

Use of the product of driving pressure and respiratory rate for predicting failure of weaning from mechanical ventilator in medical patients

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Abstract

Background : Respiratory workload increment in the process of mechanical ventilation withdrawal is critical for the determination of weaning outcome. Pressure, tidal volume (Vt) and respiratory rate (RR) are considered as patient's respiratory power, albeit being affected by excessive respiratory load. We aimed to evaluate the performance of driving pressure (DP)×RR to predict the outcome of weaning.

Methods : Plateau pressure (Pplat) and positive end-expiratory pressure tot (PEEPtot) were measured during mechanical ventilation, viz., (1) brief deep sedation, (2) on volume support ventilation of MV with Vt 6 ml/kg and a PEEP of 0 cm H₂O, (3) Pplat and PEEPtot were measured by holding breath for 2s after inhalation and exhalation, respectively. The DP was determined as Pplat minus PEEPtot. The highest RR was recorded within 3 min during spontaneous-breathing trial (SBT). Patients that were able to tolerate SBT for 1 h were directly extubated. These measurements correlated well with weaning outcome. Notably, patients in the "failure" group failed the SBT, died, while others required reintubation or noninvasive ventilation within 48 h of extubation.

Results : Out of the 61 patients studied, 22 failed weaning. During the withdrawal of ventilation, DP×RR was 134.2 ± 33.2 cmH₂O·breaths/min and 238.5 ± 61.7 cmH₂O·breaths/min ($P = 0.00$), DP was 7.9 ± 1.6 cmH₂O and 9.7 ± 2.3 cmH₂O ($P = 0.00$), in the "success" and "failure" groups, respectively. The DP×RR index greater than 170 cmH₂O·breaths/min had a sensitivity of 95.5% and a specificity of 89.7%, while DP index greater than 8.1 cmH₂O had 81.8% sensitivity and 64.1% specificity to predict weaning failure.

Conclusions : Measurement of DP×RR during withdrawal of ventilation may help predict weaning outcome. Noticeably, high DP×RR increased the likelihood of weaning failure.

1. Background

It has been shown that as soon as the factors causing the respiratory failure starts were removed, the weaning from mechanical ventilation should be initiated. However, even with the spontaneous-breathing trial (SBT) being used worldwide, more than 10% of extubations failed [1]. There are many weaning parameters, such as tracheal airway occlusion pressure at 0.1 s (P_{0.1}) [2], rapid shallow breathing index (RSBI) [3], and CROP index (respiratory compliance, RR, oxygenation, maximum inspiratory pressure) [4]. Most importantly, RSBI seems to be the most substantial single parameter to predict weaning success with positive predictive value (PPV), negative predictive value (NPV), sensitivity and specificity of 0.78, 0.95, 0.97, and 0.64 respectively [3]. Nonetheless, this index had low PPV and specificity. At present, it is difficult for clinicians to choose the accurate timing of withdrawal of mechanical ventilation. In this study, we sought to identify a new parameter to improve accuracy and precision of weaning.

Currently, a number of observational studies have demonstrated an association between lung injury or mortality and mechanical power [5-6]. As an important element of mechanical power, high DP is associated with greater mortality and poor diaphragmatic function [7-9]. Airway driving pressure represents the cyclic strain which is related to volume change. Usually, this is a physiological way of adjusting Vt to the residual lung size (respiratory system compliance). Both power and driving pressure (DP) are effective indicators of weaning outcome. By extension, pressure applied to multiply volume

change is the work that reflects respiratory workload, while affecting the outcome of weaning [10]. Thus, we postulated that DP \times respiratory rate (RR) could be a predictor of weaning in patients with respiratory failure. In order to assess the predictive value (PV), we did an observational trial to investigate the utility of this index during weaning from mechanical ventilation (MV) to predict weaning outcomes.

2. Methods

This study was performed between March 2017 and June 2019 in the affiliated Changshu hospital of Xuzhou medical university. All the patients were recruited from the medical intensive care unit. The participants were enrolled into the study when they were ready for weaning from MV. Prior to the study, *ethical approval* for this study *was obtained from the ethics committee of affiliated Changshu hospital of Xuzhou medical university* (ID number: 0056-2017). All the patients or their relatives gave written informed consent prior to the investigation.

2.1 Patient selection

Inclusion criteria included age \geq 18 years, and MV for more than 24 h. The readiness of the patients for weaning largely dependent on their ability to meet all the criteria: $\text{PaO}_2/\text{FIO}_2 > 200 \text{ mmHg}$, using $\text{PEEP} \leq 5 \text{ cmH}_2\text{O}$ and fraction of inspired oxygen (FIO_2) ≤ 0.4 , stable hemodynamic (heart rate ≤ 140 beats/min, absence or low-dose vasopressors required i.e., dopamine or dobutamine $\leq 5-10 \text{ ug/kg}\cdot\text{min}$), good consciousness (Glasgow coma scale ≥ 13), stable metabolism (i.e. acceptable electrolyte levels), effectiveness of cough, and in the recovery stage of disease.

2.2 Exclusion Criteria

Exclusion criteria included age less than 18 years, and MV for less than 24 h, pregnancy, end-stage tumor, neuromuscular disease, presence of pneumothorax, flail chest, large pleural effusion, patients with severe deformity, obesity, organ failure and lack of informed consent.

2.3 Study Design

The patients who met the aforementioned inclusion criteria were injected intravenously with remifentanil 0.2 mg for brief deep sedation. Next, the patients were put on triggering assisted breaths on volume support ventilation of MV with V_t 6 ml/kg of ideal body weight and a PEEP of 0 cmH_2O . Respiratory mechanical parameters (peak inspiratory pressure, P_{plat} and PEEP_{tot}) were recorded. P_{plat} and PEEP_{tot} were measured by holding breath for 2 s after inhalation and exhalation, respectively. The DP was measured as P_{plat} minus PEEP_{tot} . When the study subjects were deemed ready for an SBT with the intent to weaning, each participant was disconnected from the ventilator to SBT for 1 h using T piece with oxygen supplementation (FIO_2 of 0.25–0.5) to achieve pulse oxygen saturation (SpO_2) $\geq 90\%$. Then, the RR was measured after SBT for 3 min, while the highest RR was recorded. After that, the DP multiplies by RR was calculated. Notably, patients who passed the 1 h SBT were directly extubated, while others were

reconnected to the ventilator with the previous ventilatory parameters if failed to the SBT. The decision to use noninvasive ventilation or reintubate after extubation was left up to the discretion of ICU team.

Criteria for passing the spontaneous breathing test:
RR/Vt \geq 105
RR \leq 35 or \leq 8 breaths/min
Spontaneous breathing tidal volume \geq 4 ml/kg
Heart rate \leq 140 beats/min or a 20% increase or decrease from baseline
Arterial blood oxygen saturation \geq 90%.

2.4 Weaning failure definition

Weaning failure or post extubation distress was defined as the inability to maintain spontaneous breathing for at least 48 h, without any form of ventilatory support [11]. Patients who failed the SBT, died, or required reintubation or noninvasive ventilation (NIV) within 48 h of discontinuation of MV were considered as having failed to wean.

2.5 Statistical analysis

Normally distributed continuous variables were expressed as means with standard deviations. The variables were compared with Student's t test for independent samples. Non-normally distributed continuous variables were compared via Mann–Whitney U test, while categorical variables were compared with the Chi-Square Test or correction of continuity. Receiver operating characteristic (ROC) curve analysis was performed to assess the capability of DP \times RR and DP to predict patients who may succeed at weaning or fail. Statistical analysis was performed with Statistical package for social sciences (SPSS) 17.0 software (SPSS, Chicago, IL, USA). A *p* values less than 0.05 were chosen to indicate the statistical significance.

3. Results

During the study period, 61 patients were recruited with 22 of them failing weaning. Fifteen (15) of 22 the patients failed to pass weaning after 1 h SBT. Also, 2 patients in the failure group were reintubated within 48 h of extubation. The remaining 5 patients were initiated on NIV within 48 h of extubation either preemptively or as rescue therapy. Importantly, 39 patients were weaned successfully (Fig 1). The mean age of the study cohort was 67.7 years, with 42 (68.9%) being male. The characteristics of the patients are summarized in Table 1. As presented in Table 1, the underlying reasons for initiation of MV were Trauma (16.4%), Pneumonia (44.3%), Toxication (11.5%), Shock (16.4%), Cardiac failure (6.6%) and Apnea (4.9%). The difference between the two groups regarding age, gender, and acute physiology as well as Chronic Health Evaluation II score were not statistically significant. The duration of ventilation and ICU length of stay were longer in the failure group ($P=0.01$, $P\leq 0.0001$) (Table 1). The patients in the failure group had significantly higher DP \times RR ($P\leq 0.0001$), and DP ($P\leq 0.0001$) in comparison with the success group. Notably, the DP \times RR was 238.5 ± 61.7 cmH₂O·breaths/min and 134.2 ± 33.2 cmH₂O·breaths/min ($P\leq 0.0001$) in the failure and success groups; while the DP was 9.7 ± 2.3 cmH₂O and 7.9 ± 1.6 cmH₂O ($P\leq 0.0001$) in the failure and success groups, respectively (Table 2). The mean value of DP \times RR and DP parameters between the two patient groups were compared in Fig 2. A DP \times RR index greater than 170

$\text{cmH}_2\text{O}\cdot\text{breaths}/\text{min}$ had a sensitivity of 95.5% and a specificity of 89.7% to determine weaning failure (area under the curve [AUC], 0.968). Likewise, a DP index greater than 8.1 cmH_2O showed 81.8% sensitivity and 64.1% specificity (AUC, 0.742) (Fig 3).

4. Discussion

It was observed in this study that $\text{DP}\times\text{RR}$ index was greater in the patients who failed weaning comparable to those who were successfully extubated from MV. In contrast with the most accurate parameter RSBI [3], our index showed similar sensitivity and higher specificity. Even RSBI has limitations, including mean RSBI value less than 105 in the failure group [12]. Moreover, RSBI requires dynamic monitoring of tidal volume during SBT, which is not convenient.

Imbalance between respiratory energy load and muscle function contribute to failure of ventilation weaning. Notwithstanding, several mechanisms may be involved, namely, alteration in airway resistance, respiratory system compliance, intrinsic positive end-expiratory pressure, and increased additional work (mechanism or intubation) are associated with excessive respiratory load. The alternative contribution of each factor affects the energy load. Actually, pressure, V_t and RR are considered as patient's respiratory power which is affected by excessive respiratory load.

Tidal breath starts from the potential energy corresponding to PEEP_{tot} and inflates the end-inspiratory value. The respiratory energy load of each tidal inflation can be kinetic (resistance and tidal elasticity) and potential (PEEP_{tot}). This energy defines the product of pressure applied while the volume change quantifies the work accomplished. Power is product of inflation energy per cycle while the number of cycles per minute which is defined as work per unit time, usually describes the intensity of energy application [13].

In this study, patients received the same V_t . Thus, $\text{pressure}\times\text{RR}$ could be referred to respiratory power of patients amidst being affected by excessive respiratory load. Three major components comprise the inflating pressure, viz., flow resistive, tidal elastic (DP), and starting pressure above the baseline value [14]. There are at least three different ways to calculate mechanical power (energy per breath times respiratory rate) with different degrees of complexity [15]. While, the pressure due to the flow is usually considered fully dispersed within the airways, this is not taken into account for the calculation of energy during tidal breathing [16]. Furthermore, for the two groups, PEEP was fixed at 0 cmH_2O . Therefore, DP relating to incremental dynamic strain plays a key role in inspiratory energy. Actually, DP is defined as the amount of cyclic parenchymal deformation imposed on ventilated and preserved lung units [17], which is most accessible at the bedside, and may serve as a marker of cyclic lung strain [18]. Mathematically, $V_t/\text{system compliance (C)}$ is the DP i.e. the applied pressure above PEEP to deliver the V_t . [19]

On the other hand, it was found in this study that the $\text{DP}\times\text{RR}$ and DP index were significantly greater in the failure group compared with the success group. Pertinently, $\text{DP}\times\text{RR}$ had higher sensitivity and specificity than the DP to predict weaning failure. Noticeably, most of the patients who were ready to

withdraw after meeting the standard had their high airway resistance being relieved. The main factors that affected the results of the withdrawal are cardiopulmonary and diaphragm functions. It was observed that when the patient changed from mechanical ventilation to SBT, the compliance of thorax or lung was poor, while the elastic load and the driving pressure of the patient increased but the evacuation failed. In addition, when the patient's primary disease did not improve, the respiratory load was high, or with poor heart and diaphragm functions. Besides, during SBT, the patient's respiratory frequency accelerated, indicating that the respiratory endurance was not enough to balance the patient's respiratory load. As a result, the patient could not maintain a stable breath, while the final result was also a failure to withdraw the machine. Weaning is a complex process involving transition from ventilatory support to spontaneous breathing. Any single parameters cannot guide the weaning well. A more global perspective which combines DP and RR does not only reflects respiratory system compliance, but also the capacity to perform work (energy) and the intensity of energy application (power). When the required pressure to produce the fixed volume is high, work rate is increased, or when RR is increased, work per unit time is high coupled with high power, indicating that the patient is more likely to fail to withdraw from mechanical ventilation.

In this study, some few limitations were identified. Different etiologies were studied together, which thereby increased the heterogeneity of the study. Despite this, the $DP \times RR$ was significantly greater in the failure group compared with the success group. There are also limitations of the study generalizability as this study did not include obese patients (a growing part of the population), patients with "organ failure" (many ICU patients), and was still a single center study. In addition, the SBT failure was included in the definition of machine withdrawal failure, thus the result was greatly affected by RR index in SBT. The observation of weaning outcomes does not mean that an intervention targeted at achieving that profile will accurately determine the timing of weaning.

5. Conclusion

The $DP \times RR$ index may serve as a novel method to predict the outcome of weaning. A greater $DP \times RR$ index is predictive of failed weaning. This combination provide a clue for physicians as to how they assess weaning readiness in critically ill patients. Because of the complexity of factors that determine the outcome of weaning, the $DP \times RR$ index serves as a good but may be an imperfect predictor. Therefore, further evidences are required to validate the finding.

Abbreviations

VT: Tidal volume; RR Respiratory rate; DP Driving pressure; Pplat Plateau pressure; PEEPtot Positive end-expiratory pressure tot; SBT: Spontaneous breathing test; RSBI Rapid shallow breathing index; PPV Positive predictive value; NPV negative predictive value; MV: Mechanical ventilation; FIO₂ Inspired oxygen; SpO₂ pulse oxygen saturation; NIV Noninvasive ventilation; ROC Receiver operating characteristic; AUC: Area under curve.

Declarations

Ethics approval and consent to participate

The study was approved by the institutional ethics committee of the hospital, The Affiliated Changshu Hospital of Xuzhou Medical University (20170056). All patients or relatives of the patients gave written informed consent prior to participation.

Consent for publication

Not applicable.

Availability of data and materials

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

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

GJ wrote large parts of the manuscript and conceived the study design and data collection. ZB B participated in the study design. HX W performed statistical analyses. LB participated in literature search. HJ reviewed the manuscript. All authors interpreted the data, contributed to the intellectual content, reviewed the manuscript, and approved the final version.

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Tables

Table.1 Patient Demographics

Variable	Success Group	Failure Group	P Value
Age,y	65.4±16.0	71.8±12.0	0.11
Male,No.(%)	29(74.4%)	15(68.2%)	0.61
APACHEII	6.4±4.4	8.6±5.1	0.08
LOV,d,median(25th,75th percentiles)	6(3,10)	14(7.5,18.25)	0.01 ^a
ICU LOS, d,median(25th,75th percentiles)	11.7±9.0	22.1±12.4	0.00 ^a
Reason for intubation			
Trauma	8(20.5%)	2(9.1%)	0.43 ^b
Pneumonia	17(43.6%)	10(45.5%)	0.89
Toxication	3(7.7%)	4(18.2%)	0.41 ^b
Shock	8(20.5%)	2(9.1%)	0.43 ^b
Cardiac failure	1(2.6%)	3(13.6%)	0.26 ^b
Apnea	2(5.1%)	1(4.5%)	1.00 ^b

Table.2 Comparison Between Diagnostic Tests

Diagnostic Test	Sensitivity(%)	Specificity(%)	PPV(%)	NPV(%)
DP×RR ≤170 (cmH ₂ O·breaths/min)	95.5	89.7	92.3	95.5
DP≤8.1(cmH ₂ O)	81.8	64.1	64.1	81.8

Figures

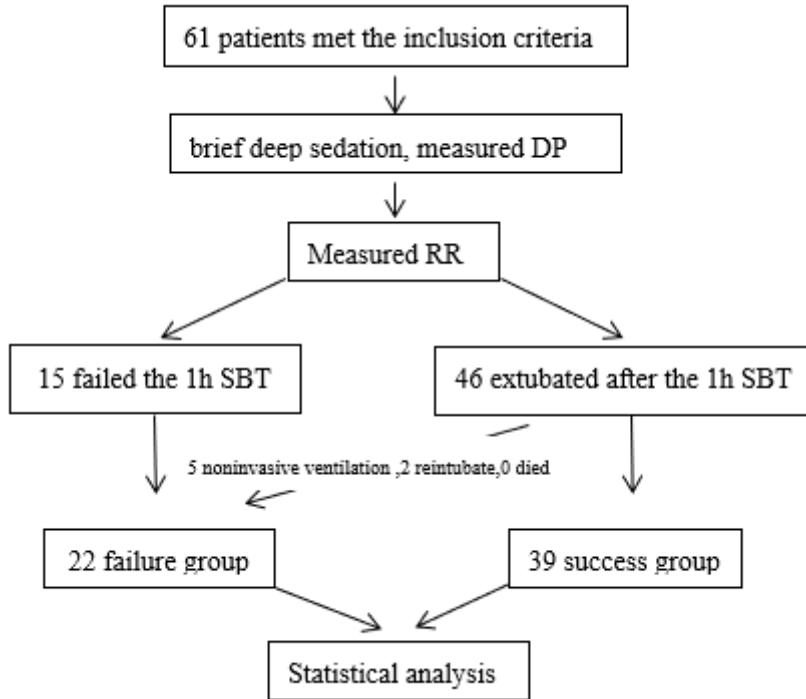


Figure 1

Flowchart of the study. DP (driving pressure); RR (respiratory rate); SBT (spontaneous breathing trial).

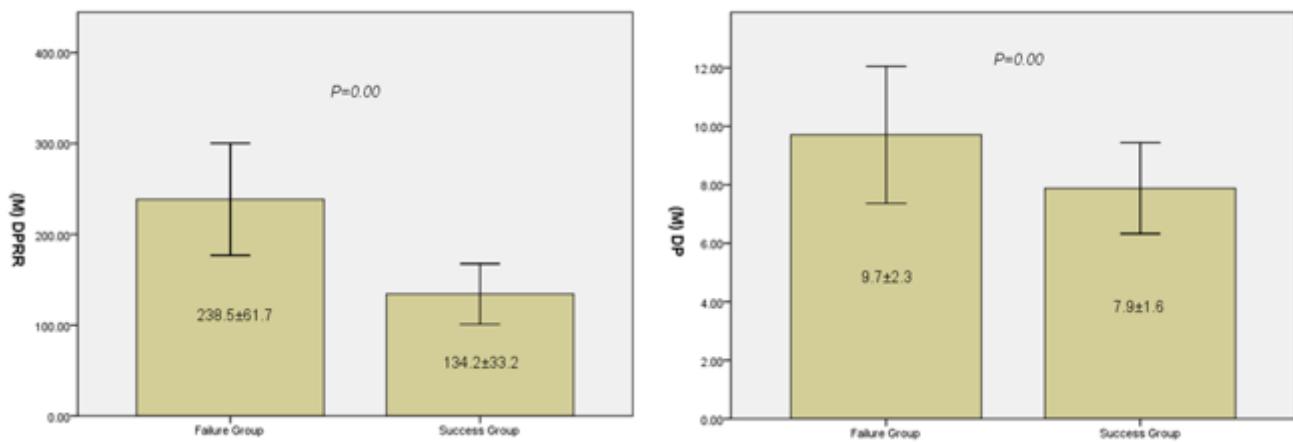


Figure 2

DP×RR,DP: Comparison of two patient group. Fig

ROC Curve

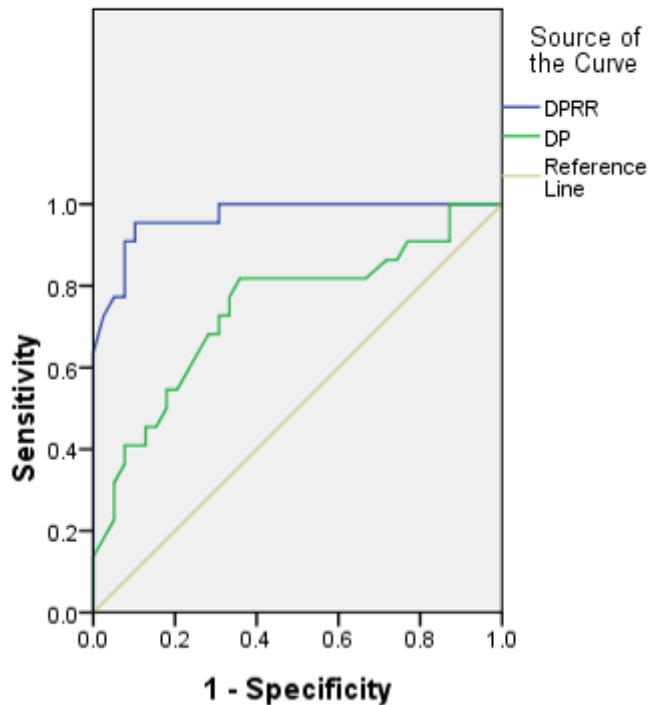


Figure 3

Receiver operating characteristic curve for DP \times RR and DP. The DP \times RR:AUC 0.968(95%CI 0.91-1.00 P \leq 0.0001), DP:AUC 0.742(95%CI 0.61-0.88 P \leq 0.0001)

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