load from the diaphragm to the rib cage muscles. Their study also showed that the contribution of ICs was strongly correlated with effort, reinforcing the idea that accessory muscle activation can serve as a sensitive marker of rising neuromechanical load [40,20]. In our cohort, this phenomenon was captured noninvasively: indeed, TFdi decreased as inspiratory effort rose, while parasternal and SCM activation increased in parallel with ΔPnose. Importantly, this pattern was observed despite a relatively limited respiratory rate at baseline, suggesting that in ECOPD the neural drive may manifest earlier through increased intensity of

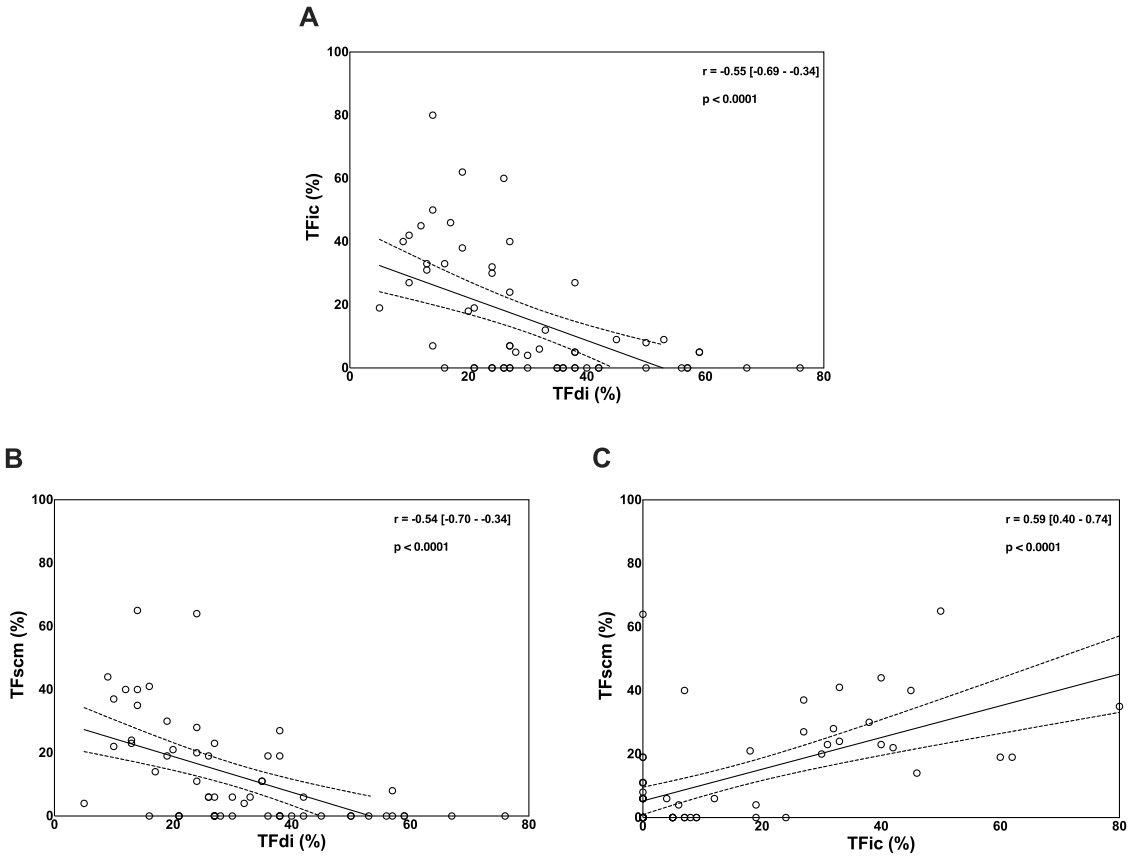

Fig. 1. Correlations between TFdi and TFic (**panel A**), TFdi and TFscm (**panel B**), and TFic and TFscm (**panel C**). TFdi was inversely correlated with both TFic (r = –0.55, $p < 0.0001$) and TFscm (r = –0.54, $p < 0.0001$), while TFic and TFscm were directly correlated (r = 0.59, $p < 0.0001$).
TFdi, diaphragmatic thickening fraction; TFic, parasternal intercostals thickening fraction; TFscm, sternocleidomastoid thickening fraction.

inspiratory effort rather than tachypnea [25,41,42]. Notwithstanding, patient-reported dyspnea was only moderate and widely dispersed, indicating that substantial effort can occur without proportionate symptom perception [43]. This uncoupling between effort and effective diaphragmatic recruitment suggests that relying on clinical assessment or effort monitoring alone may be insufficient. In this line, muscle-specific indices could provide a more accurate assessment of ventilatory adaptation at the bedside. Therefore, US-derived indices offer additional physiological information compared with conventional predictors such as pH, $PaCO_2$, dyspnea score, and clinical signs of increased respiratory drive (i.e. RR). Indeed, they directly capture the pattern and intensity of inspiratory muscle recruitment that precedes overt clinical deterioration. This physiological insight seems particularly relevant in the context of non-invasive support, where cumulative studies have demonstrated a beneficial effect of HFNC in acute hypercapnic respiratory failure due to ECOPD [30,44]. In our study, nearly one-third of patients failed HFNC, a proportion in line with that reported (26 %) by Tan et al. in patients with moderate acidosis (pH 7.25–7.35) [45–47]. Our data suggest that patient selection may be critical. Responders to HFNC showed progressive recovery of diaphragmatic thickening, whereas non-responders exhibited rising accessory muscle activation despite stable respiratory rate and only moderate dyspnea. This imbalance likely reflects insufficient diaphragmatic reserve, with accessory recruitment acting as an early marker of HFNC inadequacy. Notably, SCM activation was already elevated at baseline in all patients who subsequently failed HFNC, and predominant IC/SCM activation was consistently present in the failure group at both time points. These observations support the concept that persistent activation of accessory inspiratory muscles—particularly the SCM—may serve as a physiological marker of instability or unresponsiveness under HFNC as well as an early predictor to the NIV escalation.

Limitations and strengths

This study has limitations. The absence of direct measurements of tidal volume and minute ventilation prevents a precise quantification of ventilatory efficiency; thus, the observed muscle patterns should be interpreted as relative markers of load distribution rather than absolute surrogates of ventilation. Similarly, another limitation is the absence of direct measurements of lung volumes, such as functional residual capacity or end-expiratory lung volume. Therefore, the assumption that diaphragmatic dysfunction and the compensatory recruitment of accessory inspiratory muscles were driven by dynamic hyperinflation remains speculative. Moreover, we did not include radiological quantification of hyperinflation nor stratification by baseline spirometry, limiting our ability to contextualize muscle performance within the degree of static or dynamic hyperinflation. These gaps emphasize that our findings primarily capture the functional adaptation of inspiratory muscles at the bedside, rather than the full mechanical picture. Nonetheless, it is physiologically plausible that a specific phenotype of COPD patients, characterized by low respiratory system elastance and a tendency to accumulate excessive lung volumes during exacerbations, may be more prone to develop such ventilatory uncoupling. In this subgroup, early activation of extra-diaphragmatic muscles could represent not only a marker of diaphragmatic inefficiency but also a signal of maladaptive mechanics associated with volume overload. Inspiratory effort was assessed noninvasively by nasal pressure swings; used as a surrogate of esophageal pressure measurement. However, this approach does not capture the portion of inspiratory work required to counterbalance the threshold load and therefore may underestimate the true mechanical

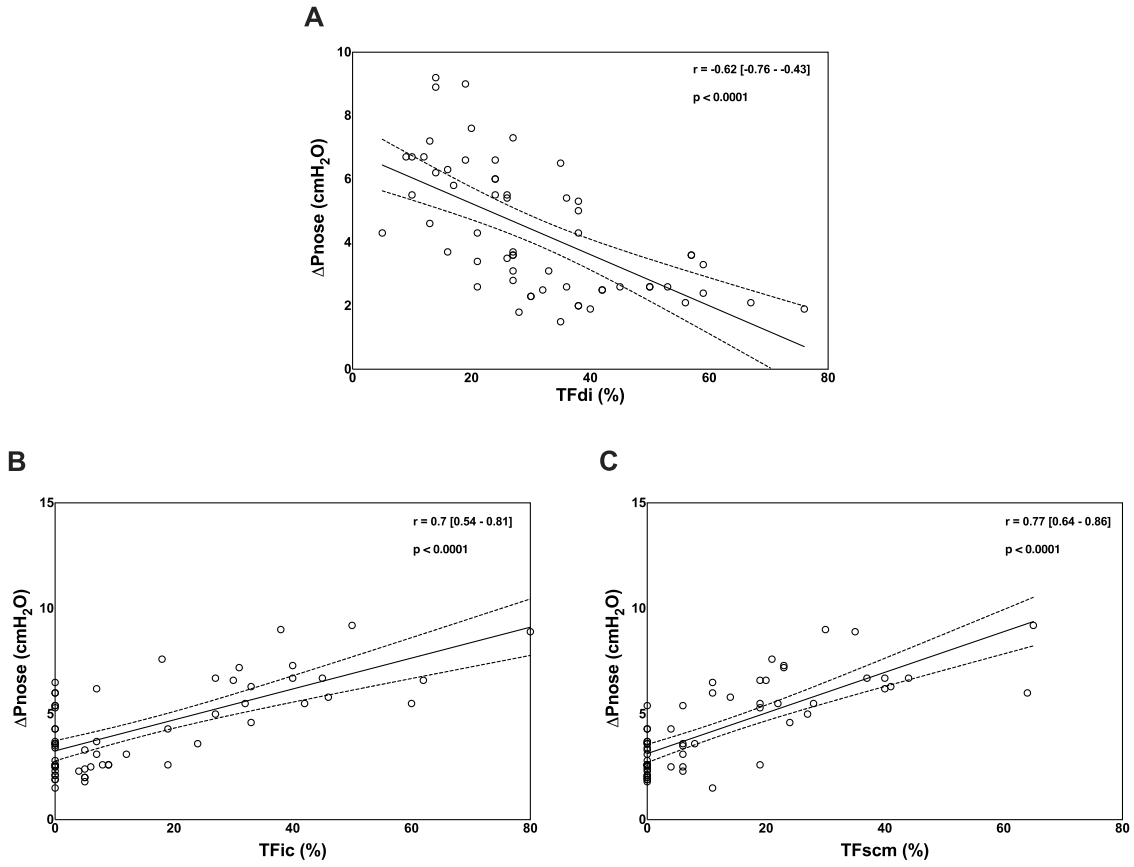

Fig. 2. Correlations between TFdi and ΔPnose (**panel A**), TFic and ΔPnose (**panel B**), and TFscm and ΔPnose (**panel C**). TFdi correlated inversely with ΔPnose (r = –0.62, $p < 0.0001$), while TFic ($r = 0.70$, $p < 0.0001$) and TFscm ($r = 0.77$, $p < 0.0001$) correlated positively.
TFdi, diaphragmatic thickening fraction; TFic, parasternal intercostals thickening fraction; TFscm, sternocleidomastoid thickening fraction.

load faced by the respiratory muscles. Yet, this limitation applied equally to all enrolled patients, thereby preserving the internal validity of our comparisons. Further, we did not assess interobserver agreement among the physicians performing the US examinations, although all had prior experience in respiratory US and previous studies have consistently demonstrated good inter- and intra-observer reproducibility in this setting [48]. A further limitation is that clinical signs such as paradoxical breathing or the Hoover sign were not systematically recorded. Their integration with US could indeed provide complementary insight into diaphragmatic weakness and rib cage distortion. Finally, given the inclusion criterion of a moderate hypercapnic respiratory failure (pH 7.25–7.35), the present findings should not be generalized to patients with more severe acidosis and/or requiring immediate NIV.

Although exploratory, present data extend previous findings from NIV cohorts [10,9], by indicating that accessory muscle activation during HFNC may help identify patients who are unlikely to benefit and should be prompted to escalation. At the same time, we feel that our study may have implications for clinical practice. First, all patients were assessed at the initiation of HFNC, providing a homogeneous and clinically relevant cohort. Second, this is to our knowledge the first study to describe SCM function activity not invasively in ECOPD. In this line, both US assessments of parasternal IC and SCM were feasible at the bedside, with SCM imaging proving technically simpler and faster to perform. The clinical value of inspiratory muscle US is supported by the growing body of literature, showing both feasibility and practical bedside assessment of the inspiratory effort, with stable acoustic windows even in critically ill patients. While operator training and methodological standardization remain important for broader adoption, limited operator training—typically involving 20 to 30 supervised examinations—has been shown enough to achieve reliable image acquisition [49]. Moreover, a complete US examination of diaphragm, IC, and SCM requires approximately 10 min. Overall, these characteristics could support its easibility as a bedside physiological tool in the management of acute respiratory care.

Conclusion

In patients with ECOPD treated with HFNC, bedside US revealed divergent patterns of inspiratory muscle recruitment: reduced diaphragmatic thickening was accompanied by compensatory activation of extra-diaphragmatic and accessory muscles, tightly associated with inspiratory effort and clinical outcome. Early trajectories of muscle activity may help to distinguish responders from non-responders, with extra-diaphragmatic activation emerging as a potential marker of insufficient diaphragmatic reserve.

Ethics approval and consent to participate

This study was conducted in accordance with Ethics Committee “Area Vasta Emilia Nord” approval (registered protocol number 165/2024). Informed consent to participate in the study was obtained from participants, as appropriate.

Consent for publication

Informed consent to allow their clinical data to be analysed and published was obtained from participants, as appropriate.

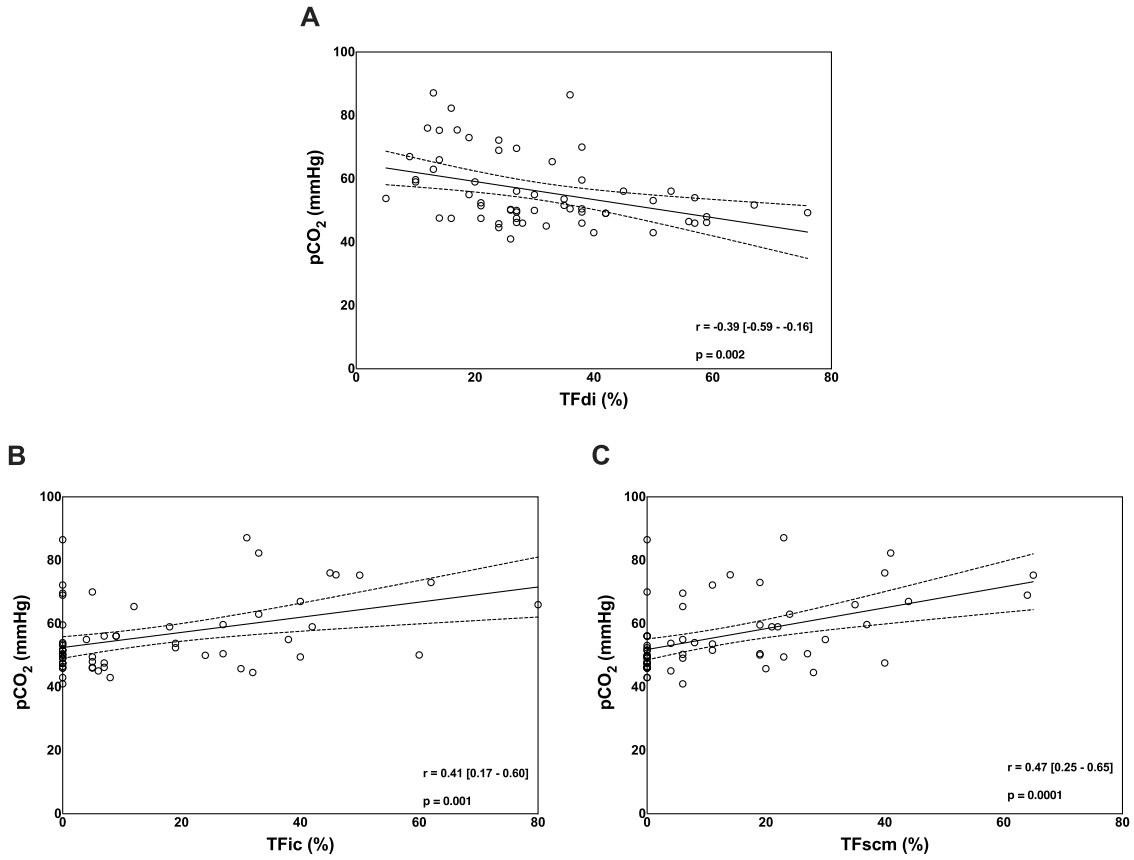

Fig. 3. Correlations between inspiratory muscle US indices and $PaCO_2$. TFdi correlated inversely with $PaCO_2$ (**panel A**, $r = –0.39$, $p = 0.002$), whereas TFic (**panel B**, $r = 0.41$, $p = 0.001$) and TFscm (**panel C**, $r = 0.47$, $p = 0.0001$) correlated positively.
TFdi, diaphragmatic thickening fraction; TFic, parasternal intercostals thickening fraction; TFscm, sternocleidomastoid thickening fraction.

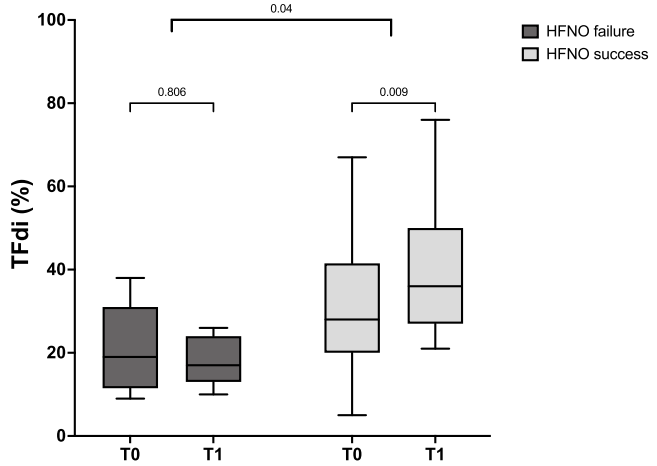

Fig. 4. Temporal evolution of diaphragm thickening fraction (TFdi) according to HFNC outcome. Box plots represent TFdi at HFNC initiation (T0) and after 2 h (T1) in patients with successful (light grey) and failed (dark grey) HFNC trials. A significant interaction was observed ($p = 0.04$), with TFdi increasing in successes and decreasing in failures, indicating divergent trajectories of diaphragmatic performance under HFNC.
HFNC, high flow nasal cannula; TFdi, thickening fraction of the diaphragm.

Availability of data and materials

Data are available at the Respiratory Disease Unit of the University Hospital of Modena, Italy, upon request.

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Author contributions

LT, RT and AMarchioni designed the study, enrolled the patients, analysed the data, and wrote the paper. JM and SB contributed to the design of the study, enrolled the patients, wrote and edited the manuscript. DP, SM and VA made substantial contributions to the literature review, data collection, and paper writing. RF, GB and Amoretti, IC, FL made substantial contribution in patients' enrolment and manuscript editing. LG, SC and BB contributed to data analysis and paper writing. DB, SS, HY and HS made substantial contribution in data interpretation and paper writing. EC designed the study, wrote, reviewed, and edited the manuscript. LT and AMarchioni share first authorship. RT and EC share senior authorship. All authors have read and approved the final version of the manuscript.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used ChatGPT in order to improve language and readability. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Declaration of competing interest

RT, IC, AM, EC, RF and LT declares patent N. 102,021,000,007,478

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ejim.2025.106649.

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