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Original article

Comparison of the pulmonary dead-space fraction derived from ventilator volumetric capnography and a validated equation in the survival prediction of patients with acute respiratory distress syndrome

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ABSTRACT

Purpose: This prospective observational study aims to evaluate the accuracy of dead-space fraction derived from the ventilator volumetric capnography (volumetric CO_2) or a prediction equation to predict the survival of mechanically ventilated patients with acute respiratory distress syndrome (ARDS).

Methods: Consecutive VD/VT measurements were obtained based upon a prediction equation validated by Frankenfield et al for dead-space ventilation fraction: VD/VT = 0.320 + 0.0106 ($PaCO_2$-$ETCO_2$) + 0.003 (RR) + 0.0015 (age) in adult patients who had infection-related severe pneumonia and were confirmed as having ARDS. Here $PaCO_2$ is the arterial partial pressure of carbon dioxide in mmHg; $ETCO_2$, the end-tidal carbon dioxide measurement in mmHg; RR, respiratory rate per minute; and age in years. Once the patient had intubation, positive end expiratory pressure was adjusted and after P_{high} reached a steady state, VD/VT was measured and recorded as the data for the first day. VD/VT measurement was repeated on days 2, 3, 4, 5 and 6. Meanwhile we collected dead-space fraction directly from the ventilator volumetric CO_2 and recorded it as Vd/Vt. We analyzed the changes in VD/VT and Vd/Vt over the 6-day period to determine their accuracy in predicting the survival of ARDS patients.

Results: Overall, 46 patients with ARDS met the inclusion criteria and 24 of them died. During the first 6 days of intubation, VD/VT was significantly higher in nonsurvivors on day 4 (0.70 ± 0.01 vs 0.57 ± 0.01), day 5 (0.73 ± 0.01 vs. 0.54 ± 0.01), and day 6 (0.73 ± 0.02 vs. 0.54 ± 0.01) (all $p = 0.000$). Vd/Vt showed no significant difference on days 1–4 but it was much higher in nonsurvivors on day 5 (0.45 ± 0.04 vs. 0.41 ± 0.06) and day 6 (0.47 ± 0.05 vs. 0.40 ± 0.03) (both p = 0.008). VD/VT on the fourth day was more accurate to predict survival than Vd/Vt. The area under the receiver-operating characteristic curve for VD/VT and Vd/Vt in evaluating ARDS patients survival was day 4 (0.974 ± 0.093 vs. 0.701 ± 0.023, p = 0.0024) with the 95% confidence interval being 0.857–0.999 vs. 0.525–0.841.

Conclusion: Compared with Vd/Vt derived from ventilator volumetric CO_2, VD/VT on day 4 calculated by Frankenfield et al's equation can more accurately predict the survival of ARDS patients.

Introduction

Acute respiratory distress syndrome (ARDS) is a life-threatening condition, which presents as progressive hypoxemia and difficulty in breathing following diffuse pulmonary interstitial and alveolar edema due to pulmonary capillary endothelial cell damage. Patients with ARDS are often critical and accompanied by other diseases or major injuries, for example, severe infection, shock, trauma and burns, etc.[1] Although medical rescue is enhancing unceasingly, the mortality rate of critical patients has not been greatly decreased. Previous studies have shown the importance of physiologic dead space and its evolution in predicting mortality in critical patients.[2–6] In clinical practice, we can directly read pulmonary dead-space fraction on the ventilator screen (in this study

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we recorded it as Vd/Vt), which may change a lot and sometimes contradictory or nonsensitive due to numerous interference factors, including high positive end-expiratory pressure (PEEP), administration of sedatives or muscle relaxants, etc. Therefore its accuracy to predict survival should be studied further. The equation VD/VT = 0.320 + 0.0106 ($PaCO_2$-$ETCO_2$) + 0.003 (RR) + 0.0015 (Age) proposed by Frankenfield et al[7] (in this study we recorded it as VD/VT) has been shown to calculate pulmonary dead-space fraction precisely and without bias, eliminating the above-mentioned disturbing factors. In this study, we compared VD/VT with Vd/Vt to evaluate their prediction accuracy of survival of ARDS patients.

Methods

Patient selection

This was a prospective observational cohort study conducted in the intensive care unit (ICU) of Tianjin Third Central Hospital, Tianjin, China. All the protocols have been approved by the Institutional Committee on Human Research, and informed consents have been obtained from the patients or their relatives. All patients with ARDS admitted to the adult ICU of our hospital between January 2014 and January 2015 were eligible for this study. Inclusion criteria were adult patients (≥18 years old) who were diagnosed as having ARDS based on the Berlin Definition for ARDS[8] and required positive pressure mechanical ventilation via an endotracheal tube. Vd/Vt was directly read from the Dräger XL ventilator (Dräger Medical, Germany) volumetric CO_2. Patients were excluded if they have pulmonary thromboembolism (PTE), history of chronic obstructive pulmonary disease (COPD), bronchiectasis or interstitial lung disease. Of 58 patients with ARDS, 46 were included in this study.

Clinical data collection

Baseline characteristics, demographic data and relevant physiologic data were recorded on the first day of study (defined as the moment when PEEP has been well adjusted and P_{high} reached a steady state after intubation). Acute physiology and chronic health evaluation (APACHE) II score and lung-injury score at the time of enrollment were calculated. The primary etiology of ARDS was assessed based on a detailed review of the clinical history. Finally, we recorded the information about the survival condition of patients within 28 days.

Measurement of dead-space fraction

Initial VD/VT measurements were obtained on the first day. VD/VT was serially measured on days 2, 3, 4, 5 and 6 following the equation: VD/VT = 0.320 + 0.0106 ($PaCO_2$-$ETCO_2$) + 0.003 (RR) + 0.0015 (Age). At the same time, we recorded Vd/Vt directly from breath-by-breath volumetric CO_2. We also recorded the arterial blood gas values, PaO_2/FiO_2, PEEP and FiO_2. Breath-by-breath volumetric CO_2 and analysis of $ETCO_2$ were obtained by the mainstream CO_2 sensor of a Dräger XL ventilator based on the non-dispersive infrared absorption principle. The machine was placed between the ventilator circuit and the patient. Measurement of dead-space fraction was conducted at the same time of arterial blood sampling, which was analyzed by a Radiometer ABL800 arterial blood gas analyzer (Radiometer, Bronshøj, Denmark). Modality of mechanical ventilation of all patients were bilevel positive airway pressure. Data were read when the patient were observed to be calm with complete respiratory rhythm.

Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences (Version 17.0, SPSS Inc, Chicago, Illinois, USA) and Med Calc statistical software (V.15.6.1). Parametric and nonparametric values were expressed as mean ± SEM, and distance between median and quartile respectively. Comparison of sampled ratios were explored by using χ^2 test. Student t test were used to compare mean values. Paired comparisons were conducted by using the Mann-Whitney test. Receiver operating characteristic (ROC) curves were obtained for the prognostic value of VD/VT and Vd/Vt, respectively. The area under the ROC curves of VD/VT and Vd/Vt were compared with Med Calc statistical software. A simple Pearson correlation was used to compare the relation of VD/VT to PEEP and PaO_2/FiO_2. A logistic regression was used to determine the association of VD/VT with mortality as the outcome. All tests were two sided and considered significant at $p < 0.05$.

Results

Baseline characteristics

A total of 46 patients with ARDS were enrolled in this study, including 18 females and 28 males with the mean age of (55.71 ± 3.01) years. Etiology of ARDS was pneumonia in 26 patients (57%), sepsis in 12 (25%), aspiration in 4 (9%) and trauma or others in 4 (9%). Of the 46 patients enrolled, 24 (52%) died and 22 (48%) survived. The demographics data, APACHE II score and lung-injury score are summarized in Table 1. Differences in PEEP and PaO_2/FiO_2 are summarized in Table 2. In this study, PEEP and FiO_2 were adjusted based upon a target $PaO_2 \geq 60$ mmHg and low tidal volume. PEEP showed no significant difference at the first 5 days, but it was much lower in survivors on day 6 (9.2 ± 0.10 vs. 14.3 ± 0.08, $p < 0.001$). PaO_2/FiO_2 was significantly higher among survivors on day 4 (273 ± 11 vs. 182 ± 56), day 5 (289 ± 20 vs. 172 ± 15) and day 6 (305 ± 29 vs. 174 ± 40, $p = 0.000$ for all).

Comparison of VD/VT and Vd/Vt between survivors and nonsurvivors

The mean VD/VT was significantly higher in nonsurvivors than in survivors from the fourth day of mechanical ventilation ($p < 0.05$, Fig. 1). As for Vd/Vt, nonsurvivors had a slightly higher mean value (0.40–0.47). However, the difference between two groups was significant only on day 5 and day 6. During the whole study period (6 days of mechanical ventilation), the mean Vd/Vt for all the patients was consistently lower than 0.5 (Fig. 2).

Table 1
Baseline data and clinical characteristics of 46 patients (mean ± SEM).

Group	Age (yr)	Female percentage	APACHE II score	Lung-injury score
Survivors ($n = 22$)	43.84 ± 3.35	32%	25 ± 0.5	2.60 ± 0.7
Non-survivor ($n = 24$)	66.59 ± 2.94	45%	28 ± 0.4	2.7 ± 0.6
Examining value	$t = -3.342$	$\chi^2 = 0.947$	$U = -2.846$	$U = -1.78$
p value	0.003	0.378	0.004	0.076