

Initial oxygenation as early predictor of mortality in acute respiratory distress syndrome: a retrospective study

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Abstract

Introduction: Acute respiratory distress syndrome (ARDS) is a major contributor to mortality and morbidity of adult patients admitted to intensive care units (ICU). Numerous scoring systems have been developed for critically ill patients with the goal of more accurately predicting clinical outcomes. However, the variability in these scores among individual patients, and consequently, their individual predictive ability is quite limited. **Aim:** To evaluate the role of initial oxygenation as an early predictor of mortality in ARDS patients. **Methodology:** One hundred and six mechanically ventilated adult patients with ARDS were enrolled retrospectively. Baseline parameters from the day of ICU admission were recorded. The details of ventilation, inspired oxygen fraction required, positive end-expiratory pressure and number of days on ventilation along with duration of hospital stay were recorded. Similarly, the status of oxygenation was assessed using PaO₂/FiO₂ (P/F) ratio. Survival of the patients was correlated with the baseline status of oxygenation. **Results:** Of the 106 patients, 65 were males and 41 female. The mean (\pm SD) age was 44 years (16.08). The difference in the P/F ratio between survivors and nonsurvivors was statistically significant. The ROC curve showed a cutoff value for P/F ratio of 108. Among survivors, the ICU stay was shorter in patients in pulmonary group compared to extrapulmonary group. **Conclusion:** Mortality is high if the baseline P/F ratio at admission is below 108. There is no difference in mortality due to lung injury caused by pulmonary or extrapulmonary aetiologies. ICU stay is longer among survivors if cause of ARDS is extrapulmonary.

Keywords: Acute respiratory distress syndrome, initial oxygenation, mortality

Introduction

Acute respiratory distress syndrome (ARDS), is associated with high mortality and morbidity in patients admitted to intensive care units (ICU).¹ The mortality rates vary from 30 to 70% even with the advances in understanding of the pathophysiology and treatment of ARDS.² The ARDS Network trial

reported an overall mortality of 35.4% at 180 days in a total trial population which composed of 83.5% ARDS patients.³ The review of Kraft *et al* in 1996 of 101 studies over the period 1967-1994, in 3264 patients, had previously suggested a stable mortality of ARDS of 50%.⁴ Numerous scoring systems have been developed for critically ill patients with the goal of more accurately predicting clinical outcomes. However, there is considerable variation in these scores among individual patients, and consequently, their individual predictive ability is limited.⁵⁻⁸ This study was done to evaluate the role of initial oxygenation status as an early predictor of mortality in ARDS patients.

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Methodology

This retrospective study included one hundred and six mechanically ventilated adult patients with ARDS (diagnosed based on the Berlin definition of ARDS) who were admitted to the medical and multidisciplinary intensive care units (ICU) of the University and Medical College Hospital between October 2012 and October 2013. The study protocol was approved by the institutional board of ethics committee. Patients less than 18 years and those with obstructive pulmonary disease were excluded.

The following parameters from the day of admission were recorded as baseline: Demographic data of the patients, severity of illness score (APACHE II), whether it was a surgical or medical admission and the cause of ARDS (pulmonary or extrapulmonary).

The details of ventilation including inspired oxygen fraction (FiO₂), positive end-expiratory pressure, number of days of mechanical ventilation and duration of hospital stay were recorded. Similarly, arterial blood gas values such as pH, partial pressure of oxygen (PaO₂), partial pressure of carbon dioxide (PaCO₂) and actual serum bicarbonate were recorded. The status of oxygenation was assessed using PaO₂/FiO₂ (P/F) ratio. Survival of the patients to hospital discharge was correlated with the baseline status of oxygenation.

Results

The data of 106 subjects with ARDS were collected, 65 of whom were male (61.3%) and 41 female patients (38.7%). The mean (± SD) age of the patients was 44 (±16.08) years. The difference in the P/F ratio between survivors and nonsurvivors were compared using Mann-Whitney Test (Table 1) and was statistically significant. The difference in the P/F ratio between pulmonary and extrapulmonary ARDS were compared using Mann-Whitney U test (Table 2) and was statistically significant.

Table 1: Comparison of P/F ratio among survivors and nonsurvivors

Outcome	Number of subjects (N)	P/F Median(IQR)	P value
Survived	58	133(109,183)	0.00 (P < 0.005)
Expired	48	89(79,121)	
Total	106		

Table 2: Comparison of initial P/F ratio between pulmonary and extrapulmonary ARDS

Outcome	Pulmonary (n)	Extrapulmonary (n)
Survived	15	43
Expired	10	38
Total	25	81
P/F Median (IQR)	103 (88,165)	122 (87,152)
P value	0.040 (P<0.005)	0.00 (P<0.005)

A receiver operating characteristic (ROC) curve was constructed and it was found that baseline P/F ratio of less than 108 has a higher mortality rate among all ARDS patients with sensitivity of 78% and specificity of 70% (Figure 1).

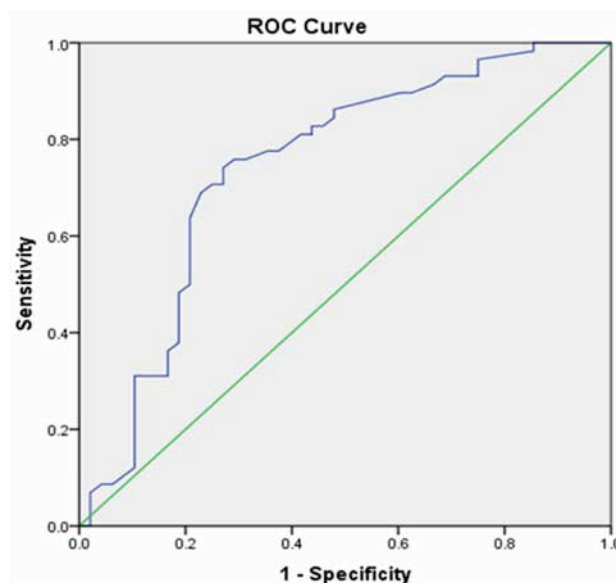


Figure 1: The area under the curve 0.74, standard error of 0.05 (95% confidence interval 0.64 – 0.84) for initial P/F ratio and survival in all patients with ARDS requiring mechanical ventilation

When ROC curve was constructed, it was found that baseline P/F ratio of 111 has a higher mortality rate among extrapulmonary ARDS with sensitivity of 76% and specificity of 71%. Similarly, a baseline P/F

ratio of 100 had a higher mortality rate among pulmonary ARDS with sensitivity of 80% and specificity of 79%.

When the pulmonary and extrapulmonary group of ARDS were compared, the median (interquartile range – IQR) stay in ICU for pulmonary group was 9 (6, 13) days and for extrapulmonary group was 12 (9, 21) days (*Figure 4*).

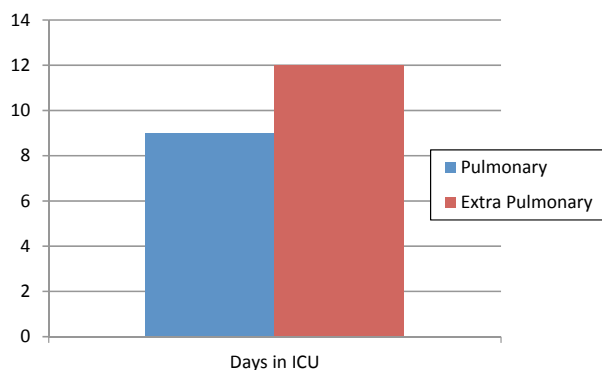


Figure 2: Number of days of stay in ICU among survivors

Discussion

Gupta *et al* tried to correlate survival from ARDS with age, aetiology, disease severity scores and organ failure using multivariate analysis and found that sepsis, APACHE III score > 57 and SAPS II score > 39 were all associated with increased risk of mortality.⁹

The value of $\text{PaO}_2/\text{FiO}_2$ as an early predictor of death in ALI/ ARDS is not known. Bone and colleagues observed that rather than the $\text{PaO}_2/\text{FiO}_2$ ratio at the onset of ARDS, a steady increase in $\text{PaO}_2/\text{FiO}_2$ during the first week of conventional therapy is characteristic of survival.⁵ Similarly, Ware *et al* found that $\text{PaO}_2/\text{FiO}_2$ at the onset of ARDS did not predict clinical outcome but if the $\text{PaO}_2/\text{FiO}_2$ remained persistently low, worse outcomes can be expected and may be a marker of failure to respond to conventional therapy.¹⁰ Thus, these authors found that in contrast to the $\text{PaO}_2/\text{FiO}_2$ ratio at admission, its trend is more predictive of mortality. A positive trend is likely to indicate a better outcome whereas no change or a negative trend is likely to predict mortality.

Other authors have suggested that oxygenation index (OI) may be a better predictor of death than $\text{PaO}_2/\text{FiO}_2$ because it includes changes in mean airway pressure as well as FiO_2 . Trachsel and colleagues found that OI, measured at any time during hospitalisation, was the best pulmonary predictor of death in a group of paediatric patients with acute hypoxic respiratory failure.⁶

In our study the difference in the $\text{PaO}_2/\text{FiO}_2$ ratio between survivors and nonsurvivors were compared using Mann-Whitney Test and was statistically significant, which suggest that $\text{PaO}_2/\text{FiO}_2$ can be used as predictor of mortality at early stage of ARDS. We did not calculate oxygenation index and our study was done in adult population.

Luhr *et al* conducted a study that included 132 intensive care patients in three countries (including medical, surgical and neurological patients) found that chronic liver disease, a $\text{PaO}_2/\text{FiO}_2$ ratio of <108 and age to be independent predictors of death.¹¹ In most studies, a low initial oxygenation abnormality as defined by the $\text{PaO}_2/\text{FiO}_2$ ratio did not predict mortality unless it was grossly abnormal.^{12,13}

Current evidence states that persistently low P/F ratio is associated with worse outcomes and may be useful as an indicator of predicting mortality in ARDS.^{5, 14} We found in our study that the $\text{PaO}_2/\text{FiO}_2$ at the onset of ARDS was independently associated with mortality. This finding disagrees with most studies in ARDS. We constructed a receiver operating characteristic (ROC) curve and it was found that baseline P/F ratio ≤ 110 has a higher mortality rate among ARDS patients, in spite of the aetiology. The ICU stay was longer in the extrapulmonary group among survivors.

In one study, it was found that there was no difference in mortality due to lung injury caused by pulmonary or extrapulmonary aetiologies.¹⁵ Further studies should specifically focus on specific subsets of these subgroups such as sepsis-related or trauma-related lung injury rather than the broad categories of pulmonary and extrapulmonary lung injury.

There were some limitations in our study. Our sample size was small and enrolment of patients was carried out at only one study centre. We included only 106 patients and a larger study would substantiate the finding better.

Conclusion

In patients with ARDS, the mortality rate is high if the baseline P/F ratio at admission is below 108. There is no difference in mortality due to lung injury caused by pulmonary or extrapulmonary aetiologies. Hospital stay is longer among survivors if cause of ARDS is extrapulmonary.

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