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Benefit of the Application of New ARDS Criteria (Berlin) Compared to Old Criteria (AECC) in a Tertiary Hospital in a Developing Country

Zulkifli Amin\(^1\), Astrid Priscilla Amanda\(^1\), Chrispian O Mamudi\(^1\)

\(^1\)Division of Respirology and Critical Illness, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia/Cipto Mangunkusumo Hospital, Jakarta, Indonesia

ABSTRACT

**Background:** There have been several ARDS definitions throughout years, including those by Laennec, Ausbagh, the Lung Injury score (LIS), and the American-European Consensus Conference (AECC) criteria in 1821, 1967, 1998, and 1994, respectively. In 2012, a new diagnostic criteria, the Berlin criteria, was published.

**Objective:** To identify benefits of implementing the Berlin criteria as compared to the AECC criteria in a tertiary hospital of a developing country

**Method:** This is a prospective, observational study conducted at a tertiary hospital in Jakarta from October 2015 to June 2016. Data was collected from ARDS patients in the emergency room, ICU, resuscitation room, and in-patient ward.

**Result:** There were 104 ARDS patients according to the Berlin criteria, while only 75 patients were diagnosed as ARDS according to the AECC criteria. Both criteria showed that majority of the patients were male; the APACHE score was <20; the Charlson comorbidity index 2; and sepsis was the most common etiology. Seven-day survival was higher in the Berlin criteria (51.9%) than in the AECC criteria (48%).

**Conclusion:** Application of the Berlin criteria in developing countries is more beneficial compared to the AECC criteria as a larger number of ARDS patients can be diagnosed, earlier diagnosis leads to earlier management thus increasing the survival rate, and excluding the use of a pulmonary artery catheter to measure the pulmonary wedge pressure

**Keywords:** Berlin, AECC, criteria, developing country.

INTRODUCTION

Laennec in 1821 described a condition characterized by pulmonary edema that occurred with no evidence of heart failure. Some terms were used to described the condition, such as double pneumonia, lung shock, and post traumatic lung.\(^1\) Asbaugh et al, in 1967 was the first to coin the term Acute Respiratory Distress Syndrome (ARDS). This condition was based on 5 clinical features including an associated risk factor, severe hypoxemia despite adequate oxygen supplementation, bilateral infiltrates on chest x-ray, decreased lung compliance, and no evidence of congestive heart failure.\(^2\) In 1998, another ARDS diagnostic criteria was made, the Lung Injury Score (LIS). There were 4 aspects of the respiratory injury, including positive end expiratory pressure (PEEP), PaO\(_2\)/FiO\(_2\) ratio, lung compliance, and infiltrates on chest X-ray. Each item was assigned a score from 1 to 4 points. The patient would be diagnosed with ARDS if the total score was more than 2.5.\(^3\)
The definition of Acute Respiratory Distress Syndrome (ARDS) according to the American-European Consensus (AECC) in 1994 was acute hypoxemia (PaO$_2$/FiO$_2$ ratio of 200 mmHg) with bilateral infiltrates on chest X-ray, without evidence of left atrial hypertension. On the other hand, Acute Lung Injury (ALI), which has a similar clinical criteria similar to ARDS, has a lower degree of hypoxemia compared to ARDS (PaO$_2$/FiO$_2$ ratio of 300 mmHg).

In 2012, a panel of experts from The European Society of Intensive Care Medicine, the American Thoracic Society, and the Society of Critical Care Medicine revised the ARDS definition. The panel agreed on the earlier concept of ARDS and further detailed the understanding of acute onset; the classification of decreased oxygenation; the minimum PEEP value; exclusion of hydrostatic pulmonary edema; and the new radiologic criterion. Further, a new classification of ARDS; mild, moderate, and severe ARDS was determined. The objective of this study was to highlight the benefits of implementing the Berlin criteria, as compared to the AECC criteria in the tertiary hospitals of developing countries.

**MATERIALS AND METHOD**

This was a prospective, observational study conducted in the emergency room, intensive care unit (ICU), high care unit (HCU), resuscitation room, and in-patient wards of a tertiary hospital in Jakarta from October 2015 to June 2016. The inclusion criteria were as follows: (1) diagnosed as ARDS based on the Berlin criteria and AECC criteria, (2) age 18 years and older. The exclusion criterion was patients discharged within less than 7 days since diagnosed as ARDS. This study has been reviewed and approved by The Health Research Ethics Committee of the Faculty of Medicine Universitas Indonesia and Dr. Cipto Mangunkusumo National General Hospital.

**Variables and Measurement**

The demographic characteristics included age and gender. The clinical characteristics reported include etiology of ARDS; ARDS classification according to the Berlin criteria and the AECC criteria; comorbidity; Charlson comorbidity index (CCI); Acute Physiology and Chronic Health Evaluation (APACHE) II score; ventilator utilization; and outcome of the patient in the following 7 days (dead or survived).

In this study, two diagnostic criteria (the Berlin criteria and AECC criteria) were applied. The specifics of each diagnostic criteria can be seen in Table 1.

<table>
<thead>
<tr>
<th>Berlin Criteria</th>
<th>AECC Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild ARDS: PaO$_2$/FiO$_2$ ratio ≤300 and &gt;200</td>
<td>PaO$_2$/FiO$_2$ ratio of 200 mmHg</td>
</tr>
<tr>
<td>Moderate ARDS: PaO$_2$/FiO$_2$ ratio 100-200</td>
<td>Bilateral infiltrates in chest X-ray</td>
</tr>
<tr>
<td>Severe ARDS: PaO$_2$/FiO$_2$ ratio &lt;100</td>
<td>No evidence of left atrial hypertension</td>
</tr>
</tbody>
</table>

The etiology of ARDS was categorized into sepsis and non-sepsis. Comorbidity was defined by the presence of a documented clinical diagnosis at the end of hospitalization. The diagnosis included were diabetes mellitus, chronic kidney disease (CKD), systematous lupus erythematos (SLE), liver cirrhosis, cerebrovascular disease (CVD), cancer, acquired immune deficiency syndrome (AIDS), and kidney transplant recipient.

The CCI is a method of measuring the severity of a patient’s co-morbidities. Each comorbidity is given a score; 1 point for myocardial infarction, congestive heart failure, peripheral vascular disease, dementia, cerebrovascular disease, chronic lung disease, connective tissue disease, gastrointestinal ulcer, mild liver disease, diabetes mellitus; 2 points for hemiplegia, moderate to severe kidney disease, diabetes with end organ damage, any tumor, leukemia, lymphoma; 3 points for moderate or severe liver disease; 6 points for autoimmune deficiency syndrome, metastatic solid tumor. The points are totaled, and then categorized into >2 and 2.

The APACHE II score is a measurement of disease severity. It is used to assess the risk of in-hospital mortality. This score is calculated within the first 24 hours of ARDS, and it is categorized into <20 and 20. Ventilator utilization is the use of a ventilator within the first 48 hours following ARDS diagnosis. Outcome of the patient is their condition after 7 days of hospitalisation, dead or survived.

**Statistical Analysis**

Analysis was conducted using the SPSS software version 20.0. For qualitative variables, a descriptive
analysis is presented as frequencies (percentage). Frequency of the quantitative variables were calculated and are presented as mean±SD. If the data was not normally distributed, the data is presented as median (interquartile range/IQR).

**RESULTS**

There were 104 ARDS patients based on the Berlin criteria and 75 patients according to the AECC criteria. The demographic and clinical characteristic of the patients are listed in Table 2 and 3.

**Table 2. Demographic Characteristic**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Berlin Criteria (n: 104)</th>
<th>AECC Criteria (n:75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean±SD</td>
<td>53.06 ± 17.103</td>
<td>52.92 ±17.584</td>
</tr>
<tr>
<td>Gender</td>
<td>Male 52 (50%)</td>
<td>Male 38 (50,7%)</td>
</tr>
<tr>
<td></td>
<td>Female 52 (50%)</td>
<td>Female 37 (49,3%)</td>
</tr>
</tbody>
</table>

**Table 3. Clinical Characteristic**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Berlin Criteria (n: 104)</th>
<th>AECC Criteria (n:75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classification of ARDS</td>
<td>Severe 26 (25%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moderate 49 (47,1%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mild 29 (27,9%)</td>
<td></td>
</tr>
<tr>
<td>Etiology of ARDS</td>
<td>Non sepsis 5 (4,8%)</td>
<td>Non sepsis 5 (6,7%)</td>
</tr>
<tr>
<td></td>
<td>Sepsis 99 (95,2%)</td>
<td>Sepsis 70 (93,3%)</td>
</tr>
<tr>
<td>APACHE II score</td>
<td>&lt;20: 67 (64,4%)</td>
<td>&lt;20: 47 (62,7%)</td>
</tr>
<tr>
<td></td>
<td>20: 37 (35,6%)</td>
<td>20: 28 (37,3%)</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>26 (25%)</td>
<td>18 (24%)</td>
</tr>
<tr>
<td>SLE</td>
<td>3 (2,9%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>CKD</td>
<td>15 (14,4%)</td>
<td>12 (16%)</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>2 (1,9%)</td>
<td>1 (1,3%)</td>
</tr>
<tr>
<td>Cancer</td>
<td>34 (32,7%)</td>
<td>22 (29,3%)</td>
</tr>
<tr>
<td>CVD</td>
<td>14 (13,5%)</td>
<td>11 (14,7%)</td>
</tr>
<tr>
<td>AIDS</td>
<td>3 (2,9%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Kidney transplant recipient</td>
<td>(1%)</td>
<td>1 (1,3%)</td>
</tr>
<tr>
<td>CCI</td>
<td>&gt;2: 28 (26,9%)</td>
<td>&gt;2: 23 (30,7%)</td>
</tr>
<tr>
<td></td>
<td>2: 76 (73,1%)</td>
<td>2: 52 (69,3%)</td>
</tr>
<tr>
<td>Ventilator</td>
<td>Yes 45 (43,3%)</td>
<td>Yes 32 (42,7%)</td>
</tr>
<tr>
<td>Outcome</td>
<td>Survived 54 (51,9%)</td>
<td>Survived 36 (48%)</td>
</tr>
<tr>
<td></td>
<td>Dead: 50 (48,1%)</td>
<td>Dead: 39 (52%)</td>
</tr>
</tbody>
</table>

The mean age of patients according to the Berlin criteria is 53.06 ± 17.103, while in the AECC criteria is 52.92 ± 17.584. Majority of the patients in both groups were male. Based on the Berlin criteria, most patients were classified as moderate ARDS, 49 (47.1%). The primary etiology of ARDS in the Berlin criteria and the AECC criteria was sepsis consisting of 99 patients (95.2%) and 70 patients (93.3%), respectively.

In both criteria, majority of patients had a Charlson comorbidity index 2, 76 patients according to the Berlin criteria (73,1%) and 52 according to the AECC criteria (69,3%). Further, an APACHE II score of <20 was most common among the participants, 67 according to the
Berlin criteria (64.4%) and 47 according to the AECC criteria (62.7%). Patient co-morbidities include diabetes mellitus, SLE, CKD, cirrhosis, cancer, CVD, AIDS, and kidney transplant recipients. Most of the patients were not ventilated. Patient survival as based on the Berlin criteria was 54 patients (51.9%), while patient survival according to the AECC criteria was 36 (48%).

**DISCUSSION**

There were 104 ARDS patients according to the Berlin criteria, while only 75 patients was diagnosed as ARDS according to the AECC criteria. This result may be attributed to the wider $\text{PaO}_2/\text{FiO}_2$ ratio range in the Berlin Criteria as compared to the AECC criteria. Thus, the advantage of the Berlin criteria in encompassing more ARDS patients as compared to previous criteria; and its ability to detect ARDS patient earlier are highlighted.

The mean age of patients diagnosed by the Berlin criteria and AECC criteria were similar (53.06 ± 17.103 and 52.92 ± 17.584, respectively). A study by Rubenfeld et al, showed that the incidence of ARDS increased with age. For patients age 15-19 years, the incidence was 16 per 100,000 person/years and the rate increased to 306 per 100,000 for patients age 75-84 years.

Males were predominant in both criteria. A study by Nadia et al, showed similar results, that males were predominant among those diagnosed with ARDS. However, a different result was showed by Daithi et al. This study reported that females are more likely to develop ARDS than males following critical injury, but the mortality rate is similar in both genders. The relationship between immune-depressing testosterone and pro-inflammatory estrogens are thought to be important factors, regardless of gender.

Sepsis is a major etiology of ARDS in both criteria. ARDS usually develops in a condition that induces systemic inflammatory response, such as sepsis, pneumonia, major trauma, multiple transfusions, aspiration, or acute pancreatitis. However, among these factors, sepsis is the most common cause of ARDS.

The APACHE II score was <20 in both criteria. Saleh et al, in their study concluded that performance of the APACHE II/III score was superior to other scores with regard to mortality prediction. Chawla et al, stated that the APACHE score is one of the factors that contributes to mortality other than shock, low $\text{PaO}_2/\text{FiO}_2$, and ARDS severity. E.Sealey et al, concluded that a higher APACHE II score was associated with increased mortality rate.

Majority of the patients in this study had a Charlson comorbidity index 2. Han-Yi Wang et al, stated that a high CCI index (2) in the emergency department revisiting patients showed higher admission rate, longer hospital stay, poorer prognosis, and high in-hospital mortality. Another study conducted by Ando et al, stated that patients with CCI 4 had poor prognosis.

The list of co-morbidities found in this study were diabetes mellitus, SLE, CKD, cirrhosis, cancer, CVD, AIDS, and kidney transplant recipients. The presence of co-morbidities (pulmonary or non-pulmonary) is one of the risk factor that contributes to mortality in ARDS patients. In addition, factors such as increasing age, worsening multi-organ dysfunction, higher APACHE II score, and acidosis contribute to mortality as well. It should be noted that this study was conducted in a tertiary hospital which accepts patients referred from another hospitals in Jakarta and other provinces of the country. Thus, the patients tend to present with more complicated diseases. Further, a large percentage of the patients have multiple co-morbidities that worsen their condition.

In both criteria, most of patients did not receive ventilation. In the Berlin criteria group, there were 59 patients (56.7%) who were not ventilated with 17 patients classified as severe ARDS. Ideally, these patients should be ventilated, but they were not due to the limited number of ventilators available at the hospital. In fact, mechanical ventilation is important for ARDS patients. Ventilation works by two mechanisms, first it allows precise titration of $\text{FiO}_2$ in the gas delivered, and secondly, it provides sufficient pressure to open some of the collapsed lung during the inspiratory phase. It is hoped that this result may provide sufficient support so hospitals can increase the number of ventilators as ventilators are of prime importance in ARDS treatment.

This study compared the Berlin criteria to the AECC criteria. In comparison, there have been several studies that compared the various ARDS diagnostic criteria. Goh et al (1998) compared the Lung Injury Score (LIS) with the AECC criteria. The results show that both criteria identified a similar group of ARDS patients. Further, Niall et al (2005) compared the diagnostic accuracy of
three ARDS diagnostic criteria: AECC criteria, LIS, and Delphi definition. It was concluded that ARDS was under-diagnosed by the clinicians.\(^{20}\)

In this study, we compared two ARDS diagnostic criteria according to patient survival. Patient survival was higher in the Berlin criteria (51.9\%) than in the AECC criteria (48\%). This may be attributed to the larger number of patients that are encompassed by the Berlin criteria compared to the AECC criteria. However, it should be noted that patients with \(\text{PaO}_2/\text{FiO}_2\) ratio \(\leq 300\) are diagnosed with ARDS, thus, earlier ARDS diagnosis can be made compared to when the AECC criteria is used. Moreover, earlier diagnosis allows earlier management of the ARDS patient, hence it can increase the survival rate of ARDS patients in general.

Moreover, the Berlin criteria rules out the use of a pulmonary artery catheter to measure the pulmonary wedge pressure. A patient can be diagnosed with ARDS whether the respiratory failure is not caused by heart failure or fluid overload, as it is based on clinical judgement.\(^{4}\) This may be beneficial in developing countries that have limited resources and facilities.

There are several limitations in this study. Firstly, the number of patients included was small as the duration of this study was short. In addition, it used descriptive statistics alone to compare the Berlin criteria and the AECC criteria. Further study using a more comprehensive statistical analysis statistic may reveal a more detailed result.

**CONCLUSION**

The Berlin criteria allows a larger number of patients to be diagnosed with ARDS as compared to the AECC criteria. There were 104 ARDS patients according to the Berlin criteria, while only 75 patients were diagnosed with ARDS according to AECC criteria. Earlier ARDS diagnosis can be made based on the Berlin criteria due to the higher \(\text{PaO}_2/\text{FiO}_2\) ratio limits implemented as compared to the AECC criteria. Earlier diagnosis allows earlier management of the ARDS patient, Hence it can increase the survival rate of ARDS patients. Additionally, the Berlin criteria excludes the use of a pulmonary artery catheter to measure the pulmonary wedge pressure which is beneficial for developing countries with limited resources and facilities. However, further investigation is required to further detail the benefits of the Berlin criteria as compared to the AECC criteria.

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11. Heffernan DS, Dossett LA, Lightfoot MA, Fremont RD, Ware LB, Sawyer RG, et al. Gender and


