Comparison of SpO2 / FiO2 Ratio and PaO2 / FiO2 Ratio as Diagnostic Criteria in Patients with ALI and ARDS

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ABSTRACT

BACKGROUND
PaO2 / FiO2 ratio has been the main criterion in defining ALI / ARDS (Acute Lung Injury / Acute Respiratory Distress Syndrome). This study is particularly aimed at utilising SpO2 / FiO2 ratio as an alternative diagnostic criterion of ALI / ARDS.

METHODS
Fifty patients with ALI / ARDS were included in the study. SpO2, PaO2 values, and serum electrolytes were measured using pulse oximetry and arterial blood gas analysis along with simultaneous measurement of FiO2.

RESULTS
SpO2 / FiO2 and PaO2 / FiO2 ratio showed a good linear correlation. By quantifying the linear regression equation, the threshold value of SpO2 / FiO2 ratio was calculated. Evidence gathered from the study demonstrated strong association between SpO2 / FiO2 and PaO2 / FiO2 ratio and it is proposed that SpO2 / FiO2 ratio calculation should be the norm to characterise oxygen impairment in ALI / ARDS, rather than just using it as an alternative diagnostic criterion.

CONCLUSIONS
Threshold values of SpO2 / FiO2 ratio can be used as an alternative to PaO2 / FiO2 ratio in the early diagnosis of ALI and ARDS.

KEYWORDS
PaO2 / FiO2 Ratio, SpO2 / FiO2 Ratio, ABG, Pulse Oximetry, ALI, ARDS

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DOI:10.18410/jebmh/2020/521

How to Cite This Article:
Janipalli VP, Moturi PK. Comparison of SpO2 / FiO2 ratio and PaO2 / FiO2 ratio as diagnostic criteria in patients with ALI and ARDS. J Evid Based Med Healthc 2020;7(44), 2520-2525. DOI: 10.18410/jebmh/2020/521

Submission 26-04-2020,
Peer Review 01-05-2020,
Acceptance 27-05-2020,
Published 02-11-2020.

BACKGROUND

Acute Lung Injury (ALI) and ARDS are devastating clinical syndromes associated with high morbidity & mortality. Even in paediatric age group ALI / ARDS is the major cause of mortality as per Leteurtre et all study[1]. P_aO_2 / F_iO_2 (Fraction of Inspired Oxygen) ratio (or P / F ratio) is one of the criteria for defining ALI / ARDS that was developed by an American European Consensus Conference (AECC)[2] in 1994. ALI is defined as P / F ratio < 300 and ARDS if P / F ratio is < 200, respectively in accordance with the AECC definitions and Bernard et al study[2]**.** The non-availability of arterial blood gas sampling may contribute to the under diagnosis of these syndromes, despite the straight forward nature of the AECC definition of ALI and ARDS.

In healthy subjects, changes in PaO2 correlate well with changes in pulse oximetric saturation (SpO_2) for oxygen saturation in the range of 80 - 100 %. However, studies in critically ill patients, especially those with ALI / ARDS, are lacking as cited by Mirinda et al[3] in their study. Furthermore, threshold values for SpO2 / FiO2 (S / F) ratios could be used as non-invasive criteria for diagnosing ALI / ARDS. The use of the S / F ratio may better facilitate the screening and rapid identification of patients with ALI / ARDS while avoiding the blood use and cost for blood gas determination. This was previously put forth by Marie Grace et al[4] in their study determination of SpO2 / fiO2 ratio in the diagnosis of patients admitted at Philippine heart centre. For example, a patient with early ARDS / ALI showing patchy asymmetric infiltrates that may be interpreted as pneumonia or segmental atelectasis with profound hypoxemia. Despite a variable radiographic appearance, the presence of bilateral infiltrates and moderate or severe hypoxemia (P / F < 300) should raise the possibility of ALI / ARDS. Since ALI and ARDS are syndromes based on non-specific radiographic and physiologic criteria, establishing a diagnosis of ALI or ARDS is not equivalent to diagnosing the precipitating cause. Utilizing S / F ratios to facilitate the clinical diagnosis of ALI / ARDS should help to address the under diagnosis of these syndromes. A volume-limited and pressure-limited ventilation strategy as proposed by eng journal of medicine[5] and Tripathi et al study[6] is the only therapeutic intervention that has been shown to significantly reduce mortality in patients with ALI. Despite being inexpensive and easy to use, this intervention has not been widely adopted. One explanation may be that ALI and ARDS are often not recognized, contributing to the failure to implement treatment strategies such as lung-protective ventilation[5] and conservative fluid management. The fact that early identification and treatment directed at the inciting causes of ALI and ARDS are imperative for resolution of lung injury and respiratory failure which is in line with the results derived in study conducted in paediatric population by Neal J. Tomas et al[7] Since pulse oximeters are now readily available in most of the hospitals and some adult studies demonstrated that routine use of pulse oximetry leads to 40 - 60 % reduction in ABG measurement without any adverse effects on patient outcomes. This study is taken up with an aim to know if the SpO2 / FiO2 can be used as an alternative to PaO2 / FiO2 in the diagnosis of ALI and ARDS in the absence of ABG analysis and also to derive threshold values of S / F ratio that correspond to P / F criteria for ALI and ARDS with good sensitivity and specificity.

Objectives

1. To study the utility of SpO2 / FiO2 ratio as an alternative for PaO2 / FiO2 ratio in the diagnostic criteria of ALI / ARDS.
2. To identify the threshold values for SpO2 / FiO2 ratio that corresponds to the PaO2 / FiO2 criteria for ALI / ARDS.

METHODS

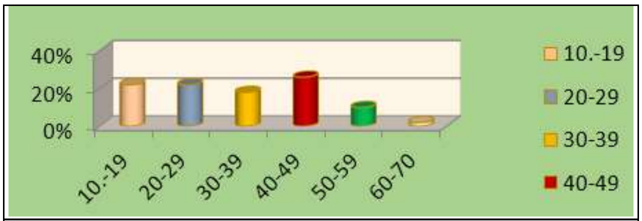
This study was conducted in patients who were admitted to a tertiary teaching hospital in Visakhapatnam, from May 2019 to January 2020. Fifty cases of ARDS / ALI were selected for the study. The inclusion criteria used for this study were bilateral (patchy, diffuse, or homogeneous) infiltrates consistent with pulmonary oedema, those who were presenting with acute hypoxemia and with no clinical evidence of congestive cardiac failure. The patients with hypotension, peripheral vascular disease, shock, significant jaundice, inadequate SpO2 trace, SpO2 > 97 %, septicaemia, SpO2 < 80 % were excluded.

- "Medaid Model 900" pulse oximeter and "Cobas B 121" ABG analyser were used.
- All patients underwent measurements of SpO_2, ABG and serum electrolytes with simultaneous recording of FiO_2.
- Before ABG was taken, procedure is explained to the patients.
- The following measures were employed to improve the accuracy of the SpO_2 measurements.
    - Optimal position and cleanliness of sensor.
    - Satisfactory waveforms.
    - No positional change.
    - No endobronchial suctioning for at least 10 min prior to the measurement.
    - No invasive procedures or ventilator setting changes for at least 30 min prior to measurement.
    - SpO_2 was observed for a minimum of 1 min before the value was recorded.
- Skin was examined for rash or other abnormalities.
- Radial and ulnar arteries are palpated and modified Allen's test is performed.
- Statistical software packages (SPSS, version 19.0); was utilized to perform analysis, graph scatter plots, analyse linear regression, ROC curves, and calculate the AUC of the ROC.

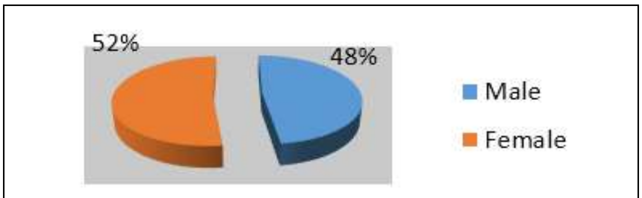
Statistical Analysis

Study was done in randomly selected fifty patients allotted in two groups. (Randomized Control Trial). The baseline parameters such as age, sex, height and weight were comparable and there is no statistical significant difference between the two groups. To analyse the graph scatter plots, linear regression, ROC curves and for calculating the AUC of the ROC in the two group's statistical software package, SPSS version 19 was used.

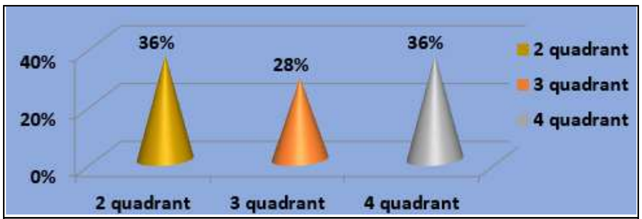
RESULTS



Age Distribution



Gender Distribution

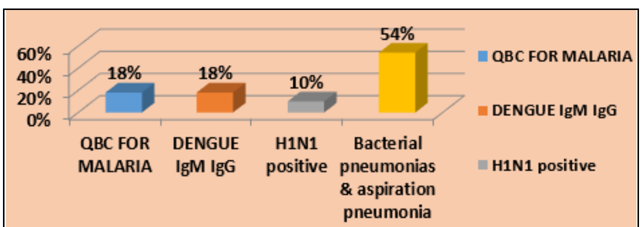


No. of Quadrants Involved

64 % had 3 / 4 quadrant disease on chest x ray

Investigations Supportive of Aetiology

- 27 cases were bacterial / aspiration pneumonias, complicated by ARDS / ALI.
- 3 cases were H1N1 flu positive.
- 41 cases were pulmonary ARDS and 9 were extra pulmonary ARDS.



Investigations Supportive of Aetiology

The PF and the SF values are higher in the patients with 2 quadrant oedema than 3 quadrant and 4 quadrant oedema. The PF and SF ratios are corresponding with the number of the quadrants of involvement in the chest x-ray. The PF and SF ratios are higher in dengue and malarial causes than other causes.

In the present study, 50 cases of ARDS / ALI were studied. Out of 50 cases 24 cases were males and 26 cases were females. Patients of all age groups are present in the study. Corresponding measurements of SpO2 and PaO2 from the patients were utilized to establish the relationship between SpO2 / FiO2 and PaO2 / FiO2 ratios. A total of 37 cases (74 %) met the PF (PaO2 / FiO2) ratio criteria for ARDS, and 13 cases (26 %) met the PF criteria for ALI.

	Range	Mean
PO_2	47 - 85	70.94
PCO_2	21 - 38.6	33.82
HCO_3	17 - 34.2	22.22
pH	7.38 - 7.57	7.456
PaO_2 / FiO_2	90 - 303	154.5 + 65
SpO_2 / FiO_2	136 - 339	207 + 61

Respiratory Parameters

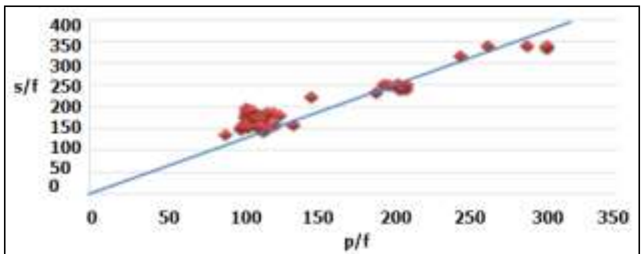
No. of Quadrants Involved in CXR	Mean PF and SF
2 Quadrants	PF = 218 ± 42 SF = 273 ± 45
3 Quadrants	PF = 112 ± 5 SF = 181 ± 8
4 Quadrants	PF = 112 ± 11 SF = 151 ± 8

Correlation of Mean PF and SF Values with Quadrants Involved

Aetiology	Mean PF and SF
Dengue Fever	PF = 245 ± 51 SF = 285 ± 49
Malaria	PF = 218 ± 45 SF = 268 ± 48
Bacterial Pneumonia & Aspiration Pneumonia	PF = 112 ± 15 SF = 142 ± 11
H1N1 FLU	PF = 113 ± 8 SF = 172 ± 11

Aetiology Wise Mean PF and SF Ratios

A scatter plot of S / F vs. P / F ratios was utilized to determine the linear relationship between the two measurements.



Scatter Plot with S / F Ratio vs. P / F Ratio Showing Linear Correlation

S / F and P / F ratios demonstrated a good linear correlation, with a correlation coefficient (r) of 0.96. Linear regression equation was used to predict the SF ratio from the PF ratio. The linear regression equation was determined from the PF and SF (SpO2 / FiO2) ratios of this study. The linear regression equation was quantified as:

SF = 68 + 0.89 X PF

[95 % confidence interval (CI) SF = (55.8 to 77.4) + (0.84 to 0.96) X PF; $p < 0.0001$].

The equation was employed to determine threshold values for S / F ratios that correlate with P / F ratios of 300 and 200, for ALI and ARDS, respectively. Based on this equation a PF ratio of 300 corresponded to an SF ratio of 335 and a PF ratio of 200 corresponded to SF ratio of 246.

	P / F < 200	P / F > 200	
S / F < 246	36	1	37
S / F > 246	3	10	13
	39	11	

Sensitivity and Specificity Determination Using S / F Ratio Threshold Value of 246

Applying the S / F ratio threshold value of 246 in place of P / F ratio of 200 in the study population, the sensitivity and the specificity obtained are

Sensitivity = 36 / 39 X 100 = 92.30

Specificity = 10 / 11 X 100 = 90.90

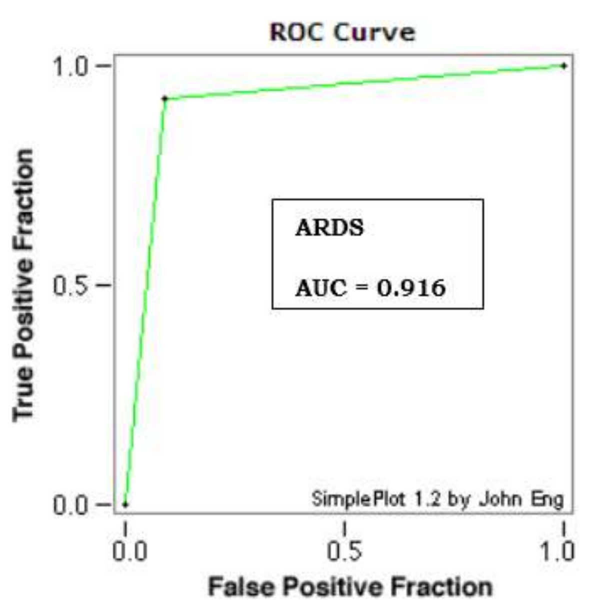
	P / F < 300	P / F > 300	
S / F < 335	45	1	46
S / F > 335	1	3	4
	46	4	

Sensitivity and Specificity Determination Using S / F Ratio Threshold Value of 335

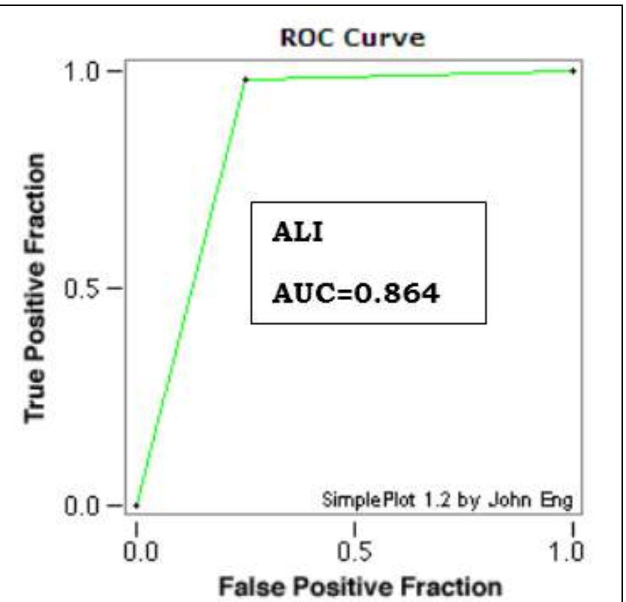
Similarly, when the S / F threshold of 335 is applied in place of the P / F ratio of 300, the sensitivity and specificity are 92.30 and 90.90 respectively.

Sensitivity = 45 / 46 X 100 = 97.82

Specificity = 3 / 4 X 100 = 75



A. ROC Curve for ARDSS / F vs. P / F Ratio of ≤ 200 of ≤ 300



B. ROC Curve for ALI S / F vs. P / F Ratio

SF ratio has an excellent discriminating ability for ARDS (AUC = 0.916) and good discriminating ability for ALI (AUC = 0.864).

DISCUSSION

ALI and ADRS are devastating clinical syndromes with high morbidity and mortality. Acute hypoxemic respiratory failure as defined by the PaO2 / FiO2 ratio is one of the criteria for ALI / ARDS. A P / F ratio ≤ 300 and ≤ 200 are utilized to define ALI and ARDS respectively. The P / F ratio is utilized to assess the degree of hypoxemia. But ABG analyser is not available in all centres. The non-availability of an arterial blood gas analysis may contribute to the under diagnosis of these syndromes. The P / F ratios in a case of bilateral pneumonia is necessary to know the patient's oxygenation status and to plan for invasive ventilation, non-invasive ventilation or oxygen therapy accordingly as discussed by C. Lobete et al[8] in their study. The changes in PaO2 correlate well with the SpO2 for oxygen saturation in the range of 80 – 100 % similar to the study conducted by Robinder et al in paediatric age group[9]. Furthermore, threshold values for S / F ratios could be used as non-invasive criteria for diagnosing ALI / ARDS.

In this study, patients who presented with acute hypoxia, showing bilateral infiltrates in chest x-ray suggestive of bilateral pneumonia with no clinical evidence of congestive heart failure were selected as there was incidence of sequential organ failure with respiratory component cited in the study conducted by Pandharipande et al[10]. ABG analysis was done for all patients, and while drawing the sample, SpO_2 was measured with a pulse oximeter and the FiO_2 being delivered to the patient was noted. The minimum SpO_2 recorded was 81 %. The SpO_2 values < 80 do not correlate well with the PaO2 values. 96 % of measurements were between 88 % to 97 %.

The present study group consisted of 50 patients, aged between 18 - 62 years with mean age of 34.08. The most frequent complaints were shortness of breath (100 %) and fever (100 %) followed by other complaints of cough (82 %), expectoration (72 %), haemoptysis (6 %), wheeze (3 %), chest pain (3 %).

Of the 50 cases, 9 were QBC for malaria positive, the mean P / F ratio in them was a little high 245 ± 51 and S / F ratio was 285 ± 49. Similarly 9 cases were dengue positive cases and in these cases also the mean P / F and S / F ratios were a little high, 218 ± 45 and 268 ± 48 respectively. The mean P / F and S / F ratios in H1N1 flu cases were very low 112 ± 7 and 174 ± 11 respectively. The outcome was very poor in H1N1 cases with 100 % mortality. Among others, in bacterial pneumonia and aspiration pneumonia cases the mean P / F and S / F ratios were 112 ± 15 and 142 ± 11 respectively.

The mean P / F and S / F ratios were 218 ± 42 and 273 ± 45 in cases where chest x-ray showed 2 quadrant consolidation. In cases showing 3 quadrant consolidation the mean P / F and S / F ratios were 112 ± 5 and 181 ± 8 respectively. And in cases showing 4 quadrant consolidation the mean P / F and S / F ratios were 112 ± 11 and 151 ± 8 respectively.

37 cases of ARDS and 13 cases of ALI based on PF ratios were identified. The S / F and P / F ratios were calculated for all the patients in the study group. A scatter plot of S / F vs. P / F ratios was utilized to determine the linear relationship between the two measurements. SpO_2 / FiO_2 and PaO_2 / FiO_2 ratios demonstrated a linear correlation. The correlation coefficient (r) was calculated as +0.96. The correlation coefficient (r) in ALI cases and ARDS cases was + 0.93 and + 0.88 respectively. The linear regression equation was quantified as SF = 68 + 0.89 X PF. The equation was employed to determine threshold values for S / F ratios that correlate with P / F ratios of 300 and 200, respectively, for ALI and ARDS. Based on this equation a PF ratio of 300 corresponded to an SF ratio of 335 and a PF ratio of 200 corresponded to SF ratio of 246.

The S / F ratio threshold of 246 accurately identified 36 of the 39 cases of ARDS in the present study (P / F ratio ≤ 200), yielding a sensitivity of 92.30 %. The same threshold value also correctly discriminated 10 of the 11 cases in which the P / F ratio was ≥ 200, for a specificity of 90.90 %. Similarly, the S / F threshold of 335 demonstrated 97.82 % sensitivity (accurately identifying 45 of the 46 cases) for discriminating ALI (P / F ratio ≤ 300) with 75 % specificity (correctly discriminating 3 of the 4 cases in which the P / F ratio was ≥ 300).

The ROC curves demonstrated that S / F ratios had excellent ability to discriminate between the patients with and without ARDS (i.e. P / F ratio ≤ 200, AUC = 0.916) and ALI (P / F ≤ 300, AUC = 0.861)

In Todd rice group's study[11] of ARDS network which evaluated a total of 1074 adult patients with ALI / ARDS, the linear regression equation was quantified as S / F = 64 + 0.84 x P / F and an S / F ratio of 235 corresponded with a P / F ratio of 200. While an S / F ratio of 315 corresponded with a P / F ratio of 300. The S / F ratio threshold values of 235 and 315 resulted in 85 % sensitivity with 85 % specificity and 91 % sensitivity with 56 % specificity, respectively, for P / F ratios of 200 and 300 which are less than the sensitivity (92 % for ARDS & 97 % for ALI) and specificity (90 % for ARDS & 75 % for ALI) of the present study.

The mean P / F ratio was 155 + 66 and mean S / F ratio was 194 + 65 in Rice's study. In the present study, mean PaO2 / FiO2 ratio is 154.5 + 65 and mean S / F ratio of 207 + 61.

Regardless of the slight differences in values generated in the above studies, the association between SF and PF ratio is quite strong. Moreover, although the PF criteria for ALI and ARDS have some relationship to outcome, the values of 200 and 300 were determined by consensus primarily to create a homogeneous diagnostic group of patients. As such, it is less important that each study finds the same SF values for PF criteria for ALI and ARDS, but rather this knowledge should aid in establishing consensus definitions for a non-invasive method to identify these patients.

The results of the present study demonstrate that pulse oximetry can substitute for PaO2 and the threshold value of S / F ratio correlate well with P / F ratio's, 335 for 300 in ALI cases and 246 for 200 in ARDS cases with 92.82 % sensitivity and 75 % specificity and 92.3 % sensitivity and 90.90 % specificity respectively. These results are close to those of the Todd Rice et al study[11] of ARDS network groups with S / F ratio threshold values of 235 & 315, corresponding to P / F ratio of 200 & 300 in identification of ALI / ARDS cases. Raluca Solmon et al results[12] are also comparable to the present study results (with S / F ratio of s245 and 312). Both are adult studies and indicate strong association between SF and PF ratios. The results are also in close association with the conclusions obtained in Mirinda et al study conducted in paediatric population[3] In the present study the measurement of SpO_2 and PaO_2 were done simultaneously whereas in the 2 major adult studies[11,12] the time difference varied from 5 - 8 minutes which may contribute to some discrepancies since changes in SpO_2 and PaO_2 may happen quickly. On the other hand, the relationships between PaO_2 and SpO_2 are affected by variables like pH, temperature, PacO2 & concentration of 2, 3 DPG. In the present study these variables were not linked to SpO_2 or ABG data as it is clinically not practical to calculate the information on all patients. The S / F ratio use in diagnostic definition for ALI / ARDS has several potential clinical applications. Firstly, it allows recognition of patients who likely have ALI / ARDS but have not undergone ABG sampling.

Secondly, it facilitates early enrolment in to clinical trials and early diagnosis to implement treatment strategies and conservative fluid management. Thirdly it allows calculation of scores such as SOFA, SAPS II, MODS scores etc. in the absence of ABG sampling. Thus the evidence gathered so far demonstrates strong association between SF and PF ratios and given the clear benefits of pulse oximetry over invasive arterial sampling, it is proposed that SF ratio calculation should be the norm to characterize oxygen impairment, rather than an alternative diagnostic criteria to P / F ratio.

It is recommended that more definitive prospective multicentre studies are needed for validity of PF / SF ratios in more heterogenous populations in critically ill patients with care to document simultaneous SpO_2 / FiO_2 and PaO_2 / FiO_2 ratios and observe the effect of other variables like pH, PCO_2, temperature and 2, 3 DPG on SpO_2. Prospective research is also required to determine whether threshold values with higher sensitivity and specificity can be derived, while maintaining clinical usefulness.

Limitations

- The SpO_2 trace is unreliable in the methemoglobinemia, sepsis, and shock.
- The measurements made with SpO2 > 97 % were excluded from analysis. At these saturations, the slope of the relationships between SpO_2 and PaO_2 becomes almost zero, and large changes in PaO_2 may result in little or no change in SpO_2. This limitation can be overcome by titrating FiO_2 to maintain saturations less than 97 %.

- The SpO_2 values < 80 does not correlate well with the PaO_2 values. So the SpO_2 / FiO_2 is not reliable when the SpO_2 of the patient is < 80 %.
- S / F ratio does not allow evaluation of acid base status or $PaCO_2$ levels.

CONCLUSIONS

Threshold values for S / F ratio can be used as an alternative to diagnose ALI / ARDS when a P / F ratio is unavailable. Utilizing the non-invasive and continuously available S / F ratio may facilitate an earlier diagnosis of ALI / ARDS allowing the application of appropriate therapies and management strategies. Future studies are needed to establish the relationship between S / F and P / F ratio in a more heterogeneous population of critically ill patients.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

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