




Predictors of Successful Weaning from Noninvasive Ventilation in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease: A Single-Center Retrospective Cohort Study

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Abstract

Purpose Noninvasive ventilation (NIV) is often required for patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD), and it can significantly reduce the need for endotracheal intubation. Currently, there is no standard method for predicting successful weaning from NIV. Therefore, we aimed to evaluate whether a weaning index can predict NIV outcomes of patients with AECOPD.

Methods This study was conducted at a single academic public hospital in northern Taiwan from February 2019 to January 2021. Patients with AECOPD admitted to the hospital with respiratory failure who were treated with NIV were included in the study. Univariate and multivariate logistic regression analyses were used to identify independent predictors of successful weaning from NIV. Receiver operating characteristic curve methodology was used to assess the predictive capacity.

Results A total of 85 patients were enrolled, 65.9% of whom were successfully weaned from NIV. The patients had a mean age of 75.8 years and were mostly men (89.4%). The rapid shallow breathing index (RSBI) ($P < 0.001$), maximum inspiratory pressure ($P = 0.014$), and maximum expiratory pressure ($P = 0.004$) of the successful group were significant while preparing to wean. The area under the receiver operating characteristic curve for the RSBI was 0.804, which was considered excellent discrimination.

Conclusion The RSBI predicted successful weaning from NIV in patients with AECOPD with hypercapnic respiratory failure. This index may be useful for selecting patients with AECOPD that are suitable for NIV weaning.

Keywords Chronic obstructive pulmonary disease · Noninvasive ventilation · Weaning · Weaning index

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Introduction

Acute exacerbation of chronic obstructive pulmonary disease (AECOPD), a common cause of respiratory failure during hospital admission and readmission, is a public health problem that is associated with increased medical costs. AECOPD is characterized by persistent airflow limitation and develops when significant exposure to irritants causes an inflammatory response in the lungs [1]. The World Health Organization reported that COPD was the fifth most common disease globally in 2020 [2], with a prevalence of 7.8–19.7% in adults [3]. Approximately, 60% of patients with COPD admitted with hypercapnic respiratory failure die in hospital [4, 5].

The 1990s saw a wealth of research emerge on the characteristics of spontaneous breathing trials and how they relate to trial performance. Studies showed that noninvasive ventilation (NIV) was successful as first-line treatment for

patients admitted to hospital with hypercapnic respiratory failure due to AECOPD [6–9]. COPD treated with NIV has lower inpatient mortality rates, shorter lengths of stay, and lower costs than treatment with invasive mechanical ventilation (IMV) [9, 10].

The weaning index for IMV is the most appropriate method to determine readiness for weaning training. However, no standard method has been shown to be a good predictor of weaning success with NIV, and there is no consensus among researchers regarding the extent and nature of weaning from NIV. It is possible that delayed weaning may expose the patient to unnecessary discomfort, increased risk of complications, and increased cost of care. The rapid shallow breathing index (RSBI) was introduced by Yang and Tobin in 1991. They found that there was a higher probability of weaning success if the RSBI was ≤ 105 and spontaneous breathing trials were successful [11, 12]. Once NIV therapy is initiated, however, the timing of withdrawal must be considered. Thus, we conducted a prospective observational study to investigate the use of a weaning index to predict weaning outcomes for patients with AECOPD requiring NIV.

Materials and Methods

Study Design and Population

To identify predictors of successful weaning from NIV for patients with AECOPD, we conducted a prospective, noninterventive study at the National Taiwan University Hospital Hsin-Chu Branch, a 637-bed academic public hospital in Hsinchu City, Taiwan. Consecutive patients (aged ≥ 20 years) hospitalized with AECOPD between February 2019 and January 2021 who were treated with NIV during hospitalization using a bi-level positive airway pressure mode (VPAP III ST-A; ResMed, UK) and a full facemask were enrolled. NIV was initiated based on the patient's respiratory status and indications, including respiratory acidosis (partial pressure of $\text{CO}_2 \geq 45$ mmHg; arterial $\text{pH} \leq 7.35$), severe dyspnea with clinical signs of respiratory muscle fatigue, or persistent hypoxemia despite supplemental oxygen therapy [13]. Subsequent ICU admission for identified cases depended on current ICU availability and the clinician's discretionary judgement, and medical treatment was provided by a respiratory therapist. The exclusion criteria were cardiovascular instability, lack of patient cooperation or a Glasgow Coma Scale (GCS) score < 13 , increased aspiration risk, recent facial trauma, upper airway obstruction, increased sputum secretion, or respiratory arrest. Patients who required NIV post-extubation, were pregnant, were transferred from another acute care facility,

required long-term continuous NIV, or signed do-not-resuscitate orders were also excluded [14–16].

Weaning Criteria and Protocol

After admission, NIV was administered 24 h/day, except during meals and for expectoration. The initial inspiratory (IPAP) and expiratory (EPAP) positive airway pressures were determined based on achieving acceptable arterial blood gas (ABG) parameters, a respiratory rate (RR) < 25 breaths/minute, and patient tolerance and comfort. All patients had an initial IPAP set at 12 cmH_2O , which was gradually increased by 2–3 cmH_2O , as tolerated, but did not exceed 25 cmH_2O . The EPAP was initially set at 5 cmH_2O and then gradually increased by 1–2 cmH_2O , as needed, to improve hypoxemia [17]. Decisions regarding the duration of NIV and whether to progress to endotracheal intubation were made by the clinical team, based on the attending physician's judgement.

The criteria and weaning protocols by Duan and Momii were modified for use in this study [18, 19]. The weaning criteria used were adequate mentation, oxygen saturation (SpO_2) $\geq 90\%$ on a fraction of inspired oxygen (FiO_2) ≤ 0.4 , $\text{pH} \geq 7.30$, a systolic blood pressure of 90–180 mmHg without vasopressor support, a body temperature of 36–38 °C, and a heart rate of 50–120 bpm [18]. Patients who met these criteria were enrolled in the weaning protocol.

The weaning protocol was performed by decreasing the IPAP and EPAP by 3 cmH_2O every 30 min, with close monitoring for worsening SpO_2 and/or RR. When the IPAP and EPAP were reduced to 15 and 5 cmH_2O , respectively, with a satisfactory SpO_2 ($\geq 90\%$) on a $\text{FiO}_2 \leq 0.4$, NIV was withdrawn and 3 L/min oxygen was administered via a nasal cannula for an additional 30 min [19]. The primary outcome was successful weaning from NIV. Weaning failure was determined by objective or subjective determination of respiratory failure based on the need for repeated NIV, intubation, high-flow nasal cannula oxygen therapy, or long-term NIV support. Weaning failure was also determined in the case of patient death within 48 h of NIV weaning [20].

Data Collection and Outcomes

Patient demographic data, including past medical history, physiological measurements, blood test results (including data on baseline arterial blood gases), COPD-associated therapy, hospital areas, other therapies, initial setting of NIV, and respiratory indices [maximal inspiratory (MIP) and expiratory (MEP) pressure, tidal volume (TV), RR, and RSBI], were extracted from medical records. The RSBI was measured using a Wright respirometer (“nSpire” Wright/Haloscale Respirometers; Hertford, UK). Patients were asked to breathe through the respirometer for 1 min, RR and

TV were measured, and RR was divided by TV to calculate the RSBI. MIP and MEP were measured with a respiratory pressure force meter (“MTC” Gas Pressure Gauge, Taoyuan, ROC). MIP was measured with a maximum inspiratory effort maintained for ≥ 1 s, and MEP was measured with a maximum respiratory effort maintained for ≥ 1 s. All parameters were recorded during the first 2 h of NIV treatment and before NIV was turned off within 2 h. The primary outcome was successful weaning from NIV, which was determined by the number of patients no longer requiring NIV support during their hospital stay. The secondary outcome was the length of hospital stay (days).

Statistical Analyses

Categorical variables are expressed as N (%). Descriptive data are reported as mean \pm standard deviation or median [interquartile range (IQR)]. Variables were evaluated for an association with NIV weaning outcome using Pearson’s chi-squared test (or Fisher’s exact test, when appropriate) for categorical data and the Student’s t test for variables with normal distribution (or Mann–Whitney U test as non-parametric methods) for numerical data. Univariate analysis was performed to determine predictive factors for successful weaning from NIV. Variables with $P < 0.2$ were entered into the multivariable logistic regression analysis to identify independent predictors of NIV weaning outcome. Odds ratios (ORs) and 95% confidence intervals (CIs) were reported for all independent predictors. Receiver operating characteristic (ROC) curve analysis was performed to determine the capacity to predict the success of NIV weaning for

different variables. All statistical analyses were conducted using IBM SPSS software version 22.0 (IBM Co., Armonk, NY, USA). A two-tailed $P < 0.05$ was considered statistically significant.

Results

During the study period, 141 eligible patients with AECOPD received NIV treatment upon admission; 56 were excluded due to their post-extubation status, non-cooperation or GCS score (< 13), episodes of respiratory arrest, or requirement for long-term continuous NIV support (Fig. 1). Eighty-five patients met the inclusion criteria, including 56 (65.9%) in the NIV weaning success group and 29 (34.1%) in the NIV weaning failure group. The average age of the patients was 75.8 ± 10.1 years; 76 (89.4%) patients were men. Additional baseline characteristics are presented in Table 1. No significant differences were detected between the two groups in terms of sex, age, body mass index, GCS score, white blood cell count, COPD severity, Acute Physiology and Chronic Health Evaluation II score, hospital areas, C-reactive protein (CRP) level, albumin level, COPD-associated therapy, therapeutic interventions (systemic steroids and antibiotics), ABG data before the initiation of NIV, and initial setting of NIV. There were significant differences between the NIV weaning success and failure groups in terms of smoking history (50 vs. 20 cases; $P = 0.020$), days on NIV until weaning (2.0 vs. 3.0 days; $P = 0.019$), average duration of NIV treatment (5.0 vs. 13.0 days; $P < 0.001$), and length of hospital stay (13.0 vs. 17.0 days; $P = 0.008$).

Fig. 1 Flowchart of participant recruitment. AECOPD, acute exacerbation of chronic obstructive pulmonary disease; GCS Glasgow Coma Scale; NIV noninvasive ventilation

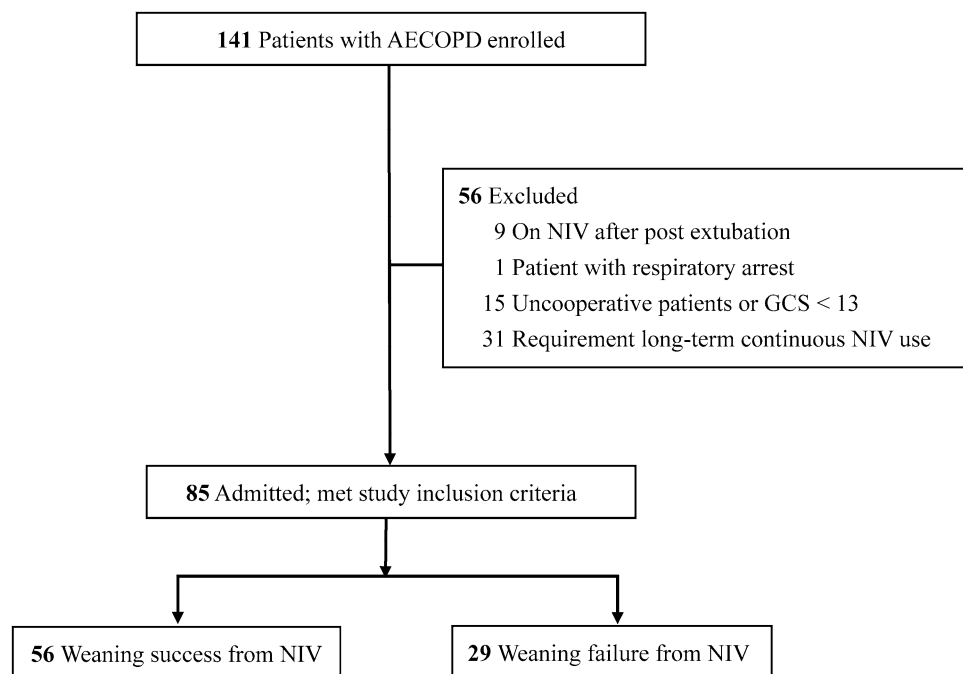


Table 1 Baseline characteristics of the study population

Characteristic	Total (N=85)	NIV weaning		
		Success (N=56)	Failure (N=29)	
Sex, male (%) ^b	76 (89.4)	52 (92.9)	24 (82.8)	0.263
Age, mean (SD), years ^a	75.8 ± 10.1	76.0 ± 10.4	75.4 ± 9.8	0.786
BMI, mean (SD), kg/m ^{2a}	22.7 ± 6.5	22.4 ± 5.8	23.3 ± 7.9	0.595
GCS, median (IQR) ^a	15.0 (15.0–15.0)	15.0 (15.0–15.0)	15.0 (15.0–15.0)	0.722
Smoking history, N (%) ^b	70 (82.4)	50 (89.3)	20 (69.0)	0.020*
WBC, median (IQR), K/ μ L ^a	9.4 (7.1–13.5)	9.4 (7.4–13.9)	9.6 (6.7–12.5)	0.704
CRP, median (IQR), mg/dL ^a	3.5 (1.2–9.6)	3.0 (0.7–9.5)	5.2 (1.5–10.5)	0.219
Albumin, median (IQR), g/dL ^a	3.2 (3.0–3.5)	3.3 (3.1–3.5)	3.2 (2.7–3.4)	0.089
COPD GOLD assessment (%)				0.105
Group A and B, N (%) ^b	24 (28.2)	19 (33.9)	5 (17.2)	
Group C and D, N (%) ^b	61 (71.8)	37 (66.1)	24 (82.8)	
APACHE II, median (IQR) ^a	12.0 (8.5–15.0)	12.0 (9.0–15.0)	12.0 (7.5–15.0)	0.824
Days on NIV until weaning, median (IQR), days ^a	2.0 (2.0–4.0)	2.0 (2.0–3.0)	3.0 (2.0–5.0)	0.019*
Average duration of NIV treatment, median (IQR), days ^a	6.0 (4.0–12.0)	5.0 (3.0–7.0)	13.0 (9.5–22.0)	<0.001*
LOS, median (IQR), day ^a	13.0 (9.5–20.5)	13.0 (9.0–17.0)	17.0 (12.0–26.0)	0.008*
Hospital area				
Diagnosis area				0.120
Emergency room, N (%) ^b	46 (54.1)	33 (58.9)	13 (44.8)	
General ward, N (%) ^b	32 (37.6)	17 (30.4)	15 (51.7)	
Intensive care unit, N (%) ^b	7 (8.2)	6 (10.7)	1 (3.4)	
Treatment area				0.547
Emergency room, N (%) ^b	2 (2.4)	2 (3.6)	0 (0.0)	
General ward, N (%) ^b	55 (64.7)	35 (62.5)	20 (69.0)	
Intensive care unit, N (%) ^b	28 (32.9)	19 (33.9)	9 (31.0)	
Comorbidities				
Diabetes mellitus, N (%) ^b	39 (45.9)	29 (51.8)	10 (34.5)	0.129
Hypertension, N (%) ^b	52 (61.2)	34 (60.7)	18 (62.1)	0.903
Congestive heart failure, N (%) ^b	11 (12.9)	5 (8.9)	6 (20.7)	0.174
Coronary artery disease, N (%) ^b	14 (16.5)	11 (19.6)	3 (10.3)	0.363
Arrhythmia, N (%) ^b	16 (18.8)	9 (16.1)	7 (24.1)	0.367
Chronic renal disease, N (%) ^b	11 (12.9)	8 (14.3)	3 (10.3)	0.742
Benign prostatic hyperplasia, N (%) ^b	16 (18.8)	8 (14.3)	8 (27.6)	0.137
Malignancies other than lung cancer, N (%) ^b	10 (11.8)	5 (8.9)	5 (17.2)	0.298
Lung cancer, N (%) ^b	6 (7.1)	4 (7.1)	2 (6.9)	>0.999
COPD therapy				
Inhaled SABA, N (%) ^b	41 (48.2)	28 (50.0)	13 (44.8)	0.651
Inhaled SAMA, N (%) ^b	28 (32.9)	17 (30.4)	11 (37.9)	0.481
Inhaled LABA, N (%) ^b	54 (63.5)	34 (60.7)	20 (69.0)	0.454
Inhaled LAMA, N (%) ^b	53 (62.4)	34 (60.7)	19 (65.5)	0.665
Inhaled corticosteroids, N (%) ^b	36 (42.4)	25 (44.6)	11 (37.9)	0.553
Long-term oxygen therapy, N (%) ^b	7 (8.2)	3 (5.4)	4 (13.8)	0.223
Pulmonary rehabilitation, N (%) ^b	17 (20.0)	12 (21.4)	5 (17.2)	0.647
Therapeutic interventions				
Systemic corticosteroids, N (%) ^b	74 (87.1)	50 (89.3)	24 (82.8)	0.499
Antibiotics, N (%) ^b	74 (87.1)	51 (91.1)	23 (79.3)	0.174
NIV initial setting				
IPAP, median (IQR), cmH ₂ O ^a	16.0 (15.0–18.5)	16.0 (15.0–19.7)	16.0 (15.0–18.0)	0.783
EPAP, median (IQR), cmH ₂ O ^a	5.0 (5.0–6.0)	5.0 (5.0–6.0)	5.0 (5.0–6.0)	0.258

Table 1 (continued)

Characteristic	Total (N=85)	NIV weaning		
		Success (N=56)	Failure (N=29)	
FiO ₂ , median (IQR), (%) ^a	35.0 (34.0–44.5)	35.0 (33.0–40.0)	35.0 (35.0–50.0)	0.094
Blood gas analysis (before the initiation of NIV)				
Arterial pH, mean (SD) ^a	7.31 ± 0.07	7.30 ± 0.75	7.32 ± 0.88	0.486
PaO ₂ , median (IQR), mmHg ^a	77.0 (62.8–98.0)	78.4 (61.7–100.5)	74.1 (65.1–87.4)	0.499
PaCO ₂ , mean (SD), mmHg ^a	60.3 ± 18.9	60.7 ± 18.7	59.3 ± 19.5	0.743
HCO ₃ , mean (SD), mEq/L ^a	29.1 ± 6.8	29.3 ± 6.7	28.9 ± 7.0	0.801
BE, median (IQR), mmol/L ^a	2.6 (– 0.7–7.0)	2.5 (– 0.6–6.1)	3.2 (– 2.2–9.7)	0.677
SaO ₂ , median (IQR), % ^a	93 (90–96)	93.5 (90.0–96.7)	92 (89.5–95.5)	0.316

APACHE II acute physiology and chronic health evaluation; BMI body mass index; BE bicarbonate; COPD chronic obstructive pulmonary disease; CRP C-reactive protein; EPAP expiratory positive airway pressure; FiO₂ fraction of inspired oxygen; GCS Glasgow Coma Scale; HCO₃ bicarbonate; IPAP inspiratory positive airway pressure; IQR interquartile range; LABA long acting beta agonist; LAMA long acting muscarinic antagonist; LOS length of hospital stay; MEP maximal expiratory pressure; MIP maximal inspiratory pressure; NIV noninvasive ventilation; PaO₂ partial pressure of oxygen; PaCO₂ partial pressure of carbon dioxide; SABA short acting beta agonist; SAMA short acting muscarinic antagonist; SaO₂ arterial oxygen saturation; SD standard deviation; WBC white blood cell

^aContinuous variables are expressed as mean ± SD or median (IQR)

^bCategorical variables are expressed as N (%)

*P < 0.05, significant

Predictive Factors for Successful Weaning from NIV

The weaning parameters and ABG findings of the two groups are shown in Table 2. Within 2 h of initiating NIV treatment, no significant differences were detected between the two groups in any of the weaning indices or ABG data. However, immediately before NIV was turned off within 2 h, the NIV weaning success group was compared to the NIV weaning failure group, the NIV weaning success group had a lower RSBI, RR, and higher VE, TV, MIP, predict MIP, and MEP, predict MEP ($P < 0.001$, < 0.001 , 0.016 , < 0.001 , 0.014 , 0.013 and 0.004 , 0.012 , respectively). There was a significant difference between the two groups in the hospital mortality rate (3 vs. 9 cases; $P = 0.002$), and there were no significant differences in readmission within 60 days of discharge.

Univariate Analysis

For the primary outcome of successful weaning from NIV, univariate analysis showed that higher MIP and MEP were associated with an increased rate of successful weaning [OR 1.026 (95% CI 1.001–1.052); $P = 0.040$ and OR 1.025 (95% CI 1.003–1.048); $P = 0.026$, respectively] after turning off NIV. Conversely, days on NIV until weaning and RSBI were inversely associated with successful weaning [OR 0.716 (95% CI 0.539–0.949); $P = 0.020$ and OR 0.970 (95% CI 0.956–0.984); $P < 0.001$, respectively] after turning off NIV.

Multivariate Analysis

We used a multivariable logistic model to examine selected factors, including sex, smoking history, albumin level, antibiotic use, COPD severity, MEP, RSBI, and days on NIV until weaning. MIP and MEP are highly correlated, as both are related to respiratory muscle strength. To address the issue of collinearity, we excluded MIP because it was less significant than MEP. Patients with a lower RSBI were significantly more likely to be weaned successfully [OR 0.976 (95% CI 0.959–0.993); $P = 0.006$] (Table 3). Hosmer and Lemeshow goodness-of-fit chi-squared test was 4.065 [$P = 0.772$ (> 0.05)].

Predictive Value of the Weaning Index

The ROC curve was analyzed by selecting the follow-up RSBI. The area under the ROC curve for NIV weaning was 0.804 (95% CI 0.706–0.901) (Fig. 2). The RSBI at a threshold of 67.4 predicted successful weaning from NIV, with a sensitivity of 82.1%, a specificity of 69.0%, a positive likelihood ratio of 2.648, and a negative likelihood ratio of 0.377 (Table 4).

Discussion

NIV is now the mainstay of therapy before endotracheal intubation and mechanical ventilation for patients with acute respiratory distress or failure due to AECOPD [22].

Table 2 Weaning parameters and arterial blood gas findings between the two groups

Clinical outcome	Total (N=85)	NIV weaning		P value
		Success (N=56)	Failure (N=29)	
Weaning index (on NIV within 2 h)				
RSBI, mean (SD), breaths/(min mL) ^a	103.1 ± 60.0	100.0 ± 60.4	109.1 ± 59.7	0.512
VE, median (IQR), L ^a	6.3 (4.8–9.1)	7.0 (5.1–9.1)	5.1 (4.2–9.3)	0.100
TV, median (IQR), mL ^a	271.0 (198.0–378.5)	275.5 (209.2–407.0)	242.0 (173.0–339.0)	0.218
RR, mean (SD), breaths/min ^a	24.8 ± 6.9	24.7 ± 6.6	25.0 ± 7.5	0.877
MIP, median (IQR), –cmH ₂ O ^a	30.0 (20.0–40.0)	34.0 (20.0–40.0)	26.0 (17.0–38.0)	0.205
MEP, median (IQR), +cmH ₂ O ^a	36.0 (22.0–44.0)	36.0 (22.5–48.0)	36.0 (21.5–41.5)	0.263
Blood gas analysis (on NIV within 2 h)				
Arterial pH, mean (SD) ^a	7.31 ± 0.07	7.31 ± 0.06	7.31 ± 0.08	0.707
PaO ₂ , median (IQR), mmHg ^a	90.0 (78.5–113.1)	91.1 (79.4–114.1)	88.0 (75.5–114.0)	0.777
PaCO ₂ , median (IQR), mmHg ^a	60.5 (48.6–67.3)	60.4 (48.2–66.1)	61.1 (48.8–68.4)	0.838
HCO ₃ , mean (SD), mEq/L ^a	29.3 ± 6.9	29.5 ± 6.9	28.9 ± 7.0	0.705
BE, mean (SD), mmol/L ^a	4.2 ± 7.7	4.0 ± 7.0	4.6 ± 8.9	0.733
SaO ₂ , median (IQR), (%) ^a	96.0 (93.0–97.0)	96.0 (94.0–97.0)	94.0 (92.5–98.5)	0.373
Weaning index (before turning off NIV within 2 h)				
RSBI, median (IQR), breaths/(min mL) ^a	53.5 (29.8–83.2)	38.5 (18.7–58.9)	84.9 (55.3–128.8)	<0.001*
VE, median (IQR), L ^a	7.4 (5.9–9.9)	7.9 (6.4–10.2)	6.2 (5.5–8.1)	0.016*
TV, median (IQR), mL ^a	408.0 (272.5–571.0)	444.5 (360.2–671.2)	264.0 (219.0–395.5)	<0.001*
RR, mean (SD), breaths/min ^a	19.8 ± 6.8	17.7 ± 6.2	23.7 ± 6.5	<0.001*
MIP, median (IQR), –cmH ₂ O ^a	36.0 (24.0–52.0)	44.0 (30.5–55.2)	30.0 (20.0–40.0)	0.014*
Predict MIP, median (IQR), (%) ^{a,c}	42.0 (29.0–61.0)	49.0 (33.2–67.7)	35.0 (24.0–47.0)	0.013*
MEP, median (IQR), +cmH ₂ O ^a	44 (28.0–60.0)	48.5 (40.0–67.0)	28.0 (20.0–50.0)	0.004*
Predict MEP, median (IQR), (%) ^{a,c}	41.0 (27.0–59.0)	44.0 (33.2–60.5)	30.0 (21.0–54.0)	0.012*
Blood gas analysis (before turning off NIV within 2 h)				
Arterial pH, mean (SD) ^a	7.41 ± 0.49	7.41 ± 0.50	7.42 ± 0.48	0.186
PaO ₂ , median (IQR), mmHg ^a	95.4 ± 34.2	92.3 ± 30.5	101.4 ± 40.6	0.257
PaCO ₂ , mean (SD), mmHg ^a	45.7 ± 10.8	45.4 ± 10.4	46.4 ± 11.6	0.704
HCO ₃ , median (IQR), mEq/L ^a	29.6 (22.8–33.6)	29.5 (22.8–33.0)	29.8 (22.6–34.1)	0.765
BE, mean (SD), mmol/L ^a	4.6 ± 6.5	4.0 ± 6.3	5.9 ± 6.9	0.235
SaO ₂ , median (IQR), (%) ^a	96.0 (94.0–97.7)	96.0 (93.2–97.0)	97.0 (94.2–98.0)	0.226
Clinical outcome (after NIV treatment)				
In-hospital mortality, N (%) ^b	12 (14.1)	3 (5.4)	9 (31.0)	0.002*
Readmission after discharge within 60 days, N (%) ^b	28 (32.9)	20 (35.7)	8 (27.6)	0.450

BE bicarbonate; IQR interquartile range; MEP maximal expiratory pressure; MIP maximal inspiratory pressure; NIV noninvasive ventilation; PaO₂ partial pressure of oxygen; PaCO₂ partial pressure of carbon dioxide; RR respiratory rate; RSBI rapid shallow breathing index; TV tidal volume; VE minute ventilation; SaO₂ arterial oxyhemoglobin saturation; SD standard deviation

^aContinuous variables are expressed as mean ± SD or median (IQR)

^bCategorical variables are expressed as N (%)

^cIncluding data from studies in the review by Evans et al. [21]. Male MIP reference: 120–(0.41 × age); female MIP reference: 108–(0.61 × age); male MEP reference: 174–(0.83 × age); female MEP reference: 131–(0.86 × age), percentage of predict MIP or MEP of percentage = real data (MIP or MEP)/reference (MIP or MEP)

*P < 0.05, significant

NIV is now recommended as a direct alternative for the management of patients with acute respiratory failure, particularly during the course of AECOPD, to preclude tracheal intubation and subsequent complications [6, 23, 24]. This is derived from the fact that, in many cases, patient

outcomes (both short- and long-term) are better with NIV than with IMV [25, 26]. There is strong evidence to suggest that this benefit is due to a reduction in the rate of ventilator-associated pneumonia and avoidance of intensive care unit admission [27, 28]. Thus far, however, there is uncertainty

Table 3 Univariate and multivariate analyses of clinical factors associated with successful weaning

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	<i>P</i> value	OR (95% CI)	<i>P</i> value
Age	1.006 (0.963–1.052)	0.783	–	–
Sex (reference, female)	2.708 (0.667–10.993)	0.163	1.274 (0.154–10.527)	0.822
Smoking history (reference, yes)	0.267 (0.084–0.847)	0.025*	0.544 (0.087–3.396)	0.515
Days on NIV until weaning, days	0.716 (0.539–0.949)	0.020*	0.825 (0.562–1.211)	0.326
Albumin, g/dL	2.561 (0.869–7.550)	0.088	2.196 (0.555–8.694)	0.262
Systemic corticosteroids (reference, yes)	1.736 (0.481–6.261)	0.399	–	–
Antibiotics (reference, yes)	0.376 (0.104–1.358)	0.135	0.405 (0.082–1.999)	0.267
COPD group (reference, C + D group)	2.465 (0.811–7.487)	0.112	1.556 (0.420–5.769)	0.508
Off NIV RSBI, breaths/(min•mL)	0.970 (0.956–0.984)	<0.001*	0.976 (0.959–0.993)	0.006*
Off NIV MIP, –cmH ₂ O	1.026 (1.001–1.052)	0.040*	–	–
Off NIV MEP; +cmH ₂ O	1.025 (1.003–1.048)	0.026*	0.996 (0.968–1.023)	0.755

Obtained through enter model construction, including only significant independent predictors; OR of NIV treatment success associated with each variable in the model

CI confidence interval; COPD chronic obstructive pulmonary disease; MEP maximal expiratory pressure; MIP maximal inspiratory pressure; NIV noninvasive ventilation; OR odds ratio; RSBI rapid shallow breathing index

**P* < 0.05, significant

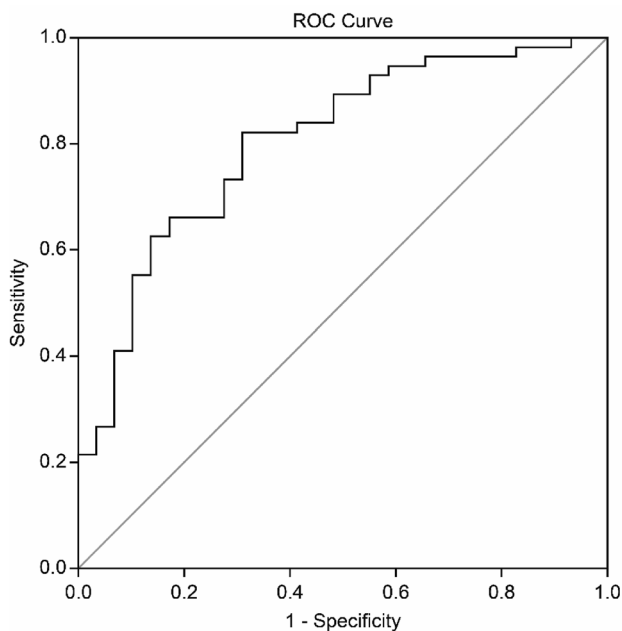


Fig. 2 Receiver operating characteristic (ROC) curve for weaning parameters. The sensitivity and specificity of the weaning parameter for each image set a priori operation point and are indicated on the curve. They are as follows: off RSBI images: sensitivity, 69.0%; specificity, 82.1%; area under the ROC curve, 0.804

regarding the best method of evaluating weaning from NIV, which generally requires the cooperation of the patient during the AECOPD recovery phase. Delayed weaning may potentially expose the patient to unnecessary discomfort and increase the risk of complications [29].

Although the RSBI was not a significant predictor of successful NIV [30], our results suggest that it is a reasonably good predictor of success for weaning a patient from not only IMV [31] but also NIV. The RSBI has been found to be an accurate index [32] that is calculated by dividing RR by TV in liters. Clinicians have successfully used this ratio in most mechanical ventilation weaning protocols. In a study by Berg et al. [15], patients were divided into two groups according to their RSBI. The assisted RSBI (aRSBI) is a criterion for weaning from IMV. The authors recorded it based on the initial level of support: high (aRSBI \geq 105) or low (aRSBI < 105). The RSBI may be useful for titrating the NIV settings, as an aRSBI \geq 105 is associated with the need for intubation and increased in-hospital mortality. According to Sellarer et al. [33], NIV can be discontinued immediately, without the need for a weaning period, allowing rapid discontinuation of NIV, if the patient's condition improves. However, our results suggest that a weaning period is essential for this to succeed.

In our study, using ROC curve analysis, an RSBI \leq 67.4 was associated with the highest sensitivity and specificity for determining successful weaning from NIV. In cases where chronic hypercapnia persists during the night for patients with AECOPD, NIV can be beneficial because it can provide gas exchange and improve night-time hypoventilation. It is not clear, however, whether long-term NIV can be used for stable chronic COPD patients with chronic comorbidities or pneumonia [34–36]. Patients with moderate-to-severe COPD frequently have persistent low-grade systemic inflammation with elevated levels of circulating inflammatory cascade molecules, such as CRP [37, 38]. Furthermore, some authors

Table 4 Analysis of NIV treatment

	AUC (95% CI)	Optimal cutoff	Sensitivity (%)	Specificity (%)	<i>P</i> at difference
Off NIV RSBI, breaths/(min mL)	0.804 (0.706–0.901)	67.4	69.0	82.1	<0.001*

Data are presented as AUC (95% CI); **P* < 0.05, predicted outcome of a significant difference in weaning success

AUC area under the receiver operating characteristic curve; CI confidence interval; NIV noninvasive ventilation; RSBI rapid shallow breathing index

**P* < 0.05, significant

have reported that high CRP levels in patients with COPD are associated with worse short- and long-term clinical outcomes [39, 40]. In our study, we found that CRP levels were not significantly associated with weaning outcomes, indicating that the mechanism of successful weaning from NIV is very complex. This suggests that NIV weaning outcomes are not entirely mediated by modulation of the immune response, or determined by the effect of lung inflammation itself, in patients with COPD. Although CRP and B-type natriuretic peptide (BNP) have high diagnostic potency for COPD patients combined with cor-pulmonale, and are positively correlated with cardiac function classification [41], CRP level may not be useful in assessing weaning outcomes for COPD patients with NIV support [42].

Our study is limited by its small sample size and observational nature. Our hospital also does not have a distinct protocol outlining when to commence NIV. Dyspnea, one of the NIV initiation criteria, may also not be clearly defined. In the future, it may be possible to use a more objective assessment scale, such as the modified Medical Research Council dyspnea or Borg scale. In addition, cor-pulmonale and ejection fraction parameters were not evaluated in this cohort study, which may affect RSBI, MEP, and MIP when weaning from NIV. Both left ventricular and right ventricular functions may interact with intra-thoracic pressure in a complex and often unpredictable fashion. In future studies, these parameters may be included and collected for adjustment additional. Our patients may differ from those treated with NIV at other hospitals, even those with AECOPD. Finally, data were not collected after discharge. Therefore, an analysis of long-term outcomes was not possible.

Conclusion

We evaluated the use of potential factors and various respiratory indices for predicting successful weaning from NIV in patients with AECOPD with hypercapnic respiratory failure. A lower RSBI immediately before turning off NIV was more likely to be associated with successful weaning. Thus, RSBI is a single clinical parameter that can be easily measured at the bedside to help predict the likelihood of successful NIV weaning in patients with AECOPD. However, additional

studies with longer follow-up periods and larger sample sizes should be conducted to further evaluate the predictive ability of the RSBI, or other potential weaning indices, for NIV in populations other than patients with COPD.

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Data Availability Data are available from the Thoracic Medicine Unit of the National Taiwan University Hsin-Chu Hospital, Taiwan.

Declarations

Conflict of interest The authors have no relevant financial or non-financial interests to disclose.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the hospital institutional review board.

Informed Consent Informed consent was obtained from all individual participants included in the study (or their next of kin).

Consent for Publication All participants have consented to the submission of the manuscript to the journal.

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