Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Parasternal intercostal muscle thickening as a predictor of non-invasive ventilation failure in patients with COVID-19

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To the editor,

Millions of patients have died from the Coronavirus disease-2019 (COVID-19), with respiratory failure being the most common presenting feature. There is wide agreement on the use of non-invasive ventilation (NIV) to manage patients with COVID-19 [1]. However, NIV failure, if not detected early, carries several hazards such as patient self-induced lung injury and unplanned intubation [2].

Therefore, it is essential to have accurate and simple tools for monitoring patient's response to NIV and facilitating the decision and timing of invasive mechanical ventilation. Assessment of diaphragmatic function provides an excellent tool for predicting the outcomes of patients with COVID-19 on admission and during weaning [3,4]. Increased activity of the intercostal muscles was observed in patients with respiratory failure and correlated with the degree of diaphragmatic dysfunction in non-COVID-19 patients [5]. This study aimed to evaluate the ability of parasternal intercostal muscle thickening fraction (PIC-TF) to predict NIV failure in patients with COVID-19.

Methods

This prospective observational study was conducted in a tertiary hospital after obtaining approval from the institutional ethics committee (N-131-2021). Before enrolment, written informed consents were obtained from the patient's next of kin. We included patients with severe COVID-19, according to the World Health Organization criteria, who were receiving NIV after the failure of simple oxygen therapy (failure to maintain peripheral oxygen saturation [SpO_2] $\geq$ 92% and/or respiratory rate $>$ 30). According to the local protocols, NIV was considered a failure, and invasive mechanical ventilation was initiated if SpO_2 was $<$ 90%, respiratory rate $>$ 35 breaths/min, respiratory acidosis, haemodynamic instability, or altered consciousness level. All patients received non-invasive mechanical ventilation, and none received high-flow nasal oxygen. The patients were managed according to local protocols and the Surviving Sepsis Campaign guidelines. All intensivists who managed the patients had no role in the data collection or radiological examination.

Within 6 h of NIV initiation, ultrasound examination of the diaphragm and intercostal muscles was performed by an intensivist who had more than 200 previous similar examinations using the LOGIQ V5 ultrasound device (GE Medical Systems Co., Ltd., China). Measurements were performed in the semi-setting position at a pressure support of 8–12 cmH_2O and a positive end-expiratory pressure of 6 cmH_2O. Intercostal muscle examination was performed using a high-frequency probe (L6-12-RS, 4–16 MHz) placed vertically at the second intercostal space 3 cm lateral to the sternal border (Fig. 1A). The cyclic respiratory changes in muscle thickening were measured using the M-mode, and PIC-TF (the percentage change in intercostal muscle thickness at peak inspiration in relation to intercostal muscle thickness at end expiration) was calculated using the following formula: {(Inspiratory muscle thickness − expiratory muscle thickness)/expiratory muscle thickness $\times$ 100} (Fig. 1B). Diaphragmatic excursion (DE) was evaluated using a low-frequency curved probe (4C-RS, 2–5 MHz) placed at one of the lower intercostal spaces in the right anterior and left midaxillary lines. Computed tomography (CT) score was evaluated by a radiologist who was blinded to clinical data [3,4].

The primary outcome of this study was the accuracy of PIC-TF in predicting a composite outcome of NIV failure or in-hospital mortality. Other outcomes included the accuracy of room air SpO_2, respiratory rate, DE, and CT score in predicting the primary outcome. The patients' vital signs, laboratory and radiological markers at admission, and outcomes were recorded.

If the incidence of NIV failure and/or in-hospital mortality in patients with severe COVID-19 is 35%, a minimum of 28 patients were needed to detect an area under the receiver operating characteristic curve (AUC) of 0.80 with a study power of 90% and alpha error of 0.05. The AUC was calculated for the accuracy of PIC-TF, DE, CT score, and SpO_2 in predicting failure of NIV and/or in-hospital mortality. Patients were divided into successful NIV group and failed NIV group and were compared according to baseline and radiological characteristics using Chi-Squared test, Mann–Whitney *U* test, and Student's *t*-test as appropriate.

Results

Thirty-five patients were screened for eligibility; seven patients were excluded because they did not meet the inclusion criteria, and 28 patients were available for the final analysis. Eleven patients had successful NIV, and 17 had failed NIV. Patients with failed NIV showed higher interleukin-6, D-dimer, PIC-TF, and CT score, and lower SpO_2 and DE (Fig. 2**A**) (**Supplementary Table**).

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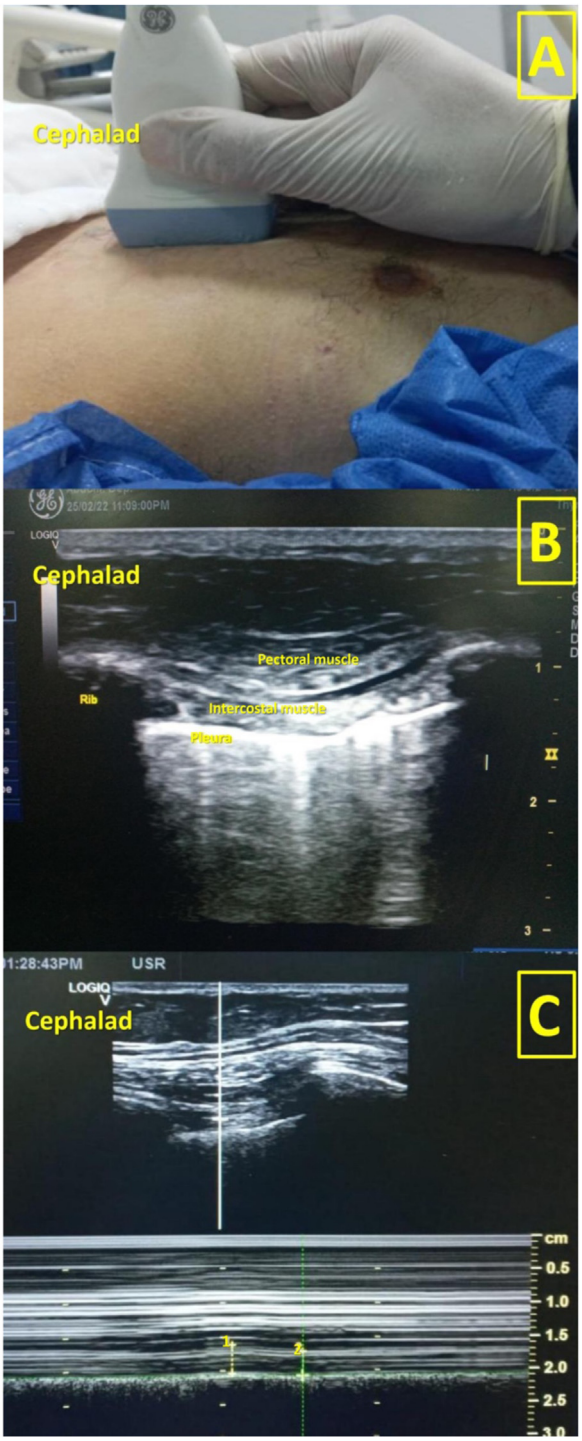


Fig. 1. Ultrasound scan of the parasternal intercostal muscle. A: The transducer is placed vertically at the second intercostal space 3 cm lateral to the sternal border; B: Ultrasound image for the intercostal muscle; C: M-mode for assessing the cyclic respiratory changes in intercostal muscle, 1: intercostal muscle thickening at peak inspiration, 2: intercostal muscle thickening at end expiration.

The AUCs (95% CI) for right and left PIC-TF for predicting NIV failure and/or in-hospital mortality were 0.83 (0.64–0.95) and 0.84 (0.65–0.95) with positive predictive values of 87 and 93% at cut-off values > 8.7 and 9.1%, respectively. The AUC for predicting the primary outcome was highest for DE, followed by PIC-TF, CT score, and SpO_2 (Fig. 2B).

AUC analysis for DE < 15 mm and PIC-TF > 9% combination revealed that this combination had a negative predictive value of 100%; however, it did not improve the specificity (92%). Fig. 3 shows a proposed stepwise approach to evaluating the intercostal muscles and diaphragm using ultrasound.

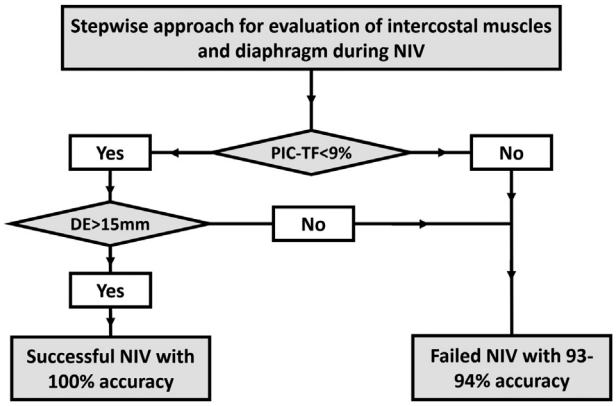


Fig. 3. A stepwise approach to evaluation of intercostal muscles and the diaphragm using ultrasound in patients receiving non-invasive ventilation. DE: diaphragmatic excursion, PIC TF: parasternal intercostal muscle thickening fraction.

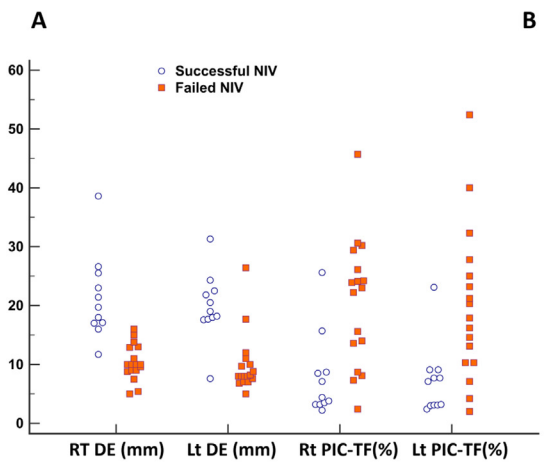
Discussion

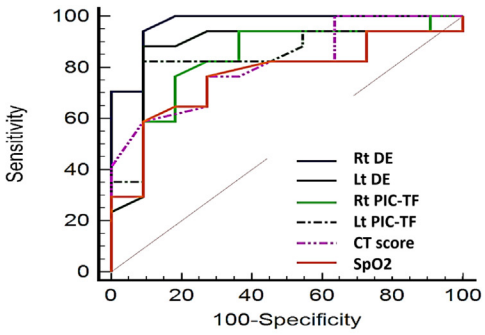
Among patients with severe COVID-19, PIC-TF had a good ability to predict NIV failure, which was higher than the CT score and SpO_2, and close to DE. Two mechanisms explain our findings. First, extra-diaphragmatic inspiratory accessory muscle activity reflects respiratory load. High activity of accessory muscles in respiratory failure has been reported in electromyographic studies [5]. Second, diaphragmatic dysfunction has been reported in patients with COVID-19 [3,4] and increased intercostal muscle thickening is a compensatory mechanism for diaphragmatic dysfunction [5].

The few available reports on intercostal muscle ultrasound showed a dose-response relationship between PIC-TF and respiratory capacity load balance during weaning [5]; however, this has not been previously explored in COVID-19. We found that both PIC-TF and DE could accurately predict NIV failure and/or in-hospital mortality. However, the intercostal muscles are more accessible and easier to examine than the diaphragm [5].

Despite the good outcomes of NIV in COVID-19, delayed detection of its failure carries serious hazards, such as patient-induced lung injury due to exaggerated swings in the pleural pressure owing to high inspiratory efforts, alveolar flooding, and pulmonary oedema due to increased transmural pressure in lung vessels, unplanned emergency intubation, which is life-threatening to the patient [2], and carries the risk of disease transmission to healthcare providers. Therefore, it is essential to have easy and accurate monitoring tools to determine the optimal timing of invasive ventilation. Our study provides a novel, easy, and accurate tool for monitoring respiratory drive and is the first to evaluate PIC-TF during NIV. A PIC-TF > 9% can predict NIV failure, with a positive predictive value of 93%. The combination of PIC-TF and DE improved the sensitivity of both variables; thus, the presence of DE > 15 mm and PIC-TF < 9% can rule out failed NIV with a 100% negative predictive value.

In conclusion, in patients with severe COVID-19, PIC-TF and DE measured within 6 h of NIV showed a good ability to predict NIV failure.





	AUC (95% CI)	Sensitivity% (95% CI)	Specificity% (95% CI)	PPV% (95% CI)	NPV% (95% CI)	Cut-off value
RT DE	0.97 (0.83-1.00)	94 (71-100)	91 (59-100)	94 (71-99)	91 (60-99)	<15mm
LT DE	0.88 (0.70-0.97)	88 (64 - 99)	91 (59-100)	94 (70-99)	83 (57-95)	<12mm
RT PIC-TF	0.83 (0.64-0.95)	77 (50-93)	82 (48-98)	87 (64-96)	69 (48-85)	>8.7%
LT PIC-TF	0.84 (0.65-0.95)	82 (57- 96)	91 (59-100)	93 (68-99)	77 (54-90)	>9.1%
CT score	0.81 (0.62-0.93)	59 (33-82)	91 (59-100)	91 (60-99)	59 (44-72)	>14
SpO2	0.77 (0.57-0.91)	59 (33-82)	91 (59-100)	91 (60-99)	59 (44-72)	<73%
PIC-TF>9% and DE<15mm	0.92 (0.76-0.99)	100 (81-100)	82(48-98)	90 (67-99)	100(66-100)	>0

Fig. 2. A: Dot plot for individual PIC-TF and DE values in patients with successful and failed NIV. B: AUC analysis for the ability of DE, PIC-TF, CT-score, and SpO_2 to predict non-invasive ventilation failure and/or in-hospital mortality. AUC: area under receiver operating characteristic curve, CI: confidence interval, CT: computed tomography, Lt DE: left diaphragmatic excursion, Lt PIC-TF: left parasternal intercostal muscle thickening fraction, NIV: non-invasive ventilation, NPV: negative predictive value, PPV: positive predictive value, Rt DE: right diaphragmatic excursion, Rt PIC-TF: right parasternal intercostal muscle thickening fraction, SpO_2: Peripheral oxygen saturation.

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Declaration of interests

The authors have no conflict of interest to declare.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.accpm.2022.101063.

References

[1] Wang Z, Wang Y, Yang Z, Wu H, Liang J, Liang H, et al. The use of non-invasive ventilation in COVID-19: a systematic review. Int J Infect Dis 2021;106:254–61. http://dx.doi.org/10.1016/j.ijid.2021.03.078.

[2] Menga LS, Berardi C, Ruggiero E, Grieco DL, Antonelli M. Noninvasive respiratory support for acute respiratory failure due to COVID-19. Curr Opin Crit Care 2022;28:25–50. http://dx.doi.org/10.1097/MCC.0000000000000902.

[3] Helmy MA, Magdy Milad L, Osman SH, Ali MA, Hasanin A. Diaphragmatic excursion: a possible key player for predicting successful weaning in patients with severe COVID-19. Anaesth Crit Care Pain Med 2021;40100875. http://dx.doi.org/10.1016/j.accpm.2021.100875.

[4] Adolf Helmy M, Magdy Milad L, Hasanin A, Mostafa M. The novel use of diaphragmatic excursion on hospital admission to predict the need for ventilatory support in patients with coronavirus disease 2019. Anaesth Crit Care Pain Med 2021;40:100976. http://dx.doi.org/10.1016/j.accpm.2021.100976.

[5] Dres M, Dubé B-P, Goligher E, Vorona S, Demiri S, Morawiec E, et al. Usefulness of parasternal intercostal muscle ultrasound during weaning from mechanical ventilation. Anesthesiology 2020;132:1114–25. http://dx.doi.org/10.1097/ALN.0000000000003191.

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