

# The guiding significance of NT-proBNP and PCT levels in mechanical ventilator of patients with chronic respiratory failure

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**Abstract. – OBJECTIVE:** To analyze the guiding significance of N-terminal pro-brain natriuretic peptide (NT-proBNP) and procalcitonin (PCT) level in mechanical ventilator used for patients with chronic respiratory failure.

**PATIENTS AND METHODS:** Eighty-two patients with simple chronic respiratory failure who were treated by mechanical ventilator were selected for this study. They were treated offline after they reached the standards of spontaneous breathing trial, and were divided into two groups: 1- the successful offline group with 59 patients and 2- the failure group with 23 patients. Differences of NT-proBNP and PCT levels, oxygenation index, average heart rate and mean arterial pressure between two groups were compared.

**RESULTS:** The NT-proBNP and PCT levels in the failure group were significantly higher than those in the success group, while oxygenation index was significantly lower in the success group. All differences were statistically significant ( $p < 0.05$ ). Comparison of average heart rate and mean arterial pressure between two groups showed no statistically significant difference ( $p > 0.05$ ).

**CONCLUSIONS:** Through multi-factor regression analyses we observed that NT-proBNP and PCT levels were independent risk factors for guiding the success rate of offline ( $p < 0.05$ ). Spontaneous breathing trial in combination with NT-proBNP and PCT levels improved the success rate of offline.

Key Words:

NT-proBNP, PCT, Chronic respiratory failure, Mechanical ventilator, Offline.

## Introduction

Early online and early offline are basic principles of assisted mechanical ventilation<sup>1</sup>. Too early offline will increase respiratory problems; while too late offline will lead to ventilator dependence and the occurrence of ventilator-related pneumonia<sup>2</sup>. Currently, offline testimony, which has

a high level of risk, includes vital signs, biochemical indexes and spontaneous breathing trial<sup>3</sup>. Prior studies showed that about 40% patients had difficulties in offline<sup>4</sup>. Currently, positive pressure ventilation (heart and lung mutual interaction) is the most popular method of mechanical ventilation. It was shown<sup>5-7</sup> that the level of N-terminal pro-brain natriuretic peptide (NT-proBNP) increased significantly, and it was relevant to prognosis. As a brand-new biological marker, procalcitonin (PCT) has important applications in the infection and inflammatory reactions<sup>8</sup>. This study presents the guiding significance of NT-proBNP and PCT levels in mechanical ventilator for patients with chronic respiratory failure.

## Patients and Methods

### Patients

Eighty-two patients who were diagnosed with simple chronic respiratory failure in our hospital between August 2014 and August 2015 were continuously selected to participate in this study. Patients with cardiac respiratory failure, central respiratory failure, trauma, post-operation, serious infection, acute respiratory distress syndrome, autoimmune disease, serious functional disorders of heart, liver and kidney and malignant tumors were all excluded. This research obtained the approval from Ethics Committee of our hospital and informed consent from patients and their families. According to standard medical treatment plans, all patients were treated by assisted mechanical ventilation treatment testimony, and offline was carried out after patients reached spontaneous breathing trial standards. According to the comprehensive judgment of relevant parameters such as clinical manifestations and vital signs of patients 48 hours after offline,

patients were divided into success group (59 patients) and failure group (23 patients). In success group, there were 38 males and 21 females, with ages ranging from 53 to 78 years with the average age of (66.3±10.5) years; 24 patients with type I respiratory failure and 35 patients with type II respiratory failure. The courses of disease ranged from 1 to 12 years with an average course of 6.4 years. In the failure group, there were 15 males and 8 females, with ages range from 52 to 83 years with the average age of (65.6±12.3) years. There were 10 patients with type I respiratory failure and 13 patients with type II respiratory failure. The courses of disease ranged from 1.5 to 13 years with the average course of 6.8 years. The comparisons of gender, age, respiratory failure types and courses of disease revealed no statistical significance ( $p>0.05$ ).

The standards of spontaneous breathing trials were<sup>9</sup>: (1) we used appropriate oxygenation, with a concentration of oxygen inhalation  $\leq 40\%$ . Positive end-expiratory pressure was 5 to 10 mmH<sub>2</sub>O, oxygenation index was  $\geq 150-300$ ; (2) the cardiovascular system was stable. Heart rate was  $\leq 140$  per minute, blood pressure was stable, and no vasoactive drugs were used; (3) body temperature was below 38°C; (4) no respiratory acidosis was observed; (5) hemoglobin was 8 to 10 g/L; (6) mental activities were relatively good, sober, and the continuous application of depressant was not necessary; (7) metabolism was stable, and the electrolytes were basically normal.

The standards of successful offline<sup>10</sup>: (1) patients could breathe spontaneously 48 hours after the removal of the orotracheal catheter (2) construction of artificial ventilator and mechanical ventilation was not necessary. Otherwise, it was regarded as a failure.

### **Observation Indexes and Detection Methods**

The differences of NT-proBNP and PCT levels, oxygenation index, average heart rate and mean arterial pressure between two groups before offline were compared.

The detection methods of NT-proBNP and PCT: 3 ml venous whole blood was transferred into EDTA anticoagulative tube. Triage BNP machine (American Biosite, San Diego, CA, USA) was used, and double antibody-sandwich ELISA method was adopted for detection. We strictly followed operating instruction, and the detection range was 5 to 5000 pg/ml. The principle was combining specific antibodies with solid phase

carrier to form solid phase antibodies; then, combining corresponding antigens in detected serum to form an immune complex. Enzyme antibody conjugates were added, antigens were combined in an immune complex to form enzyme labeled antibody-antigen-solid phase antibody complex. Substrates were added, and the content of antigens was measured. PCT kit was provided by Roche Diagnostics Products Co., Ltd. (Shanghai, China), and electrochemical luminous double antibody sandwich method was used for detection. Monoclonal PCT antibodies of biotinylation and monoclonal PCT antibodies marked by Ruthenium complexes were incubated first to form an antigen-antibody sandwich complex. Then, magnetic beads particles of packaged chain enzyme avidin were added for further incubation, antigen-antibody complex and magnetic beads were combined with biotin and streptomycin interactions. Furthermore, reaction fluid was absorbed into detection cell, and magnetic beads were attached to the electrode surface through electromagnetic interaction. Those not combined with magnetic beads were removed by cleaning fluid; electricity was added to electrodes to make complex glow chemically. Luminous intensity was measured by multiplier phototube, and detection results obtained from the software automatically.

### **Statistical Analysis**

All data were analyzed using SPSS 19.0 statistical software (SPSS Inc., Chicago, IL, USA), measurement data were represented as mean±standard deviation, and t-test was adopted for comparison among groups. Enumeration data were represented by cases or percentages, X<sup>2</sup>-test was used for comparison among groups, Logistic examination was employed for multi-factor regression analysis, and  $p<0.05$  was considered statistically significant.

## **Results**

### **The Comparisons of Detection Indexes**

The NT-proBNP and PCT levels in the failure group were significantly higher than those in the success group, while oxygenation index was significantly lower in the failure group. All differences were statistically significant ( $p<0.05$ ). Comparisons of average heart rate and mean arterial pressure between two groups showed that the differences had no statistical significance ( $p>0.05$ ) (Table I).

**Table I.** The comparisons of detection indexes.

Groups	NT-proBNP (pg/ml)	PCT (ng/ml)	Oxygenation Index	Average heart rate (min)	Mean arterial pressure (mm Hg)
Success group	465.2±43.6	0.34±0.03	243.7±35.2	85.4±7.2	93.4±8.3
Failure group	769.8±75.4	0.79±0.05	176.8±42.6	89.7±6.9	90.7±7.8
<i>t</i>	5.627	5.764	4.923	0.524	0.239
<i>p</i>	0.032	0.031	0.037	0.168	0.463

### Multi-factor Regression Analysis

Gender, age, respiratory failure types, courses of disease, NT-proBNP and PCT levels, oxygenation index, average heart rate and mean arterial pressure were included in multi-factor regression analysis. Results showed that NT-proBNP and PCT levels were independent risk factors of guiding the success of offline ( $p < 0.05$ ) (Table II).

### Discussion

The purpose of mechanical ventilation is to rectify the lack of O<sub>2</sub> and retention of CO<sub>2</sub>. Among other purposes we can add rectifying ventilator fatigue, ensuring the safety of operative period, ensuring the safety of depressant and muscle relaxant and changing the relationship between pressure and volume. For patients with simple chronic respiratory failure, early effective respiration support could rapidly remedy the oxygenation disorders, acid-base imbalance and metabolic disorders<sup>11</sup>. With the gradual decline in patients' mechanical ventilation level and the gradual spontaneous respiration recovery, the testimony and opportunity of offline can be assessed<sup>12</sup>.

Based on standards of spontaneous breathing trial which is widely applied in current clinical researches, the final successful offline rate is 71.95%, which is not ideal. Our results revealed that the NT-proBNP and PCT levels in the failure group were significantly higher than those in the success group, while oxygenation index was significantly lower. Comparisons of average heart rate and mean arterial pressure between two groups showed that the differences were statistically significant. Through multi-factor regression analyses, we found that

NT-proBNP and PCT levels were independent risk factors in guiding the success of offline. In the offline process, due to the evacuation of positive pressure ventilation, the intrapleural pressure declines. This decline can reduce the pressure of atrium dextrum and increase the volume of returned blood, which can induce or aggravate functional insufficiency of the right heart. During the process of mechanical ventilation evacuation, patients are usually switched from assisted ventilation to spontaneous respiration while the intrapleural pressure reduces. This change increases the difference between intravascular pressure and intrapleural pressure, and increases the left ventricular afterload<sup>13</sup>. Moreover, it can reduce the atrium dextrum pressure and increase the venous return as well as left ventricular preload, which can induce or aggravate functional insufficiency of the left heart<sup>14</sup>. Furthermore, after offline, neural and humoral regulation disorders are triggered, sympathy is activated, and the levels of adrenaline, renin and natriuretic peptide A surge<sup>15</sup>. It was shown that<sup>16</sup> NT-proBNP could be used as the prognostic indicator for predicting assisted mechanical ventilation of chronic respiratory failure.

In normal conditions, calcitonin is produced by thyroid C cells, while after serious infections it may be secreted from other cells, such as peripheral blood mononuclear cells. The content of PCT in plasma in healthy individuals is very low, inducible secretion is strictly limited, and the contacts between cells play an important role<sup>17</sup>. As a kind of marker with high specificity, the serum concentration of PCT has a good correlation with the severity of the diseases<sup>18</sup>. The occurrence and aggravation of chronic respiratory failure are closely related to pulmonary infections, and assisted mechanical ventilation is also a very strong stres-

**Table II.** Multi-factor regression analysis.

Factors	$\beta$	Wald	<i>p</i>	OR	95% CI
NT-proBNP	0.127	6.412	0.019	2.745	1.623-4.023
PCT	0.236	6.329	0.022	2.563	1.127-5.632
Oxygenation Index	1.524	1.234	0.538	0.748	-0.234-2.427

sor<sup>19</sup>. Prior studies revealed that<sup>20</sup> PCT, as an inflammatory marker, was significantly correlated to the prognosis of the disease.

## Conclusions

Spontaneous breathing trial in combination with NT-proBNP and PCT levels can improve the success rate of offline.

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## Conflicts of interest

The authors declare no conflicts of interest.

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