

Research Article

Integrated Respiratory, Hemodynamic, and Cardiac Predictors of Prolonged Mechanical Ventilation in Acute Exacerbation of Chronic Obstructive Pulmonary Disease

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Abstract

Background

Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is an important cause of intensive care unit admission and respiratory failure. Although respiratory abnormalities are central to ventilatory dependence, hemodynamic instability and cardiac dysfunction may contribute substantially to delayed liberation from mechanical ventilation. This study evaluated the integrated association of respiratory, hemodynamic, and cardiac parameters with prolonged mechanical ventilation in patients with AECOPD requiring invasive ventilatory support.

Methods

A prospective observational study was conducted among 300 adults admitted to the intensive care unit with AECOPD requiring invasive mechanical ventilation. Clinical characteristics, arterial blood gas parameters, respiratory mechanics, hemodynamic variables, electrocardiographic findings, cardiac biomarkers, and echocardiographic

measurements were recorded during the first 24 hours of ICU admission. Prolonged mechanical ventilation was defined as invasive mechanical ventilation for more than 7 days. Patients were categorized into prolonged and non-prolonged ventilation groups. Multivariable logistic regression was performed to identify independent predictors.

Results

Of 300 patients, 92 (30.7%) required mechanical ventilation for more than 7 days. Compared with patients ventilated for ≤ 7 days, those with prolonged ventilation had lower admission pH, higher PaCO₂, lower PaO₂/FiO₂ ratio, higher respiratory rate, greater intrinsic PEEP, more frequent hypotension, higher lactate, greater heart-rate burden, elevated high-sensitivity cardiac troponin-I, higher NT-proBNP, and lower left ventricular ejection fraction. On multivariable analysis, admission pH ≤ 7.25 (adjusted odds ratio [aOR] 3.42, 95% CI 1.72–6.82), PaCO₂ ≥ 70 mmHg (aOR 2.71, 95% CI 1.39–5.29), intrinsic PEEP ≥ 10 cmH₂O (aOR 3.08, 95% CI 1.56–6.09), mean

arterial pressure <65 mmHg (aOR 2.86, 95% CI 1.39–5.87), elevated hs-cTnI (aOR 2.48, 95% CI 1.25–4.91), NT-proBNP $\geq$ 1800 pg/mL (aOR 2.76, 95% CI 1.39–5.48), and left ventricular ejection fraction <40% (aOR 2.34, 95% CI 1.12–4.88) were independently associated with prolonged ventilation.

Conclusion

Prolonged mechanical ventilation in AECOPD appears to reflect an integrated interaction between severe respiratory derangement, hemodynamic compromise, and cardiac dysfunction. Early assessment of these three domains may improve risk stratification and facilitate individualized ventilator-weaning strategies.

Keywords: chronic obstructive pulmonary disease; acute exacerbation; mechanical ventilation; prolonged ventilation; respiratory failure; hemodynamic instability; cardiac dysfunction; troponin; NT-proBNP; echocardiography

Introduction

Chronic obstructive pulmonary disease (COPD) is a major chronic respiratory disorder characterized by persistent airflow limitation and respiratory symptoms. Acute exacerbations represent periods of worsening respiratory symptoms that frequently require intensified treatment and may result in hospitalization, intensive care admission, non-invasive ventilation, or invasive mechanical ventilation. Current GOLD guidance recognizes acute respiratory acidosis, persistent hypoxemia, respiratory muscle fatigue, and severe clinical deterioration as important indicators for ventilatory support.¹⁻³

Acute exacerbation of COPD requiring invasive mechanical ventilation is associated with substantial morbidity. Respiratory acidosis and severe hypercapnia are established indicators of acute respiratory decompensation. Previous studies have demonstrated associations between low arterial pH, elevated PaCO₂, impaired

functional status, and severity scores with the need for mechanical ventilation.⁴

However, the duration of mechanical ventilation cannot be explained by respiratory variables alone. Dynamic hyperinflation and intrinsic positive end-expiratory pressure (PEEP) can increase the work of breathing and impair venous return. Consequently, severe airflow obstruction may have secondary hemodynamic effects, particularly in patients with limited cardiovascular reserve.

Cardiovascular disease is common among patients with COPD. Chronic hypoxemia, pulmonary vascular disease, right ventricular dysfunction, coronary artery disease, heart failure, and arrhythmias may coexist with COPD and become clinically important during an acute exacerbation. Previous studies have identified cardiac comorbidity and chronic heart failure as factors associated with severe outcomes and increased ventilatory requirements in AECOPD.

Recent multicenter evidence further suggests that cardiovascular dysfunction during the early period of ventilatory support is associated with failure of non-invasive ventilation and prolonged invasive mechanical ventilation. Earlier international data also identified cardiovascular and renal dysfunction among factors associated with poor outcomes in mechanically ventilated AECOPD.⁵⁻⁸

Despite these observations, respiratory, hemodynamic, and cardiac variables are frequently examined independently. An integrated approach may provide a more clinically meaningful assessment of patients who are likely to remain ventilator-dependent.⁹⁻¹⁰

Therefore, the present study evaluated the independent and combined associations of respiratory, hemodynamic, and cardiac parameters with prolonged mechanical ventilation in patients admitted with AECOPD.

Objectives

1. To determine the proportion of AECOPD patients requiring prolonged invasive mechanical ventilation.
2. To evaluate respiratory, hemodynamic, and cardiac characteristics associated with prolonged ventilation.
3. To identify independent predictors of mechanical ventilation lasting more than 7 days.
4. To assess whether an integrated multivariable model incorporating the three physiological domains improves prediction of prolonged ventilation.

Materials and Methods

Study Design and Setting

A prospective observational study was conducted at Sahiwal Medical College over a 24-month period.

Study Population

Adult patients aged ≥ 40 years with a documented diagnosis of COPD who were admitted with an acute exacerbation and required invasive mechanical ventilation were eligible.

AECOPD was defined clinically as an acute worsening of respiratory symptoms requiring additional treatment.

Inclusion Criteria

Patients were included if they:

- were aged ≥ 40 years;
- had established COPD based on previous clinical or spirometric documentation;
- presented with an acute exacerbation;
- required endotracheal intubation and invasive mechanical ventilation;
- had arterial blood gas analysis performed before or shortly after initiation of invasive ventilation.

Exclusion Criteria

Patients were excluded if they had:

- primary bronchial asthma without established COPD;
- acute major trauma;
- postoperative respiratory failure;
- established neuromuscular respiratory failure;
- pregnancy;
- known terminal malignancy receiving end-of-life care;
- incomplete admission physiological or cardiac data.

Definition of Prolonged Mechanical Ventilation

The primary outcome was prolonged invasive mechanical ventilation, defined as mechanical ventilation for >7 consecutive days.

Patients were divided into:

- **Non-prolonged ventilation:** ≤ 7 days
- **Prolonged ventilation:** >7 days

Respiratory Variables

The following respiratory variables were recorded within the first 24 hours:

- respiratory rate;
- arterial pH;
- PaCO_2 ;
- PaO_2 ;
- $\text{PaO}_2/\text{FiO}_2$ ratio;
- serum bicarbonate;
- peak airway pressure;
- plateau pressure;
- intrinsic PEEP;
- ventilatory driving pressure;
- initial ventilator mode;
- requirement for rescue ventilatory interventions.

A pH ≤ 7.25 was considered severe respiratory acidosis, while $\text{PaCO}_2 \geq 70$ mmHg was considered marked hypercapnia.

Hemodynamic Variables

Hemodynamic assessment included:

- systolic blood pressure;
- mean arterial pressure;
- heart rate;
- shock index;
- serum lactate;

- vasopressor requirement;
- urine output during the first 24 hours.

Hemodynamic instability was defined as mean arterial pressure <65 mmHg and/or requirement for vasopressor support.

Cardiac Assessment

Cardiac assessment included:

- electrocardiography;
- high-sensitivity cardiac troponin-I;
- NT-proBNP;
- echocardiographic left ventricular ejection fraction;
- right ventricular systolic function;
- estimated pulmonary artery systolic pressure;
- evidence of significant valvular disease.

Cardiac dysfunction was defined as the presence of reduced left ventricular systolic function, significant right ventricular dysfunction, clinically significant heart failure, or a major cardiac biomarker elevation in the appropriate clinical context.

Statistical Analysis

Data were analyzed using statistical software. Continuous variables were expressed as mean $\pm$ standard deviation and categorical variables as frequencies and percentages.

Patients with prolonged and non-prolonged ventilation were compared using the independent-samples t-test or Mann–

Whitney U test for continuous variables and the chi-square test or Fisher's exact test for categorical variables.

Variables with clinical relevance and those demonstrating an association on univariable analysis were entered into multivariable logistic regression.

The primary dependent variable was prolonged mechanical ventilation (>7 days). Adjusted odds ratios (aORs) with 95% confidence intervals (CIs) were reported. Statistical significance was considered at $p < 0.05$.

Results

Patient Characteristics

A total of 300 patients with AECOPD requiring invasive mechanical ventilation were included. The mean age was 67.4 ± 10.2 years and 216 (72.0%) were male.

Overall, 92 patients (30.7%) required mechanical ventilation for more than 7 days, while 208 (69.3%) were successfully liberated from invasive ventilation within 7 days.

Patients with prolonged ventilation had a greater burden of severe respiratory abnormalities at admission. They also demonstrated a higher frequency of hypotension, elevated lactate, cardiac biomarker elevation, and echocardiographic abnormalities

Table 1. Baseline Respiratory, Hemodynamic and Cardiac Characteristics of the Study Population

Variable	Total (n=300)	Ventilation ≤ 7 days (n=208)	Ventilation >7 days (n=92)	p-value
Age, years	67.4 ± 10.2	66.1 ± 9.7	70.2 ± 10.7	0.001
Male sex	216 (72.0%)	151 (72.6%)	65 (70.7%)	0.73
Current/former smoker	264 (88.0%)	181 (87.0%)	83 (90.2%)	0.44
Previous ICU admission	102 (34.0%)	61 (29.3%)	41 (44.6%)	0.009

Variable	Total (n=300)	Ventilation ≤ 7 days (n=208)	Ventilation >7 days (n=92)	p-value
Long-term oxygen therapy	78 (26.0%)	43 (20.7%)	35 (38.0%)	0.002
Respiratory rate, /min	31.2 $\pm$ 7.4	29.4 $\pm$ 6.3	35.2 $\pm$ 8.1	<0.001
pH	7.26 $\pm$ 0.09	7.29 $\pm$ 0.07	7.20 $\pm$ 0.10	<0.001
PaCO ₂ , mmHg	67.8 $\pm$ 18.9	63.1 $\pm$ 16.5	78.4 $\pm$ 20.5	<0.001
PaO ₂ /FiO ₂ ratio	178 $\pm$ 72	194 $\pm$ 70	142 $\pm$ 67	<0.001
Intrinsic PEEP, cmH ₂ O	8.1 $\pm$ 3.6	7.1 $\pm$ 3.0	10.4 $\pm$ 3.9	<0.001
Plateau pressure, cmH ₂ O	23.1 $\pm$ 5.8	22.2 $\pm$ 5.2	25.1 $\pm$ 6.5	<0.001
MAP <65 mmHg	87 (29.0%)	43 (20.7%)	44 (47.8%)	<0.001
Heart rate ≥ 120 /min	111 (37.0%)	64 (30.8%)	47 (51.1%)	0.001
Lactate ≥ 2.5 mmol/L	99 (33.0%)	49 (23.6%)	50 (54.3%)	<0.001
Vasopressor requirement	69 (23.0%)	30 (14.4%)	39 (42.4%)	<0.001
hs-cTnI above upper reference	118 (39.3%)	63 (30.3%)	55 (59.8%)	<0.001
NT-proBNP ≥ 1800 pg/mL	96 (32.0%)	49 (23.6%)	47 (51.1%)	<0.001
LVEF <40%	55 (18.3%)	27 (13.0%)	28 (30.4%)	0.001
RV dysfunction	71 (23.7%)	38 (18.3%)	33 (35.9%)	0.001
Pulmonary hypertension	93 (31.0%)	53 (25.5%)	40 (43.5%)	0.002
Significant arrhythmia	49 (16.3%)	25 (12.0%)	24 (26.1%)	0.003

Respiratory and Hemodynamic Outcomes

Severe respiratory acidosis was considerably more common among patients requiring prolonged ventilation. Similarly, marked hypercapnia and intrinsic PEEP elevation were significantly associated with prolonged ventilatory support.

Hemodynamic deterioration was also more frequent in the prolonged ventilation group. Vasopressor use and elevated lactate were particularly prominent.

Table 2. Respiratory and Hemodynamic Risk Factors According to Duration of Mechanical Ventilation

Risk factor	≤7 days n (%)	>7 days n (%)	Odds ratio (95% CI)	p-value
pH ≤7.25	47 (22.6%)	51 (55.4%)	4.25 (2.51–7.19)	<0.001
PaCO ₂ ≥70 mmHg	62 (29.8%)	49 (53.3%)	2.68 (1.62–4.44)	<0.001
PaO ₂ /FiO ₂ <150	56 (26.9%)	44 (47.8%)	2.48 (1.49–4.12)	0.001
Respiratory rate ≥30/min	108 (51.9%)	66 (71.7%)	2.36 (1.38–4.03)	0.002
Intrinsic PEEP ≥10 cmH ₂ O	41 (19.7%)	48 (52.2%)	4.44 (2.63–7.51)	<0.001
Plateau pressure ≥25 cmH ₂ O	48 (23.1%)	39 (42.4%)	2.45 (1.46–4.12)	0.001
MAP <65 mmHg	43 (20.7%)	44 (47.8%)	3.51 (2.09–5.90)	<0.001
Lactate ≥2.5 mmol/L	49 (23.6%)	50 (54.3%)	3.85 (2.31–6.43)	<0.001
Vasopressor requirement	30 (14.4%)	39 (42.4%)	4.37 (2.49–7.67)	<0.001
Shock index ≥1.0	49 (23.6%)	39 (42.4%)	2.39 (1.42–4.02)	0.001

Cardiac Predictors

Cardiac abnormalities were more frequent among patients who required prolonged ventilation. Elevated hs-cTnI was present in 59.8% of prolonged-ventilation patients compared with 30.3% of those ventilated for ≤7 days.

Similarly, NT-proBNP elevation, reduced LVEF, right ventricular dysfunction, pulmonary hypertension, and significant arrhythmia were significantly associated with prolonged ventilation.

Table 3. Cardiac Characteristics Associated With Prolonged Mechanical Ventilation

Cardiac variable	≤7 days n (%)	>7 days n (%)	Odds ratio (95% CI)	p-value
hs-cTnI above reference range	63 (30.3%)	55 (59.8%)	3.43 (2.05–5.75)	<0.001
hs-cTnI markedly elevated	31 (14.9%)	31 (33.7%)	2.90 (1.63–5.16)	<0.001
NT-proBNP ≥1800 pg/mL	49 (23.6%)	47 (51.1%)	3.39 (2.03–5.66)	<0.001
LVEF <40%	27 (13.0%)	28 (30.4%)	2.92 (1.62–5.27)	<0.001
RV dysfunction	38 (18.3%)	33 (35.9%)	2.50 (1.43–4.37)	0.001
Pulmonary hypertension	53 (25.5%)	40 (43.5%)	2.25 (1.35–3.76)	0.002

Cardiac variable	≤7 days n (%)	>7 days n (%)	Odds ratio (95% CI)	p-value
Significant arrhythmia	25 (12.0%)	24 (26.1%)	2.58 (1.35–4.91)	0.004
Chronic heart failure	31 (14.9%)	27 (29.3%)	2.37 (1.31–4.30)	0.004
Ischemic heart disease	42 (20.2%)	31 (33.7%)	2.01 (1.18–3.43)	0.010

Multivariable Analysis

Variables representing the three physiological domains were entered into a multivariable logistic regression model.

Severe respiratory acidosis, marked hypercapnia, increased intrinsic PEEP, hemodynamic instability, elevated lactate, cardiac biomarker elevation, elevated NT-proBNP, and reduced LVEF remained independently associated with prolonged mechanical ventilation.

Table 4. Multivariable Logistic Regression Analysis of Predictors of Prolonged Mechanical Ventilation

Predictor	Adjusted OR	95% CI	p-value
Age ≥70 years	1.72	0.94–3.15	0.078
Previous ICU admission	1.63	0.89–2.98	0.111
pH ≤7.25	3.42	1.72–6.82	<0.001
PaCO ₂ ≥70 mmHg	2.71	1.39–5.29	0.003
PaO ₂ /FiO ₂ <150	1.88	0.99–3.57	0.054
Intrinsic PEEP ≥10 cmH ₂ O	3.08	1.56–6.09	0.001
Plateau pressure ≥25 cmH ₂ O	1.69	0.87–3.28	0.118
MAP <65 mmHg	2.86	1.39–5.87	0.004
Lactate ≥2.5 mmol/L	2.43	1.25–4.73	0.009
Vasopressor requirement	2.11	0.99–4.48	0.053
hs-cTnI above reference	2.48	1.25–4.91	0.009
NT-proBNP ≥1800 pg/mL	2.76	1.39–5.48	0.004
LVEF <40%	2.34	1.12–4.88	0.024
RV dysfunction	1.81	0.91–3.60	0.091

Predictor	Adjusted OR	95% CI	p-value
Significant arrhythmia	1.96	0.89–4.32	0.094

The model demonstrated good discrimination for prolonged mechanical ventilation, with an estimated area under the receiver operating characteristic curve of **0.84**.

Discussion

This study evaluated prolonged mechanical ventilation in AECOPD using an integrated respiratory, hemodynamic, and cardiac framework. Approximately one-third of patients in the study required invasive mechanical ventilation for more than 7 days. The principal finding was that prolonged ventilation was not associated with respiratory variables alone. Severe respiratory acidosis, marked hypercapnia, and elevated intrinsic PEEP remained important predictors, while hemodynamic instability and cardiac abnormalities independently contributed to the risk.¹¹⁻¹³ Respiratory failure remains the central reason for ventilatory support in AECOPD. Previous studies have demonstrated that low pH and elevated PaCO₂ are associated with the requirement for mechanical ventilation. In one cohort of patients with acute respiratory failure due to COPD, pH ≤ 7.28 and PaCO₂ ≥ 68.6 mmHg were independently associated with the need for mechanical ventilation. The present findings extend this observation by demonstrating that severe hypercapnic respiratory acidosis may also identify

patients likely to remain ventilator-dependent for longer periods.¹⁴⁻¹⁵

Intrinsic PEEP was another important respiratory predictor. Dynamic hyperinflation is a recognized consequence of severe airflow obstruction and can increase inspiratory workload while producing adverse cardiovascular effects. In the present cohort, intrinsic PEEP ≥ 10 cmH₂O remained independently associated with ventilation beyond 7 days. This finding supports the concept that respiratory mechanics may provide information beyond conventional arterial blood gas measurements.¹⁶⁻¹⁷

Hemodynamic instability was also strongly associated with prolonged ventilation. Patients with MAP below 65 mmHg and elevated lactate had substantially higher rates of prolonged ventilatory dependence. This may reflect the interaction between severe respiratory mechanics and cardiovascular reserve. Dynamic hyperinflation can reduce venous return and compromise cardiac output, while infection, hypoxemia, acidosis, pulmonary hypertension, and underlying

cardiovascular disease may further impair systemic perfusion.¹⁸⁻¹⁹

The cardiac findings are particularly relevant. Elevated hs-cTnI and NT-proBNP were independently associated with prolonged ventilation after adjustment for respiratory and hemodynamic factors. Cardiac biomarker elevation during AECOPD does not necessarily indicate acute coronary occlusion; it may reflect myocardial strain, hypoxemia, tachycardia, right ventricular pressure overload, or concomitant cardiovascular disease. Therefore, biomarker results should be interpreted in conjunction with clinical findings, ECG, and echocardiography.²⁰

Reduced LVEF was independently associated with prolonged ventilation. This finding is consistent with previous evidence that cardiovascular comorbidity and chronic heart failure increase the likelihood of severe outcomes and ventilatory support in AECOPD. Similarly, previous mechanically ventilated AECOPD cohorts have identified cardiovascular dysfunction as an important determinant of outcome.

Recent multicenter evidence provides additional support for this integrated model. In a large international analysis of patients receiving ventilatory support for AECOPD, cardiovascular failure during the first day of

ventilatory support was independently associated with prolonged invasive mechanical ventilation. This observation is important because cardiovascular dysfunction may be both a consequence of severe respiratory disease and an independent contributor to failure of ventilator liberation. The findings also have implications for weaning. Conventional weaning assessment focuses predominantly on respiratory parameters such as gas exchange, respiratory muscle strength, and spontaneous breathing tolerance. However, cardiac dysfunction can become apparent during reductions in positive pressure support. Patients with limited cardiovascular reserve may therefore benefit from early echocardiographic assessment and careful hemodynamic monitoring during the liberation process.

The present study supports a multidimensional approach in which respiratory mechanics, systemic perfusion, and cardiac function are evaluated together. Such an approach may help clinicians identify patients at increased risk of prolonged ventilatory dependence earlier in the ICU course.

Clinical Implications

The findings suggest that assessment of AECOPD patients requiring invasive

ventilation should extend beyond arterial blood gases.

A practical assessment during the initial ICU period may include:

1. Respiratory domain

- pH;
- PaCO₂;
- PaO₂/FiO₂;
- respiratory rate;
- intrinsic PEEP;
- plateau pressure.

2. Hemodynamic domain

- MAP;
- heart rate;
- lactate;
- vasopressor requirement;
- urine output.

3. Cardiac domain

- ECG;
- hs-cTnI;
- NT-proBNP;
- LVEF;
- right ventricular function;
- pulmonary pressure estimation.

The combination of these variables may provide a more comprehensive assessment than any individual marker.

Strengths

The principal strength of this study was the integrated evaluation of three physiological

domains that are frequently considered separately.

Additional strengths included:

- prospective collection of physiological variables;
- standardized definition of prolonged ventilation;
- incorporation of respiratory mechanics;
- inclusion of both left- and right-sided cardiac assessment;
- multivariable adjustment for potentially confounding factors.

Limitations

Several limitations should be considered.

First, this was a single-center observational study, which may limit generalizability.

Second, cardiac biomarker elevation during AECOPD is not specific for primary cardiac disease and may result from systemic stress or right ventricular strain.

Third, echocardiographic measurements may vary according to operator experience and loading conditions.

Fourth, the study focused on patients who already required invasive mechanical ventilation and therefore does not identify predictors of initial intubation.

Finally, although the integrated model demonstrated good discrimination, external validation in an independent cohort would be required before clinical implementation.

Conclusion

Prolonged mechanical ventilation in patients with acute exacerbation of COPD is associated with abnormalities across respiratory, hemodynamic, and cardiac domains. Severe respiratory acidosis, marked hypercapnia, elevated intrinsic PEEP, hypotension, elevated lactate, cardiac biomarker elevation, increased NT-proBNP, and reduced left ventricular systolic function were independently associated with ventilation lasting more than 7 days.

These findings support an integrated physiological approach to risk stratification in critically ill patients with AECOPD. Early recognition of respiratory mechanics abnormalities together with hemodynamic and cardiac dysfunction may help identify patients at increased risk of delayed ventilator liberation and may facilitate individualized monitoring and weaning strategies.

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