Fluctuations of driving pressure during mechanical ventilation indicates elevated central venous pressure and poor outcomes

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Abstract
Inappropriate mechanical ventilation may induce hemodynamic alterations through cardiopulmonary interactions. The aim of this study was to explore the relationship between airway pressure and central venous pressure during the first 72 h of mechanical ventilation and its relevance to patient outcomes. We conducted a retrospective study of the Department of Critical Care Medicine of Peking Union Medical College Hospital and a secondary analysis of the MIMIC-III clinical database. The relationship between the ranges of driving pressure and central venous pressure during the first 72 h and their associations with prognosis were investigated. Data from 2790 patients were analyzed. Wide range of driving airway pressure (odds ratio, 1.0681; 95% CI, 1.0415–1.0953; \( p < 0.0001 \)) were independently associated with mortality, ventilator-free time, intensive care unit and hospital length of stay. Furthermore, wide range of driving pressure and elevated central venous pressure exhibited a close correlation. The area under receiver operating characteristic demonstrated that range of driving pressure and central venous pressure were measured at 0.689 (95% CI, 0.670–0.707) and 0.681 (95% CI, 0.662–0.699), respectively. Patients with high ranges of driving pressure and elevated central venous pressure had worse outcomes. Post hoc tests showed significant differences in 28-day survival rates (log-rank (Mantel–Cox), 184.7; \( p < 0.001 \)). In conclusion, during the first 72 h of mechanical ventilation, patients with hypoxia with fluctuating driving airway pressure have elevated central venous pressure and worse outcomes.

Keywords
fluctuation, driving pressure, central venous pressure, outcome

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Introduction
Despite a lot of attention focused on respiratory mechanism during mechanical ventilation, little data were found about the interaction between the respiratory mechanism and hemodynamics in changing patients’ outcome. Positive pressure mechanical ventilation has a favorable hemodynamic effect by increasing the intrathoracic pressure and changing the heart–lung interactions.1,2 The most classic was patients with acute respiratory distress syndrome (ARDS); hemodynamic instability appears to be one of the major determinants of mortality.3 One potential mechanism is the dysfunction of the right ventricle (RV) and pulmonary vasculature.4 As a result, the RV fails to deliver adequate cardiac output to the left-sided circulation, thus resulting in systemic hypoperfusion and multiple organ dysfunction.5

An increasing number of studies have focused on the risk factors for right ventricular dysfunction during mechanical ventilation.6

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Central venous pressure (CVP) monitoring directly measures the right atrial pressure, and without sufficient cardiac compensation, a significantly increased CVP could serve as an indicator of impending right ventricular dysfunction.7,8 Our previous study has shown that patients with elevated mean airway pressure (Pmean) and elevated CVP (ECVP) had worse outcomes.9 What is more, we have also revealed that ECVP was independently associated with the occurrence of pulmonary hypertension in new onset ARDS.10 Therefore, in this study, we explored the relationship of the airway pressure level during mechanical ventilation with the CVP and other hemodynamic parameters to reveal the effects on patient outcomes.

Methods

Data source

We performed a retrospective study among patients in the Department of Critical Care Medicine of Peking Union Medical College Hospital from May 2013 to December 2017 using the administrative database. We identified patients with hypoxia admitted with invasive mechanical ventilation, and detailed inclusion and exclusion criteria were listed as follows. The Institutional Research and Ethics Committee of the Peking Union Medical College Hospital approved this study for human subjects.

For the limited records of respiratory characteristic measurement, a secondary analysis was conducted with data collected from the MIMIC-III open-source clinical database (version 1.4, released on 2 September 2016), which was developed and is maintained by the Massachusetts Institute of Technology (MIT), Philips Healthcare, and Beth Israel Deaconess Medical Center (BIDMC).11 Information derived from the electronic medical records of 46,476 unique critical care patients admitted to the intensive care units (ICUs) at BIDMC between 2001 and 2012 is included in this free accessible database.11 MIMIC-III data are compliant with the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Use of the MIMIC-III database was approved by the Institutional Review Boards of BIDMC and MIT, and a waiver of informed consent was granted.

Patients

All patients in the database were screened. The inclusion criteria in this study were as follows: (1) hypoxia with an oxygen index (PaO2/fraction of inspired oxygen (FiO2)) <300 mmHg at the time of ICU admission; (2) received invasive volume-controlled or pressure-controlled mechanical ventilation for ≥72 h; (3) with complete medical records including available CVP measurements and other hemodynamic records during the first 72 h; (4) adequate sedation and analgesia with the level of sedation assessed with the Ramsay Sedation Scale (Score 1) or Richmond Agitation-Sedation Scale (Score −5). For patients with multiple ICU stays, only data related to the first ICU admission were considered. The patients who were younger than 18 years old were excluded, measurements of plateau pressure (Pplat) <5 was excluded to avoid the risk that small numbers of record may not truly represent patients’ physiological status.

Outcome

Respiratory parameters were recorded during the first 72 h, and the difference between the Pplat and positive end expiratory pressure (PEEP) was calculated as the driving airway pressure (DP). The range of DP (R-DP) is the difference between its maximum and minimum values.

\[
R - DP = (\text{Pplat} - \text{PEEP})_{\max} - (\text{Pplat} - \text{PEEP})_{\min}
\]

As is shown in our previous study,12 ECVP was correlated with poor outcomes and prolonged treatment in critical care settings. Mean CVP level during the first 72 h after ICU admission was recorded. The clinical data of the patients involved in this study included also respiratory rate (RR), FiO2, PaO2, PaCO2, Plat Pressure, PEEP, heart rate (HR), mean arterial pressure (MAP), Simplified Acute Physiology Score II (SAPS II), Sequential Organ Failure Assessment (SOFA), and Acute Physiology and Chronic Health Evaluation II, and the data were recorded during the first 72 h after ICU admission. All the data used in the statistical analyses were an average of the values collected during the first 72 h after ICU admission as to reflect the actual condition of the patient’s circulatory and respiratory systems and avoid errors. Mortality, ventilator-free time, ICU, and hospital length of stay were analyzed as prognostic outcomes.

Statistical analysis

The unreasonable values were considered missing values, and CVP over 25 mmHg was considered over abnormal outliers and recorded as 25 mmHg. Descriptive analysis was performed. All data are expressed as the mean ± SD or median (25–75th percentiles) unless otherwise specified. For the continuous variables, data were analyzed using the t test. Variables were introduced into a multivariate logistic regression model if significantly associated with mortality. Effect estimates were analyzed using the COX proportional-hazards regression for other prognostic outcome. Discrimination of values was performed using receiver operating characteristic (ROC) analysis using the Hanley–McNeil test. Comparisons of two continuous variables were performed using Pearson’s Correlation Coefficient. Survival curves up to day 28 were estimated using the Kaplan–Meier method, and the log rank (Mantel–Cox) test was used to estimate differences among the predefined groups. All comparisons were two-tailed, and p value <0.05.
was required to exclude the null hypothesis. Statistical analyses were performed using the SPSS 13.0 software package (SPSS, Chicago, IL).

Results

Basic characteristics

Patients. During the study period (from May 2013 to December 2017), a total of 12,395 patients were admitted to Critical Care Medicine department of PUMCH, and 3238 patients with hypoxia based on oxygen index were admitted and underwent invasive mechanical ventilation over 72 h; 2289 among them had adequate sedation and control mode of mechanical ventilation. The patients without detailed respiratory characteristic (n = 1387) were excluded from this study. Finally, except patients without CVP monitor (n = 525), 377 patients were included in this study. Among the 46,476 ICU patients and 61,532 ICU admissions in the MIMIC-III v1.4 databases, a total of 17,219 patients with hypoxia were admitted with invasive mechanical ventilation over 72 h, and 12,361 with adequate sedation and without spontaneous breathing. Among these 12,361 patients, 1413 patients who kept detailed records of respiratory and hemodynamic characteristics, especially Pplat and CVP, were included in this study as illustrated in Fig. 1.

The demographic and clinical characteristics of all patients included in this study after ICU admission are shown in Table 1. The majority of patients were male and most were admitted from the emergency room. Based on mortality, we divided patients into groups of survivors and nonsurvivors. Regarding to etiology of hypoxia, group of survivors were mostly composed of patients with cardiovascular condition, and group of nonsurvivors were patients with sepsis. In terms of respiratory condition, the R-DP, Pplat, PEEP, and RR were significantly higher in nonsurvivors than in survivors. Regarding hemodynamic data, compared with survivors, nonsurvivors had a higher CVP (p < 0.0001) in both databases. The SOFA scores were significantly higher in the nonsurvivor group than in the survivor group.

Risk factors for mortality in mechanically ventilated ICU patients

A multivariate logistic regression analysis was used to examine the possible risk factors for a poor prognosis (Table 2). The variables taken into account were R-DP, CVP, age, RR, FiO₂, PaO₂, PaCO₂, Pplat, PEEP, HR, MAP, SAPS II score, and SOFA score. Finally, R-DP and CVP were included in the regression equation (p < 0.00001). The odds ratio (OR) of R-DP and CVP was 1.0681 (95% CI, 1.0415–1.0953) and 1.0904 (95% CI, 1.0589–1.1228) in MIMIC-III database respectively.

R-DP were associated with mortality

R-DP in the 72 h of ventilation after admitted was also associated with ventilator-free time, ICU, and hospital length of stay (Fig. 2a). The ROC curve was drawn with mortality (Fig. 2b). The area under the curve (AUC) for R-DP was 0.689 (95% CI, 0.670–0.707). The cutoff value of R-DP was 12.4 cmH₂O, based on the maximum Youden index. Based on the cutoff of the R-DP, all the participants were divided into low R-DP group and high R-DP group. Both respiratory and hemodynamic conditions worsened between the low R-DP group and the high R-DP group (Table 3).

Relationships among mortality, CVP, and dynamic driving airway pressure

The Pearson correlation was used to explore the relationship between R-DP and CVP (Fig. 3a). The correlation coefficient was 0.4049 in PUMCH database, and 0.4493 in MIMIC-III database (p < 0.0001). Furthermore, the ROC curve of CVP was also drawn and the AUC was 0.681 (95% CI, 0.662–0.699), the cutoff value of CVP was

![Fig. 1. Flowchart showing step-by-step selection of patients included in the study.](image-url)
Table 1.1. The general characteristics of the patients from PUMCH included in this study.

| Characteristics | PUMCH, n = 377 | MIMIC-III, n = 2413 |
|-----------------|----------------|---------------------|
| Survivors, n = 317 | Nonsurvivors, n = 60 | Survivors, n = 1978 | Nonsurvivors, n = 435 | P |
| Age, yr, median (IQR) | 61.9 (44.1–79.7) | 60.0 (43.7–76.3) | 61.9 (50.5–79.7) | 67.1 (51.3–82.9) | 0.0093 |
| Gender, n (%) | Male 192 (60.6) | 34 (57.6) | Male 1301 (63.8) | 261 (60) | 0.0004 |
| R-DP | 9.7 (4.7–14.7) | 15.8 (8.8–22.8) | 9.7 (4.5–8.7) | 8.0 (5.1–10.9) | <0.0001 |
| CVPmean | 9.5 (7.2–11.8) | 11.4 (8.9–13.9) | 9.5 (7.2–11.8) | 11.4 (8.9–13.9) | <0.0001 |
| PaCO2 | 40.2 (30.4–50.0) | 45.7 (30–61.4) | 42.0 (30.4–50.0) | 45.7 (30–61.4) | <0.0001 |
| RR | 17.6 (14.9–20.3) | 19.2 (16.0–22.4) | 17.6 (14.9–20.3) | 19.2 (16.0–22.4) | <0.0001 |
| Pplat | 21.6 (15.6–26.6) | 24.1 (17.3–30.9) | 21.6 (15.6–26.6) | 24.1 (17.3–30.9) | <0.0001 |
| PEEP | 6.6 (4.5–8.7) | 8.0 (5.1–10.9) | 6.6 (4.5–8.7) | 8.0 (5.1–10.9) | <0.0001 |
| HR | 92.9 (76.9–108.9) | 96.7 (80.2–113.2) | 92.9 (76.9–108.9) | 96.7 (80.2–113.2) | <0.0001 |
| MAP | 79.7 (79.5–99.9) | 89.2 (79.7–98.7) | 79.7 (79.5–99.9) | 89.2 (79.7–98.7) | 0.0001 |
| SOFA | 9.7 (6.4–13.4) | 11.1 (7.9–14.3) | 9.7 (6.4–13.4) | 11.1 (7.9–14.3) | 0.0001 |

R-DP: range of driving pressure; CVP: central venous pressure; RR: respiratory rate; Pplat: plateau pressure; PEEP: positive end expiratory pressure; HR: heart rate; MAP: mean arterial pressure; SAPS II: Simplified Acute Physiology Score II; SOFA: Sequential Organ Failure Assessment; IQR: interquartile range.

Table 1.2. The general characteristics of the patients from MIMIC-III included in this study.

| Characteristics | MIMIC-III, n = 2413 |
|-----------------|---------------------|
| Survivors, n = 1978 | Nonsurvivors, n = 435 | P |
| Age, yr, median (IQR) | 65.1 (50.5–79.7) | 67.1 (51.3–82.9) | 0.0093 |
| Gender, n (%) | Male 1301 (63.8) | 261 (60) | 0.0004 |
| Admission type | Elective 636 (32.2) | 30 (6.9) | 0.0001 |
| | Urgency 43 (2.2) | 11 (2.5) | 0.0001 |
| | Emergency 1299 (65.6) | 394 (90.6) | 0.0001 |
| Initial diagnosis | Sepsis 234 (11.8) | 156 (35.9) | 0.0001 |
| | Respiratory condition 90 (4.6) | 53 (12.2) | 0.0001 |
| | Cardiological condition 1129 (57) | 57 (13.1) | 0.0001 |
| | Digestive condition 166 (8.4) | 76 (17.5) | 0.0001 |
| | Others 359 (18.2) | 93 (21.3) | 0.0001 |
| Comorbidities | Basic pulmonary disease 213 (1.2) | 68 (15.6) | 0.0001 |
| | R-DP 9.9 (4.5–15.3) | 14.0 (7.8–20.2) | <0.0001 |
| | CVPmean 12.5 (8.5–16.5) | 16.6 (10.2–23.0) | <0.0001 |
| | RR 18.6 (15.2–22) | 21.3 (16.9–25.7) | <0.0001 |
| | PaCO2 40.8 (35.6–46) | 39.9 (31.8–48) | 0.0018 |

Discussion

To explore the relationships between mechanical ventilation parameters and RV function, we reviewed the hemodynamic and ventilation parameters during the first 72 h of ICU admission. We found that the nonsurvivors had significantly worse respiratory and hemodynamic disorders than survivors, a wide range of DP and ECVP were risk factors associated with a poor outcome in critically ill patients who received mechanical ventilation. We also found that when the DP ranged widely, the CVP showed a gradual increasing trend as analyzed by Pearson correlation, further indicating the correlation of mechanical ventilation and hemodynamic disturbances, especially in patients with hypoxia.

In patients with ARDS, RV dysfunction, especially acute cor pulmonale (ACP), is associated with high mortality and long-term disability. It still occurs in approximately one of five patients even under protective mechanical ventilation. A clinical risk score based on four variables (pneumonia as the cause of ARDS, driving pressure, PaO2/FiO2 ratio, and PaCO2) has a reasonable discriminatory ability and good calibration for detecting early ACP in the derivation and validation cohorts. DP was recently reported as the venti-
lung distension on pulmonary capillaries and, consequently, on RV afterload and function.

However, RV dysfunction still occurs in ARDS patients who are ventilated according to the lung-protective ventilation. Therefore, we hypothesized that not only the DP itself but also the range of DPs may indicate the range of lung strain, which contributes to the stress placed on pulmonary capillaries. Based on multivariate regression, the R-DP was selected as an independent risk factor for a poor outcome; the OR was 1.0681 (95% CI, 1.0415–1.0953). In addition, the AUC for R-DP was 0.689 (95% CI, 0.670–0.707). This verified that not only the airway pressure itself during mechanical ventilation but also the fluctuation in DP also contributes to poor outcomes. The influencing factors on DP includes, but is not limited to, static compliance of the respiratory system, chest wall elastance, diaphragmatic function, etc. Effect of specific factors and their contribution among fluctuation in DP still need our further study.

### Table 2. Multivariate logistic regression analysis for possible risk factors for prognosis.

| Variable | B   | SE  | p     | OR       | 95% CI for OR |
|----------|-----|-----|-------|-----------|---------------|
| R-DP     | 0.0659 | 0.0129 | <0.0001 | 1.0681 | 1.0415–1.0953 |
| CVP      | 0.0865 | 0.0150 | <0.0001 | 1.0904 | 1.0589–1.1228 |
| Age      | 0.0047 | 0.0054 | 0.3823 | 1.0047 | 0.9942–1.0153 |
| RR       | 0.0867 | 0.0191 | <0.0001 | 1.0906 | 1.0506–1.1321 |
| PaCO₂    | -0.0256 | 0.0114 | 0.0246 | 0.9747 | 0.9531–0.9967 |
| PaO₂     | -0.0114 | 0.0020 | <0.0001 | 0.9887 | 0.9848–0.9926 |
| FiO₂     | 0.0072 | 0.0073 | 0.3284 | 1.0072 | 0.9928–1.0218 |
| Pplat    | -0.0153 | 0.0152 | 0.3156 | 0.9848 | 0.9559–1.0147 |
| PEEP     | 0.0317 | 0.0295 | 0.2832 | 1.0141 | 1.0040–1.0243 |
| MAP      | -0.0066 | 0.0080 | 0.4087 | 0.9934 | 0.9780–1.0091 |
| SAPSII   | 0.0541 | 0.0066 | <0.0001 | 1.0556 | 1.0421–1.0693 |
| SOFA     | -0.0146 | 0.0277 | 0.5974 | 0.9855 | 0.9334–1.0405 |

OR: odds ratio; R-DP: range of driving pressure; CVP: central venous pressure; RR: respiratory rate; Pplat: plateau pressure; PEEP: positive end expiratory pressure; HR: heart rate; MAP: mean arterial pressure; SAPS II: Simplified Acute Physiology Score II; SOFA: Sequential Organ Failure Assessment.

### Fig. 2. The relationships between R-DP and the prognostic outcome. (a) Relationship between R-DP and ventilator-free time, ICU length of stay, and hospital length of stay. (b) Receiver operating characteristic curve of R-DP.

AUC: area under the curve; NLR: negative likelihood ratio; PLR: positive likelihood ratio; PPV: positive predictive value, YI: Youden index.
The effects of mechanical ventilation on RV afterload have been illustrated by echocardiography\(^1\)\(^8\)\(^,\)\(^9\)\(^,\)\(^19\); these effects may result in increased CVP, and more cardiac work may be required to produce a high CO. Without sufficient cardiac compensation, the significantly increased CVP could indicate RV dysfunction.\(^1\) From the results of the regression analysis, we learned that ECVP was also an independent risk factor for poor prognosis; the OR of CVP was 1.0904 (95% CI, 1.0589–1.1228), and the AUC was 0.681 (95% CI, 0.662–0.699). Therefore, it is necessary to balance the RV function with the ventilator settings.

As the R-DP and CVP increased, mortality showed a gradually increasing trend, and Pearson correlation showed a close relationship between these variables, indicating that a wide range of DP was associated with ECVP. We wonder the reason is that inappropriate mechanical ventilation may induce hemodynamic alterations, a fluctuation in DP may indicate severity of destroyed pulmonary capillaries, accompanied with deteriorated function of the RV, and finally result in hemodynamic disturbances and poor outcomes. As in set similar conditions of tidal volume after admission, DP is mainly determined by the compliance of the relaxed respiratory system. During ARDS, the decrease in lung compliance (CRS) is attributable to the reduction in the airspace volume due to alveoli collapse as a result of inflammatory cells, fluid, and superimposed pressure, along with impairment of surfactant function.\(^2\)\(^0\) CRS is a marker of disease severity because CRS varies in proportion to the number of aerated and recruitable lung units.\(^2\)\(^1\) Our study further raises the suspect that pathologic pulmonary vascular tension in patients with hypoxia may be further destroyed by inappropriate mechanical ventilation, and revealed as widely range of DP as well as worsen RV function characteristic.

Therefore, we wonder whether fluctuation in DP could reveal the progression of morbidity and direct the adjustment of ventilation parameters. When the DP is fluctuating, shifting lung-protective ventilation to circulatory-protective ventilation should be considered.\(^2\)\(^2\) Cardiac function should be closely assessed by ultrasound before and during mechanical ventilation. Airway Pplat, Pmean, and PEEP should be adjusted until stable, and ventilation in the prone position could be instituted to avoid pulmonary hypertension and right heart dysfunction caused by excessive airway pressure.\(^2\)\(^3\)\(^,\)\(^2\)\(^4\)

There are several limitations in our study. First, this study is a retrospective study and it is limited by the source of data used. Therefore, no causal relationships among R-DP, CVP, and mortality could be established. Additionally, DP and CVP data could only be assessed in patients who record the corresponding evaluation during the first 72 h after ICU admission, which may lead to bias in selecting specific patients. Thus, our results cannot be

### Table 3. Parameters of respiratory condition and hemodynamics in the different groups.

| Characteristics          | Low R-DP, n = 1579 | High R-DP, n = 834 | p       |
|--------------------------|--------------------|--------------------|---------|
| Age, yr, median (IQR)    | 65.8 (51.5–80.1)   | 64.8 (49–80.6)     | 0.1744  |
| Gender, n (%)            |                    |                    |         |
| Male                     | 1042 (66.0)        | 520 (62.4)         |         |
| CVPmean                  | 11.8 (7.9–15.7)    | 16.0 (10.9–21.1)   | <0.0001 |
| RR                       | 18.7 (15.3–22.1)   | 20.0 (15.9–24.1)   | <0.0001 |
| PaCO2                    | 40.7 (35.1–46.3)   | 40.7 (34.4–47)     | 0.8859  |
| PaO2                     | 154.7 (103.8–205.6)| 136.9 (94.3–179.5)| <0.0001 |
| FiO2                     | 53.9 (44.3–63.5)   | 55.9 (45.5–66.3)   | <0.0001 |
| Pplat                    | 21.3 (16.3–26.3)   | 23.5 (17.5–29.5)   | <0.0001 |
| PEEP                     | 6.6 (4–9.2)        | 7.8 (4.5–11.1)     | <0.0001 |
| HR                       | 86.9 (74.7–99.1)   | 89.2 (75.2–103.2)  | <0.0001 |
| MAP                      | 76.4 (67.8–85)     | 76.1 (67.2–85)     | 0.4421  |
| SAPS II                  | 43.5 (29–58)       | 47.4 (32–62.8)     | <0.0001 |
| SOFA                     | 6.8 (3.5–10.1)     | 8.1 (4.4–11.8)     | <0.0001 |
| ICU stay time            | 7.2 (2.2–8.7)      | 9.6 (3.2–12.9)     | <0.0001 |
| hospital stay time       | 14.8 (6.8–18.2)    | 16.5 (7.4–21.1)    | 0.0065  |
| Mortality, n (%)         | 178 (11.3)         | 257 (30.8)         |         |

R-DP: range of driving pressure; CVP: central venous pressure; RR: respiratory rate; Pplat: plateau pressure; PEEP: positive end expiratory pressure; HR: heart rate; MAP: mean arterial pressure; SAPS II: Simplified Acute Physiology Score II; SOFA: Sequential Organ Failure Assessment.

### Fig. 3. The relationship between R-DP and CVP, and the prognostic significance. (a) Relationship between R-DP and CVP based on Pearson correlation. (b) Prognostic significance of R-DP and CVP.

R-DP: range of driving pressure; CVP: central venous pressure.
generalized to patients who did not undergo continuous treatment in ICU during the first three days, the associations of R-DP (or other variables) with CVP may be overemphasized in such situations. We would like to explore the effect of R-DP and CVP on prognosis and their relationship in prospective study in the future. Second, in our study, a significantly increased CVP could serve as an indicator of impending right ventricular dysfunction. However, ECVP occurs frequently in critical care settings and may be caused by several conditions, such as heart failure, pericardial disease, and especially as a surrogate of intravascular volume. As a matter of fact, we found the proportion of patients with cardiological condition was far less in non-survivor group than survivor group. Therefore, we do not think basic heart dysfunction could account for ECVP in nonsurvivor group. What is more, recent studies have challenged the validity of ECVP in critical care settings; it might indicate an impediment to the venous return and microcirculatory blood flow as well as accompanying lung edema. ECVP may work as a preliminary indicator of increased pulmonary vascular resistance or right ventricular dysfunction.

In conclusion, fluctuated DP and ECVP were associated with a worse outcome in patients with hypoxia who received mechanical ventilation during the first 72 h after ICU admission in our study, and further indicate the interaction between the respiratory mechanism and hemodynamics, and the impact on patient outcome. Therefore, “circulation-protective ventilation” should be considered to remedy these deleterious effects associated with the lung-protective ventilation strategy, thereby decreasing the incidence of hemodynamic disorders.

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Authors’ contributions
D.-W.L. designed the experiment. J.-Y.M. drafted and revised the manuscript. D.-K.L. assembled input data, X.D. helped to draft the manuscript, H.-M. Z. participated in the design of the study, Y.L. helped to revise the manuscript. X.-T.W. conceived of the study and participated in its design and coordination. All authors have read the manuscript and approved of the version to be published.

Availability of data and materials
The datasets supporting the conclusions of the current study are available from the corresponding author on reasonable request. Please contact corresponding author if you want to request the dataset.

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.

Conflict of interest
The author(s) declare that there is no conflict of interest.

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