

## Can Alveolar-Arterial Oxygen Pressure Difference be used to Diagnose Acute Respiratory Distress Syndrome in Pneumonia Patients?

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### Abstract

Alveolar-arterial oxygen pressure difference (P[Aa]O<sub>2</sub>) can reflect pulmonary ability to exchange oxygen; it shows good correlation with the oxygenation index (OI), which is important in diagnosing acute respiratory distress syndrome (ARDS). This study explored the ability of P(Aa)O<sub>2</sub> in diagnosing ARDS in pneumonia patients.

### Methods

We selected patients with community-acquired pneumonia and sepsis in the intensive care unit (ICU) of the People's Hospital of Qiandongnan Miao and Dong Autonomous Prefecture; we measured P(Aa)O<sub>2</sub> and the OI under anoxic conditions upon their admittance to the ICU. We divided the patients into

ARDS and non-ARDS groups. We compared the differences in P(Aa)O<sub>2</sub> and OI; we analyzed the correlation between P(Aa)O<sub>2</sub> and ARDS. To assess the diagnostic ability of P(Aa)O<sub>2</sub> for ARDS, we drew the receiver operating characteristic (ROC) curve.

### Result

We found that P(Aa)O<sub>2</sub> in the ARDS group was greater than in the non-ARDS group ( $t = 8.875$ ,  $P < 0.001$ ); the OI in the ARDS group was smaller than in the non-ARDS group ( $t = -6.956$ ,  $P < 0.001$ ). There was a positive correlation between P(Aa)O<sub>2</sub> and ARDS ( $r = 0.718$ ,  $P < 0.001$ ). The area under the ROC curve for P(Aa)O<sub>2</sub> in the diagnosis of ARDS was 0.931 (0.873–0.988); the cutoff value was 214.70 mmHg, the sensitivity was 89.50%, and the specificity was 85.00%.

### Conclusion

We conclude that P(Aa)O<sub>2</sub> is a good reference index in diagnosing ARDS.

### Introduction

Pneumonia is a common disease of the respiratory system and has a high incidence. If diffuse pulmonary lesions and hypoxemia develop, acute respiratory distress syndrome (ARDS) may result <sup>1</sup>. ARDS patients frequently need to undergo intensive care unit (ICU) treatment owing to that dangerous, complex condition <sup>2</sup>. Currently, there is no specific treatment for ARDS; the mortality rate can attain

40%–50%<sup>3-5</sup>. Early diagnosis and active, effective intervention measures are important toward improving the success rate. According to the Berlin definition, the oxygenation index (OI) constitutes an important indicator for the clear diagnosis and risk stratification of ARDS<sup>6</sup>; the OI can be used as a standard for clinical diagnosis and developing a guide treatment plan. Alveolar-arterial oxygen pressure difference (P[Aa]O<sub>2</sub>) is the difference between alveolar and arterial oxygen partial pressure; it can be used to accurately assess pulmonary ventilation and pulmonary oxygen uptake<sup>7</sup>. ARDS presents the pathological features of diffuse pulmonary inflammation and dysfunctional oxygen exchange. Both P(Aa)O<sub>2</sub> and OI can reflect the state of pulmonary oxygen exchange. To provide a reference for clinical practice, the present study evaluated the effectiveness of P(Aa)O<sub>2</sub> in diagnosing ARDS in pneumonia patients.

## Material and Methods

### Subjects

We selected the study participants among 206 patients with community-acquired pneumonia (CAP) and sepsis who were admitted to the ICU of the People's Hospital of Qiandongnan Miao and Dong Autonomous Prefecture from January 1, 2016 to April 10, 2022. We excluded 22 patients with cardiac insufficiency, 18 with lung malignancy, and 10 with chest trauma; thus, 156 patients were enrolled in this study. They comprised 108 men and 48 women, aged 56–80 years (mean 69.74 ± 6.72 years); there were 76 cases of ARDS and 80 of non-ARDS.

### CAP Diagnostic Criteria

The criteria were as follows: A, community onset; B, pneumonia-related clinical manifestations-(1) recent coughing, expectoration, or aggravation of original respiratory disease symptoms; (2) fever; (3) signs of pulmonary consolidation or audible moist wheezing; (4) peripheral blood leukocytes >10 × 10<sup>9</sup>/L or <4 × 10<sup>9</sup>/L; C, chest imaging showed new patchy infiltrates, consolidation of the lobe or segment, and ground-glass or interstitial changes. We were able to confirm the clinical diagnosis of CAP if we found any of criteria A–C and had excluded the following: pulmonary tuberculosis; pulmonary tumor;

noninfectious pulmonary interstitial disease; pulmonary edema; atelectasis; pulmonary embolism; pulmonary eosinophilic infiltration; and pulmonary vasculitis<sup>8</sup>.

### Sepsis Diagnostic Criteria

We followed the definition and diagnostic criteria of sepsis 3.0 jointly issued by the American Society of Critical Care Medicine and European Society of Critical Care Medicine<sup>9</sup>.

### ARDS Diagnostic Criteria

The criteria were as follows: A, onset time within 1 week after known predisposing factors, new respiratory symptoms, or exacerbation of original symptoms; B, increased opacity of both lungs in chest imaging that could not be satisfactorily explained by pleural effusion, atelectasis, or nodules; C, pulmonary edema with respiratory failure that could not be accounted for by cardiac failure or fluid overload; D, hypoxemia with an OI ≤300 mmHg<sup>6</sup>.

### Treatment

We treated all patients with antibiotics according to standard practice; they received expectorants, anti-asthmatics, nutritional support, and mechanical ventilation as necessary. We undertook the timing and mode of ARDS mechanical ventilation according to guidelines for such ventilation<sup>6,8</sup>.

### Exclusion Criteria

We excluded patients with complicated cardiac insufficiency, pulmonary poisoning, lung malignancy, and pulmonary trauma. We also excluded patients with incomplete data.

### Measurements

Patients were assessed for ARDS within 24 hours of ICU admission; we divided them into ARDS and non-ARDS groups. After patient admission to hospital, 2 ml of arterial blood was withdrawn under anoxic conditions; we immediately undertook blood gas analysis (REDU ABL800 blood gas analyzer, Denmark, according to manufacturer instructions) to determine P(Aa)O<sub>2</sub> and OI. We compared the two groups with respect to gender, age, and P(Aa)O<sub>2</sub> and OI levels. We examined the correlation

between P(Aa)O<sub>2</sub> and ARDS. To analyze the diagnostic ability of P(Aa)O<sub>2</sub> for ARDS, we drew the receiver operating characteristic (ROC) curve.

**Statistical Analysis**

We employed SPSS 24.0 statistical software for data analysis. To test the normality of the measurement data, we applied the Kolmogorov-Smirnov method. We expressed the measurement data of normal distribution as mean ± standard deviation. We applied the following: an independent-sample *t* test for group comparison; the  $\chi^2$  test for count data; the Pearson correlation analysis for correlation between P(Aa)O<sub>2</sub> and ARDS; *r* for expression; and ROC curve analysis to assess the diagnostic ability of P(Aa)O<sub>2</sub> for ARDS. We considered a *P* value below 0.05

statistically significant.

**Results**

We observed no significant differences in gender, age, P(Aa)O<sub>2</sub>, and OI between the two groups ( $\chi^2/t = 0.681, 0.461; P >0.05$ ). P(Aa)O<sub>2</sub> in the ARDS group was greater than in the non-ARDS group (*t* = 8.875; *P* <0.001; OI in the ARDS group was smaller than in the non-ARDS group (*t* = -6.956; *P* <0.001. The differences were statistically significant (Table 1). Our ROC curve analysis showed that the area under the curve for the diagnostic ability of P(Aa)O<sub>2</sub> for ARDS was 0.931 (0.873–0.988). The cutoff value was 214.70 mmHg, the sensitivity 89.50%, and the specificity 85.00% (Figure 1).

Table 1. Gender, age, P(Aa)O<sub>2</sub>, and OI in the ARDS and non-ARDS groups

group	Number of cases (n)	Male/Female (n/n)	Age(year)	P(A-a)O <sub>2</sub> (mmHg)	OI(mmHg)
ARDS group	76	56/20	70.11±7.32	314.28±108.37*	140.53±68.79*
non-ARDS group	80	52/28	69.40±6.17	132.55±66.1	342.58±60.53
$\chi^2/t$ value		0.681	0.461	8.875	-6.965
<i>P</i> value		0.280	0.646	0.000	0.000

Note: \* compared with the non-ARDS group, *P*<0.01

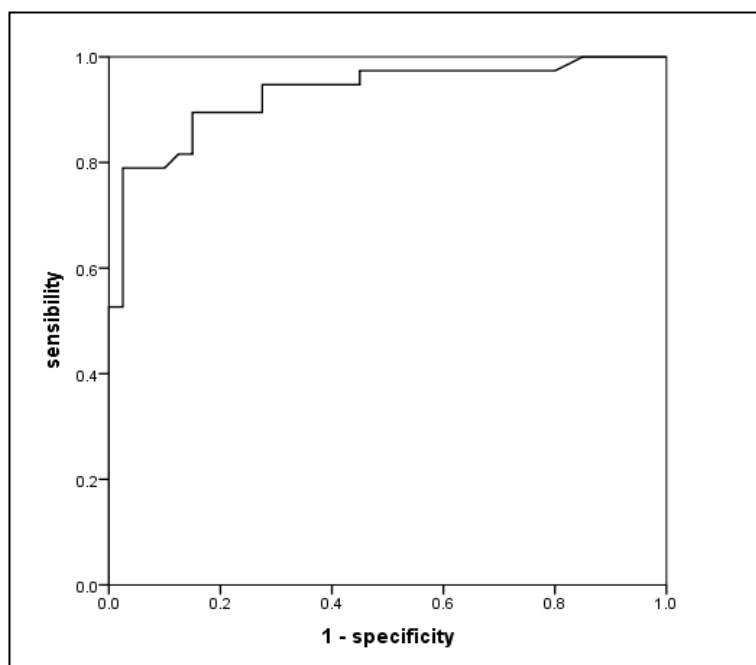


Figure 1. ROC curve for the diagnostic ability of P(Aa)O<sub>2</sub> for ARDS

## Discussion

Serious lung inflammation in sepsis patients may directly lead to pulmonary injury. It can arise as an inflammatory response to pulmonary capillary endothelial cells and alveolar epithelial cells damaged by a significant increase in alveolar capillary wall permeability; it may spread extensively in the lung and produce pulmonary interstitial edema<sup>10-14</sup>. The result can be impaired oxygen exchange, lung compliance, and significantly reduced pulmonary function<sup>15</sup>. ARDS is clinically characterized by stubborn hypoxemia. ARDS is a common cause of death among ICU patients with severe pulmonary infection; the fatality rate is high and treatment is difficult<sup>16</sup>. Reportedly, most patients who recover suffer severe sequelae<sup>17-18</sup>, which makes it difficult for them to lead normal lives. For ARDS patients with severe pulmonary infection, timely effective preventive measures, appropriate determination of ARDS status, and well-timed effective intervention are key to successful treatment<sup>3</sup>. ARDS patients have an imbalance between ventilation and blood flow ratio, resulting in a decreased respiratory quotient; simultaneously, there is reduced arterial oxygen partial pressure, leading to an increase in  $P(Aa)O_2$ <sup>19-20</sup>. Studies have shown that  $P(Aa)O_2$  can accurately reflect ARDS patients' intrapulmonary shunt and diffuse dysfunction;  $P(Aa)O_2$  can precisely evaluate pulmonary gas exchange capacity, which correlates well with pulmonary oxygen level and function<sup>7,21</sup>. Thus, monitoring  $P(Aa)O_2$  can help evaluate dynamic changes in pulmonary lesions in ARDS patients, which is advantageous in individual management of ARDS.

As a common diagnostic and risk stratification indicator for ARDS, OI provides a reference for medical treatment<sup>22</sup>. In the present study,  $P(Aa)O_2$  correlated negatively with OI ( $r = -0.555, P < 0.001$ ), indicating that  $P(Aa)O_2$  has diagnostic ability for ARDS. This investigation showed that when  $P(Aa)O_2$  was greater than 214.70 mmHg, the sensitivity and specificity of  $P(Aa)O_2$  were 89.50% and 85.00%, respectively, in diagnosing ARDS; this finding underlines the clinical value of  $P(Aa)O_2$  in such diagnosis.  $P(Aa)O_2$  is appropriate owing to the pathology of ARDS, which is an oxygen exchange disorder caused by

inflammation:  $P(Aa)O_2$  has high sensitivity in reflecting pulmonary oxygen exchange. Some studies have reported the significance of  $P(Aa)O_2$  for ARDS. Wang and Associates suggested that  $P(Aa)O_2$  can provide a clear early warning for ARDS in patients with severe pneumonia<sup>23-24</sup>.  $P(Aa)O_2$  can be used for the stratified diagnosis and guiding treatment of ARDS patients<sup>25</sup>. Yang et al. suggested that  $P(Aa)O_2$  may play an important role in indicating the severity of ARDS in patients with pulmonary infection; it can also be used to assess the risk of fatality<sup>26</sup>.  $P(Aa)O_2$  may be employed as an important reference indicator for judging clinical efficacy. Zhang et al. found that  $P(Aa)O_2$  dynamic monitoring was effective in making a dynamic assessment for pulmonary disease and could be used to guide clinical treatment<sup>27</sup>. Yu et al.<sup>20</sup> and Shen et al.<sup>28</sup> suggested that  $P(Aa)O_2$  can guide the withdrawal of mechanical ventilation in ARDS patients. The clinical application of  $P(Aa)O_2$  for ARDS patients was confirmed in the present study.

Some limitations of this study deserve mention. We had relatively few cases, and we selected only sepsis patients from one central ICU; their conditions were quite severe, so there could have been some significant deviation in the cutoff value we determined. We measured  $P(Aa)O_2$  directly by blood gas analysis with arterial blood, which was simple, convenient, and repeatable. However, whether  $P(Aa)O_2$  is as convenient a measure as OI requires further prospective clinical studies regarding the ability to assess ARDS and its practicability.

## Conclusion

$P(Aa)O_2$  is a good diagnostic index for pneumonia patients with ARDS complications.

## Declarations

## Competing Interests

The authors have no conflicts of interest to declare

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### Ethical Approval

The research was approved by the medical ethics committee of the people's Hospital of Qiandongnan Miao and Dong Autonomous Prefecture.

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