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Procalcitonin kinetics to guide sequential invasive-noninvasive mechanical ventilation weaning in patients with acute exacerbation of chronic obstructive pulmonary disease and respiratory failure: procalcitonin's adjunct role

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ABSTRACT

How to identify the optimum switch point of sequential invasive and noninvasive ventilation is the focus of clinical attention on the patients suffering from acute exacerbation of chronic obstructive pulmonary disease (AECOPD) complicated by acute respiratory failure (ARF). This study aims to explore the clinical significance of taking the change rate of procalcitonin (PCT) as identifying the timing of weaning on the mechanical ventilation for the patients of AECOPD followed by ARF as a complication. There were altogether 140 patients of AECOPD complicated with ARF, who were randomly selected and divided into a study group and a control group respectively. A change rate of serum PCT level exceeding 50% was taken as the switch point selection of tracheal intubation removal for the patients of the study group, while the 'pulmonary infection control (PIC) window' was done for those in the control group. With CRP, IL-6, TNF-a, $PaCO_2$, PaO_2, and Lac having been detected before and after treatment to them all, clinical indexes were obtained and compared between these two groups. The CRP, TNF-a, and IL-6 levels of the patients in the study group after treatment ($p < 0.05$) were lower than those in the control group. There was no significant difference in $PaCO_2$, PaO_2, and Lac between these two groups before and after treatment ($p > 0.05$). Even so, some other indexes available for the study group of patients were found to be lower than those for the control group ($p < 0.05$) in the following aspects: duration of invasive ventilation support, total time of mechanical ventilation support, incidence rate of ventilator-associated pneumonia, 48-hour reintubation rate, incidence rate of upper gastrointestinal bleeding, hospitalization time of critical respiratory illness, total hospitalization time, RICU treatment cost, total treatment cost, and mortality. It is preferable to take the change rate of PCT level exceeding 50% as the switch point of weaning time in sequential mechanical ventilation rather than the PIC window.

Abbreviations

AECOPD: acute exacerbation of chronic obstructive pulmonary disease; ARF: acute respiratory failure; PCT: procalcitonin; PaO_2: the oxygen partial pressure; $PaCO_2$: the partial pressure of carbon dioxide; TNF-a: serum tumor necrosis factor-a; IL-6: interleukin-6; CRP: serum C-reactive protein; PIC window: pulmonary infection control window; RICU: respiration and intensive care unit

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1. Introduction

Ventilator-supporting therapy is one of the primary means for treating the patients affected with acute exacerbation of chronic obstructive pulmonary disease (AECOPD) complicated by acute respiratory failure (ARF). In China, over 80% of AECOPD cases present as a result of bronchial-pulmonary infection [1,2]. In accordance with the different extents to which an assisted respiration support is given to the patients, there are two therapies applied clinically: non-invasive (NIV) ventilator support and invasive (IV) ventilator support. Although the former is increasingly suggested as a primary option follow various kinds of guidelines, the latter (invasive) therapy has also developed to be an efficient method under certain conditions, especially for the patients who are diagnosed with severe AECOPD or COPD followed by pneumonia. The implementation of invasive ventilator-assisted support to patients with AECOPD complicated by ARF does work well to

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quickly open the airway to relieve airway spasm, destroy carbon dioxide retention or severe hypercapnia, improve oxygenation, and promptly rectify ARF [3,4]. This therapy in an application, however, would give rise to an increase in alveolar pressure, causing pneumothorax to happen in a greater likelihood. The incidence of pulmonary infection, upper gastrointestinal bleeding, ventilator-associated pneumonia, and ventilator dependence will also increase [5–7] at the same time. Nevertheless, in the case where early extubation is conducted, there will be some other problems concerned, such as incomplete relief of ARF, and increased incidence of endotracheal intubation, etc. Therefore, it is of great importance to determine the optimum timing of sequential invasive-noninvasive ventilator switching at all time [8,9]. Previously, the judgment of the switch point of sequential invasive-noninvasive ventilator therapy mostly relied on the operator's personal clinical experience or the theoretical guidance of pulmonary infection control (PIC) window [10,11]. The PIC window on the other hand was described as a temporary period of controlled lung infection following artificial airway reconstruction, sputum drainage, and antibiotic application [12], which had some shortcomings including long withdrawal time, high pulmonary infection rate, and low tolerability for the patients. Up to date, the studies have indicated that serum PCT is the primary serum biological marker for determining the severity of illness in patients with COPD [13,14]. The level of serum PCT will not only mark the inflammatory response to bacterial infection but also demonstrate the oxidative stress in one's body. It can change rapidly in a short period, correlated with the illness severity of the patients with AECOPD to some extent [15]. However, It is still not clear yet whether the application of PCT changing rate could be helpful to identify the switch point of transitioning and weaning in the patients from invasive to noninvasive mechanical ventilation [16,17]. The purpose of this study is to put forward the index of PCT change rate and explore the value of determining the time point of reasonable weaning during mechanical ventilation for the patients with AECOPD complicated with ARF according to the change rate of serum PCT levels.

2. Study objects and methods

2.1. Objects

A total of 140 patients with AECOPD complicated with ARF and coma were enrolled from June to December 2018, including 70 males and 70 females at the age of 63.16 ± 3.19 on average. The diagnosis of chronic obstructive pulmonary disease is in line with what is stipulated for AECOPD by the Respiratory Branch of the Chinese Medical Association in 2017. The criteria supporting the judgment of ARF included $PaCO_2$ > 45 mmHg or PaO_2 < 60 mmHg. The patients admitted for the study should be diagnosed with: a) AECOPD [18], b) ARF [19], and c) be in a state of unconsciousness or coma. And those in other cases as follows should be excluded from the study: a) malignant pulmonary tumor or interstitial lung disease, b) severe hepatorenal insufficiency, c) severe systemic disease and connective tissue disease, d) systemic bacterial infection in other parts. This study has been approved by the local hospital research ethics committee, and all the treatment plans have been informed to the patients and their families with consent obtained the forms signed in the end.

2.2. Grouping

All of the patients were given urgent treatment under invasive ventilator support after admission. After the patients were conscious, they were weaned by SIMV +PSV Mode according to the conventional invasive ventilation method, and then switched to PSV mode. The minimum required parameters of weaning for all patients were as follows: gradually reduce the frequency of SIMV to eight times/min, PSV level to 12 cmH_2O, and PEEP level to 5 cmH_2O. If the condition remained stable for the patient, the clinicians

Table 1. Comparison of baseline clinical data between the two groups.

Group	n	Gender (M) n(%)	Age (years)	Body mass index (Kg/m^2)	Prior exacerbations (times/year)	Respiratory rate (times/min)	Heart rate(times/min)	Duratiton (years)
Study group	70	43 (61.43)	63.37 ± 5.84	26.83 ± 2.09	2.86 ± 1.44	35.87 ± 4.90	127.86 ± 10.94	23.19 ± 5.36
Control group	70	41 (58.57)	63.10 ± 5.72	25.95 ± 2.37	2.90 ± 1.37	36.13 ± 5.32	131.05 ± 12.37	24.05 ± 4.87
t	-	0.784	0.905	0.750	0.873	0.698	0.992	0.963
P	-	*>0.05*	*>0.05*	*>0.05*	*>0.05*	*>0.05*	*>0.05*	*>0.05*
Group	n	Glasgow coma scale	PH	Comorbidities, n(%)				
				OSAS	asthma overlap	Hypertension	Diabetes mellitus	Cardiopathy
Study group	70	8.75 ± 1.04	7.18 ± 0.09	14 (20.00)	3 (4.29)	8 (11.42)	9 (12.86)	5 (7.14)
Control group	70	8.90 ± 0.99	7.19 ± 0.11	13 (18.57)	5 (7.14)	7 (10.00)	10 (14.29)	4 (5.71)
t	-	0.974	0.879	0.690	0739	0.903	0.672	0.768
P	-	*>0.05*	*>0.05*	*>0.05*	*>0.05*	*>0.05*	*>0.05*	*>0.05*

considered how to wean and extubate According to the different withdrawal methods, the patients were divided into a study group (n = 70) and a control group (n = 70). Before treatment, the differences between the two groups are of statistical significance in terms of gender, age, course of the disease, Glasgow coma score, PH, respiratory rates, heart rates, concomitant basic diseases, and other demography data ($p > 0.05$), *see* Table 1.

2.3. Procedures

After admission, 3 ml of radial venous blood was drawn from each patient in these two groups on an empty stomach in the morning every day. The circulating PCT concentrations were detected through the Elecsys BRAHMS immunoassay (Roche Diagnostics, Mannheim, Germany). The serum tumor necrosis factor-a (TNF-a) and interleukin-6 (IL-6) were measured by use of the enzyme-linked immunosorbent assay (Elisa), and so was the level of C-reactive protein(CRP) by the immune turbidimetry, the ratio of total leukocyte to neutrophil by the automatic hematology analyzer, and the levels of $PaCO_2$, PaO_2, and Lac by the automatic blood gas analyzer. The change rate of serum PCT level at different time points was calculated based on the data obtained on the first day after admission as the reference line. The patients of the study group experienced a change rate of serum PCT level exceeding 50% in 24 hours, which was judged as a case where the patients could be treated by discarding the tracheal intubation and converting from invasive ventilator support to sequential noninvasive ventilation support. In comparison, the optimum time of withdrawal from invasive ventilator support for the patients in the control group was properly determined with the coming-up of the 'pulmonary infection control (PIC) window' during hospitalization. The PIC window diagnosis conforms to the 1st edition of 'Intensive Care Medicine' compiled by the Chinese Medical Association's Critical Medicine Branch in 2017, whose diagnostic criteria are as follows: a) signification absorption of pulmonary inflammatory exudative lesions on X-ray film, b) reduced airway secretion, c) thinness of sputum and powerful expectoration, d) no fever, e) decrease of peripheral white blood cell count, and f) reduced ventilator support.

2.4. Clinical indexes

Comparisons were made between the two groups of patients in terms of the time of invasive ventilation support, total mechanical ventilation support time, the incidence of ventilator-associated pneumonia, 48-hour reintubation rate, the incidence of upper gastrointestinal bleeding, respiratory critical illness hospitalization time, total hospitalization time, RICU treatment cost, total treatment cost, and clinical mortality. The 48-hour reintubation rate refers to the proportion in which the patients were given endotracheal intubation mechanical ventilation support again within 48 hours due to the fact that their conditions had deteriorated to the extent that ARF occurred after the first invasive ventilation support treatment. The diagnosis of ventilator-associated pneumonia follows the guidelines for the diagnosis and treatment of hospital-acquired pneumonia and ventilator-associated pneumonia [20]. Moreover, the invasive ventilation support time refers to the total days during which endotracheal intubation was performed, further invasive ventilator support treatment elapsed, and intubation was standby (d). And upper gastrointestinal bleeding refers to the indwelling gastric tube and extraction of gastric juice. The gastric juice is generally tested positive for occult blood.

2.5. Statistical analysis

The SPSS19.0 statistical software was used for data analysis. The measurement data were analyzed by means of Student's *t*-test, and expressed as mean ± standard deviation, while the enumeration data were compared by virtue of the χ^2 test, and represented by percentage (%). $P < 0.05$ indicated that the difference is of statistical significance.

3. Results

3.1. Comparisons of serum CRP, TNF-a, and IL-6 levels between the two groups before and after treatment

The differences in the levels of serum CRP, TNF-a, and IL-6 between the two groups were of no statistical significance before treatment ($p > 0.05$), but not after treatment ($p < 0.05$) since the levels of CRP, TNF-a, and IL-6 in the study group were lower than those in the control group. *See* Table 2.

Table 2. Comparison of the levels of serum CRP, TNF-a, and IL-6 between the two groups.

Group	n	TNF-α (μg/L)		CRP (mg/L)		IL-6 (pg/ml)	
		Before T	After T	Before T	After T	Before T	After T
study group	70	45.92 ± 4.37	25.57 ± 6.10[a]	29.87 ± 2.45	8.26 ± 1.71[a]	57.09 ± 4.17	29.53 ± 4.81[a]
control group	70	48.26 ± 5.36	35.71 ± 5.83[a]	30.73 ± 3.83	15.93 ± 3.76[a]	59.04 ± 5.21	37.04 ± 5.36[a]
t	-	1.504	10.050	1.583	15.543	1.561	8.725
P	-	0.092	<0.000	0.116	<0.000	0.067	<0.000

T: treatment. a: there was a significant difference before and after treatment ($p < 0.05$).

Table 3. Comparison of blood gas analysis indexes between the two groups before and after treatment.

Group	n	PaCo2(mmHg) Before T	PaCo2(mmHg) After T	PaO2 (mmHg) Before T	PaO2 (mmHg) After T	Lac (mmol/L) Before T	Lac (mmol/L) After T
study group	70	98.78 ± 10.52	53.80 ± 5.53[a]	71.39 ± 4.45	94.38 ± 2.35[a]	3.27 ± 0.53	1.78 ± 0.37[a]
control group	70	102.53 ± 8.78	51.65 ± 4.29[a]	73.73 ± 3.83	95.48 ± 3.21[a]	3.31 ± 0.48	1.80 ± 0.45[a]
t	-	1.436	1.280	1.357	0.904	0.468	1.804
P	-	0.136	0.151	0.215	0.318	0.641	0.390

T: treatment. a: there was a significant difference before and after treatment ($P < 0.05$).

3.2. Comparisons of blood gas analysis indexes between the two groups before and after treatment

Compared with the indexes before the treatment, it is found that the $PaCO_2$ level declined, the PaO_2 level elevated, and the serum lactic acid level fell after treatment. There was a significant difference in each of the two groups ($p < 0.05$). Furthermore, both before and after treatment, there was no significant difference in PaO_2 and Lac between the two groups ($p > 0.05$). Although the $PaCO_2$ levels of the patients in the study group rose slightly, there was still no significant difference between the two groups ($p > 0.05$). See Table 3.

3.3. Comparisons of clinical indexes

After comparing the data collected from the two groups in terms of invasive ventilation support time, total mechanical ventilation support time, the incidence of ventilator-associated pneumonia, 48-hour reintubation rate, the incidence of upper gastrointestinal bleeding, hospitalization time for critical respiratory illness, total hospitalization time, RICU treatment cost, total treatment cost and mortality, all the above for the patients in the study group were lower than those in the control group. The differences between the two groups were concluded to be of statistical significance ($p < 0.05$). *See* Table 4.

4. Discussion

COPD, as a common chronic respiratory disease in clinical practice, is also one kind of lung disease at a high rate of incidence clinically, manifesting a decline in lung function over time [21,22]. Some of the patients may even be obsessed with recurrent clinical symptoms, whose life quality is affected in a large part [23–25]. As shown by epidemiological data, AECOPD is one of the most common diseases among the inpatients in the respiratory and critical diseases department of the hospital [26], and ARF is the most common complication with the AECOPD patients. When it comes to the severe cases, most of the patients often appear to be delirious, and some may lose consciousness to be in a state of coma. Even worse, this may imperil their lives [27]. A ventilator-assisted support therapy is the primary method suitable for treating patients with ARF. Depending on the different extents of using assisted respiratory support measures, there are two treatment methods in clinical practice: one is invasive respirator-assisted ventilation, and the other noninvasive respirator-assisted ventilation [28,29]. Indwelling endotracheal intubation for mechanical ventilation can effectively dilate the airway of spastic obstruction, reduce carbon dioxide retention, improve the state of ventilation and oxygenation, and promote the rapid improvement of the patients' conditions [30]. Although invasive mechanical ventilation is the primary approach of treatment for the patients with ARF in a state of unconsciousness, it does not work well to the patients with COPD

Table 4. Comparison of clinical efficacy between the two groups.

Group	n	invasive ventilation support time (d)	whole mechanical ventilation support time (d)	the incidence of ventilator-associated pneumonia, n (%)	the incidence of upper gastrointestinal bleeding, n (%)	48-hour reintubation rate, n (%)
study group	70	2.10 ± 1.02	6.90 ± 1.65	2 (2.86)	3 (4.29)	4 (5.71)
control group	70	4.53 ± 1.28	8.99 ± 1.61	11 (15.71)	9 (12.86)	3 (4.29)
t or x^2	-	12.42	7.585	2.054	2.942	2.679
P	-	*< 0.000*	*< 0.000*	*< 0.05*	*< 0.05*	*> 0.05*
Group	n	RICU Hospitalization time (d)	total hospitalization time (d)	RICU treatment cost (thousand CNY)	Total treatment cost (thousand CNY)	mortality, n(%)
study group	70	2.25 ± 0.87	8.70 ± 1.38	6.89 ± 2.65	10.98 ± 1.76	2 (2.86)
control group	70	5.52 ± 2.41	11.48 ± 3.09	11.35 ± 3.06	14.79 ± 3.73	3 (4.29)
t or x^2	-	10.68	6.873	9.218	7.729	0.673
P	-	*< 0.000*	*< 0.000*	*< 0.000*	*< 0.000*	*> 0.05*

because the functions of their airway structural defense barrier would be attenuated with a higher risk of bacterial infection due to the existence of irreversible airway obstruction lesions, reduction of mucosal surface cilia, mucosal hyperemia and edema, and mucous glandular cell hyperplasia and hypertrophy [31,32]. Apart from that, since the patients with COPD are also affected by long-term malnutrition, unsatisfactory development of respiratory muscles, and abatement of physical strength, it is more likely for them to become heavily dependent on ventilators so that there is much more difficulty in taking away the assisted respiratory equipment after invasive mechanical ventilation support treatment. In view of the fact that long-term use of invasive ventilator support measures could aggravate pulmonary infection, and lengthen the ventilator's standby time, which in consequence would increase the probability of ventilator dependence and other risks, it is of great concern clinically to make every effort to minimize the time of invasive ventilator support [33]. At present, the sequential invasive-noninvasive respirator-assisted ventilation has already been developed as the primary approach for treating patients with AECOPD complicated with ARF [34,35]. In the past, the time point of conversion between invasive and noninvasive ventilator support measures was mainly decided by the doctors based on their clinical experience, which, however, is still lacks of quantitative parameters to support such a decision due to the differences among individuals. Over the last few years, some studies have come up with the concept of 'pulmonary infection control window,' pointing out that using 'PIC window' as the switch point of invasive-noninvasive ventilator transferring could significantly reduce the occurrence of ventilator-associated pneumonia and other related complications [36,37]. Some clinical practice has also validated that the relying-on of PIC window does reduce the patients' reintubation rate within 48 hours. However, since taking the PIC window as the switch point requires a comprehensive analysis of various subjective and objective factors, the clinical data acquisition is tedious, toilsome, and time consuming [38]. This in fact will give rise to a problem of time delay, which will not be conducive to the timely adjustment of treatment. According to the statistics in some studies, that the 'PIC window' was used as the switch point of weaning and extubation in the process of sequential invasive-noninvasive ventilation would remarkably prolong the intubation standby time of the patients, and increase the incidence of ventilator-associated pneumonia. Some patients may have great difficulties in weaning ventilators owing to their heavy dependence on them [39]. In most cases, patients with COPD have a long medical history with some problems of alveolar expansion, emphysema, and airway structural remodeling, whose organic structural defense functions are destroyed to various extents. Therefore, their respiratory tracts are more susceptible to the external environment, inducing bacterial or viral infections as a result. The invasive endotracheal intubation also damages the respiratory structure barrier and increases the probability of infections. At the same time, because COPD is a chronic long-term deterioration process, during which with the increasing respiratory burden, the patients will gradually lose weight, and their respiratory muscle strength will decrease. Once intubated, it would be more common for the patients to evolve with more dependence on the ventilator. Therefore, identifying an optimum switch point to abandon an invasive ventilator has become the focus of clinical attention.

Under normal circumstances, PCT is a polypeptide of a small molecular weight substance secreted by thyroid C cells. Its serum concentration in vivo is tiny with secretion level being constant or stable, which is unlikely to be disturbed by renal function, age, gender, and other factors [40,41]. On the occasion when the body is complicated with bacterial infection or severe systemic reaction syndrome, the tissues in the whole body will secrete PCT that is the main biological marker to distinguish bacterial or viral infection. Studies have shown that the significant inclination of PCT level can be used as a biomarker to indicate the existence of bacterial infection [42]. On the other hand, the fluctuating PCT level during a certain period time can guide the clinical use of antibiotics to patients with AECOPD. It also demonstrated in the previous studies that the utilization of PCT levels, in comparison with the empirical use of antibiotics, to guide the treatment of patients with AECOPD could significantly shorten the time of taking antibacterial drugs. In recent years, some studies have further shown that the increase of PCT level is also an indicator of oxidative stress and inflammatory immune response in patients' body [43,44]. As to the patients who have just received a major surgery to suffer severe trauma, their tissue cells in the whole body would secrete PCT, resulting in a significant rise in PCT level. Most of the patients with AECOPD complicated with ARF have acute systemic inflammatory response syndrome at the same time. The concentration of PCT is positively correlated with the severity of the illness in a linear model. Because it is convenient to detect PCT besides sickbeds, and its reproducibility is precise as well, this study proposes to use the change rate of the PCT algorithm over a period of time as an indicator for identifying the optimum switch point of withdrawing invasive ventilators. Based on the comprehensive analysis of clinical significance, it was found in the study that the indexes obtained from the patients in the study group were apparently lower than those for the patients in the control group in terms of invasive ventilation support

time, total mechanical ventilation support time, incidence of ventilator-associated pneumonia, 48-hour reintubation rate, the incidence of upper gastrointestinal bleeding, hospitalization time for critical respiratory illness, total hospital stay time, RICU treatment cost, total treatment cost of the hospitalization and mortality. The result has proved that it is reliable to use the change rate of PCT algorithm to assist in determining the switch point when the sequential invasive-noninvasive ventilator support therapy is being applied to the patients with AECOPD complicated with ARF. After a further blood gas analysis, it has been shown that the resulted data turned for better for the patients in both groups after ventilator-assisted ventilation treatment. Although the extent of improvement of $PaCO_2$ in the study group was smaller than that in the control group, such a difference was of no statistical significance between them. In the meanwhile, the studies in the past also showed that patients with COPD are fairly capable of tolerating hypercapnia to some extent due to their long-term carbon dioxide retention. Therefore, the effort of normalizing $PaCO_2$ in clinical practice is rarely regarded as a decisive factor to determine whether the patient should be withdrawn from the ventilator or not. The scientific basis, on which the change rate of the PCT algorithm is taken as evidence to support the withdrawal of ventilator assistance in treating the patients with AECOPD complicated with ARF, might be related to the fact that PCT concentration could reflect the state of oxidative stress in a part. Serum CRP, TNF-a, and IL-6 are all common parameters of the clinical inflammatory response process, and their elevated levels reflect the severity of microinflammation in the body [45,46] This is in close relation with oxidative stress and systemic tissue inflammatory response syndrome. This study showed no significant difference in the levels of serum CRP, TNF-a, and IL-6 between the two groups before treatment. However, all the three levels above for the patients in the study group were lower than those in the control group. The difference between them was of statistical significance. Furthermore, the study results also proved that severe oxidative stress and systemic tissue inflammatory response syndrome still exist in patients with AECOPD complicated with ARF. The elevation of the PCT algorithm in the early stage mostly reflects the level of immune inflammation, which is closely related to the oxidative stress state in the patients' bodies. At present, more emphasis of the research on the relationship between PCT and AECOPD are put on applying PCT algorithm to guiding the use of clinical antibiotics rather than some other aspects [47]. Therefore, the results obtained from this study will be of some help to guide how to select the switch point when a transfer should be properly made between invasive and noninvasive sequential ventilation supports to the patients with COPD, and provide quantifiable and objective indicators for clinical needs, minimizing the inconsistency of subjective judgment among different doctors. Yet there is one deficiency with regard to this study, that is, samples having been taken are in such a small size that the conclusion needs to be further explored.

Several key points of the study should be taken into account. First, For most patients with AECOPD and respiratory failure, noninvasive ventilation is still the first choice. As is known to all, invasive mechanical ventilation is not the standard of care for AECOPD. It is rather the NIV, which has become the standard either by its effectiveness or by the prevention of other clinical episodes. Second, whether the patient with AECOPD is conscious or not is the main criterion to decide whether to use invasive or noninvasive mechanical ventilation therapy. In other words, in general, coma is a relative contraindication of noninvasive ventilation. For patients in a coma state, even if the procalcitonin level decreased significantly, whether to wean or not also needs comprehensive evaluation. Fortunately, all the patients in the group recovered their consciousness within 24 hours, and they were conscious before extubation. It is to say, they can adapt to the treatment of noninvasive assisted ventilation. Third, part of the patients enrolled in this study was complicated with pulmonary infection. Bronchial-pulmonary infection might lead to the aggregation of COPD symptoms and accelerate the progression of acute respiratory failure. Procalcitonin, as a biomarker of bacterial infection, plays an important role in the diagnosis and treatment of pneumonia. Perhaps, this might cause some selection bias. For the index of procalcitonin change rate proposed in this study, previous studies have also obtained a lot of basis in the study of sepsis [48,49]. When one kind of disease causes a systemic inflammatory reaction, the whole body tissue and cells can secrete procalcitonin, leading to a rapid and abrupt rise in the level of procalcitonin in circulating blood. Once the patient's condition improves, the level of procalcitonin will quickly fall back. We acknowledge that it is a very complicated topic to master the ideal time point of successful weaning for AECOPD patients. It would be difficult to assimilate that the procalcitonin shift alone could discriminate weaning and even less extubation. One of the advantages of this study might be the kinetic index of procalcitonin is proposed firstly in this field. This is urgently necessary for clinicians. Some clinicians would be tempted to have a discriminative biomarker to strengthen decision-making power. The novel use of procalcitonin is still interesting and if having an appropriate setting, it may be useful in clinical practice [50]. Maybe, if it could be integrated with the weaning criteria, we may come near to some convincing conclusions.

We will continue in-depth in future work, and constantly improve the clinical significance of the procalcitonin kinetic.

To sum up, some clinicians would be tempted to have a discriminative marker to strengthen decision-making power on the weaning from invasive to non-invasive mechanical ventilation. this paper looks at a novel point about using the halving of procalcitonin as a cue of the question. The study has shown that when the change rate of serum PCT level > 50% rather than the routine PIC window is taken as the optimum switch point of weaning time in the application of sequential mechanical ventilation therapy for the patients with AECOPD complicated with ARF and coma, it will significantly reduce the time of invasive ventilator-assisted support, lower down the incidence of ventilator-associated pneumonia and upper gastrointestinal bleeding as well, shorten the stay time in RICU and the total hospitalization time, and cut down the patient's treatment cost. After the change rate of serum PCT level >50% selected for the patients to receive treatment in sequence from invasive to non-invasive ventilation support, both the incidence of reintubation within 48 hours and the clinical mortality do not increase at all, Although one source of weakness in this study which could have affected the measurements of procalcitonin kinetic was that we should provide much more detailed information to ensure that the research conclusion does not produce the conclusion bias caused by confounding factors, which include defining the population, the interventions, including the ventilatory parameters for both invasive and non-invasive ventilation, and so on, this approach is worth recommending for application in clinical practice.

Contributors

Hao-hua LIN proposed the study and wrote the first draft. All of the authors contributed to the study's design and interpretation and to further drafts and provided their final approval for the completed manuscript.

Disclosure statement

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

Ethical approval

The Ethical Committee approved the present study of Rongcheng People's Hospital in ShanDong Province.

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