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Derivation and validation of SpO₂/FiO₂ ratio to impute for PaO₂/FiO₂ ratio in the respiratory component of the Sequential Organ Failure Assessment (SOFA) Score

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Abstract

Objective—The Sequential Organ Failure Assessment (SOFA) score is validated to measure severity of organ dysfunction in critically ill patients. However, in some practice settings, daily arterial blood gas (ABG) data required to calculate the respiratory component of the SOFA score are often unavailable. The objectives of this study were to derive SpO₂/FiO₂ (SF) ratio correlations with the PaO₂/ FiO₂ (PF) ratio to calculate the respiratory parameter of the SOFA score, and to validate the respiratory SOFA obtained using SF ratios against clinical outcomes.

Patients and measurements—We obtained matched measurements of SpO₂ and PaO₂ from two populations: Group 1- patients undergoing general anesthesia and Group 2- patients from the ARDS network -low versus high tidal volume for the Acute Respiratory Management of ARDS (ARMA) database. Using a linear regression model, we first determined SF ratios corresponding to PF ratios of 100, 200, 300 and 400. Second, we evaluated the contribution of positive end expiratory pressure (PEEP) on the relationship between SF and PF, for patients on PEEP in centimeters of water (cm H₂O) of <8, 8–12 and >12. Third, we calculated the SOFA scores in a separate cohort of ICU patients using the derived SF ratios and validated them against clinical outcomes.

Results—The total SOFA scores calculated using SF ratios and PF ratios were highly correlated (Spearman's rho 0.85, p<0.001) in all patients and in the 3 stratified PEEP categories (<8 cm H₂O, Spearman's rho 0.87, p<0.001; PEEP 8–12 cm H₂O, Spearman's rho 0.85, p<0.001; PEEP>12 cm H₂O, Spearman's rho 0.85, p<0.001). The respiratory SOFA scores based on SF ratios and PF ratios correlated similarly with ICU length of stay and ventilator-free days, when validated in a cohort of critically ill patients.

Conclusion—The total and respiratory SOFA scores obtained with imputed SF values correlate with the corresponding SOFA score using PF ratios. Both the derived and original respiratory SOFA scores similarly predict outcomes.

Introduction

Advances in modern medicine have resulted in marked improvements in patients' survival of diseases that were once considered to be fatal. Concurrently, there has also been a tremendous growth in the elderly population with many surviving into their 8th and 9th decades.(1) These changing demographics, along with the sheer increase in the volume and acuity of patients admitted to hospitals, necessitate the need for scoring systems to describe evolving morbidity, treatment endpoints, organ dysfunction, and predictors of mortality.(2)

The Sequential Organ Failure Assessment (SOFA)(3) score is one such scoring system, which allows daily evaluation of organ dysfunction in critically ill patients. The SOFA score was validated as a measure of severity of illness over time within patients, and thus can be used to follow the course of organ dysfunction and response to treatment.(4) The SOFA score has become the premier scoring system of patients in multi-organ failure, given its high specificity and sensitivity as a predictor of morbidity and mortality in critically ill patients.(2–6)

The SOFA score is based on six organ categories comprised of the respiratory, cardiovascular, nervous, hepatic, renal and coagulation systems.(3) Each of these categories is graded from a score of 1 (least organ dysfunction) to 4 (severe organ dysfunction), based on predefined cutoffs that are easily measured in the Intensive Care Unit (ICU) (Table 1). Of these, the severity of respiratory dysfunction is measured in the SOFA score by PaO₂/FiO₂ (PF) ratios, which require a daily arterial blood gas measurement if the SOFA score is to be followed during the course of an ICU admission. (3) Often these blood gas data are not available on a daily basis; hence the clinical and research utility of the SOFA and other scoring systems are reduced dramatically. Recently, Rice et. al.(7) determined the SF ratios corresponding to PF ratios of 200 and 300 to assist in the diagnosis of acute respiratory distress syndrome (ARDS) and acute lung injury (ALI) respectively; however the corresponding SF values for PF ratios of 100 and 400 needed for the SOFA score are presently unavailable. Furthermore, it is not known if the level of positive end expiratory pressure (PEEP) required adds predictive value to the PF or SF ratios. While PEEP does not affect the oxyhemoglobin curve and hence the relationship between SpO₂ and PaO₂, PEEP may impact the PF ratio by improving ventilation perfusion matching. The aims of this study, therefore, were to expand on the work done by Rice et al.(7) and derive and validate a reliable system to utilize SF ratios to impute for the PF ratios in assessing the respiratory parameters of the SOFA score, providing clinicians and researchers the ability to monitor daily SOFA scores even when arterial blood gas data are not available.

Methods

The study was approved by Institutional Review Board at Vanderbilt University Medical Center and involved two phases; Phase 1-derivation phase, followed by Phase 2-validation phase. In Phase 1, matched measurements of oxygen saturation by pulse oximetry (SpO₂) and partial pressure of oxygen in arterial blood (PaO₂) were obtained from 2 groups of patients: Group 1: those undergoing general anesthesia at Vanderbilt University Medical Center from 2002 to 2007 and Group 2: patients from the ARDS network -low versus high tidal volume for the Acute Respiratory Management of ARDS (ARMA) database.(8) We limited data points to those with SpO₂ > 98% to maximize matched data in the linear range of the sigmoidal association between SpO₂ and PaO₂ in the oxyhemoglobin curve, and at the

same time maintain clinical relevance and adequate sample size, given that it is unlikely that patients with higher SpO₂ would have PF ratios of less than 400 and thus impact the SOFA score. SF ratios corresponding to PF ratios of 100, 200, 300 and 400 were then derived. In Phase 2, the SOFA scores calculated by using these SF ratios were validated against outcomes in a 3rd group of surgical and trauma ICU patients.

Patients

In group 1, the intraoperative data points were obtained from a computerized query of the Microsoft SQL2003 database providing storage for data from Vanderbilt University's electronic anesthesiology documentation system, the Vanderbilt Perioperative Informatics Medical System (VPIMS)©. Data queried from the database included intraoperative pulse oximetry (SpO₂) values (Nellcor pulse oximeters via a Philips Intellivue MP 90 monitor) and time correlated intraoperative partial pressure of oxygen (PaO₂) determinations made by arterial blood sampling (Laboratory Gem Premier 3000, Instrumentation Technology) in all mechanically ventilated (MV) adults, undergoing general anesthesia. We excluded patients who were scheduled for cardiovascular surgeries, due to the potential effect of cardiopulmonary bypass and hypothermia on blood gas data, and those having thoracotomies with resultant lung resection or hypo-inflation for surgical purposes. In group 2, PaO₂ and corresponding SpO₂ values were obtained from the ARMA study database of patients with acute respiratory distress syndrome (ARDS).(8)

In our discussions with experts in the field - both clinicians and researchers - the unmet need in this area was to develop an easy to use and reliable imputation for PF ratios by using SF threshold values, without having the clinicians and research personnel perform difficult calculations, incorporating the covariates that may have played a role in this relationship. Hence a decision was made first to develop a model without any covariates, enabling the calculation of the SOFA score when only SpO₂ was available in a broad range of patients. To study the possible contribution of PEEP to the predictive value of SF and PF, we evaluated a second model to determine the relationship between SF and PF ratios within 3 categories of PEEP support: <8 centimeters of water (cm H₂O), 8–12 cm H₂O and > 12 cm H₂O.

Statistical analysis

The best fitting association between SF and PF ratios was described by a linear association between log (10) transformed SF and PF. Using the equation derived from the linear regression model, SF ratios corresponding to PF ratios of 100, 200, 300 and 400 were determined in the entire study population consisting of the anesthesia and ARMA databases. The possible contribution of PEEP to the predictive value of SF and PF was examined by stratifying for <8 cm H₂O PEEP, 8–12 cm H₂O PEEP and >12 cm H₂O PEEP, in only the patients in the ARMA database with data on levels of PEEP. Linear regression was then fitted between log (10) transformed SF and PF separately within each stratum. SF threshold values correlating with PF ratios of 100, 200, 300 and 400 were determined separately within each of the 3 PEEP categories, using the equation derived from the models.

To validate the use of SF ratios, the respiratory component of the SOFA score (SOFA respiratory -SF) and the total SOFA (SOFA-SF) were calculated in a cohort of 100 trauma and surgical ICU patients using the derived SF ratio thresholds and were correlated with the respiratory component of the SOFA score (SOFA respiratory-PF) and the total SOFA (SOFA-PF) based on PF values. The SOFA respiratory-SF and SOFA respiratory-PF were then correlated with important outcomes, such as ICU length of stay and ventilator free days, in the same trauma and surgical ICU cohort.

Results

One thousand seven hundred and forty two matched measurements of SpO₂ and PaO₂ were obtained from patients undergoing anesthesia at Vanderbilt University Medical Center and 2986 measurements from patients in the ARMA database. The best fitting association between SF and PF ratios in the total sample of 4728 matched measurements was described by a linear relationship between the transformed logarithmic value of the SF and PF ratios, with the regression equation $\text{Log}(\text{PF})=0.48+0.78 \times \text{Log}(\text{SF})$ and R-square of 0.31 (Figure 1). SF threshold values correlating with PF ratios of 100, 200, 300 and 400 were determined, using the equation derived from the model (Table 2).

Of the 2986 patients in the ARMA database, 2916 patients had documented PEEP support and were included in the stratified analysis by PEEP. The associations between SF and PF for the 3 models incorporating levels of PEEP (PEEP <8 cm H₂O, n=1107; PEEP 8–12 cm H₂O, n=1404 and PEEP >12 cm H₂O, n= 405), were best described by the following 3 equations: $\text{Log}(\text{PF})= 0.06 + 0.94 \times \text{Log}(\text{SF})$, $\text{Log}(\text{PF})= -0.13 + 1.01 \times \text{Log}(\text{SF})$ and $\text{Log}(\text{PF})= -0.47 + 1.17 \times \text{Log}(\text{SF})$, respectively, with corresponding R-square of 0.58, 0.61 and 0.59 (Figure 2). SF threshold values correlating with PF ratios of 100, 200, 300 and 400, according to level of PEEP are shown in Table 3.

The SOFA respiratory-SF and PF and total SOFA-SF and PF were well correlated (Table 4). Both the SOFA respiratory-SF and PF scores correlated with outcomes when validated in a cohort of 100 surgical and trauma intensive care unit patients (Table 4). Table 5 shows that the SOFA respiratory-SF and PF and total SOFA-SF and PF are correlated in the different PEEP categories and both predict outcomes similarly.

Discussion

In this study, we have taken multiple approaches for both clinicians and critical care researchers, to ensure confidence in using pulse oximetry data to calculate a reliable and valid severity of illness score over a wide range of patients in both the operating room and ICU. Our data show that the total SOFA scores calculated by imputing the derived SF ratios (for PF values of 100, 200, 300 and 400) are highly correlated with the total SOFA scores calculated with the PF ratio, and that the respiratory component of the SOFA scores are moderately correlated. In addition, the SF based respiratory SOFA score predicted outcomes when validated in a cohort of trauma and surgical critically ill patients. These findings provide support for using SF ratios to calculate SOFA scores when arterial blood gas data are not available. A second aim of our study was to determine if stratifying for PEEP improved the predictive value of the SF ratio for the PF ratio. Though the correlations between SF and PF for the 3 strata of PEEP were similar (r-squares of 0.58, 0.61 and 0.59, respectively), subtle differences existed in the SF threshold values for corresponding PF ratios depending on the level of PEEP. Thus level of PEEP may not significantly alter the relationship between SF and PF, and the differences in SF thresholds may not be clinically relevant. However the additional PEEP stratified analysis may provide more precise SF ratios for researchers, incorporating SOFA scores in their studies.

The utility of having a validated model for substituting SF ratios for PF ratios could go beyond the confines of the objective of this study. Extension of this work would allow the correlation we derived for SF vs. PF ratios to be applied to other severity of illness scores such as the Acute Physiology and Chronic Health Evaluation II score (APACHE II),(9) that require a PaO₂ or PF ratios for their calculation.

Our study has several strengths and limitations that should be mentioned. First, we studied a heterogeneous group of patients, who were either undergoing general anesthesia or were part

of the ARMA study. This strength, along with the large number of paired observations, increases the generalizability of the study given that both surgical and medical patients with varying degrees of pulmonary dysfunction were studied. However, this strength in generalizability is limited by poorer correlation between SF and PF ratios (a lower R-square value), when evaluated in the entire population. This is primarily driven by the group of patients undergoing general anesthesia, who are often oxygenated to maintain saturations above 95%, thus limiting the number of SpO₂ measurements in the linear part of the oxyhemoglobin curve. Second, we did not have the levels of PEEP in the patients undergoing general anesthesia, and so the models incorporating the categories of PEEP were limited to the ARMA database of the ARDS network's NIH cohort.(8) Third, in the effort to develop an easy to apply method of completing the SOFA score, we designed a model that did not incorporate covariates such as hemoglobin, age, comorbid illnesses, smoking history, body mass index and positioning of patient (supine versus prone). While it is possible that incorporation of these covariates would have strengthened the model, it would have made the regression equation impractical for daily use.

Conclusion

The respiratory and total SOFA scores obtained with imputed SF values correlate with the respiratory and total SOFA score using PF ratios. Both the derived and original respiratory SOFA score predicted outcomes similarly. SF ratios therefore provide an alternative method for calculating the respiratory component of the SOFA score when the PF ratios are unavailable due to the lack of arterial blood gas data.

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Abbreviations

SpO₂	Oxygen saturation by pulse oximetry
PaO₂	Partial pressure of oxygen in arterial blood
FiO₂	Fraction of inspired oxygen
SF	SpO ₂ /FiO ₂ ratio
PF	PaO ₂ /FiO ₂ ratio
SOFA	Sequential Organ Failure Assessment
PEEP	Positive End Expiratory Pressure
ICU	Intensive Care Unit
ARDS	Acute Respiratory Distress Syndrome
ARMA	Acute Respiratory Management of ARDS
MV	Mechanically Ventilated
SOFA-SF	SOFA score calculated using SpO ₂ /FiO ₂ ratio
SOFA-PF	SOFA score calculated using PaO ₂ /FiO ₂ ratio

SOFA respiratory-SF	The respiratory component of the SOFA score calculated using SpO ₂ /FiO ₂ ratio
SOFA respiratory-PF	The respiratory component of the SOFA score calculated using PaO ₂ /FiO ₂ ratio

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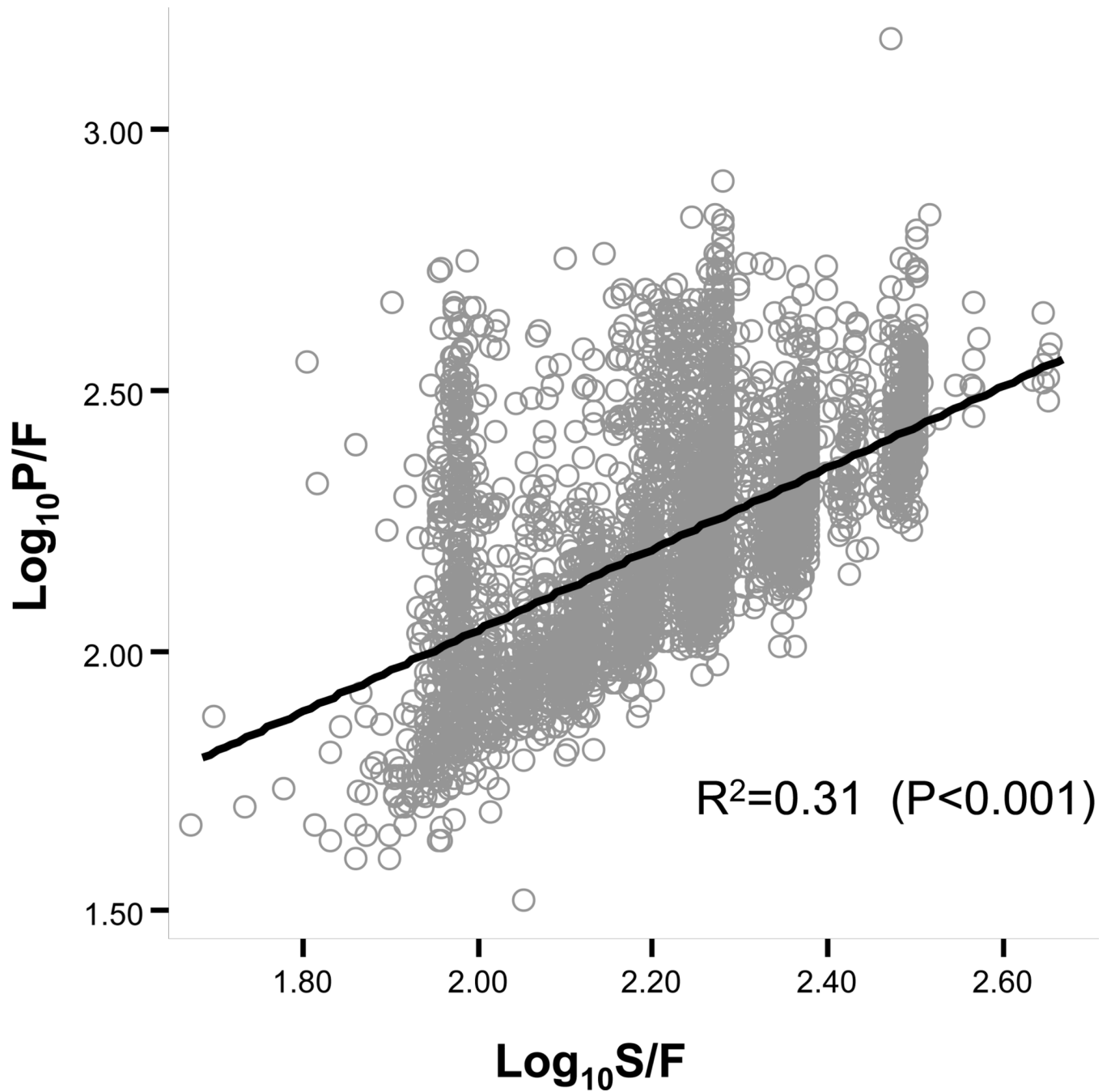


Figure 1.

Linear regression describing association between $\text{SpO}_2/\text{FiO}_2$ and $\text{PaO}_2/\text{FiO}_2$ in the combined anesthesia and ARMA database.

The association between $\text{SpO}_2/\text{FiO}_2$ and $\text{PaO}_2/\text{FiO}_2$ was best described by a linear association between \log_{10} transformed $\text{PaO}_2/\text{FiO}_2$ values $\text{SpO}_2/\text{FiO}_2$ and. R-square for the model was 0.31 indicating that 31% variability in $\text{PaO}_2/\text{FiO}_2$ was due to $\text{SpO}_2/\text{FiO}_2$.

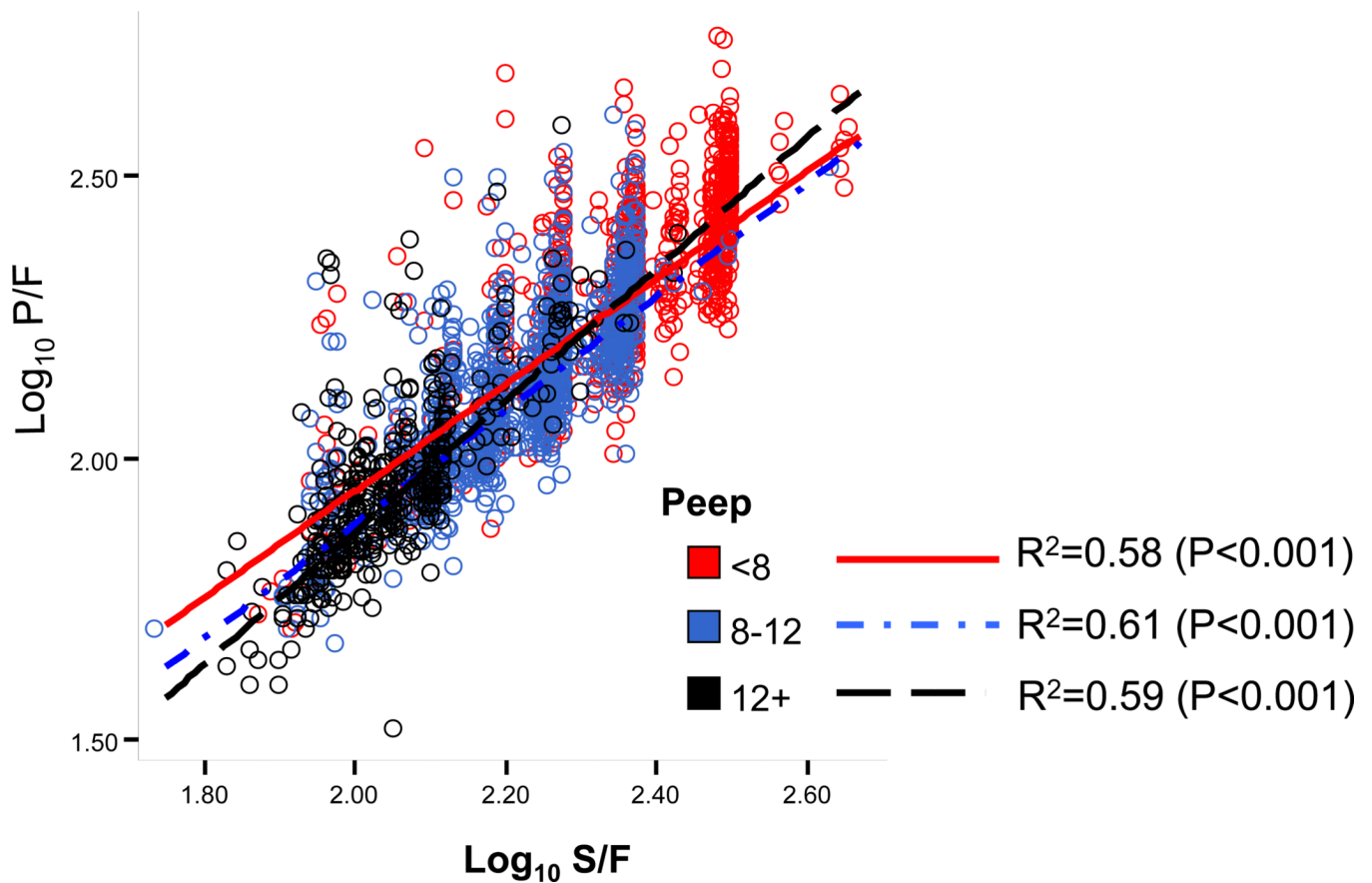


Figure 2.

Linear regression describing association between $\text{SpO}_2/\text{FiO}_2$ and $\text{PaO}_2/\text{FiO}_2$, stratified by level of positive end expiratory pressure in the ARMA database. The association between $\text{SpO}_2/\text{FiO}_2$ and $\text{PaO}_2/\text{FiO}_2$, stratified by the level of PEEP, was best described by a linear association between the log transformed values of $\text{SpO}_2/\text{FiO}_2$ and $\text{PaO}_2/\text{FiO}_2$. R-square for the 3 models (PEEP <8 cm H₂O, n=1107; PEEP 8–12cm H₂O, n=1404 and PEEP >12 cm H₂O, n= 405) were 0.58, 0.61 and 0.59, respectively.

Table 1

The Sequential Organ Failure Score (SOFA)*

SOFA score	Respiratory PaO ₂ /FiO ₂ ratio	Cardiovascular Mean Arterial Pressure / vasopressors*	Nervous Glasgow coma score	Hepatic Bilirubin, mg/dl	Renal Creatinine, mg/dl (or urine output)	Coagulation Platelets (×10 ³ /mm ³)
1	<400	<70 mm/Hg	13-14	1.2-1.9	1.2 - 1.9	<150
2	<300	dopamine 5 or dobutamine (any dose)	10-12	2-5.9	2.0 - 3.4	<100
3	<200	dopamine > 5, epinephrine 0.1 or norepinephrine	6-9	6-11.9	3.5 - 4.9 (or < 500 ml/d)	<50
4	<100	dopamine > 15, epinephrine > 0.1 or norepinephrine > 0.1	<6	>12	> 5.0 (or < 200 ml/d)	<20

* Vasopressor drug doses are in mcg/kg/min

Table 2

Derivation of SpO₂/FiO₂ values corresponding to PaO₂/FiO₂ ratios in the combined anesthesia and ARMA database *

SOFA Respiratory score	PaO ₂ /FiO ₂	SpO ₂ /FiO ₂
1	<400	<512
2	<300	<357
3	<200	<214
4	<100	<89

* Data derived from 4728 matched SpO₂/FiO₂ and PaO₂/FiO₂ measurements from the combined anesthesia and ARMA database

Table 3Derivation of SpO₂/FiO₂ values corresponding to PaO₂/FiO₂ stratified by PEEP in the ARMA database *

SOFA Respiratory score	PaO ₂ /FiO ₂ ratio	SpO ₂ /FiO ₂ ratio		
		PEEP <8	PEEP 8-12	PEEP >12
1	<400	<502	<515	<425
2	<300	<370	<387	<332
3	<200	<240	<259	<234
4	<100	<115	<130	<129

* Data derived from 2916 matched SpO₂/FiO₂ and PaO₂/FiO₂ measurements from the ARMA database of the ARDS network's NIH study(8)

Table 4Validation of SOFA scores derived from SpO₂/FiO₂ from the combined anesthesia and ARMA database *

	Spearman's rho	p-value
SOFA-PF vs. SOFA-SF	0.85	<0.001
SOFA respiratory-PF vs. SOFA respiratory-SF	0.50	<0.001
ICU LOS vs. SOFA respiratory-PF	0.26	0.005
ICU LOS vs. SOFA respiratory-SF	0.36	0.013
Ventilator free days vs. SOFA respiratory-PF	-0.28	0.005
Ventilator free days vs. SOFA respiratory-SF	-0.33	0.025

* Validation performed by calculating SF based SOFA scores and correlating against PF based SOFA scores and clinical outcomes in a separate cohort of surgical and trauma ICU patients.

Table 5Validation of SOFA scores derived from SpO₂/FiO₂, stratified by the PEEP level, from the ARMA database

	Spearman's rho, p-value		
	PEEP <8	PEEP 8–12	PEEP >12
SOFA-PF vs. SOFA-SF	0.87, <<0.001	0.85, <0.001	0.85, <0.001
SOFA respiratory-PF vs. SOFA respiratory-SF	0.45, <0.001	0.41, <0.001	0.47, <0.001
ICU LOS vs. SOFA respiratory-PF	0.28, <0.006		
ICU LOS vs. SOFA respiratory-SF	0.36, <0.001	0.27, 0.007	0.35, <0.001
Ventilator free days vs. SOFA respiratory-PF	-0.28, 0.005		
Ventilator free days vs. SOFA respiratory-SF	-0.31, 0.002	-0.25, 0.011	-0.32, 0.001

* Validation performed by calculating PEEP stratified SF based SOFA scores and correlating against PF based SOFA scores and clinical outcomes in a cohort of surgical and trauma ICU patients.