Utility of Pulse Oximetry Oxygen Saturation (SpO₂) with Incorporation of Positive End-Expiratory Pressure (SpO₂ * 10/FiO₂ * PEEP) for Classification and Prognostication of Patients with Acute Respiratory Distress Syndrome

Pratibha Todur, Anitha Nileshwar, Souvik Chaudhuri, Nitin Gupta, Srikant Natarajan, and Shwethapriya Rao

1 Department of Respiratory Therapy, Manipal College of Health Professions, Manipal Academy of Higher Education, Manipal 576104, Karnataka, India
2 Department of Anaesthesiology, Kasturba Medical College, Manipal Academy of Higher Education, Manipal 576104, Karnataka, India
3 Department of Critical Care Medicine, Kasturba Medical College, Manipal Academy of Higher Education, Manipal 576104, Karnataka, India
4 Department of Infectious Diseases, Kasturba Medical College, Manipal Academy of Higher Education, Manipal 576104, Karnataka, India
5 Department of Oral Pathology & Microbiology, Manipal College of Dental Sciences, Mangalore 575001, Karnataka, India

Correspondence should be addressed to Souvik Chaudhuri; souvikchaudhuri1207@gmail.com

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Background. Conventionally, PaO₂/FiO₂ (P/F ratio) has been used to categorize severity of acute respiratory distress syndrome (ARDS) and prognostication of outcome. Recent literature has shown that incorporation of positive end-expiratory pressure (PEEP) into the P/F ratio (PaO₂ * 10/FiO₂ * PEEP or P/FP* 10) has a much better prognostic ability in ARDS as compared to P/F ratio. The aim of this study was to correlate SpO₂ * 10/FiO₂ * PEEP (S/FP* 10) to PaO₂ * 10/FiO₂ * PEEP (P/FP* 10) and evaluate the utility of S/FP* 10 as a reliable noninvasive indicator of oxygenation in ARDS to avoid repeated arterial blood sampling.

Aim. To evaluate if pulse oximetry is a reliable indicator of oxygenation in ARDS patients by calculating SpO₂ * 10/FiO₂ * PEEP (S/FP* 10). The primary objective was to determine the correlation of S/FP* 10 to P/FP* 10 ratio in ARDS patients. The secondary objective was to determine the cut-off value of S/FP* 10 ratio to predict severe ARDS and survival.

Methods. Patients aged 18–80 years on invasive mechanical ventilation (MV) diagnosed with ARDS as defined by the Berlin definition were included. The values of PaO₂, FiO₂, and SpO₂ were collected at three different time points. They were at baseline, i.e., after intubation and initiation of MV (within one hour of intubation), day one (1–24 hours of MV), and day three (48–72 hours of MV). The primary outcome was survival at the end of intensive care unit (ICU) stay. Results. A total of 85 patients with ARDS on invasive MV were included. The data points were obtained at baseline, day one, and day three of MV. S/FP* 10 ratio has an excellent correlation to P/FP* 10 ratio at baseline and day three of invasive MV (r = 0.831 and 0.853, respectively; p < 0.001) and has a strong correlation on day one of invasive MV (r = 0.733, p < 0.001). S/FP* 10 ratio ≤ 116 at baseline has excellent discriminant function to be categorized as severe ARDS as per Berlin definition (AUC: 0.925, p < 0.001, 90% sensitivity, 93% specificity, CI: [0.862–0.980]). The increase in S/FP* 10 ratio by ≥ 64.40 from baseline to day three of MV is a good predictor of survival (AUC: 0.877, p < 0.001, 73.5% sensitivity, 97% specificity, CI: [0.803–0.952]). Conclusion. S/FP* 10 has a strong correlation to P/FP* 10 in ARDS patients. S/FP* 10 ≤ 116 has an excellent discriminant function to be categorized as severe ARDS. The S/FP* 10 ratio on day three of MV and the change in S/FP* 10 ratio from baseline and day one to day three of MV are good predictors of survival in ARDS patients. This trial is registered with CTRI/2020/04/024940.
1. Introduction

The severity, oxygenation status, and extent of lung injury in acute respiratory distress syndrome (ARDS) have traditionally been assessed by the ratio of partial pressure of arterial oxygen to fraction of inspired oxygen (PaO₂/FiO₂ or P/F ratio) as per the Berlin definition [1]. However, the P/F ratio is often misleading in predicting the extent of lung injury [2, 3]. Two different mechanically ventilated patients with the same P/F ratio may have different positive end-expiratory pressures (PEEP). As the application of PEEP will improve the PaO₂, calculating a P/F ratio without taking PEEP into account may be misleading [2]. A recent study has shown that PaO₂ * 10/FiO₂ * PEEP (P/FP * 10) ratio has a significantly better predictive ability for mortality in ARDS patients when compared to P/F ratio alone [2]. However, as these values change significantly during the course of mechanical ventilation (MV) in a patient, repeated arterial sampling is required which is associated with increased chances of infection, blood loss, patient discomfort, and costs [4, 5].

2. Aim

The aim of this study is to evaluate oxygen saturation by pulse oximetry (SpO₂) as an alternative noninvasive reliable indicator of oxygenation by calculating SpO₂ * 10/FiO₂ * PEEP (S/FP * 10) ratio. SpO₂ measurement is widely available, is conducive to use, enables continuous monitoring, and is reliable [6]. To the best of our knowledge, this is the first study that has incorporated the concept of PEEP into SpO₂/FiO₂ (S/F) to evaluate its accuracy in predicting severe ARDS and survival. The primary objective of the study was to determine the correlation of the S/FP * 10 ratio to P/FP * 10 in patients with ARDS. The secondary objective was to determine the cut-off value of the S/FP * 10 ratio to predict severe ARDS and survival.

3. Materials and Methods

3.1. Study Setting and Approvals. It was a single-centre prospective observational study conducted at the level III intensive care units (ICUs) of a tertiary care medical college from September 2020 to September 2021. This data was a secondary analysis of an ongoing prospective observational study approved by the Institutional Ethics Committee (IEC: 765/2019) and is registered in India’s Clinical Trial Registry (CTRI/2020/04/024940).

3.2. Inclusion Criteria. The inclusion criteria were as follows: all patients between the ages of 18 and 80 years with ARDS, as defined by the Berlin definition, and on invasive mechanical ventilation.

3.3. Exclusion Criteria. The exclusion criteria were as follows:

(i) Patients with COVID-19.
(ii) Patients with documented barotrauma (air leak syndromes).
(iii) Patients with penetrating chest injuries.
(iv) Patients planned for palliative care.

3.4. Sample Size. The sample size was based on the primary objective of assessment of correlation between two quantitative variables considering the expected correlation coefficient between PaO₂ * 10/FiO₂ * PEEP (P/FP * 10) and SpO₂ * 10/FiO₂ * PEEP (S/FP * 10) as at least 0.3, with power of 80% and alpha error of 5%. The following formula was used to calculate sample size (n):

\[ n = \frac{(Z_{1-\beta} + Z_{1-(\alpha/2)})^2}{r^2(1-r^2)} \]

where \( r \) is the correlation coefficient, \( Z_{1-\beta} \) is the desired confidence level, and \( 1 - \beta \) is the power; thus, \( n = 85 \).

3.5. Methodology. All patients admitted to the ICU were screened daily for eligibility. Those who met the inclusion criteria were enrolled, after obtaining written informed consent from the legally authorized representatives.

The flowchart depicting the methodology is shown in Figure 1.

In Figure 1, ABG = arterial blood gas, MV = mechanical ventilation, PaO₂ = partial pressure of arterial oxygen, SpO₂ = pulse oximetry oxygen saturation, FiO₂ = fraction of inspired oxygen, PEEP = positive end-expiratory pressure, P/FP * 10 = (PaO₂ * 10)/(FiO₂ * PEEP), S/FP * 10 = (SpO₂ * 10)/(FiO₂ * PEEP), P/FP * 10 (B) = the value obtained at one hour after intubation and before initiation of MV, S/FP * 10 (B) = corresponding values of S/FP * 10 day one, P/FP * 10 (D1) = worst values of P/FP * 10 day one (within 1–24 hours of intubation), S/FP * 10 (D1) = corresponding values of S/FP * 10 day one, P/FP * 10 (D3) = worst values of P/FP * 10 day three (within 48–72 hours of intubation), S/FP * 10 (D3) = corresponding values of S/FP * 10 day three, P/FP * 10 (D3) = change in S/FP * 10 from baseline to day three, P/FP (D3–D1) = change in S/FP * 10 from day one to day three, P/FP (D3–D1) = change in P/FP * 10 from baseline to day three, and P/FP (D3–D1) = change in S/FP * 10 from day one to day three.

Sequential Organ Failure Assessment (SOFA) score on ICU admission was noted. PaO₂ values were noted using the worst ABG during three defined time periods. The three time periods taken for the study were as follows: baseline (B: within one hour of intubation), day 1 (D1: 1–24 hours after intubation), and day 3 (D3: 48–72 hours after intubation). The FiO₂, SpO₂, and corresponding PEEP value set on the ventilator were also noted. The difference between day three and day S/FP * 10 values [S/FP (D3–D1)] as well as the difference between the values of S/FP * 10 between that of day 3 and day 1.
and baseline \([S/FP (D3-B)]\) were also calculated. Similarly, the difference between day three and day one \([P/FP*10 (D3-B)]\) as well as the difference between day three and baseline \([P/FP*10 (D3-D1)]\) were calculated. MV days, length of stay in ICU (ICU LOS), and outcomes in terms of survival at the end of ICU stay were also noted.

### 4. Statistical Analysis

The analysis of data was done using SPSS (Statistical Package for the Social Sciences) software (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, version 22.0 Armonk, NY: IBM). Mean and standard deviation (SD) for the variables following parametric distribution were calculated. The analysis was performed for the three unique data points (baseline, day one, and day three of MV), and repeated data points were not aggregated for the purpose of analysis.

For correlation of the variables \([P/FP*10]\) and \([S/FP*10]\), the Pearson correlation test was used, and the correlation coefficient \(r\) was calculated. Pearson’s correlation coefficient \(r<0.4\) was considered as weak correlation, \(0.4–0.59\) was considered moderate correlation, \(r\) within \(0.6–0.79\) was considered as strong correlation, and \(r>0.8\) was considered as excellent correlation. Additionally, the correlation analysis was also conducted for those patients with high PEEP (\(\geq 10\) cm H\(_2\)O). The main correlation analysis of \(S/FP*10\) and \(P/FP*10\) included patients at all PEEP levels (PEEP <\(10\) cm H\(_2\)O as well as PEEP \(\geq 10\) cm H\(_2\)O). However, we separately did a sub-analysis of the correlation of \(S/F\) to \(P/F\) and \(S/FP*10\) to \(P/FP*10\) at the three time points. This separate sub-analysis was done because clinicians often repeat ABG for patients with higher PEEP levels, and thus it is this category of patients that is likely to benefit the most if the non-invasively determined \(S/FP*10\) correlated to \(P/FP*10\) at all the three time points.

A receiver operating characteristic (ROC) was plotted for the ability of \([P/FP*10 (B, D1, D3)]\) and \([S/FP*10 (B, D1, D3)]\) to predict survival. Similarly, ROC curves were plotted for \([S/FP (D3-B)], [S/FP (D3-D1)], [P/FP (D3-B)], and [P/FP (D3-D1)]\) to predict survival. Area under curve (AUC) within \(0.91–1.0\) was considered excellent, \(0.81–0.90\) was considered good, and \(0.71–0.80\) was considered fair. A \(p\) value <\(0.05\) was taken as statistically significant and \(p\) value <\(0.001\) as statistically highly significant.
To compare the reliability of S/FP to predict outcomes as compared to P/FP, the comparison of the ROC curves was done using the DeLong test using MedCalc software version 20.111 (Ostend, Belgium).

5. Results

A total of 85 patients with ARDS receiving invasive mechanical ventilation were included in the study. Six patients died between day one and day three. At the end of the ICU stay, 49 (58%) patients survived. The demographic characteristics and values of the variables of the 85 ARDS patients are depicted in Table 1.

The correlation of P/FP ≥ 10 and S/FP ≥ 10 at baseline, day one, and day three of MV was stronger than the correlation of P/F and S/F on the respective days (Table 2). For the subgroup of patients with PEEP ≥ 10 cm H₂O, the same correlation was observed as in all patients (Table 2). The scatterplot depicting correlation of S/FP ≥ 10 and P/FP ≥ 10 at all levels of PEEP at all the three time points is shown in Figure 2.

P/FP ≥ 10 (B) = (PaO₂ * 10)/(FiO₂ * PEEP) at baseline (the value obtained at one hour after intubation and initiation of MV); S/FP ≥ 10 (B) = (SpO₂ * 10)/(FiO₂ * PEEP) at baseline (the corresponding values obtained at one hour after intubation and MV).

P/FP ≥ 10 (D1) = (PaO₂ * 10)/(FiO₂ * PEEP) at day 1 (worst values of P/FP ≥ 10 within 1–24 hours of intubation); S/FP ≥ 10 (B) = (SpO₂ * 10)/(FiO₂ * PEEP) at day 1 (the corresponding values of S/FP ≥ 10 within 1–24 hours of intubation).

P/FP ≥ 10 (D3) = (PaO₂ * 10)/(FiO₂ * PEEP) at day 3 (worst values of P/FP ≥ 10 within 48–72 hours of intubation); S/FP ≥ 10 (D3) = (SpO₂ * 10)/(FiO₂ * PEEP) at day 3 (the corresponding values of S/FP ≥ 10 within 48–72 hours of intubation). PEEP: positive end-expiratory pressure.

Among all the P/FP ≥ 10 and S/FP ≥ 10 ratios at baseline, day one, and day three and the changes in the ratios from baseline to day one to day three of MV, the change in P/FP ≥ 10 (D3-B) has the best ability to predict survival in ARDS patients, with AUC of 0.902 and a cut-off ≥ 34.25 (Table 3). Among the S/FP ≥ 10 ratios, the S/FP ≥ 10 (D3-B) has the highest AUC and specificity to predict survival (AUC: 0.877, p < 0.001, sensitivity: 73.5%, specificity: 97%, CI: 0.803–0.952, cut-off ≥ 64.40). The AUC values of the P/FP ≥ 10 (B), P/FP ≥ 10 (D1), P/FP ≥ 10 (D3), S/FP ≥ 10 (B), S/FP ≥ 10 (D1), S/FP ≥ 10 (D3), S/FP ≥ 10 (D3-B), and S/FP ≥ 10 (D3-D1) with their respective cut-off values are depicted in Table 3.

The ROC curves of the P/FP ≥ 10 (B), P/FP ≥ 10 (D1), P/FP ≥ 10 (D3), S/FP ≥ 10 (B), S/FP ≥ 10 (D1), and S/FP ≥ 10 (D3) to predict survival are depicted in Figure 3.

In Figure 3, PaO₂ = partial pressure of arterial oxygen, SpO₂ = pulse oximetry oxygen saturation, FiO₂ = fraction of inspired oxygen, PEEP = positive end-expiratory pressure, P/FP ≥ 10 (B) = (PaO₂ * 10)/(FiO₂ * PEEP) (the value obtained at one hour after intubation and initiation of mechanical ventilation), S/FP ≥ 10 (B) = (SpO₂ * 10)/(FiO₂ * PEEP) (the corresponding values obtained at one hour after intubation and MV).

To compare the reliability of S/FP to predict outcomes as compared to P/FP, the comparison of the ROC curves was done using the DeLong test using MedCalc software version 20.111 (Ostend, Belgium).
As per our results, the moderate ARDS category will be S/FP*10 (B) ≥116 and ≤190. In order to compare the reliability of S/FP to predict outcomes as compared to P/FP, the comparison of the ROC curves was done using the DeLong test using MedCalc software version 20.111. The ROC of the S/FP*10 to P/FP*10 at three time points (baseline, day one, and day three) to predict outcome in terms of survival was calculated. It showed that the null hypothesis was acceptable, and there was no statistically significant difference in the AUC between the ROC curves of S/FP*10 (B) and P/FP*10 (B), S/FP*10 (D1) and P/FP*10 (D1), and S/FP*10 (D3) to P/FP*10 (D3) for survival outcome prediction (p = 0.054, p = 0.681, and p = 0.264, respectively). Similarly, there was no difference in the AUC of the ROC curves between S/FP (D3-D1) and P/FP (D3-D1) as well as S/FP (D3-B) and P/FP (D3-B) to predict survival (p = 0.087 and 0.463, respectively).

### 6. Discussion

A recent study has concluded that in ARDS patients, when PEEP is integrated into the P/F ratio, the validity to predict hospital mortality is amplified [2]. The authors stated that the incorporation of PEEP into the P/F ratio enables the reflection of lung compliance and lung recruitment during the evaluation of the severity of ARDS [2]. The setting of

<table>
<thead>
<tr>
<th>Time points</th>
<th>Pearson correlation coefficient (r) between P/FP and S/F</th>
<th>p value</th>
<th>Pearson correlation coefficient (r) between P/FP<em>10 and S/FP</em>10</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All enrolled patients</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Baseline (n = 85)</td>
<td>0.660</td>
<td>&lt;0.001</td>
<td>0.831</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Day 1 (n = 85)</td>
<td>0.580</td>
<td>&lt;0.001</td>
<td>0.733</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Day 3 (n = 79)</td>
<td>0.766</td>
<td>&lt;0.001</td>
<td>0.853</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Values with PEEP ≥10 cm H2O</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Baseline (n = 39)</td>
<td>0.634</td>
<td>&lt;0.001</td>
<td>0.687</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Day 1 (n = 26)</td>
<td>0.625</td>
<td>0.001</td>
<td>0.726</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Day 3 (n = 31)</td>
<td>0.851</td>
<td>&lt;0.001</td>
<td>0.881</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Figure 2: Scatterplot depicting correlation of S/FP*10 and P/FP*10 at all levels of PEEP at baseline (Panel (a)), day one (Panel (b)), and day three (Panel (c)). PEEP: positive end-expiratory pressure.
PEEP in most cases of severe ARDS has been said to be approximately 8 cm H₂O, which is low [2, 7]. In the abovementioned study, the AUC for prediction of mortality in cases of PEEP of about 8 cm H₂O was higher for P/FP \( \times 10 \) (0.775) as compared to AUC of 0.691 for P/F ratio [2]. The sensitivity to predict mortality was also higher for P/FP \( \times 10 \) (84.3%) compared to 65% for P/F [2]. The authors of the study included a correction factor of 10 for the P/FP as a PEEP of about 10 cm H₂O is commonly set as the initial ventilator setting [2, 8]. The other reason why factor 10 was chosen was that a regression line plotted in the study between P/F ratio and PEEP intersected the P/F of value 150 mmHg (which usually discriminates the survivors and

<table>
<thead>
<tr>
<th>Variables</th>
<th>Cut-off value</th>
<th>AUC</th>
<th>p value</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>S/FP ( \times 10 ) (B)</td>
<td>( \geq 162 )</td>
<td>0.558</td>
<td>0.391</td>
<td>52</td>
<td>53</td>
<td>0.427–0.689</td>
</tr>
<tr>
<td>P/FP ( \times 10 ) (B)</td>
<td>( \geq 187.6 )</td>
<td>0.635</td>
<td>0.046</td>
<td>69</td>
<td>58</td>
<td>0.507–0.763</td>
</tr>
<tr>
<td>S/FP ( \times 10 ) (D1)</td>
<td>( \geq 157.5 )</td>
<td>0.545</td>
<td>0.508</td>
<td>53</td>
<td>53</td>
<td>0.416–0.674</td>
</tr>
<tr>
<td>P/FP ( \times 10 ) (D3)</td>
<td>( \geq 257.5 )</td>
<td>0.900</td>
<td>&lt;0.001</td>
<td>80</td>
<td>87</td>
<td>0.833–0.968</td>
</tr>
<tr>
<td>S/FP ( \times 10 ) (D3)</td>
<td>( \geq 243.75 )</td>
<td>0.872</td>
<td>&lt;0.001</td>
<td>78</td>
<td>77</td>
<td>0.787–0.956</td>
</tr>
<tr>
<td>S/FP ( \times 10 ) (D3-B)</td>
<td>( \geq 64.40 )</td>
<td>0.877</td>
<td>&lt;0.001</td>
<td>73.5</td>
<td>97</td>
<td>0.803–0.952</td>
</tr>
<tr>
<td>S/FP ( \times 10 ) (D3-D1)</td>
<td>( \geq 75.62 )</td>
<td>0.821</td>
<td>&lt;0.001</td>
<td>71.4</td>
<td>80</td>
<td>0.728–0.914</td>
</tr>
<tr>
<td>P/FP ( \times 10 ) (D3-B)</td>
<td>( \geq 34.25 )</td>
<td>0.902</td>
<td>&lt;0.001</td>
<td>81.6</td>
<td>90</td>
<td>0.834–0.970</td>
</tr>
<tr>
<td>P/FP ( \times 10 ) (D3-D1)</td>
<td>( \geq 28.56 )</td>
<td>0.876</td>
<td>&lt;0.001</td>
<td>83.7</td>
<td>80</td>
<td>0.798–0.953</td>
</tr>
</tbody>
</table>

Diagonal segments are produced by ties.

Figure 3: Receiver operating characteristic curves to predict survival for P/FP \( \times 10 \) and S/FP \( \times 10 \) at baseline, day 1, and day 3. The P/FP \( \times 10 \) (D3) has an AUC of 0.900 and a cut-off \( \geq 257.5 \) to predict survival, followed by S/FP \( \times 10 \) (D3) with a cut-off \( \geq 243.75 \) and an AUC of 0.872.

Figure 4: The ROC of the change in the P/FP \( \times 10 \) and S/FP \( \times 10 \) ratios from baseline and day one to day three to predict survival. The AUC of the P/FP (D3-B) is the highest (AUC: 0.902, cut-off \( \geq 34.25 \)), followed by the AUC of S/FP (D3-B) (AUC: 0.877, cut-off \( \geq 64.40 \)).
Figure 5: ROC curve depicting the discriminant function of S/FP * 10 (B) to be categorized as severe ARDS as per Berlin definition (AUC: 0.925, \( p < 0.001 \), cut-off value \( \leq 116 \), CI: [0.862–0.988]). S/FP * 10 (B) = (SpO2 * 10)/(FiO2 * PEEP) (the values obtained at one hour after intubation and mechanical ventilation).

Figure 6: ROC curve depicting the discriminant function of S/FP * 10 (B) to be categorized as mild ARDS as per Berlin definition (AUC: 0.773, \( p < 0.001 \), cut-off value \( \geq 190 \), sensitivity: 69%, specificity: 74%, 95% CI: [0.672–0.875]). S/FP * 10 (B) = (SpO2 * 10)/(FiO2 * PEEP) (the values obtained at one hour after intubation and mechanical ventilation).

A recent study on 1034 ARDS patients concluded that mortality prediction from oxygenation could be more conclusively done on day three (after 48 hours) of ARDS onset [16]. As the most common cause of mortality in ARDS is multi-organ dysfunction, which evolves and progresses over time, oxygenation values on the third day (after 48 hours) are likely to have a better predictive value for non-survivors at a PEEP of 10 cm H2O [2]. We used the same factor (10) to be multiplied by the S/FP ratio as was done in the previous study [2]. For our study, we wanted to use a noninvasive, easily plausible, and continuous oxygen monitoring method such as SpO2 after incorporating the PEEP into S/F ratio for correlation to the P/FP * 10. The P/FP * 10 ratio has now proven to be more pertinent as compared to the P/F ratio for prognostication of outcomes in ARDS patients [2]. Thus, we evaluated the correlation of S/FP * 10 to P/FP * 10 in ARDS patients at baseline, day one, and day three of MV. The reason for selecting the baseline and the worst values of S/FP * 10 up to day one of MV for correlation to P/FP * 10 was based on previous ARDS studies that demonstrated that compared to baseline oxygenation, values at 24 hours are more significant to predict outcomes [9–11]. Another study concluded that 6–12 hours of ARDS onset accurately predicted outcomes and was the optimal time for recruitment of patients into clinical research [12]. Thus, we selected the time interval between one hour and 24 hours of MV as day one. After initiation of MV, an ABG done within one hour has been proven to improve mechanical ventilation intervention and monitoring, by significantly detecting respiratory acidosis [13]. Thus, we chose the S/FP * 10 and P/FP * 10 values within one hour of MV initiation as baseline for correlation analysis. The strength of correlation between S/FP * 10 and P/FP * 10 in our study was more than the correlation between P/F and S/FP at the respective time intervals. A study comparing the correlation between only SpO2 and PaO2 was done previously, which showed that the Pearson correlation coefficient was 0.423 only [14]. If FiO2 is incorporated in the correlation, the strength of the correlation improves to about 0.580–0.766 as we found in our study. However, if PEEP is incorporated, the strength of correlation increases and is highly significant (0.733–0.853) as we found in our study. Moreover, in patients with PEEP \( \geq 10 \) cm H2O, there is a good correlation of S/FP * 10 and P/FP * 10, which is excellent on day three (0.881). This is clinically very significant because it is in this group of ARDS patients who require a higher PEEP that frequent ABG is ordered to evaluate the P/F ratios. Often as the days of MV progress from day one to day three, the need for placing an invasive arterial catheter for repeated ABG is often contemplated upon. The findings of the excellent correlation between S/FP * 10 and P/FP * 10 on day three in our study shows that the need for invasive arterial catheter placement for the purpose of frequent ABG monitoring as days of MV progress, can be avoided. Even though previous literature shows a good correlation between S/F ratio and P/F ratio, PEEP component which is so crucial was not incorporated previously [15].
mortality [16–18]. Therefore, we selected the P/FP * 10 and S/FP * 10 values at day three (48–72 hours after MV), apart from baseline (0–1 hour after MV) and day one (1–24 hours after MV), to predict survival. The S/F ratio complements the P/F ratio; thus, S/F has also been incorporated to reflect respiratory status in the modified Sequential Organ Failure Assessment (mSOFA) score [19].

However, the S/FP * geometrical mean over a certain time period is more helpful in predicting mortality of ICU stay was 0.784 [24]. However, we found that, rather than the P/FP * 10 and S/FP * 10 at baseline or at day one, it is the change in P/FP * 10 and S/FP * 10 from baseline to day three of MV that has the highest AUC to predict survival (AUC of 0.902 and 0.877, respectively). In our study, the S/FP (D3–D1) ≥64 and S/FP (D3–D1) ≥75 have good validity for predicting survival with AUC of 0.877 and 0.821, respectively. Other than PEEP, indices of ventilator parameters such as mean airway pressure and plateau pressure have also been incorporated into P/F ratio for better predictor of outcomes, but these require paralyzing the patient for accurate measurement [2]. Thus, incorporation of PEEP into S/F ratio and assessing the change may be a practical yet reliable predictor of outcome in ARDS patients.

Apart from the correlation to the P/F ratio and prediction of survival, we felt that another utility of S/FP * 10 that should be examined is its discriminating ability to predict severe ARDS category as per Berlin criteria. The discrimination ability should also be examined early, after intubation (baseline), so that clinicians may plan interventions in severe ARDS patients accordingly. We found that the S/FP * 10 (B) ≤116 has excellent discrimination ability to predict severe ARDS category with an AUC of 0.925 and 90% sensitivity along with 93% specificity. This was much higher than the AUC of 0.839 for S/F to predict P/F >200 as per recently concluded study results [25]. However, the study included hypoxemic patients, and not patients with ARDS [25].

We evaluated the ability of S/FP * 10 (B) to predict severe ARDS, as these patients require early assiduous treatment planning and interventions such as lung-protective ventilation, prone ventilation, neuromuscular blockade, and a targeted negative fluid balance and are at greater risk of multiple organ dysfunction [26].

The correlation between S/FP * 10 and P/FP * 10 at baseline (r = 0.831), day one (r = 0.733), and day three (r = 0.853) in our study was much higher compared to the correlation between S/F ratio and P/F ratio in the above-mentioned study (r = 0.66). Thus, the consideration of PEEP applied strengthens the correlation between S/FP * 10 and P/FP * 10 ratios.

In the study done by Pandharipande et al., the authors concluded that the correlation of S/F and P/F was unaffected by the various levels of PEEP (<8 cm H₂O, 8–12 cm H₂O, and ≥12 cm H₂O) [27]. The results of our study were similar in the aspect that we found that, even in the subgroup of patients with higher PEEP ≥10 cm H₂O, the correlation of P/F and S/F and P/FP and S/FP was similar to that of the entire study. In a previous study on P/FP * 10, Palanidurai et al. studied its utility for predicting mortality in ARDS only on the day of intubation [2]. However, the authors concluded in their hypothesis that the predictive ability of P/FP * 10 to predict mortality will improve over 24–72 hours [2]. This is exactly what we found in our study. Not only did the P/FP * 10 have an excellent predictive value for survival at 48–72 hours, but S/FP * 10 also had a good predictive ability for survival at 48–72 hours, as compared to baseline and day one.

Thus, clinicians may use the S/FP * 10 parameters in a mechanically ventilated ARDS patient, rather than repeated ABGs to predict survival. However, the S/FP * 10 values at baseline or on day one were not able to predict survival. Our findings were like the results of the trial by Chiu et al., where the authors concluded that the change in oxygenation status over 48 hours of ARDS onset, rather than baseline values, is significant [16]. The change in oxygenation as depicted by S/FP * 10 change in our study being an important predictor of survival is also theoretically validated by previous studies [22, 23]. In situations when a patient’s oxygenation improves after prone position ventilation, the change in oxygenation will be significant in 48 hours after a single proning session [22]. Such patients are more likely to survive as compared to those in whom there is no significant improvement in oxygenation over a period of MV.

In a study done by Fukuda et al. on hypoxemic respiratory failure patients who had bilateral lung field opacities, the AUC of S/F ratio at 24 hours of ICU admission to predict mortality of ICU stay was 0.784 [24]. However, we found that, rather than the P/FP * 10 and S/FP * 10 at baseline or at day one, it is the change in P/FP * 10 and S/FP * 10 from baseline to day three of MV that has the highest AUC to predict survival (AUC of 0.902 and 0.877, respectively). In our study, the S/FP (D3–D1) ≥64 and S/FP (D3–D1) ≥75 have good validity for predicting survival with AUC of 0.877 and 0.821, respectively. Other than PEEP, indices of ventilator parameters such as mean airway pressure and plateau pressure have also been incorporated into P/F ratio for better predictor of outcomes, but these require paralyzing the patient for accurate measurement [2]. Thus, incorporation of PEEP into S/F ratio and assessing the change may be a practical yet reliable predictor of outcome in ARDS patients.

Apart from the correlation to the P/F ratio and prediction of survival, we felt that another utility of S/FP * 10 that should be examined is its discriminating ability to predict severe ARDS category as per Berlin criteria. The discrimination ability should also be examined early, after intubation (baseline), so that clinicians may plan interventions in severe ARDS patients accordingly. We found that the S/FP * 10 (B) ≤116 has excellent discrimination ability to predict severe ARDS category with an AUC of 0.925 and 90% sensitivity along with 93% specificity. This was much higher than the AUC of 0.839 for S/F to predict P/F >200 as per recently concluded study results [25]. However, the study included hypoxemic patients, and not patients with ARDS [25].

We evaluated the ability of S/FP * 10 (B) to predict severe ARDS, as these patients require early assiduous treatment planning and interventions such as lung-protective ventilation, prone ventilation, neuromuscular blockade, and a targeted negative fluid balance and are at greater risk of multiple organ dysfunction [26].

The correlation between S/FP * 10 and P/FP * 10 at baseline (r = 0.831), day one (r = 0.733), and day three (r = 0.853) in our study was much higher compared to the correlation between S/F ratio and P/F ratio in the above-mentioned study (r = 0.66). Thus, the consideration of PEEP applied strengthens the correlation between S/FP * 10 and P/FP * 10 ratios.
group of patients with various PEEP levels. Furthermore, in
the above-mentioned study, when the contribution of PEEP
was accounted for, the correlation between S/F and P/F was
stronger as compared to the correlation between S/F and P/F
without contribution of PEEP, as we found in our study [27].

The study’s strengths are that it has incorporated the
concept of PEEP into a noninvasive method of oxygenation
assessment (S/FP * 10) in ARDS patients to predict survival.
The need for doing repeated ABGs may be avoided. This is
important as, apart from the risk of infection and costs,
arterial cannulation may even lead to devastating compli-
cations such as symmetrical peripheral gangrene [28]. The
excellent correlation of S/FP * 10 to P/FP * 10 at higher
PEEP on day three may help avoid arterial cannulation for
repeated P/F or P/FP assessment in patients with PEEP
≥10 cm H2O, as the days of MV progress in ICU. Similar to
the manner in which a change in SOFA scores predicts
mortality, the study could validate that the change in P/
FP * 10 as well as S/FP * 10 ratio over 48 hours after intu-
bilation is a reliable predictor of survival. The study could also
conclude that S/FP * 10 is able to predict severe ARDS
category patients early after intubation, with an excellent
discriminant function.

The study has certain limitations. It was a single-centre
study. In addition, we did not plot the ROC of S/FP * 10 to
predict survival at different levels of PEEP as done by
Palanidurai et al. in their study on P/FP * 10 [2]. We assessed
the discriminant function of S/FP * 10 to predict only severe
ARDS, and not mild or moderate ARDS. The limitations of
pulse oximetry use like poor waveform, hypothermia, shock,
and methemoglobinemia decreases the utility of S/FP ratio
as compared to P/FP ratio [25].

7. Conclusions

S/FP * 10 has a strong correlation to P/FP * 10 in ARDS
patients at baseline, day one, and day three of MV, which is
stronger than the correlation between S/F and P/F ratios at
the respective time intervals. S/FP * 10 (B) ≤116 has an
excellent discriminant function to predict severe ARDS
category. On day three after initiation of MV, S/FP ≥244
has a good predictive ability for survival, whereas an increase
in S/FP (D3–B) by ≥64 and increase in S/FP (D3–D1) by ≥75
also have good predictive ability for survival.

Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ARDS</td>
<td>Acute respiratory distress syndrome</td>
</tr>
<tr>
<td>PaO2</td>
<td>Partial pressure of arterial oxygen</td>
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<tr>
<td>FiO2</td>
<td>Fraction of inspired oxygen</td>
</tr>
<tr>
<td>PEEP</td>
<td>Positive end-expiratory pressure</td>
</tr>
<tr>
<td>P/F ratio</td>
<td>PaO2/FiO2, partial pressure of arterial oxygen to inspiratory oxygen fraction ratio</td>
</tr>
<tr>
<td>P/FP * 10</td>
<td>PaO2 * 10/FiO2 * PEEP</td>
</tr>
<tr>
<td>SpO2</td>
<td>Pulse oximetric oxygen saturation</td>
</tr>
<tr>
<td>S/F ratio</td>
<td>SpO2/Fio2, partial pressure of arterial oxygen to inspiratory oxygen fraction ratio</td>
</tr>
<tr>
<td>S/FP * 10</td>
<td>SpO2 * 10/FiO2 * PEEP</td>
</tr>
<tr>
<td>ICU LOS</td>
<td>Length of stay in intensive care unit</td>
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</table>

MV: Mechanical ventilation
CI: Confidence interval
APACHE II: Acute physiology and chronic health evaluation score
SOFA: Sequential Organ Failure Assessment score.

Data Availability

The data sets used and analyzed during the current study are
available from the first and corresponding author upon
reasonable request. The data are not publicly available due to
them containing information that could compromise re-
search participant privacy/consent.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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