Use of the modified Glasgow Coma Scale score to guide sequential invasive-noninvasive mechanical ventilation weaning in patients with AECOPD and respiratory failure

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Received December 16, 2019; Accepted May 7, 2020

DOI: 10.3892/etm.2020.8884

Abstract. Sequential invasive-noninvasive ventilation (NIV) improves the outcomes of patients with respiratory failure caused by acute exacerbation of chronic obstructive pulmonary disease (AECOPD); however, there is no clear consensus on the optimal timing of the switch to sequential invasive-NIV in these patients. In the present study, a potential role for the modified Glasgow Coma Scale (GCS) score to guide sequential weaning was investigated. Patients with AECOPD and respiratory failure were prospectively recruited from three study centers (Wenling Hospital Affiliated to Wenzhou Medical University, the First Affiliated Hospital of Wenzhou Medical University and Changsha Central Hospital) between January 1st 2016 and December 31st 2018. Patients were randomly assigned to group A and B, with the switching point for sequential weaning strategy in the two groups being a modified GCS score ≥13 and 10 points, respectively. Each group included 240 patients. Baseline demographic characteristics were comparable in the two groups. The duration of invasive mechanical ventilation (IMV) in group A was significantly shorter than that in group B. However, there were no significant between-group differences with respect to the incidence of re-intubation, ventilator-associated pneumonia, in-hospital mortality or the length of hospital stay. Use of a modified GCS score ≥13 as the switching point for sequential invasive-NIV may help decrease the duration of IMV in patients with AECOPD and respiratory failure.

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Abbreviations: AECOPD, acute exacerbation of chronic obstructive pulmonary disease; APACHE II, Acute Physiology and Chronic Health Enquiry; ABG, arterial blood gas; BMI, body mass index; COPD, chronic obstructive pulmonary disease; GCS, Glasgow Coma Scale; HR, heart rate; ICU, intensive care unit; IMV, invasive mechanical ventilation; MBP, mean blood pressure; NIV, noninvas; OI, oxygenation index; $PaCO_2$, partial pressure of arterial CO_2; PaO, partial pressure of arterial oxygen; PIC, pulmonary infection control; RR, respiratory rate; SBT, spontaneous breathing trial; VAP, ventilator-associated pneumonia

Key words: acute exacerbation of chronic obstructive pulmonary disease, respiratory failure, invasive mechanical ventilation, noninvasive ventilation, Glasgow Coma Scale

Introduction

Chronic obstructive pulmonary disease (COPD) accounts for a major proportion of global morbidity and mortality (1). An estimated 384 million people aged ≥30 years are believed to be affected by COPD [global prevalence: 11.7% (8.4-15.0%)] (1). Hospitalization in the intensive care unit (ICU) is required for ~12-18% of patients with COPD due to acute exacerbations (2), with the mortality rate of these patients approaching 15% (3). Invasive mechanical ventilation (IMV) is the primary choice of treatment for 5.9-26.0% of patients with acute exacerbation of COPD (AECOPD), especially comatosed patients (4,5). Despite the development of protective lung ventilation strategies and the optimization of treatment for respiratory failure, the reported incidence of AECOPD-induced respiratory failure is >24.5% (6). Prolonged IMV may lead to ventilator-associated pneumonia (VAP), ventilator-associated lung injury and difficulty in weaning from mechanical ventilation, which can exacerbate respiratory distress and necessitate the continuation of invasive ventilation (7,8). Prolonged endotracheal intubation can also lead to airway injury, tracheoesophageal fistula and other potentially serious complications (7). Furthermore, long-term endotracheal intubation reduces the quality of life of patients and leads to a poor prognosis; therefore, timely weaning from mechanical ventilation is an important factor for the use of IMV (8).

Sequential invasive-noninvasive ventilation (NIV) is a widely used strategy to decrease the duration of IMV.

However, there is no clear consensus on the optimal switching point (5). Excellent results have been reported with the use of a pulmonary infection control (PIC) window as the switching point for the implementation of a sequential ventilation strategy (9). However, the PIC approach is mostly based on x-ray imaging findings and does not take into account the lag time between the appearance of x-ray findings and clinical manifestations (9).

Indeed, patients with AECOPD and respiratory failure who exhibit a high level of consciousness and cooperation, typically benefit from NIV, while impaired consciousness has been identified as a risk factor for extubation failure (10,11). Previous studies have investigated the use of a modified Glasgow Coma Scale (GCS) score for evaluating the level of consciousness of intubated patients (12,13). the modified GCS score was found to be a more objective, quantitative measure of the overall clinical condition. The present study aimed to compare two weaning strategies entailing the use of different levels of modified GCS score (13 vs. 10 points) as the switching point for the sequential invasive-NIV in patients with AECOPD.

Materials and methods

Study participants. In this prospective, randomized, controlled study, consecutive patients with AECOPD who received intubation for respiratory failure at the ICU of 3 hospitals (Wenling Hospital Affiliated to Wenzhou Medical University, the First Affiliated Hospital of Wenzhou Medical University and Changsha Central Hospital) were recruited between January 1st 2016 and December 31st 2018. The Ethics Committee of the Wenling Hospital Affiliated to the Wenzhou Medical University approved the research protocol for this study. Written informed consent was obtained from all patients prior to their enrolment.

The inclusion criteria were as follows: i) Age ≥18 years; ii) patients who received IMV for respiratory failure; iii) patients who met the COPD diagnostic criteria in the 2017 guidelines of the Global Initiative for Chronic Obstructive Lung Disease (14); iv) partial pressure of arterial oxygen (PaO_2) and CO_2 ($PaCO_2$) in arterial blood gas (ABG) analysis <60 mmHg; and v) no absolute contraindications to NIV (15). The exclusion criteria were as follows: i) Acute stroke, acute pulmonary embolism, cardiogenic pulmonary edema or other causes of acute respiratory failure; ii) death within 3 days of admission; iii) active upper gastrointestinal bleeding; iv) treatment discontinuation; or v) readmission to the ICU <3 months following enrolment with the study. A total of 283 patients qualified for the inclusion criteria, with 240 patients finally included after screening. A total of 141 men and 99 women were included in the current study (mean age, 55.3±9.1 years; age range, 31-86 years). All the enrolled patients were randomly assigned to groups A and B, and there were no significant between-group differences with respect to sex, age or body mass index (BMI). A schematic illustration of the study design and patient-selection criteria is presented in Fig. 1.

Groups and definitions of the modified GCS score. Using a random number table, subjects were randomly assigned to group A and B, based on the use of modified GCS score ≥13 or 10 points, respectively, as the switching point for sequential weaning strategy. The detailed definition of the modified GCS score is shown in Table I.

Treatment protocols. All subjects received the following treatments: Anti-infective agents, antispasmodics, glucocorticoids (methylprednisolone, 40-80 mg/day), anti-inflammatory agents, expectorants, nutritional support and sedatives, as well as measures for maintaining internal homeostasis. Dexmedetomidine was used as the first-line sedative, which was administered as an intravenous bolus infusion over 10 min at a dose of 1 μg/kg, followed by 0.2-0.8 μg/kg/h using a micro-pump. The infusion rate was titrated to maintain a Richmond Agitation-Sedation score between-2 and +1 (16). The daily neurological wake-up test consisted of 3 components: Eye-opening in response to verbal command, eye tracking and shaking hands-on instruction if the sedation was in the target range. If the above criteria were not met, the sedative dose was adjusted until the target was reached.

Weaning protocol. The parameters of mechanical ventilation were calibrated based on the results of the ABG analysis and the disease course. In Group A, patients were ventilated with synchronized intermittent mandatory ventilation mode, with the addition of pressure support ventilation or the assist/control mode. The respiratory rate (RR) was set at 13-18 cycles/min and tidal volume at 8-10 ml/kg to maintain the arterial partial pressure of CO_2 ($PaCO_2$) at 35-50 mmHg. The inspired oxygen fraction and positive end-expiratory pressure were adjusted to maintain arterial oxygen saturation of ≥90%. IMV was switched to NIV (Philips Medical Systems, Inc.) if the patients remained stable for 3 h after achieving the target modified GCS score in their respective groups (13 points in Group A and 10 points in Group B). Subsequently, the spontaneous/timed mode was applied, with an inspiratory positive airway pressure of 12-14 cmH_2O and expiratory positive airway pressure of 5 cmH_2O, which were gradually increased to the appropriate level within 5-20 min of switching to NIV.

Data collection and outcomes. Data pertaining to the baseline characteristics and indices at admission were collected, including the Acute Physiology and Chronic Health Enquiry score, modified GCS score, mean arterial blood pressure (MBP) and oxygenation index (OI). Indices such as the MBP, OI, heart rate (HR), RR and results of the ABG analysis were also measured before and 3 h after weaning to NIV. The primary outcome was the duration of invasive ventilation. Other outcomes included the incidence of VAP, re-intubation rate, in-hospital mortality and the length of hospital stay.

Statistical analysis. All statistical analyses were conducted using SPSS 25.0 (for Windows; IBM Corp.). Continuous variables are expressed as the mean ± (SD). Between-group differences with respect to continuous variables were assessed using the unpaired Student's t-test. Categorical variables are expressed as ratios and between-group differences were assessed using the χ^2 test. All statistical analyses were two-sided, and $P<0.05$ was considered to indicate a statistically significant difference.

Table I. Modified GCS.

Score	Eye	Verbal	Motor
1	Does not open eyes	No response to speech	Makes no movements
2	Opens eyes in response to painful stimuli	Response to loudly call	Extension to painful stimuli
3	Opens eyes in response to voice	Understanding error	Abnormal flexion to painful stimuli
4	Opens eyes spontaneously	Slow understanding of speech	Flexion/withdrawal from painful stimuli
5	N/A	Correct understanding of speech	Localizes painful stimuli
6	N/A	N/A	Obeys commands

The modified GCS evaluates 3 parameters: Eye, verbal and motor responses. The separate scores of these 3 parameters as well as their combined scores are considered. The lowest possible GCS, the sum, score is 3 (deep coma or death), whereas the highest is 15 (fully conscious person). N/A, not applicable. GCS, Glasgow Coma Scale.

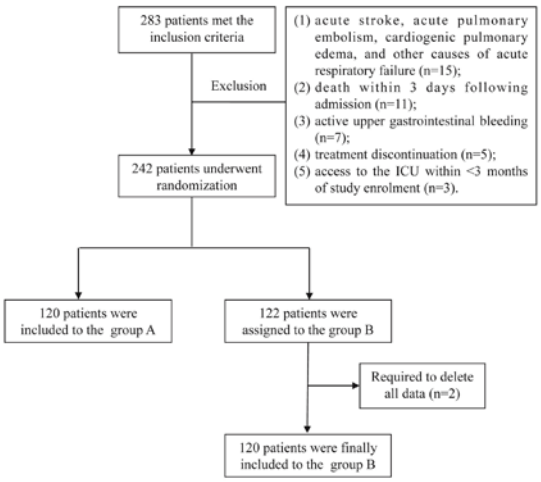

Figure 1. Schematic illustration of the study design and patient-selection criteria. ICU, intensive care unit.

Results

Baseline characteristics. A total of 240 patients [141 men and 99 women; mean age ± SD: 55.3±9.1 (range 31-86) years] qualified the study selection criteria and were enrolled; of these 120 patients each were randomly assigned to groups A and B. The baseline demographic characteristics of patients in the two groups were comparable at the time of randomization (Table II). There were no significant between-group differences with respect to sex, age or BMI. There were no significant differences with respect to concomitant diseases such as cardiovascular diseases, cerebrovascular diseases, diabetes and chronic kidney disease. Likewise, there were no significant between-group differences with respect to MBP, HR, respiratory rate, OI or arterial blood analysis at admission.

Safety and efficiency of sequential weaning as guided by two different modified GCS scores. Patients in groups A and B underwent extubation followed by sequential NIV upon reaching modified GCS score of ≥13 points and 10, respectively. There were no significant between-group differences with respect to OI, MBP, PaO_2 and $PaCO_2$ ($P>0.05$; Table III) both before extubation and at 3 h after extubation.

Primary and secondary outcomes. The duration of IMV in group A was significantly shorter than that in Group B (Table IV). However, there were no significant between-group differences with respect to the incidence rate of re-intubation, VAP, in-hospital mortality or the length of hospital stay.

Discussion

The present study was a randomized clinical trial conducted at three ICUs in Eastern China. It was found that sequential NIV, guided by a modified GCS score, was an effective and safe weaning strategy in AECOPD patients undergoing IMV. Moreover, the use of a modified GCS score ≥13 points as the criterion to switch to sequential NIV, decreased the duration of invasive ventilation in ICU patients with AECOPD-induced respiratory failure, as compared to a modified GCS score ≥10 points. However, there were no significant differences with respect to the incidence of re-intubation, VAP, hospital mortality or the length of hospital stay.

The identification of a timely and optimal 'switching point' is the key to an effective sequential ventilation strategy (9). Use of spontaneous breathing trial (SBT) to predict the successful withdrawal of the IMV is recommended by the European Respiratory Society, the American Thoracic Society, the European Society of Intensive Care Medicine, the Society of Critical Care Medicine and the Société de Réanimation de langue Française (17). It is believed that the duration of SBT should be between 30-120 min (18); however, it is not clear whether the same duration is applicable to patients who require mechanical ventilation because of different diseases. It has been found that SBT may cause a delay in weaning and may also cause VAP, which in turn may contribute to increased mortality (19). In China, the switching point is mainly the PIC window, as proposed by the Beijing Institute of Respiratory Diseases (20), while other countries, such as England, have employed a 48-h window for this purpose (21). However, both of these strategies have certain limitations. The former ignores the time-lag between the appearance of imaging findings and the onset of clinical manifestations, and does not take

Table II. Baseline characteristics of the study population.

Variables	Group A, n=120	Group B, n=120	t/χ^2 value	P-value
Male	75 (62.5%)	66 (55.0%)	-0.464[a]	0.496
Age, years	57±8	54±10	0.693[b]	0.489
BMI, kg/m^2	21.87±3.79	20.33±2.51	0.702[b]	0.484
Primary diseases				
Cardiovascular disease	19 (15.83%)	22 (18.33%)	0.265[a]	0.607
Cerebrovascular disease	25 (20.83%)	17 (14.17%)	1.847[a]	0.174
Diabetes	16 (13.33%)	22 (18.33%)	1.126[a]	0.289
Chronic kidney disease	9 (7.50%)	6 (5.00%)	0.640[a]	0.424
APACHE II	23.89±4.32	22.90±3.79	0.768[b]	0.452
MBP, mmHg	102.59±20.03	98.25±21.92	1.251[b]	0.224
OI, mmHg	158.26±32.82	161.13±26.57	0.42[b]	0.813
Heart rate, bpm	87.23±15.81	85.62±17.19	0.853[b]	0.392
Respiratory rate, bpm	21.21±5.14	19.68±4.17	1.35[b]	0.187
pH value	7.21±1.51	7.25±1.90	0.148[b]	0.881
PaO2, mmHg	58.35±11.24	56.09±9.83	1.649[b]	0.105
PaCO2, mmHg	85.19±17.53	82.39±18.07	1.276[b]	0.207

[a]χ2 value, [b]t-value. APACHE II, Acute Physiology and Chronic Health Enquiry score; BMI, body mass index; GCS, Glasgow Coma Scale; MBP, mean blood pressure; OI, oxygenation index; $PaCO_2$, arterial partial pressure of CO_2; PaO_2, arterial partial pressure of O_2.

Table III. Indices before and 3 h after extubation.

				Comparison between Group A and B	
Time	Variables	Group A	Group B	t value	P-value
Before extubation	MBP, mmHg	101.50±19.53	105.37±17.63	0.672	0.506
	OI, mmHg	222.16±40.83	225.25±43.09	1.298	0.192
	PaO_2, mmHg	88.65±19.26	87.58±17.30	1.034	0.316
	$PaCO_2$, mmHg	44.26± 12.64	43.60± 10.25	0.685	0.493
3 hours after extubation and noninvasive ventialtion	MBP, mmHg	102.86±22.69	102.56±20.35	0.857	0.389
	OI, mmHg	210.29±37.47	213.06±37.31	0.831	0.408
	PaO_2, mmHg	81.55±21.63	84.63±22.65	0.658	0.514
	$PaCO_2$, mmHg	45.75±16.14	48.32±11.74	0.693	0.491

MBP, mean blood pressure; OI, oxygenation index; PaO_2, partial pressure of arterial oxygen; $PaCO_2$, partial pressure of arterial CO_2.

Table IV. Primary and secondary outcomes.

Variables	Group A (n=120)	Group B (n=120)	t/χ^2 value	P-value
Hospital mortality (n, %)	8 (6.67%)	10 (8.33%)	0.240[a]	0.624
Duration of IMV (days)	4.13±1.04	4.96±0.69	2.003[b]	0.045
Incidence of VAP (n, %)	3 (7.5)	6 (15.0)	1.127[a]	0.288
Re-intubation (n, %)	2 (5.0)	5 (12.5)	1.409[a]	0.235
Length of hospital stay (days)	15.85±3.87	17.16±5.02	1.485[b]	0.152

[a]χ^2 value, [b]t-value. IMV, invasive mechanical ventilation; VAP, ventilator-associated pneumonia.

account of noninfective factors. The latter strategy overlooks inter-individual variability among patients.

There are 3 prerequisites for the application of sequential NIV: A high level of consciousness, a certain degree of

cooperation and appropriate compliance; therefore, the changes in consciousness should be factored while considering the switch to noninvasive respiratory support (22). The main causes of AECOPD-induced respiratory failure are pulmonary infection, ventilatory insufficiency or respiratory muscle fatigue (9). Therefore, the level of consciousness tends to vary with the development, exacerbation or improvement of AECOPD (22). The GCS score is widely used for the assessment of awareness. It is an objective measure for the dynamic assessment of the overall and physical condition of patients with COPD with severe respiratory failure at each stage of the disease (23). Patients with endotracheal intubation cannot speak even if they are conscious (24). Therefore, the GCS scoring system has been improved by modifying the correct response instead of using speech (23). A previous study found that it was safe and feasible to initiate sequential NIV if modified GCS score ≥13 points, and that it was acceptable to stablely maintain for 3 h (25). The sequential ventilation strategy was found to reduce the discomfort, restlessness and pain induced by intubation, and increased patient trust and coordination. This resulted in a higher rate of successful weaning, lower incidence of re-intubation and shorter length of hospital stay. Chen *et al* (26) found that the use of modified GCS score ≥10 points was a more suitable criterion for initiating the switch to sequential invasive-non-invasive weaning. In the present study, the two weaning strategies, which were guided respectively by 'improved GCS ≥13 points' and 'improved GCS ≥10 points', were compared. The use of the modified GCS score ≥13 points as the criterion to switch to sequential NIV was associated with a shorter duration of invasive ventilation in ICU patients with AECOPD-induced respiratory failure as compared to using the modified GCS score ≥10 points.

In conclusion, using a improvement of the modified GCS score ≥13 points as the switching point for sequential invasive-NIV may significantly improve the prognosis of patients with AECOPD with respiratory failure.

Acknowledgements

Not applicable.

Funding

This study was supported by the Wenling Science and Technology Bureau Project (grant no. 2014C31BA0032).

Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

JBZ and JQZ designed/performed most of the investigation, data analysis and wrote the manuscript. LXC, XJ and LLC provided statistics assistance. YS, SZ, JM, HF, JX, MD, LY, XW, HW, JYZ and YW contributed to interpretation of the data and analyses. All of the authors have read and approved the manuscript.

Ethics approval and consent to participate

The Ethics Committee of the Wenling Hospital Affiliated to the Wenzhou Medical University approved the research protocol for this study. Written informed consent was obtained from all patients prior to their enrolment.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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