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Association Between Peripheral Blood Oxygen Saturation (SpO_2)/ Fraction of Inspired Oxygen (FiO_2) Ratio Time at Risk and Hospital Mortality in Mechanically Ventilated Patients

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ABSTRACT

Introduction: Acute respiratory failure requiring mechanical ventilation is a leading cause of mortality in the intensive care unit. Although single peripheral blood oxygen saturation/fraction of inspired oxygen (SpO2/FiO2) ratios of hypoxemia have been evaluated to risk-stratify patients with acute respiratory distress syndrome, the utility of longitudinal SpO2/FiO2 ratios is unknown.

Objective: To assess time-based SpO2/FiO2 ratios ≤ 150—SpO2/FiO2 time at risk (SF-TAR)—for predicting mortality in mechanically ventilated patients.

Methods: Retrospective, observational cohort study of mechanically ventilated patients at 21 community and 2 academic hospitals. Association between the SF-TAR in the first 24 hours of ventilation and mortality was examined using multivariable logistic regression and compared with the worst recorded isolated partial pressure of arterial oxygen/fraction of inspired oxygen (P/F) ratio.

Results: In 28,758 derivation cohort admissions, every 10% increase in SF-TAR was associated with a 24% increase in adjusted odds of hospital mortality (adjusted odds ratio = 1.24; 95% confidence interval [CI] = 1.23-1.26); a similar association was observed in validation cohorts. Discrimination for mortality modestly improved with SF-TAR (area under the receiver operating characteristic curve [AUROC] = 0.81; 95% CI = 0.81-0.82) vs the worst P/F ratio (AUROC = 0.78; 95% CI = 0.78-0.79) and worst SpO2/FiO2 ratio (AUROC = 0.79; 95% CI = 0.79-0.80). The SF-TAR in the first 6 hours offered comparable discrimination for hospital mortality (AUROC = 0.80; 95% CI = 0.79-0.80) to the 24-hour SF-TAR.

Conclusion: The SF-TAR can identify ventilated patients at increased risk of death, offering modest improvements compared with single SpO2/FiO2 and P/F ratios. This longitudinal, noninvasive, and broadly generalizable tool may have particular utility for early phenotyping and risk stratification using electronic health record data in ventilated patients.

INTRODUCTION

Acute hypoxemic respiratory failure (AHRF) requiring mechanical ventilation is associated with substantial morbidity and mortality.[1-3] Although intensive care unit (ICU) severity of illness scoring systems such as the Acute Physiology and Chronic Health Evaluation (APACHE), Simplified Acute Physiology Score (SAPS), and Sequential Organ Failure Assessment (SOFA) are widely used to identify patients at increased risk of mortality, they are not explicitly used to characterize the severity of AHRF.[3] Thus, inexpensive, noninvasive, and readily available markers of disease severity are needed for diagnosis, phenotyping, and prognostication in patients with AHRF.

Research in AHRF severity has focused primarily on the acute respiratory distress syndrome (ARDS) using arterial blood gas (ABG) analysis of partial pressure of arterial oxygen(PaO_2)/ fraction of inspired oxygen (FiO_2) (PaO2/FiO2) ratios, with mortality inversely proportional to PaO2/FiO2 ratios.[4,5] However, despite widespread familiarity with use of PaO2/FiO2 ratios, clinical recognition of ARDS remains poor. In a recent large multinational study, clinicians failed to recognize ARDS in 40% of patients, and recognized only 1 in 3 patients when ARDS criteria were first met.[6] Therapies, including lung protective ventilation,[7] and early use of paralysis[8,9] have shown mortality benefit in ARDS, but not surprisingly, when recognition is poor, so is adoption of these strategies.[10] Selected prior studies also suggest that similar therapies could have benefit in isolated AHRF.[11-13]

Inconsistent use of PaO2/FiO2 ratios may be a barrier to AHRF classification and prognostication. Several studies suggest that repeated measurements of the PaO2/FiO2 ratio 24 or more hours after ARDS onset may improve the accuracy of classification and prognosis.[5,14-17] However, the absence of standardized practices regarding ABG use and the increasing focus on early identification and treatment of patients with AHRF limit the utility of ABG-based, reactive evaluation strategies. Furthermore, there is a surprising paucity of information regarding severity of illness classification and risk stratification in patients with non-ARDS AHRF, and recent work suggests mortality rates may be comparable in patients with ARDS and non-ARDS AHRF, with similar degrees of hypoxemia.[2] These studies highlight the need for more readily available severity classification methods to facilitate early recognition, phenotyping, and assessment of

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therapeutic response in both patients with ARDS AHRF and patients with non-ARDS AHRF.

These issues could be addressed through use of pulse oximetry-based peripheral blood oxygen saturation (SpO_2)/FiO_2 (SpO_2/FiO_2) ratios, which are ubiquitously available and noninvasive. Studies suggest that SpO2/FiO2 and PaO2/FiO2 ratios are reasonably well correlated, particularly when PaO2/FiO2 ratios are less than 300,[18-22] and ARDS mortality and ventilator days are similar when disease severity is defined by SpO2/FiO2 ratios.[22] Because SpO2/FiO2 ratios can be measured frequently, they can be used to calculate an SpO2/FiO2 ratio time-at-risk (SF-TAR) profile—the duration of time during which the patient's SpO2/FiO2 ratios are under a certain hypoxemic threshold. The SF-TAR may help identify patients with persistent hypoxemia and mitigate misclassification issues resulting from transient clinical worsening or isolated errors in charting. This is particularly salient because the severity of respiratory failure is dynamic, with patients experiencing both worsening and improving hypoxemia even within a single day.

We hypothesized that the SF-TAR would be significantly associated with mortality among unselected ventilated patients, with similar discrimination compared with PaO2/FiO2 ratios, facilitating its use as a dynamic and ubiquitously available prognostic measure.

METHODS

This retrospective cohort study was approved by the institutional review boards of Kaiser Permanente Northern California (KPNC) and the University of California, Davis (UCD).

Derivation Cohort

We retrospectively evaluated all adult, mechanically ventilated ICU patients in 21 hospitals in the KPNC integrated health care delivery system between 2010 and 2013, using a previously validated algorithm.[23-27] We included patients whose hospitalizations included an overnight stay, began in a KPNC hospital, and were not for peripartum care.

Hourly Oxygenation Ratios and Correlation

During mechanical ventilation, we calculated patients' hourly oxygenation ratios (PaO2/FiO2 ratio and SpO2/FiO2 ratio) using electronic medical record (EMR)-derived data. When patients had multiple PaO2/FiO2 or SpO2/FiO2 ratios recorded during a single hour, we calculated an hourly weighted average. We truncated PaO2/FiO2 and SpO2/FiO2 values at the 0.05th percentile (28.0 and 52.3, respectively) and the 99.95th percentile (743 and 480, respectively) to remove nonphysiologic extreme values that may result from data entry errors during clinical charting in the EMR.

We assessed the correlation between all hourly PaO2/FiO2 and SpO2/FiO2 ratios using Pearson correlation coefficients when the PaO2/FiO2 and SpO2/FiO2 ratios were limited to values less than or equal to 400 and oxygen saturations less than or equal to 96%, assuming that these ranges would be associated with more accurate assessment of hypoxemia.[18] To help visualize the relationship between PaO2/FiO2 and SpO2/FiO2 ratios over time, we randomly selected 6 patients ventilated for 5 or more days with PaO2/FiO2 values of 5 or greater and displayed oxygenation ratios over the first week of ventilation (see Supplemental Figure 1[a]).

SpO2/FiO2 Ratio Time at Risk

We calculated the SF-TAR value as the proportion of time during the first 24 hours of mechanical ventilation that a patient had severe hypoxemia, defined by an SpO2/FiO2 ratio less than 150 (corresponding to a PaO2/FiO2 ≤ 100).[20] An SpO2/FiO2 ratio threshold < 150 was used to calculate the SF-TAR after an exploratory analysis of the SpO2/FiO2-TAR using SpO2/FiO2 ratios corresponding to mild (SpO2/FiO2 ratio 235-314), moderate (SpO2/FiO2 ratio 150-234), and severe (SpO2/FiO2 ratio < 150) revealed a more linear relationship between the SF-TAR and hospital mortality using the severe threshold (see Supplemental Figure 2[a]). We thus grouped the continuous SF-TAR values into 11 categories: 0%, 1% to 10%, 11% to 20%, 21% to 30%, 31% to 40%, 41% to 50%, 51% to 60%, 61% to 70%, 71% to 80%, 81% to 90%, and 91% to 100% of the time with an SpO2/FiO2 ratio less than 150. We determined hospital mortality and 95% confidence intervals for each.

Multivariable Logistic Regression Analysis

We estimated the independent effect of increasing SF-TAR values (as ordinal categories based on 11 groups) on the prespecified primary outcome of hospital mortality with a multivariable logistic regression model adjusted for age, sex, ICU severity of illness as measured by the SAPS3 score,[28] total duration of ventilation, and additional measures of acute and chronic severity of illness: the Laboratory and Acute Physiology Score, version 2 (LAPS2) and the COmorbidity Point Score, version 2 (COPS2).[23-25,27] We compared the discrimination of this model against an identical model replacing SF-TAR with the worst PaO2/FiO2 and SpO2/FiO2 ratios in the first 24 hours of ventilation when available. We compared model discrimination using area under the receiver operating characteristic curve (AUROC). In post hoc analyses, we also calculated the AUROC of models using SF-TAR values from only the first 6 or 12 hours of ventilation.

Validation Cohorts

We used similar experimental procedures with data from the Medical Information Mart for Intensive Care (MIMIC) III database[29] and UCD Health. We identified patients from the MIMIC and UCD study cohorts from a larger inpatient sample of adult patients (≥ 18 years) whose hospitalizations included an overnight stay. We then identified a subset of ICU patients who underwent invasive mechanical ventilation on the basis of previously validated algorithms (https://github.com/MIT-LCP/mimic-code/blob/master/concepts/durations/ventilation-durations.sql). Analysis was limited to the first episode of mechanical ventilation during a hospitalization. Patient characteristics are described in Supplemental Table 1.[a]

For each patient in the validation cohorts, SpO2/FiO2 (and PaO2/FiO2) ratios were calculated by feeding forward all charted SpO_2 (or PaO_2) and FiO_2 measurements until a replacement

value for either was recorded during times when patients were classified as under mechanical ventilation by the just-mentioned algorithm. A new SpO2/FiO2 (or PaO2/FiO2) ratio was thus calculated every time that either the SpO_2 (or PaO_2) or FiO_2, or both were changed. Each PaO2/FiO2 measurement was paired with the most recent SpO2/FiO2 measurement taken within the previous hour. All PaO2/FiO2 measurements taken more than an hour after any SpO2/FiO2 measurements were discarded. These PaO2/FiO2-SpO2/FiO2 pairs were used to calculate the correlation between the 2 measures. We truncated the averaged PaO2/FiO2 and SpO2/FiO2 ratios at the 0.05th (45 and 65, respectively) and 99.95th (1100 and 414, respectively) percentiles in MIMIC and the 0.05th (28 and 52.3, respectively) and 99.95th (743 and 480, respectively) percentiles in the UCD cohort. The mortality regression models were adjusted for age, sex, and either hospital length of stay (MIMIC) or highest (SOFA score (UCD).[30]

Continuous data are presented as the mean and standard deviation (SD) or median (interquartile range [IQR]); categorical data are presented as number (percentage). All analyses were conducted using Stata/SE version 14.1 (StataCorp, College Station, TX) and R version 3.2.2.

Table 1. Patient characteristics of Kaiser Permanente Northern California derivation cohort (N = 28,758)

Variable	Value
Age, y, mean (SD)	65.4 (15.6)
Male sex, no. (%)	16,248 (56.5)
Hospitalized through ED, no. (%)	19,168 (66.7)
First hospital ward or location, no. (%)	
Intensive care unit	13,662 (47.5)
Operating room	7042 (24.5)
Hospital ward	6620 (23.0)
Stepdown unit	1345 (4.7)
Other	89 (0.3)
Hospital length of stay, d, mean (SD)	14.2 (23.3)
Full code status at time of admission, no. (%)	27,362 (95.2)
Predicted eSAPS3 hospital mortality, % (SD)	30.3 (19.1)
Observed hospital mortality, no. %	7112 (24.7)

ED = Emergency Department; eSAPS3 = electronic Simplified Acute Physiology Score 3; SD = standard deviation.

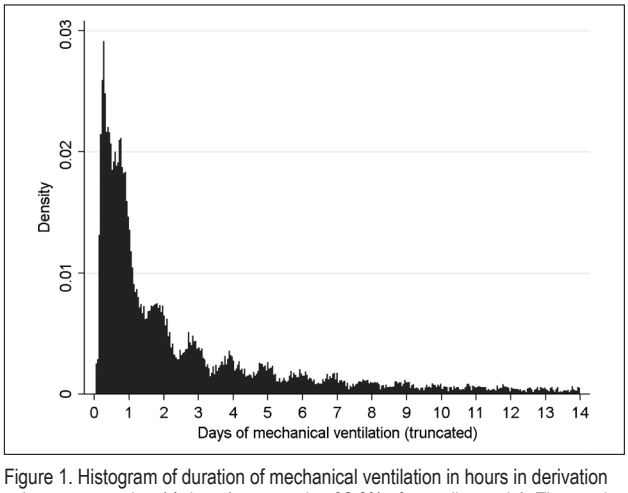

Figure 1. Histogram of duration of mechanical ventilation in hours in derivation cohort, truncated at 14 days (representing 92.6% of overall sample). The x-axis represents elapsed days. The y-axis represents frequency of patients with that duration of ventilation

RESULTS

Derivation Cohort

We included 28,758 hospitalizations with mechanical ventilation in the ICU, occurring among 25,944 unique patients (Table 1). The patients' mean age (SD) was 65.4 (15.6) years. Two-thirds of patients were admitted through the Emergency Department. The mean hospital length of stay (SD) was 14.2 (23.3) days. Figure 1 displays the duration of mechanical ventilation through day 14; the median duration of ventilation was 37 hours (IQR = 15-110).

Oxygenation Ratios

A total of 3,505,707 hourly SpO2/FiO2 ratio values were available, with a median value of 250 (IQR = 218-326); 173,576 hourly PaO2/FiO2 ratio values were available, with a median value of 214 (IQR = 134-307). SpO2/FiO2 ratio values were much more frequently available than PaO2/FiO2 values across all ranges (Supplemental Table 2[a]). During ventilation, the number of recorded PaO2/FiO2 ratios was substantially lower than the number of SpO2/FiO2 ratios across all quintiles of recorded values (see Supplemental Table 3[a]). The SpO2/FiO2 and PaO2/FiO2 ratios were moderately to strongly correlated when SpO2/FiO2 and PaO2/FiO2 ratios were available in the same hour (0.47) or when restricted to PaO2/FiO2 ratios at or below 400 and SpO2/FiO2 ratios derived from saturations less than or equal to 96% (0.68). Visual inspection of concurrent SpO2/FiO2 and PaO2/FiO2 ratios, performed to complement the correlation analysis, revealed periods of relative concordance and discordance between individual SpO2/FiO2 and extrapolated PaO2/FiO2 ratios. Supplemental Figure 1[a] shows a random sample of 6 ventilation episodes for illustrative purposes.

SpO2/FiO2 Ratio Time at Risk

Hospital mortality increased as the proportion of time with an SpO2/FiO2 ratio below 150 (SF-TAR) increased over the first 24 hours of mechanical ventilation (Figure 2 and Supplemental Table 4[a]). In the first 24 hours of ventilation, patients with an SF-TAR of 0% (n = 10,703) had a hospital mortality rate of 16.4%. Among patients with a 24-hour SF-TAR of 91% to 100% (n = 1405), the mortality rate was 70.2%.

SF-TAR and PaO2/FiO2 Ratio Comparisons

A total of 86.1% of patients had at least 1 PaO2/FiO2 ratio during the first 24 hours of ventilation (Supplemental Table 2[a]). Discrimination for hospital mortality in the adjusted logistic regression model was modestly higher with the SF-TAR (AUROC = 0.81, 95% CI = 0.81-0.82) than with the worst PaO2/FiO2 ratio (AUROC = 0.78, 95% CI = 0.78-0.79,

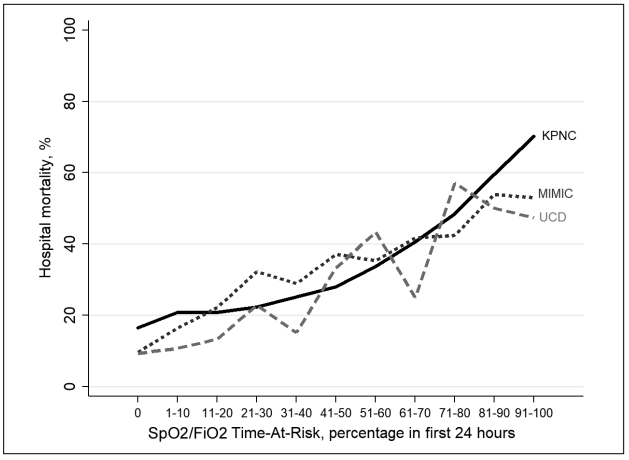

Figure 2. Hospital mortality in all 3 patient cohorts across increasing levels of peripheral blood oxygen saturation/fraction of inspired oxygen (SpO2/FiO2) ratio time-at-risk categories on day 1 of ventilation.
KPNC = Kaiser Permanente Northern California; MIMIC = Medical Information Mart for Intensive Care; UCD = University of California, Davis.

p < 0.001). Results were similar when SF-TAR was compared with the single worst SpO2/FiO2 ratio in the first 24 hours (AUROC = 0.79; 95% CI = 0.79-0.80, p < 0.01). Even when SF-TAR data were limited to either the first 6 or 12 hours of mechanical ventilation, the AUCs for these models were both 0.80 (95% CI = 0.79-0.80 and 0.80-0.81, respectively). Each 10% increase in SF-TAR during the first 24 hours of ventilation was associated with a 24% increase in the odds of hospital mortality (adjusted odds ratio = 1.24, 95% CI = 1.23-1.26, p < 0.001).

Validation Data

The MIMIC cohort included 13,755 hospitalizations with mechanical ventilation. The patients' mean age (SD) was 63.1 (16.0) years, and the median duration of ventilation was 22 hours (IQR = 9-75; Supplemental Table 1[a]). Correlation between SpO2/FiO2 and PaO2/FiO2 ratios was moderate at 0.49 when both values were available concurrently. The hospital mortality rate was 9.7% among patients with SF-TAR of 0% and was 53.0% among those with SF-TAR of 91% to 100% (Figure 2 and Supplemental Table 4[a]). Each 10% increase in SF-TAR was associated with an adjusted odds ratio of 1.26 for hospital mortality (95% CI = 1.23-1.30, p < 0.001).

The UCD cohort included 1088 hospital encounters involving mechanical ventilation where SpO2/FiO2 and PaO2/FiO2 ratios were available concurrently. The mean age (SD) was 54.9 (17.0) years; the median duration of mechanical ventilation was 35 hours (IQR = 12 to 126 hours; see Supplemental Table 1[a]). Correlation between SpO2/FiO2 and PaO2/FiO2 values was 0.50 for all values and 0.56 when comparisons were restricted to SpO2/FiO2 values with saturation less than or equal to 96%. The hospital mortality rate was 9.3% in patients with an SF-TAR of 0% and was 47.4% with an SF-TAR of 91% to 100% (Figure 2 and Supplemental Tables 4 and 5[a]). Each 10% increase in SF-TAR was associated with an adjusted odds ratio for hospital mortality of 1.21 (95% CI = 1.12-1.31, p < 0.001) when a SOFA score lacking the respiratory subscore was included in the model, and 1.16 (95% CI = 1.08-1.28, p < 0.001) using the full SOFA score.

DISCUSSION

In this study, we examined the value of using SpO2/FiO2 ratios to predict mortality among a mixed population of mechanically ventilated patients. Although individual SpO2/FiO2 ratios are ubiquitously available and frequently assessed, they were not consistently correlated with PaO2/FiO2 ratios, which were substantially less available or even unavailable in a sizable proportion of ventilated patients. We thus developed a longitudinal measure of oxygenation (SF-TAR) that is based on the percentage of time that patients exhibited severe hypoxemia (SpO2/FiO2 ratio < 150), and we tested its utility for identifying patients at increased risk of death. In 3 independent datasets, we found that the SF-TAR during the first 24 hours of ventilation was significantly associated with hospital mortality and that the SF-TAR could discriminate between survivors and nonsurvivors at least as well as the current ABG-based gold standard for quantifying severity and prognostication in AHRF.

This study has several implications for diagnosis and prognostication in patients with AHRF, including those with and without ARDS. Recent studies have shown that clinician recognition of ARDS remains poor, with several barriers that hamper both diagnosis and classification of severity.[6,31,32] Lack of standardized timing and frequency of ABG sampling may be a contributory factor.[33,34] Additionally, initiatives to reduce unnecessary testing in the ICU may further decrease the availability of ABG-derived PaO2/FiO2 values.[35-38] In contrast to ABGs, the SpO_2 values are ubiquitously available, can be frequently or continuously measured, and are free of risk. Thus, our data suggest that use of SpO2/FiO2 ratios, either as single worst values or when used in a longitudinal SF-TAR approach, should play a central role in improving the recognition of disease severity and prognostication of mortality in mechanically ventilated patients, with and without ARDS, particularly when SpO_2 is less than or equal to 96%, when estimates of hypoxemia by SpO2/FiO2 are more accurate.[39]

We developed the SF-TAR to represent a metric that characterizes both the magnitude and duration of acute hypoxemia. Several studies have demonstrated improved prognostic performance with repeated measurement of PaO2/FiO2 ratios after changing to standardized ventilator settings within the first 48 hours of ARDS, or after using standardized ventilator settings with reassessment at 24 hours.[14-17,40] Although limited to patients with ARDS, these studies support incorporating the response to initial interventions over time as a means of improving prognostication in patients with AHRF. Furthermore, there is increasing recognition that single timepoint evaluations of hypoxemia severity contribute to misclassification of patients because patients dynamically improve and worsen even during a single day.

Our finding that SF-TAR in the first 6 hours of ventilation, independent of ventilator settings or indication for ventilation,

has nearly the discriminatory power of the 24-hour value is particularly important, highlighting its potential to improve the early recognition of disease subtypes for clinical trial enrollment and to identify severely ill patients meriting protocolized care pathways. Further extension of time-based clinical phenotyping metrics like the SF-TAR may also facilitate improved characterization of the molecular basis of common AHRF subtypes, as demonstrated by the recent recognition of ARDS endotypes with potential differential response to therapies.[41-43] The SF-TAR may offer additional advantages in clinical applications in that its performance does not depend on repeated collection of ABG samples or application of standardized ventilator settings that may be difficult and costly to implement outside a clinical study.

We demonstrated that SpO_2-based measures have prognostic value in a mixed population of patients. Ventilated patients without ARDS face substantial short- and long-term morbidity and mortality, and recent data suggest that mortality in patients with non-ARDS AHRF may be similar to those with ARDS when severity of illness at ICU admission is similar.[34,44,45] Given mounting evidence that lung protective ventilation may also benefit patients without ARDS,[11,46,47] quantifying the severity and duration of hypoxemia using the SF-TAR may help to identify additional predictors of adverse outcomes in this understudied population. Although we did not explicitly identify patients with ARDS, our findings are broadly consistent with prior work demonstrating the value of SpO2/FiO2 ratios for classification and prognostication in ARDS.[18-22]

Use of frequently available values like the SF-TAR may offer future utility for characterizing the course of impending or progressive respiratory failure. This may be particularly relevant for patients at high risk of ARDS and those with early acute lung injury. Future work should evaluate patients with respiratory failure who are treated with noninvasive mechanical ventilation or high-flow nasal cannula.[48-51] Our finding that even relatively short SF-TAR intervals performed similarly to the worst PaO2/FiO2 ratio in 24 hours may facilitate development of automated surveillance tools to improve the efficiency of clinical trial screening, the timeliness of enrollment, and the accuracy of AHRF classification for studies.[52] Temporal metrics like the SF-TAR may also enable new technology-leveraged approaches to the management of patients with AHRF. For example, EMR-based early warning systems could use SF-TAR-based risk as a clinical decision support trigger that may be more resistant to false alarms from periodic low SpO2/FiO2 ratios resulting from low pulse oximetry signal quality or charting errors. In addition, most current warning score systems fail to include or simply dichotomize oxygen saturation values.[53] The SF-TAR-based triggers could be incorporated into automated surveillance systems designed to detect evolving hypoxemic respiratory failure at early time points when gradual escalation in the intensity of respiratory support may mask overt hypoxemia. Although we evaluated SF-TAR only during mechanical ventilation, future work should include longitudinal hypoxemia metrics in patients before invasive mechanical ventilation, as well as in those who never need it.

This study has several strengths. We developed the SF-TAR in a large, contemporary, community-based multicenter cohort of more than 28,000 ventilated patients, and we validated the association between SF-TAR and mortality in 2 academic medical center-based cohorts totaling more than 14,000 additional patients, suggesting the generalizability of our findings. Our use of real-world EMR data, with the potential for data quality errors, further reinforces the generalizability of the SF-TAR. Finally, all 3 patient samples incorporated medical and surgical patients, with and without ARDS, suggesting broad clinical utility.

Our study also has several limitations. First, the correlation between SpO2/FiO2 and PaO2/FiO2 ratio values was lower here than in previous studies, likely reflecting patient heterogeneity, unsynchronized measurement of SpO2/FiO2 and PaO2/FiO2 values, and potential EMR data quality issues.[18] This finding suggests that single-time-point SpO2/FiO2 ratios derived from routine clinical data entry may have limitations for clinical phenotyping or clinical decision support triggers, particularly when SpO_2 values are close to 100%. Second, although the SF-TAR exhibited significantly higher discrimination than the worst single PaO2/FiO2 or SpO2/FiO2 values, the incremental increase in performance was modest. If the primary use of noninvasive hypoxemia metrics were only to drive early recognition of risk, isolated SpO2/FiO2 ratio values might still represent the simplest and most rapid approach to risk stratification. Further research focused specifically on the first hours after intubation may help to clarify whether the SF-TAR offers advantages over isolated SpO2/FiO2 ratios. Third, we evaluated only a single SpO2/FiO2 ratio threshold to quantify the SF-TAR, and it is possible that a different threshold value might improve SF-TAR performance.

The fourth limitation of this study is that we evaluated the performance of the SF-TAR using data only from the first 24 hours of mechanical ventilation, and it is possible that an SF-TAR derived from later time bins such as day 2 of mechanical ventilation might have improved discrimination for mortality.[16,54,55] Fifth, we did not assess for ARDS in our patients given the high likelihood of diagnostic inaccuracy associated with the clinical underrecognition of ARDS and thus its diagnostic coding in the EMR.[6] Whether SF-TAR is equally predictive with and without ARDS, as well as for individual ARDS risk factors, remains unclear, and future research using prospectively identified cohorts may clarify this question. Sixth, the SF-TAR was not designed to replace the PaO2/FiO2 ratio or other diagnostic criteria for ARDS. Because of this and our inability to confidently identify true-positive and true-negative ARDS cases in our EMR-derived datasets, we did not test the diagnostic accuracy of the SF-TAR for ARDS.

CONCLUSION

We found that extended periods of severe hypoxemia (SpO2/FiO2 ratio < 150) were significantly associated with mortality in a nearly linear fashion in 3 large independent cohorts. The SF-TAR, even in the first 6 hours of ventilation, had discrimination for mortality comparable with the single worst PaO2/FiO2 ratio in 24 hours. These data reinforce the clinical utility of SpO2/FiO2 ratios in patients with AHRF and highlight

the potential value of severity of illness metrics that incorporate assessment of organ dysfunction over time. Our findings also suggest that the SF-TAR may be a useful metric for diagnosis and prognostication when one is using electronic health record-derived data in mechanically ventilated patients. ❖

[a] Supplemental Material is available at: www.thepermanentejournal.org/files/2020/19.113Suppl.pdf

Disclosure Statement

Drs Adams, Rogers, and Liu received funding from the National Institutes of Health (NIH) National Heart, Lung, and Blood Institute related to the submitted work during the study (K12HL108964 [Adams], K23HL125663 [Rogers], NIH R35GM128672 [Liu]). The study was supported by the Permanente Medical Group Delivery Science research program. Dr Taylor received grant support from the NIH during the study (UL1 TR001860). The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. Drs Schuler, Marelich, Fresco, Riedl, Baker, and Escobar have no conflicts of interest to disclose.

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Kathleen Louden, ELS, of Louden Health Communications performed a primary copy edit.

Authors' Contributions

Jason Y Adams, MD, MS; Angela J Rogers, MD, MPH; and Vincent X Liu, MD, MSc, conceived and designed the study. Jason Y Adams, MD, MS; Alejandro Schuler, MS, PhD; Sandra L Taylor, PhD; Albert W Riedl, MS; and Vincent X Liu, MD, MSc, coordinated and performed data collection and statistical analyses. All authors participated in analysis and interpretation of study data. Jason Y Adams, MD, MS; Angela J Rogers, MD, MPH; and Vincent X Liu, MD, MSc, wrote the first draft of the manuscript, and all authors participated in revision of the manuscript for important intellectual content. Jason Y Adams, MD, MS; and Vincent X Liu, MD, MSc, obtained funding for the study, and Vincent X Liu, MD, MSc, provided overall study supervision. Jason Y Adams, MD, MS; Angela J Rogers, MD, MPH; and Vincent X Liu, MD, MSc, had full access to the data used in the study and take full responsibility for the integrity of the data and the accuracy of the data analysis. Vincent X Liu, MD, MSc, was responsible for the final decision to submit the manuscript.

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