

Assessment of extravascular lung water by measuring the number of pulmonary ultrasound B-lines before and after CBP in patients with MODS

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Abstract

To determine whether the change in the number of pulmonary ultrasound B-line can accurately assess the extravascular lung water (EVLW) before and after continuous bedside blood purification (CBP) in patients with multiple organ dysfunction syndrome (MODS).

Seventy-six patients with MODS who underwent CBP were examined within 24 hours before and after CBP using pulmonary ultrasound to detect the number of ultrasound B-line or using pulse indicator continuous cardiac output method to examine extravascular lung water, blood oxygenation index, and B-type natriuretic peptide (BNP) content. The correlation of the change in the number of B lines before and after CBP treatment with the negative balance of 24 hours liquid, the change of oxygenation index, and BNP content were analyzed.

In the 76 patients, CBP treatment significantly decreased EVLW, the number of B-line, and BNP ($P < .05$ for all), while it significantly increased the oxygenation index ($P < .05$). Correlation analysis showed that the decrease in B-line number after CBP treatment was positively correlated with the 24 hours negative lung fluid balance, decrease of EVLW, oxygenation index improvement, and decreased BNP content. The change in the numbers of pulmonary ultrasound B-line can accurately assess the change of EVLW before and after CBP treatment and reflect the efficiency of ventilation in the lungs and the risk of heart failure.

Thus, it can replace pulse indicator continuous cardiac output as an indicator for evaluating EVLW in patients with MODS treated with CBP.

Abbreviations: CBP = continuous bedside blood purification, EVLW = extravascular lung water, MODS = multiple organ dysfunction syndrome, PICCO = pulse indicator continuous cardiac output.

Keywords: continuous blood purification, extravascular lung water, multiple organ dysfunction syndrome, pulmonary ultrasound B-line

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The study was approved by the Ethics Committee of our hospital and met the medical ethics standards. All treatments and tests received informed consent from patients or their families.

The authors have no conflicts of interest to disclose.

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

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1. Introduction

Multiple organ dysfunction syndrome (MODS) is a serious dysfunctional critical complication of various illnesses such as severe infection, trauma, shock, major surgery, etc, occurring simultaneously or sequentially in clinics in 2 or more organs or systems on the basis of excessive stress response and excessive systemic inflammatory response.^[1,2] Its mortality is higher than 40%, ranking the first among all deaths due to critical illnesses.^[3,4] Continuous bedside blood purification (CBP) is an important modality for the treatment of MODS.^[5,6] CBP not only can remove metabolic wastes in the body, but more importantly, it can maintain the stability of the body's volume status and mitigate the pulmonary edema caused by high-volume status.^[7] Therefore, assessment of the volume status and extravascular lung water (EVLW) before and after CBP treatment of patients with MODS is particularly critical for guiding CBP treatment.

Clinically, most patients with MODS have different degrees of fluid retention, and the lungs are the first to be involved. The increased interstitial water could reduce gas exchange rate and blood oxygenation index, while it could increase pulmonary circulation resistance, blood B-type natriuretic peptide (BNP) content, thereby inducing heart failure.^[8] Currently, the patients' capacity is mainly assessed by clinical symptoms, weight changes, blood pressure, heart rate, edema, and vascular filling degree.^[9] This method is very subjective and cannot effectively evaluate the volume load. Although central venous pressure and changes in

pulmonary wedge pressure are sometimes used as objective evaluation indicators, they are unable to accurately reflect the volume change.^[10] The new pulse indicator continuous cardiac output (PiCCO) method combines the transpulmonary temperature dilution technique and the technique analyzing the area under the arterial pulse wave curve to rationally convert hemodynamic monitoring into volume monitoring and is able to accurately monitor intrapulmonary blood volume and EVLW,^[11] but PiCCO monitoring requires puncture of deep veins and femoral artery. Thus, it is often traumatic and prone to catheter-related infections. Moreover, PiCCO monitoring kit is expensive, causing more than 10,000 Yuan each, which significantly increases the medical burden of patients and severely limits its clinical application.

Ultrasound monitoring of severely diseased patients is a dynamic assessment process for multitarget detection of MODS patients using ultrasound technology, and an important means to determine treatment options and guide fine adjustment.^[12,13] The ultrasound B-line appears as a laser-like, vertical, nonattenuating hyperechoic artifact (also known as a pulmonary ultrasound comet tail) that extends from the pleural line to the bottom of the screen in ultrasound images. Pulmonary ultrasound B-line is sensitive to changes in lung gas and water equilibrium. Thus, it could be used for early identification of pulmonary edema.^[14] The use of bedside severe ultrasound to monitor the number of pulmonary B-line is highly correlated with using PiCCO to monitor EVLW.^[15] It has been reported that pulmonary ultrasound monitoring of EVLW and inferior vena cava diameter changes in patients with chronic renal failure who subjected to interrupted hemodialysis can assess patients' pulmonary edema and volume load status.^[16] However, whether the accuracy of using bedside pulmonary ultrasound B-line to assess EVLW and volume load in MODS patients undergoing CBP in the intensive care unit can meet or exceed that of PiCCO has not been reported yet.

This study aimed to use the changes in the number of pulmonary B-lines monitored by using bedside B ultrasound to determine its accuracy in assessment of volume status and EVLW of patients with CBP, and to determine whether bedside B ultrasound could be a more accurate and cost-effective substitute of PiCCO in evaluating volume status and EVLW of MODS patients subjected to CBP.

2. Materials and methods

2.1. Patients

Seventy-six adult patients with MODS who underwent CBP treatment from February 2017 to February 2020 in our hospital were enrolled in this study. MODS were diagnosed, staged, and graded based on the criteria established in the 1995 by National Critical Care Medicine Association in China. The study was approved by the Ethics Committee of our hospital and met the medical ethics standards. All treatments and tests received informed consent from patients or their families. Patients were excluded if they have pulmonary fibrosis, pneumothorax, massive pleural effusion, and other diseases that could affect ultrasound examination and if they were unable to be monitored by PiCCO. These patients were at age of 27 to 86 years old with average of 67.9 ± 16.6 and had APACHE II score of 28.0 ± 5.0 . Among them, 42 were males and 34 were females, 30 had pulmonary infection, 9 had acute severe pancreatitis, 11 had multiple injuries, 11 had abdominal infection, 7 had blood-borne

infection, 6 had acne infection, and 2 submandibular space infection.

2.2. CBP treatment

Extracorporeal circulation was established for all patients by placing single-needle double lumen tube via internal jugular vein or femoral vein using the Seldinger technique. CBP was performed using CVVHDF mode of the Prismaflex bedside continuous blood filtration system from Sweden's Campbell and the associated pipe filters. Modified Port formula was used as the replacement fluid. The pre- and postdilution and hemodialysis flow rate were set at 800 mL/h, the blood flow rate was set at 150 to 200 mL/min, and the initial ultrafiltration rate was set at $8 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$. Unfractionated heparin was applied during CBP for anticoagulation. The activated partial thromboplastin time was measured and maintained at 1.5 to 2.5 times of the normal value by adjusting the amount of heparin. Patients with contraindications to heparin were given citrate for anticoagulation. Fluid loss was calculated according to the method published in Surgery. Briefly, the daily fluid intake, output, and insignificant loss were observed. The actual net negative balance per kg body weight at 24 hours after CBP was calculated.

2.3. Pulse indication continuous cardiac output (PiCCO) monitoring

All patients were placed in a supine position. A deep venous catheter was placed via the internal or subclavian vein and a PiCCO catheter was placed via the femoral artery. The catheter electrode was connected to the monitor of the PiCCO module, and the venous pressure end of the deep vein monitor center was connected to the PiCCO temperature sensor. The cardiac output was measured by thermodilution. In brief, 15 mL of ice-cold (0°C) physiological saline was rapidly infused ($<5 \text{ s}$) from the deep venous catheter for 3 consecutive times. The average of the measurement results was automatically calculated and input into the monitor, which was recalibrated each time before use. The EVLW was measured at 24 hours before and after CBP.

2.4. Bedside measurement of the number of pulmonary ultrasound B-line at both sides of patients with severe MODS

The patient was placed in the supine position and subjected to ultrasound examination using a color Doppler ultrasound system with a 3.5 MHz convex probe following the 28-point scanning technique recommended by the guide for bedside ultrasound.^[17] The front and bilateral chest walls were fully exposed and patients were asked to breath calmly. The two-dimensional ultrasound imaging mode was selected and the probe was placed perpendicular to the chest wall to longitudinally scan the rib gaps. A total of 28 intersection points among the parasternal line, the midline of the clavicle, the anterior tibiofibular line, the midline of the iliac crest, and the intercostal space (the 2nd to 5th of the right chest and the 2nd to 4th of the left chest) are observed and recorded. The total of pulmonary ultrasound B-line are added up. To ensure the reliability and repeatability of test results, the last 20 patients in this study were randomly inspected in 2 testers. One is a professional sonographer, the other is a nephrologist trained by ultrasound. The consistency of 2 testers can be evaluated by intraclass correlation coefficient (Fig. 1).

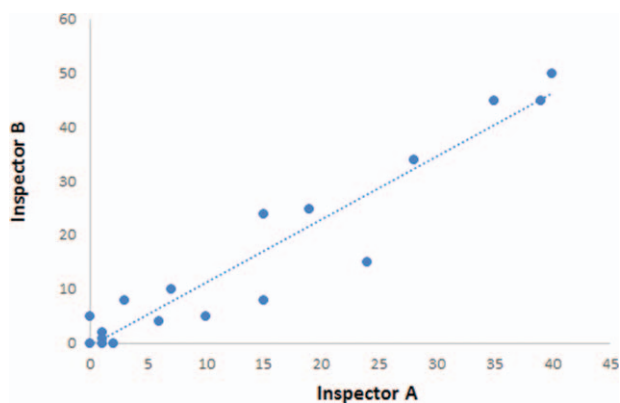


Figure 1. Evaluation of pulmonary ultrasound difference among different operators. The last 20 patients in this study were randomly inspected by two doctors. The inspector A is a professional sonographer and the inspector B is a nephrologist trained by ultrasound. $P < .05$.

2.5. Statistical analysis

The SPSS 19.0 software package was used for statistical analysis. All measurement data were denoted as $\bar{x} \pm s$. The paired sample t test was used to compare the mean before and after treatment. Pearson correlation analysis was used for univariate correlation analysis with $P < .05$ being significant in statistics.

3. Results

3.1. Amelioration of pulmonary ultrasound B-line, EVLW, and 24 hours negative lung fluid balance after 24 hours CBP in patients with MODS

All 76 patients with MODS completed 24 hours CBP. The mean number of B-lines decreased significantly after treatment

(Fig. 2A). The EVLW also decreased significantly after treatment (Fig. 2B). Pearson correlation analysis showed that the reduced number of B lines after CBP treatment was positively correlated with the decrease of EVLW (Fig. 2C) and the 24 hours negative lung fluid balance (Fig. 2D). These data suggest that the lowered number of B-lines was highly correlated with the reduction in lung fluid, and can be used as an index for detecting the contents of lung fluid before and after CBP and an index for 24 hours negative lung fluid balance.

3.2. Amelioration of oxygenation index and BNP after 24 hours CBP in patients with MODS

The oxygenation index improved significantly after CBP (Fig. 3A). By contrast, BNP decreased significantly (Fig. 3B). Correlation analysis showed that after CBP treatment, the decreased number of B-lines was correlated with the increase in oxygenation index (Fig. 3C) and the decrease in BNP (Fig. 3D). These results also suggest that the lowered number of B-lines after CBP could be used not only to reflect the EVLW content but also to evaluate the efficiency of pulmonary oxygen exchange before and after CBP and the risk of right heart failure.

4. Discussion

EVLW refers to the fluid distributed outside the pulmonary blood vessels, including intracellular fluids, alveolar fluids, and interstitial fluids.^[18] A change in EVLW is closely related to the degree of pulmonary edema caused by an abnormal accumulation of fluid outside pulmonary blood vessels. The amount of EVLW reflects the severity of pulmonary edema. Therefore, monitoring EVLW is of significance for understanding the pathophysiological function of pulmonary edema and judging the prognosis of patients of this kind.^[19] In the generation and development of MODS, the order of occurrence of these vital

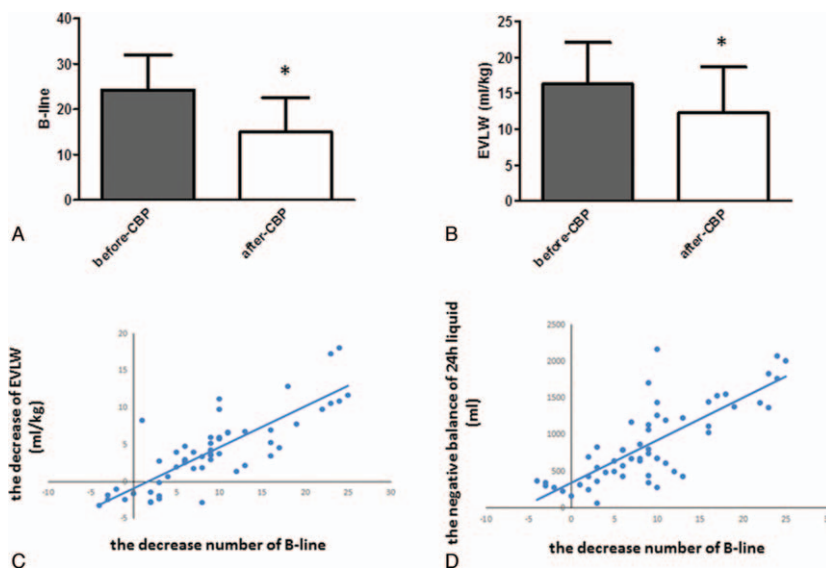


Figure 2. Amelioration of pulmonary ultrasound B-line, EVLW and 24 hours negative lung fluid balance after 24 hours CBP in patients with MODS. All 76 patients with MODS completed 24 hours CBP. A, The mean number of pulmonary ultrasound B-lines. B, The changes of EVLW. C, Correlation analysis between the reduced number of pulmonary ultrasound B-lines and the decrease of EVLW ($r = 0.779$). D, Correlation analysis between the reduced number of pulmonary ultrasound B-lines and the negative balance of 24 hours lung liquid ($r = 0.776$). $^*P < 0.05$ compared with before-CBP. CBP = continuous bedside blood purification, EVLW = extravascular lung water, MODS = multiple organ dysfunction syndrome, PICCO = pulse indicator continuous cardiac output.

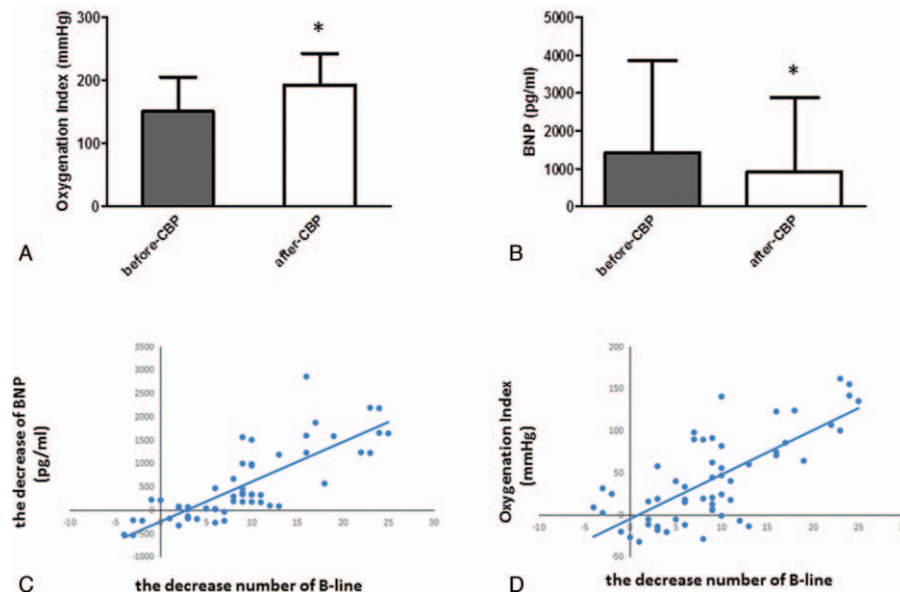


Figure 3. Amelioration of oxygenation index and BNP after 24 hours CBP in patients with MODS. All 76 patients with MODS completed 24 hours CBP. A, The changes of oxygenation index. B, The changes of BNP. C, Correlation analysis between the reduced number of pulmonary ultrasound B-lines and the decrease of BNP ($r=0.785$). D, Correlation analysis between the reduced number of pulmonary ultrasound B-lines and the increase of oxygenation index ($r=0.719$). * $P < .05$ compared with before-CBP. CBP = continuous bedside blood purification, MODS = multiple organ dysfunction syndrome, BNP = B-type natriuretic peptide.

organ dysfunctions is of their own strict regularity. Due to the lungs' anatomical characters, their rich and fine endothelial cells are easily damaged, resulting in vascular contraction, increased capillary permeability, and finally, occurrence of pulmonary edema. Thus, pulmonary edema is the clinically critical condition for MODS with the earliest occurrence and highest incidence and will lead to a fall in lung compliance, rise in respiratory membrane thickness, drop in lungs' ventilation efficiency, lower in oxygenation index, and finally myocardial hypoxemia. In addition, it will also result in an enlargement in lung circulation resistance, increase in BNP, and a rise in heart failure risk.^[20,21] In this case, the detection of EVLW becomes very important. A chest X-ray is the classic means used commonly to diagnose pulmonary edema. The typical X-ray presentations of pulmonary edema are pulmonary vasodilation, blood stasis, and increased lung markings. However, radiographing an eligible chest film is affected by multiple factors, and could pulmonary edema be diagnosed only when EVLW develops to a certain level, meaning that it is lagging behind the appearance of clinical symptoms. CT has its higher resolution and better tissue contrast. Furthermore, its tomogram eliminates the influence of tissue structure overlap. Thus, comparing with ordinary radiography, CT is easier used to diagnose pulmonary edema. However, a computerized tomograph is characteristic of huge device and complex operation. Therefore, it is not suitable to be used for bedside monitoring. In other words, it is not suitable for critically ill patients. Based on pulmonary thermodilution principle, PiCCO has become an important technique for monitoring cardiac output and EVLW. The correlative coefficient between the PiCCO-tested parameter and the EVLW estimated through the so-called golden standard pulmonary weighting method was 0.96.^[22] PiCCO-monitoring method, affected by lung resection, local pulmonary vasoconstriction, as well as necessary deep vein puncture and femoral artery puncture, will cause bigger trauma that easily complicates

with catheter-related infections. In addition, the PiCCO-monitoring kit is expensive, which is inevitable to aggravate the patient's medical burden, all of which limit its clinical application. Ultrasonic diagnosis for patients with severe lung edema has been limited for a long time because the ultrasound beam cannot be conducted in gas. When the ultrasound beam is perpendicularly incident on the pleura-lung surface, reverberating artifacts in ultrasound images could appear as multiple, equidistantly arranged, high-echo lines with orderly decreased intensity, that is, the so-called A-line by Lichtenstein. When the amount of lung fluid increases, the ratio of gas/water changes and the acoustic impedance between gas and liquid enlarges. At this time, a strong reverberation bursts itself at the gas-water interface with a "cometary tail sign" named the B-line, a high echo line perpendicular to the pleural line.^[23] Recently, Lichtenstein proposed a FALLS draft, clearly indicating that in the course of fluid anabiosis in shock patients, the use of pulmonary ultrasound detection can avoid excessive fluid therapy.^[24] Trezzi et al found that after patients received hemodialysis, the number of their B-lines lessened evidently and the decreased number of B-lines was significantly correlated with their body weight loss. These clinic evidences further confirm that the B line can be used as an indicator to assess the level of lung fluid.^[25]

Our study also has some limitation. First, this is a retrospective case-control study, the data collected was limited. Second, MODS were diagnosed, staged, and graded based on the criteria established in the 1995 by National Critical Care Medicine Association in China, other countries and regions may have slightly different criteria for these cases. Finally, we excluded the patients with pulmonary fibrosis, pneumothorax, massive pleural effusion, and other diseases that could affect ultrasound examination and if they were unable to be monitored by PiCCO, so the results cannot be applied to these patients.

5. Conclusions

This study applied pulmonary ultrasound with the change in pulmonary ultrasound B-lines to evaluate the 24 hours negative lung fluid balance in MODS before and after CBP treatment and to compare the evaluated results with the EVLW obtained through the PiCCO. The results showed that the pulmonary ultrasound B-lines not only have high correlation to their EVLW before and after CBP, but also have certain correlation to their blood oxygenation indexes and BNP contents before and after CBP. These findings revealed that using the number of B-lines obtained through pulmonary ultrasound to assess EVLW is a highly sensitive, specific, simple, noninvasive, ease to follow-up, and predictable method. Using it to detect the volumetric states of patients with MODS not only can accurately and rapidly determine their illness so as to, reduce the risk of infection due to invasive examination, but also can relieve their medical burden. Overall, this method is of importance for the individualized management of the volumetric loads of patients with MODS.

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