Ultrasonographic measurement of the diaphragm movement during cough and extubation outcomes

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Abstract

Background: A cough peak flow (CPF) of <60 L/min was significantly associated with increased risk of extubation failure after a successful spontaneous breathing trial (SBT). Passive cephalic excursion of the diaphragm (PCED), measured by ultrasonography during cough expiration, was reported to predict CPF in healthy adults. We hypothesized that PCED, diaphragm peak velocity, or both, during cough, as measured by ultrasonography, might predict CPF and extubation outcome in mechanically ventilated patients. This study attempted to identify associations of ultrasonographic indices of the diaphragm with simultaneously measured CPF and to investigate the predictive values of ultrasonographic indices for extubation outcomes after a successful SBT.

Methods: Two hundred fifty-two (252) mechanically ventilated patients with a successful SBT were enrolled in the prospective cohort study. Right hemidiaphragm passive cephalic excursion and peak velocity were measured by ultrasonography during voluntary cough expiration with maximum effort. CPF was measured simultaneously with ultrasonographic measurements.

Results: A multiple regression model adjusted for age and sex showed a significant association between PCED and CPF (P < 0.001, adjusted beta coefficient 11.4, 95% CI 8.88−14.0, adjusted R^2 = 0.287) and between diaphragm peak velocity and CPF (P < 0.001, adjusted beta coefficient 1.71, 95% CI 1.91−2.24, adjusted R^2 = 0.235). The areas under the curves of PCED, diaphragm peak velocity, and CPF for extubation failure were 0.791 (95% Cl 0.668−0.914), 0.587 (95% Cl 0.426−0.748), and 0.765 (95% Cl 0.609−0.922), respectively.

Conclusions: PCED measured by ultrasonography significantly predicted CPF and extubation failure after a successful SBT.

Backgroud

Cough strength is important for clearing secretions and protecting the airway and thus in successful extubation [1, 2]. Several parameters have proposed to evaluate cough strength, including maximum expiratory pressure, cough gastric pressure, cough bladder pressure, and cough peak flow (CPF)[3−8]. A CPF of < 60 L/min was significantly associated with increased risk of extubation failure in patients with a successful spontaneous breathing trial (SBT)[8−10]. Cough strength is mainly determined by contraction of abdominal expiratory muscles, which can be evaluated by measuring intra-abdominal pressure (gastric pressure or bladder pressure) during cough[4, 7]. The pressure gradient between the thoracoabdominal cavity and airway during cough generates air flow to the mouth, as well as passive cephalic excursion of the diaphragm (PCED). We recently reported that PCED during the cough expiratory phase is a significant predictor of CPF in healthy adults[11]. Ultrasonographic measurement of cough strength in mechanically ventilated patients, when feasible, would not require special devices, such as a peak flow meter (which must be connected to the endotracheal tube), or a ventilator from which an accurate CPF value can be recorded. We hypothesized that PCED, peak velocity of the diaphragm, or both, during the cough

expiratory phase might predict CPF and thus extubation outcome. The aims of this study were to identify associations of ultrasonographic indices with simultaneously measured CPF and to evaluate the predictive value of ultrasonographic indices for extubation outcomes after a successful SBT.

Methods

Study design

This single-center, prospective cohort study was approved by the Institutional Review Board of Tokyo Bay Urayasu Ichikawa Medical Center. A waiver of informed consent was obtained because the study exposed patients to less than minimal risk.

Patients

The study was performed in the medical–surgical intensive care unit (ICU) during the period from May 2017 through October 2018. All mechanically ventilated patients 18 years or older who had been endotracheally intubated and had passed an SBT of longer than 30 minutes with a Richmond Agitation Sedation Scale score of −2 to 2 were eligible for inclusion. Sedation was interrupted in all patients at 30 to 120 minutes before the SBT. The SBT was conducted on pressure support ventilation with a pressure support of 5 cm H_2O, a positive end-expiratory pressure (PEEP) of ≤8 cm H_2O, and a fraction of inspiratory oxygen (FiO_2) of ≤0.50. All patients with a positive result on the Confusion Assessment Methods for the ICU (ICU-CAM) instrument were actively reoriented to the situation, and only those able to follow instructions to produce a voluntary cough were included. Patients with "comfort care only" or "do not reintubate" status were excluded. Patients were also excluded if upper airway obstruction was documented or suspected. Each eligible patient was included in the analysis only once. The success of an SBT was determined by using the standard Tokyo Bay Urayasu Ichikawa Medical Center (TBUIMC) Respiratory Care Weaning Protocols (namely, no evidence of severe anxiety, dyspnea, or excessive accessory muscle use; a rapid shallow breathing index [RSBI] of ≤105 breaths/min/L; and adequate gas exchange, i.e., SaO2 ≥90% with FiO_2 ≤0.50 and PEEP ≤8 cm H_2O).

Observations and measurements

Patients in a supine position were instructed to produce two coughs with maximum effort within 10 minutes before extubation. A CX50 ultrasound device (Philips, The Netherlands) was used to assess ultrasonographic indices of the diaphragm with a sector transducer (3.5 MHz). The transducer was positioned on the abdominal wall just below the lowest right rib, between the midaxillary line and mammillary line in the longitudinal scanning plane to the cephalic direction, with the liver as an acoustic window [12-15]. The angle of the transducer was adjusted so that the ultrasound beam was perpendicular to the posterior third of the right hemidiaphragm[16]. Because PCED and diaphragm peak velocity cannot be measured simultaneously, PCED was measured during the first cough, and diaphragm peak velocity was measured during the second cough. To measure PCED, the M-mode interrogation line was adjusted to ensure that it was perpendicular to the movement of the posterior one-third of the right

hemidiaphragm[14, 15]. PCED was measured on the vertical axis of the M-mode and was traced from the end of inspiration to the end of cough expiration (Figure 1). Peak velocity of the diaphragm was measured by placing the tissue Doppler imaging cursor at the posterior one-third of the right hemidiaphragm (Figure 2)[15]. Simultaneous measurement of CPF was performed for both coughs by using the internal flow meter of the ventilator (PB840, Covidien, Mansfield, MA, USA)[17]. Four critical care fellows with at least 2 years of experience in diaphragm ultrasonography performed the evaluations. Attending physicians who were responsible for clinical decisions, including extubation and re-intubation, were blinded to the results of all cough measurements.

Definitions of extubation success and failure

Extubation failure was defined as re-intubation within 72 hours after extubation. Use of prophylactic or therapeutic noninvasive positive pressure ventilation without consequent re-intubation was not regarded as extubation failure.

Sample size

The predicted extubation failure rates were 8% in all patients, and 5% to 6% in patients who were able to follow instructions, as indicated by the past extubation failure rates in our ICU[7]. Thus, we estimated that the sample size needed to determine the cutoff value with an area under the curve (AUC) of 70% and a power of 0.8 would be 12 for the extubation failure group and 233 for the extubation success group [18]. We therefore planned to recruit 250 patients for this study.

Statistical analysis

The primary study outcome was extubation failure. Secondary outcomes included in-hospital mortality and length of hospital stay. Pearson coefficients were calculated to show correlations between variables. To determine whether ultrasonographic indices predicted CPF, we constructed regression models with CPF as the dependent variable, and PCED and diaphragm peak velocity as independent variables. If a model showed a significant association between an independent variable and CPF, an adjusted regression model was constructed with age, sex, and height. A Bland–Altman plot was constructed to analyze agreement between measured and predicted CPF, as determined by ultrasonographic indices. Cutoff values of ultrasonographic indices and CPF for extubation failure were estimated with receiver operator characteristic (ROC) analysis. A multivariable-adjusted logistic regression model was used to calculate odds ratios for extubation failure based on PCED, diaphragm peak velocity, and CPF adjusted for acute physiology and chronic health evaluation (APACHE) II score. The t-test was used to compare the means of variables. The Fisher exact test was used to compare grouped data such as sex, Confusion Assessment Method for the Intensive Care Unit (CAM-ICU), and in-hospital mortality. A two-tailed P value of 0.05 was considered to indicate statistical significance. R3.3.3 (R Foundation for Statistical Computing, Vienna, Austria) was used for all statistical analyses except the adjusted regression model, which was constructed with STATA version 14 (Stata Corp, College Station, TX, USA).

Results

Patients

A total of 252 patients were included in the analyses. Flowchart of the study inclusion is shown in additional figure 1. Twelve patients (4.8%) were re-intubated within 72 hours after extubation. APACHE II score, Simplified Acute Physiology Score (SAPS) II, duration of mechanical ventilation, length of ICU-stay and in-hospital mortality were significantly higher in the extubation failure group than in the extubation success group (Table 1). Table 2 shows indications for intubation.

Associations between PCED and CPF and between diaphragm peak velocity and CPF

The Pearson coefficient was 0.496 (p<0.001) for the correlation between PCED and CPF and 0.347 (p<0.001) for the correlation between diaphragm peak velocity and CPF. A simple regression model with CPF as the dependent variable in relation to PCED showed significant associations between PCED and CPF (P < 0.001, beta coefficient 11.9, 95% CI 9.28−14.5, adjusted R^2 = 0.243, Figure. 3) and between diaphragm velocity and CPF (P < 0.001, beta coefficient 1.97, 95% CI 1.44−2.49, adjusted R^2 = 0.175, Figure. 4). A multiple regression model adjusted for age and sex showed modestly stronger associations between PCED and CPF (P < 0.001, adjusted beta coefficient 11.4, 95% CI 8.88−14.0, adjusted R^2 = 0.287) and between diaphragm velocity and CPF (P < 0.001, adjusted beta coefficient 1.71, 95% CI 1.91−2.24, adjusted R^2 = 0.235). Height was not used in the regression models because it was not significantly associated with CPF in relation to PCED or diaphragm peak velocity.

The equation for predicting CPF with PCED, age, and sex in mechanically ventilated patients was

Predicted CPF = PCED (cm) × 11.4 − age (years) × 0.197 + male sex × 10.2 + 50.5.

The equation for predicting CPF with diaphragm velocity, age, and sex in mechanically ventilated patients was

Predicted CPF = diaphragm peak velocity (cm/sec) × 1.71 − age (years) × 0.009 + male sex × 14.9 + 43.2,

where male sex = 1 and female sex = 0.

Bland−Altman plots were used to assess agreement between measured CPF and CPF predicted by PCED, age, and sex and between measured CPF and CPF predicted by diaphragm peak velocity, age, and sex (Figure 5 and 6). The differences between predicted CPF and measured CPF were larger at higher values in both PCED and diaphragm peak velocity.

Ultrasonographic indices, CPF, and extubation outcome

PCED and CPF were significantly lower in the extubation failure group than in the extubation success group (mean PCED: 1.22 ± 0.67 cm vs 2.32±1.13 cm, p=0.001; mean CPF: 47.1 ± 21.3 L/min vs 71.1 ±

26.9 L/min, p=0.003), while diaphragm peak velocity did not significantly differ between the two groups (Table 1). A PCED less than 1.6 cm and CPF less than 50 L/min were significantly associated with extubation failure, after adjusting for APACHE II score (adjusted OR for PCED: 7.28; 95% CI, 1.88−28.3, p < 0.001; adjusted OR for CPF: 6.1; 95% CI, 1.81−20.6, p < 0.001). Figure 7 shows the ROC curves of PCED, diaphragm peak velocity, and CPF to predict extubation failure. The AUCs of PCED, diaphragm peak velocity, and CPF for extubation failure were 0.791 (95% CI 0.668−0.914), 0.587 (95% CI 0.426−0.748), and 0.765 (95% CI 0.609−0.922), respectively. The specificity and sensitivity for extubation failure with a PCED of ≤1.6 cm H_2O were 0.708 and 0.750, respectively. The specificity and sensitivity for extubation failure with a CPF of ≤50 L/min were 0.741 and 0.666, respectively. There was no significant difference in predictive accuracy between PCED and CPF (p=0.61).

Discussion

The present results show that PCED during voluntary cough significantly predicted CPF and that low PCED was significantly associated with extubation failure. As a predictor of extubation failure, PCED appears to be as accurate as CPF after a successful SBT. These results are consistent with those of previous studies, which reported that low CPF was significantly associated with extubation failure and that PCED was significantly correlated with CPF in healthy adults [8, 9, 17-21]. This is the first study to investigate associations of ultrasonographic indices of diaphragm movement during cough with simultaneously measured CPF and extubation outcome in mechanically ventilated patients.

Diaphragm excursion was positively correlated with inspiratory volume in previous studies[22, 23]. Our results suggest that cough inspiratory volume is important in generating adequate CPF and that PCED is therefore closely associated with CPF. The coefficients in the equation for predicting CPF with PCED in patients with endotracheal tubes in this study were significantly different from those for healthy adults[15], mostly because of the absence of glottic closure secondary to endotracheal tubes and the consequent absence of a "compressive phase" before cough expiration.

The association between diaphragm peak velocity and CPF was weaker than that between PCED and CPF. In addition, diaphragm peak velocity did not differ significantly between the extubation failure and success groups. These results are consistent with those reported by a study of the associations of PCED and diaphragm peak velocity with CPF in healthy adults, which showed a weak association of diaphragm velocity with CPF in women only[15]. A possible explanation for our result is that diaphragm peak velocity is merely the highest velocity at one point and does not reflect the entire cough process. It might be high even for a small cough with a tidal volume that is too low to generate adequate airflow and CPF.

The Bland−Altman plots showed that the predictive accuracy of PCED was not sufficiently high for high CPF values. Because the main use of PCED is to identify patients with weak cough, the substantial variability in high values would not be clinically relevant.

The incidence of extubation failure in the present study was lower (4.8%) than previously reported incidences, which ranged from 10% to 20%[24-27]. This was expected because our ICU is a mixed medical and surgical ICU that cares for a substantial number of patients after elective surgery. In addition, we excluded patients who could not or would not produce a voluntary cough as instructed.

The main advantage of the present method of estimating cough strength is that it is simple and noninvasive. It does not require special mechanical ventilators or devices, such as a peak flow meter, to be connected to the endotracheal tube when measuring cough strength. Future studies should investigate how to best utilize PCED for clinical decision-making before extubation. An example of such clinical application would be cautious preparation before extubation, because of the possible need for re-intubation of a patient with a successful SBT but low PCED.

This study has limitations that warrant mention. In theory, PCED is affected by respiratory system mechanics such as compliance of the lung and chest wall and airway resistance. Second, maximum expiratory pressure—another index of expiratory muscle strength—was not measured for comparison with PCED. Third, the high percentage of patients undergoing elective surgery and the limited duration of mechanical ventilation may have resulted in a lower prevalence of diaphragmatic dysfunction, which could limit the generalizability of the present results. Fourth, cardiac function was not recorded in the study, and the analysis did not exclude the influence of cardiac function on extubation outcome. Fifth, although patients were instructed to cough while supine, as this position simplifies ultrasonographic measurement, the semi-recumbent position might yield more accurate estimates. Lastly, the sample size of the present study was not sufficiently large for comparison of diagnostic accuracies between CPF and PCED.

Conclusions

In conclusion, PCED significantly predicted CPF and extubation failure after a successful SBT.

List Of Abbreviations

CPEF: cough peak expiratory flow; SBT: spontaneous breathing trial; PCED: passive cephalic excursion of the diaphragm; TBUIMC: Tokyo Bay Urayasu Ichikawa Medical Center; ICU: intensive care unit; PEEP: positive end-expiratory pressure; FiO_2: fraction of inspiratory oxygen; RSBI: rapid shallow breathing index; AUC: area under the curve; ROC: receiver operator characteristic; APACHE: acute physiology and chronic health evaluation; CAM-ICU: Confusion Assessment Method for the Intensive Care Unit; SAPS: Simplified Acute Physiology Score; CI: confidence interval

Declarations

Ethics approval and consent to participate:

This study was approved by the Institutional Review Board of Tokyo Bay Urayasu Ichikawa Medical Center. A waiver of informed consent was obtained because the study exposed patients to less than minimal risk.

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Tables

Table 1. Patient baseline characteristics and cough variables in each group

Characteristics	Extubation success	Extubation failure	p value
Number of patients, n	240	12	
Male sex, n (%)	156 (65)	9 (75)	0.552
Age y, mean±SD	66.7±14	69.3±15	0.535
BMI, mean±SD	23.6±4.9	23.3±5.1	0.829
CAM-ICU, positive (%)	58 (24)	4 (33)	0.496
RASS±SD	-0.53±0.84	-0.50±0.80	0.907
APACHE II score, mean±SD	16.5±5.9	21.0±7.86	0.011
SAPS II score, mean±SD	38.2±13.1	52.6±11.3	<0.001
Duration of MV days, mean±SD	2.58±2.42	5.33±3.06	<0.001
P/F ratio, mean±SD	341±235	323±106	0.79
Tidal volume ml, mean L±SD	473±150	415±90.4	0.183
Minute ventilation L, mean L±SD	7.09±2.21	7.57±2.02	0.465
RSBI, mean breaths/min/L±SD	38.4±18.6	48.7±19.9	0.063
Length of ICU stay days, mean±SD	4.01±4.80	10.7±3.26	<0.001
ICU mortality, n (%)	9 (3.8)	1 (8.3)	0.392
CPEF L/min, mean±SD	71.1±26.9	47.1±21.3	0.003
PCED cm, mean±SD	2.32±1.13	1.22±0.67	0.001
Velocity cm/sec, mean±SD	10.7±5.91	8.79±3.95	0.268

Abbreviations: SD = standard deviation

BMI = body mass index; GCS = Glasgow coma scale

CAM-ICU = confusion assessment method for the intensive care unit

RASS = Richmond agitation sedation scale

APACHE = acute physiology and chronic health evaluation; SAPS = simplified acute physiology score

MV = mechanical vemtilation; P/F = PaO2/FiO2

RBSI = rapid shallow breathing index; ICU = intensive care unit

CPEF = cough peak expiratory flow

PCED = passive cephalic excursion of diaphragm

Table 2. Indications for intubation

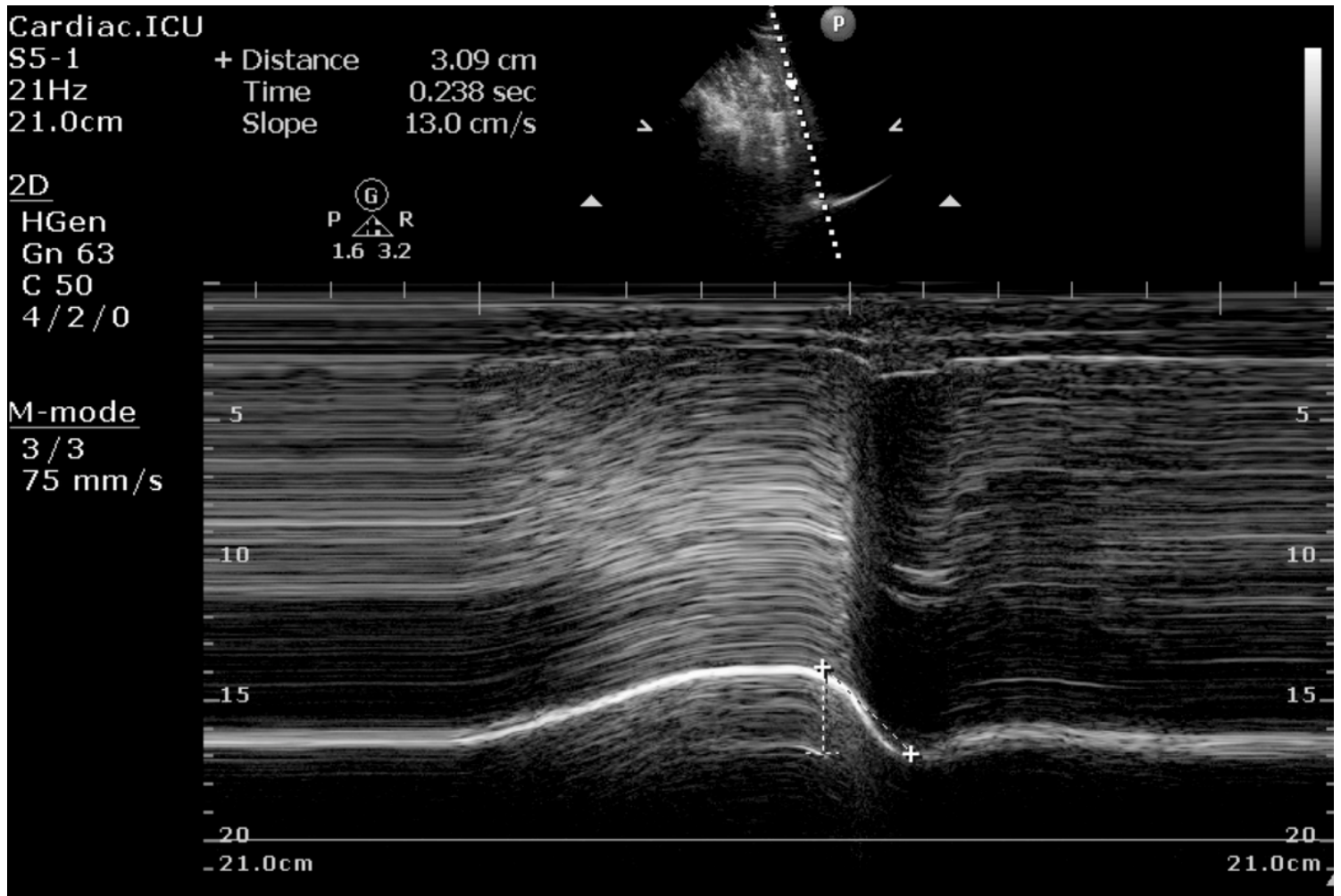| Characteristics	Extubation success	Extubation failure
Emergent surgery	43	5
Elective surgery	75	0
Altered mental status	7	0
Acute coronary syndrome	17	1
Congestive heart failure	21	0
Pneumonia	12	1
Sepsis	18	1
COPD	6	0
Drug intoxication	2	0
Hemorrhagic stroke	11	2
Ischemic stroke	2	0
Gastrointestinal bleeding	5	0
Others	21	2

Figures

Figure 1

M-mode ultrasonographic measurement of passive cephalic excursion of the diaphragm (PCED) during the cough expiratory phase
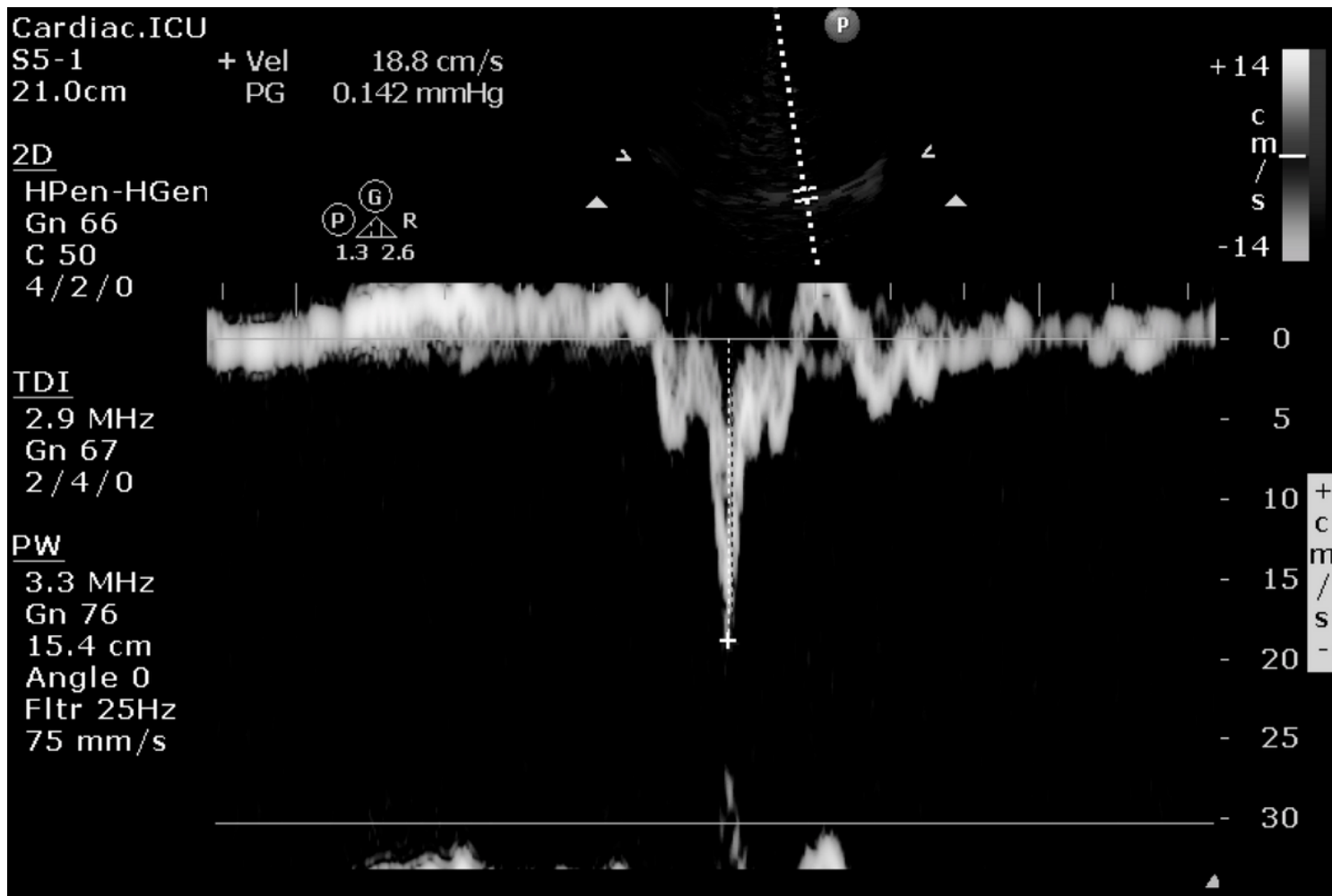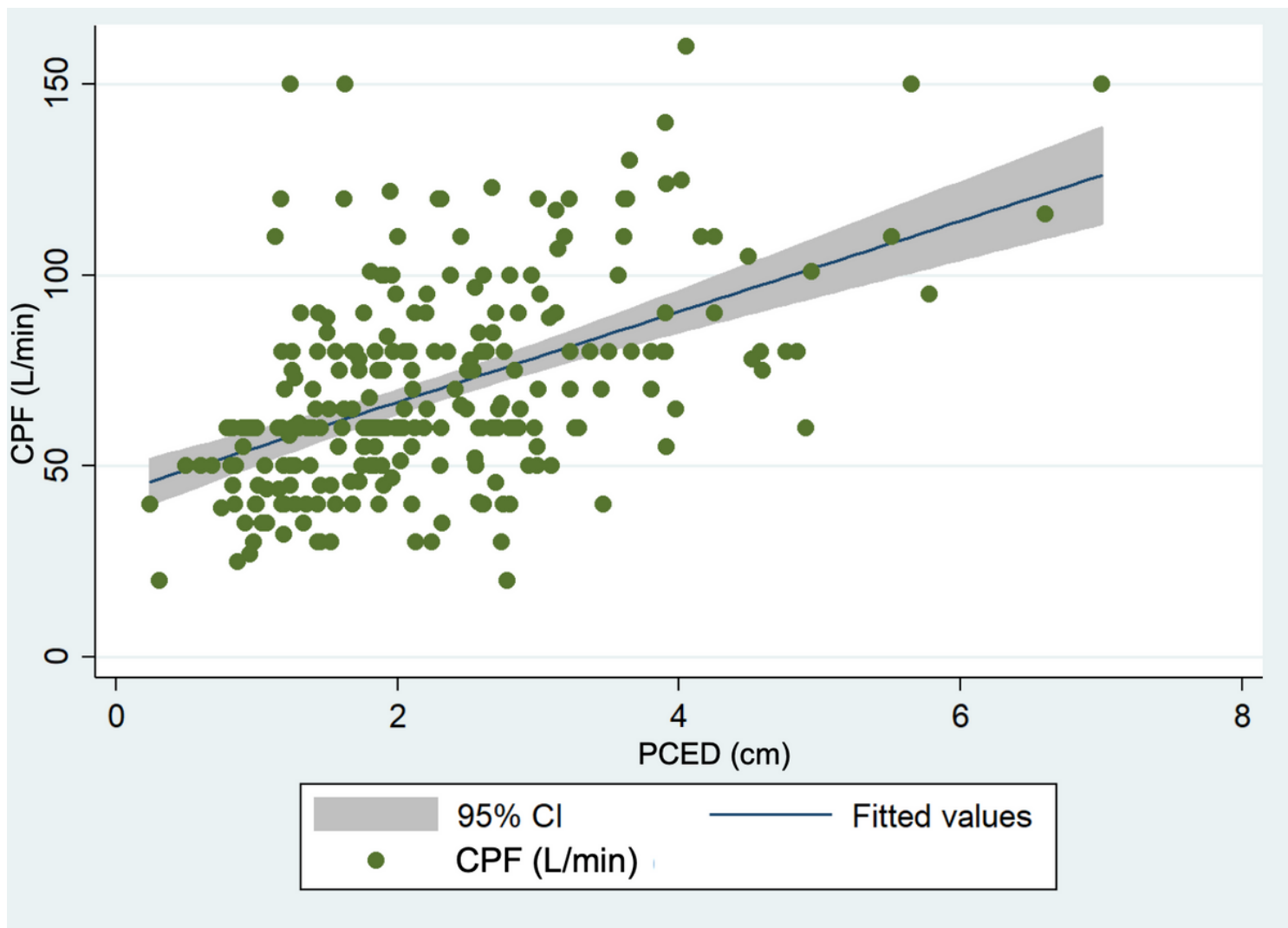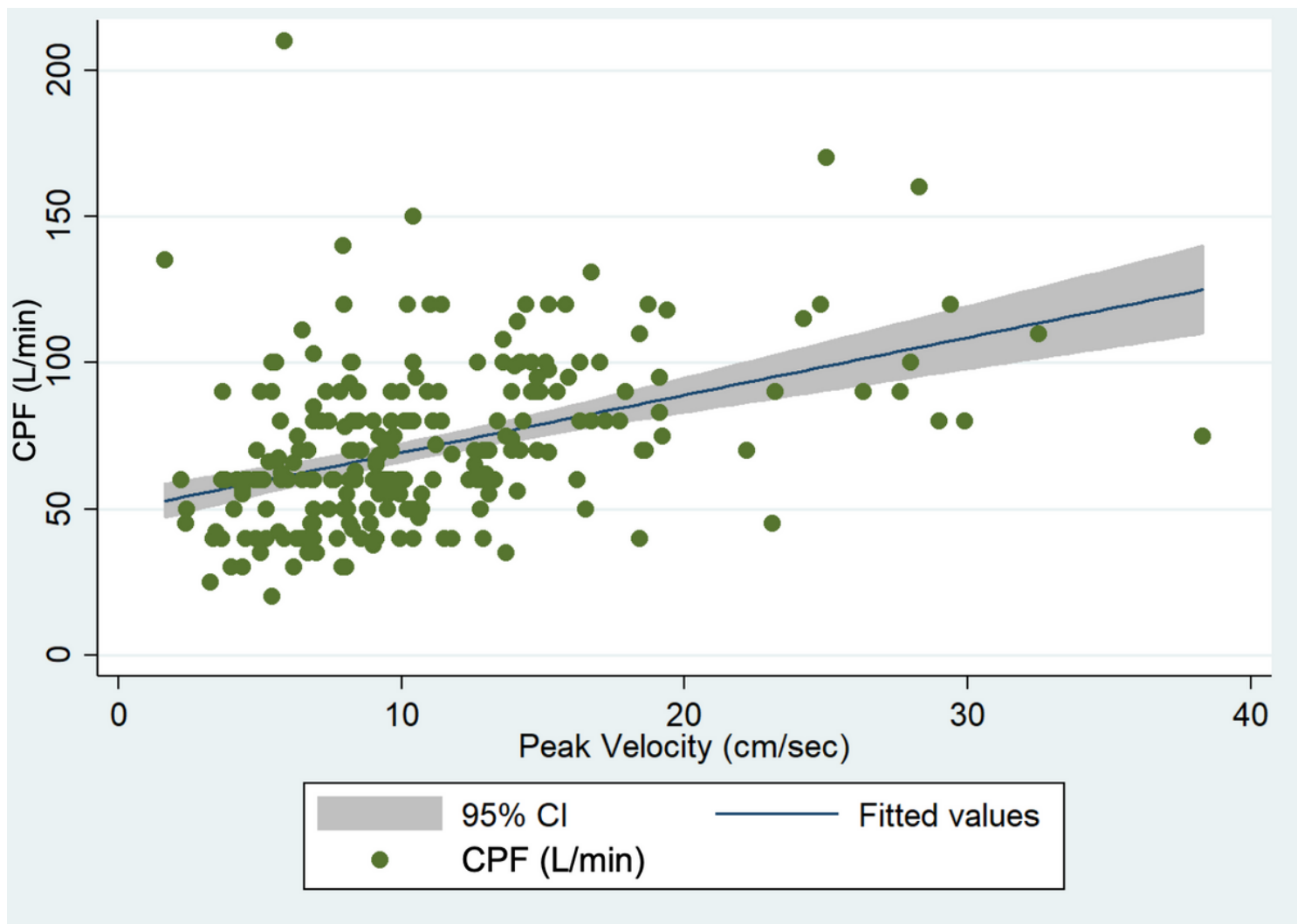
Figure 2

Measurement of diaphragm peak velocity during the cough expiratory phase by tissue Doppler ultrasonography
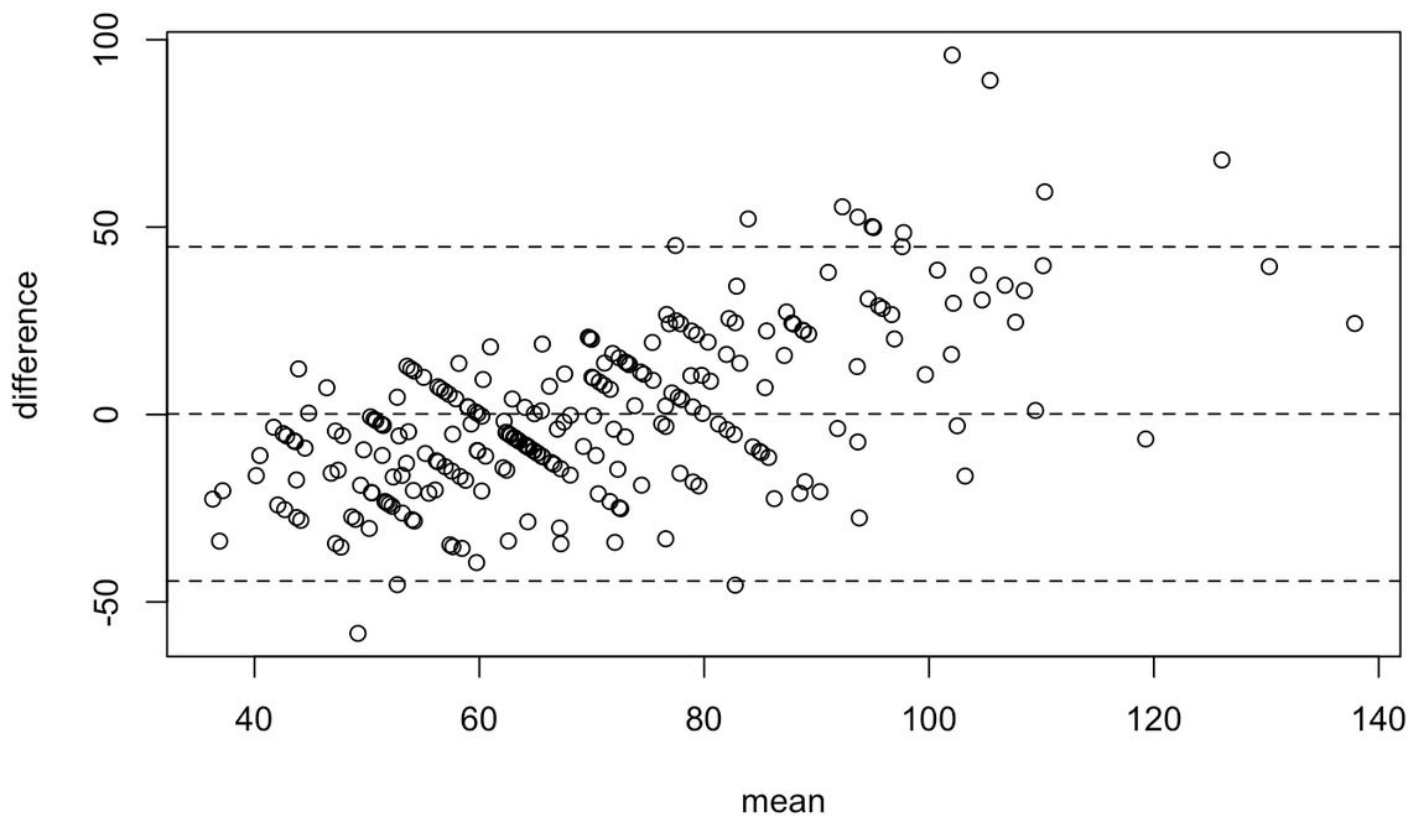
Figure 3

Simple linear regression line, with CPF as the dependent variable, in relation to passive cephalic excursion of diaphragm (PCED) Simple linear regression line showing a positive correlation between diaphragm excursion and CPF (P < 0.001, beta coefficient 11.9, 95% CI 9.28−14.5, adjusted R2 = 0.243).
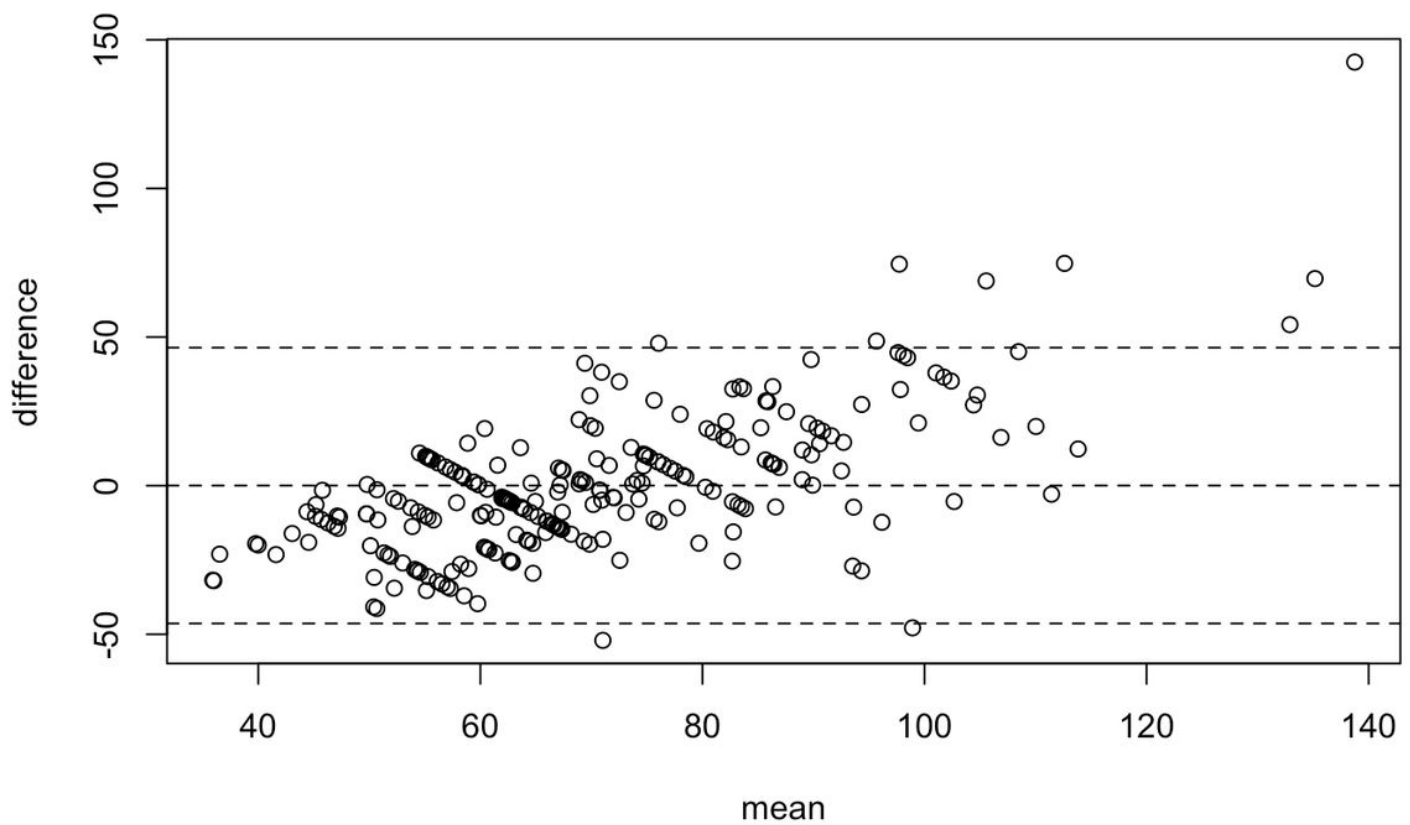
Figure 4

Simple linear regression line, with CPF as the dependent variable, in relation to diaphragm velocity Simple linear regression line showing a positive correlation between diaphragm velocity and CPF (P < 0.001, beta coefficient 1.97, 95% CI 1.44−2.49, adjusted R2 = 0.175).
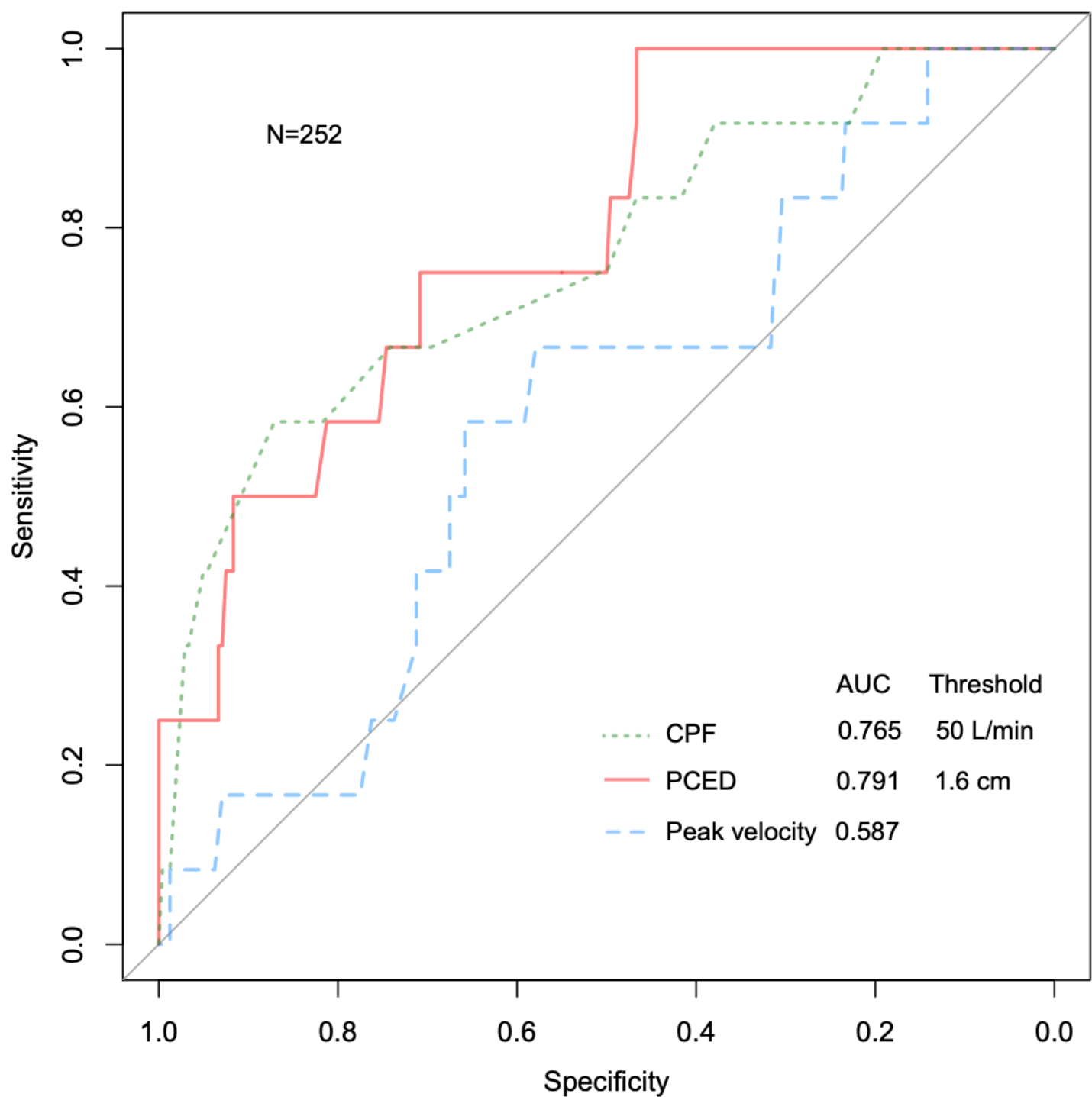
Figure 5

Bland−Altman plot showing the difference between CPF and predicted CPF using PCED, sex, and age The bias was 0.15, and the bias ± 2SD was −44.4 to 44.7.

Figure 6

Bland–Altman plot showing the difference between CPF and predicted CPF using diaphragm peak velocity, sex, and age The bias was 0.0333, and the bias ± 2SD was −46.3 to 46.4.

Figure 7

ROC curves for PCED, diaphragm peak velocity and CPF to predict extubation failure.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- AdditionalFigure1.pdf