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Characterizing the Racial Discrepancy in Hypoxemia Detection in Venovenous Extracorporeal Membrane Oxygenation: An Extracorporeal Life Support Organization Registry Analysis

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Abstract

Purpose—Skin pigmentation influences peripheral oxygen saturation (SpO_2) compared to arterial saturation of oxygen (SaO_2). Occult hypoxemia ($SaO_2 \leq 88\%$ with $SpO_2 \geq 92\%$) is associated with increased in-hospital mortality in venovenous-extracorporeal membrane oxygenation (VV-ECMO) patients. We hypothesized VV-ECMO cannulation, in addition to race/ethnicity, accentuates the SpO_2-SaO_2 discrepancy due to significant hemolysis.

Methods—Adults (≥ 18 years) supported with VV-ECMO with concurrently measured SpO_2 and SaO_2 measurements from over 500 centers in the Extracorporeal Life Support Organization Registry (1/2018–5/2023) were included. Multivariable logistic regressions were performed to examine whether race/ethnicity was associated with occult hypoxemia in pre-ECMO and on-ECMO SpO_2-SaO_2 calculations.

Results—Of 13,171 VV-ECMO patients, there were 7772 (59%) White, 2114 (16%) Hispanic, 1777 (14%) Black, and 1508 (11%) Asian patients. The frequency of on-ECMO occult hypoxemia was 2.0% ($N = 233$). Occult hypoxemia was more common in Black and Hispanic patients *versus* White patients (3.1% versus 1.7%, $P < 0.001$ and 2.5% versus 1.7%, $P = 0.025$, respectively). In multivariable logistic regression, Black patients were at higher risk of pre-ECMO occult hypoxemia versus White patients (adjusted odds ratio [aOR] = 1.55, 95% confidence interval [CI] = 1.18–2.02, $P = 0.001$). For on-ECMO occult hypoxemia, Black patients (aOR = 1.79, 95% CI = 1.16–2.75, $P = 0.008$) and Hispanic patients (aOR = 1.71, 95% CI = 1.15–2.55, $P = 0.008$) had higher risk versus White patients. Higher pump flow rates (aOR = 1.29, 95% CI = 1.08–1.55, $P = 0.005$) and on-ECMO 24-h lactate (aOR = 1.06, 95% CI = 1.03–1.10, $P < 0.001$) significantly increased the risk of on-ECMO occult hypoxemia.

Conclusion—SaO_2 should be carefully monitored if using SpO_2 during ECMO support for Black and Hispanic patients especially for those with high pump flow and lactate values at risk for occult hypoxemia.

Keywords

Pulse oximetry; Arterial blood gas; Venovenous extracorporeal membrane oxygenation; Racial/ethnical disparities; Hypoxemia

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Introduction

Arterial blood gas (ABG) analysis is the gold-standard method to measure arterial oxygen saturation (SaO_2) as it directly measures the partial pressure of oxygen in arterial blood [1]. Pulse oximetry is a standard non-invasive continuous method of monitoring peripheral oxygen saturation (SpO_2) via measurement of hemoglobin saturation through spectroscopy. Darker skin pigmentation may worsen occult hypoxemia (previously defined as $SaO_2 \leq 88\%$ despite $SpO_2 \geq 92\%$) [2] as was seen in a cohort of 10,001 intensive care unit (ICU) patients where Black patients experienced occult hypoxemia threefold more than White patients [3]. In a study of respiratory failure patients 6 h before extracorporeal membrane oxygenation (ECMO) cannulation, the frequency of pre-ECMO occult hypoxemia in Black patients was higher than in White patients [2]. However, this study analyzed only pre-ECMO oxygen saturation values and did not account for clinically relevant covariates, such as hemolysis or vasopressor usage.

In addition to skin pigmentation bias, SpO_2 is also unable to distinguish between oxygen bound to hemoglobin (oxyhemoglobin), carbon monoxide bound to hemoglobin (carboxyhemoglobin), or oxidized hemoglobin (methemoglobin or sulfhemoglobinemia), which can further cause inaccurate pulse oximetry readings [4, 5]. This is particularly important in ECMO patients, where accurate oxygenation measurements are critical and their complex physiology [6] can further influence the accuracy of these measurements. Specifically, high ECMO pump flow rate and larger cannula size [7] can cause hemolysis due to mechanical shearing of red blood cells [8–10], leading to formation of carboxyhemoglobin and thus causing inaccurate SpO_2 measurements. This phenomenon was observed in a cohort of 40 venovenous (VV)-ECMO patients; however, this study is limited by small sample size and did not account for ECMO-relevant covariates or race/ethnicity in their analyses. [11]

We sought to address these previous limitations using concurrently measured SpO_2 and SaO_2 data points within a multicenter, international cohort of ECMO patients, to examine for discrepancy by race/ethnicity. In addition, we hypothesized that ECMO-induced hemolysis would worsen occult hypoxemia in VV-ECMO patients. Finally, as the single-lumen cannula may require greater resistance of perfusion and overall pump flow to maintain adequate perfusion, we also hypothesized that single *versus* double-lumen cannulation strategies may impact the SpO_2-SaO_2 discrepancy.

Methods

Study Design and Population

This study was approved by the Johns Hopkins Hospital Institutional Review Board (IRB00216321) on 10/22/2019. The study title is “Retrospective Analysis of Outcomes of Patients on Extracorporeal Membrane Oxygenation”. All procedures were followed in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975. The Extracorporeal Life Support Organization (ELSO) Registry is an international multicenter registry from over 500 ECMO centers [12]. The Registry collects demographic information,

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pre-ECMO comorbidities, pre-ECMO and on-ECMO laboratory and hemodynamic information, on-ECMO complications, and outcomes. Comorbidity information was recorded using *International Classification of Diseases, 10th Revision (ICD-10)* codes.

We included patients who were (1) 18 years of age or older; (2) supported with VV-ECMO; and (3) had data on race/ethnicity. We excluded repeat ECMO runs within individual patients, patients without data on hypoxemia, and patients with extreme outlier values for the difference between SpO_2 and SaO_2.

Definitions

SpO_2 was defined as the non-invasive pulse oximeter measured oxyhemoglobin saturation, while SaO_2 was the percent arterial blood oxyhemoglobin saturation from ABG. Pre-ECMO ventilator-type settings included conventional ventilation, high-frequency oscillatory ventilation, other high-frequency ventilation (high-frequency jet ventilation or percussive ventilation), other non-specified ventilations, and no ventilation. Pre-ECMO mechanical circulatory support included intra-aortic balloon pump, Impella®, and left ventricular assist device. Pre-ECMO vasopressor infusions included dopamine, epinephrine, norepinephrine, phenylephrine, and vasopressin. Pre-ECMO inotrope infusions included dobutamine, enoximone, levosimendan, milrinone, nicardipine, nitroglycerin, nitroprusside, and tolazoline. Infusions were treated as a binary covariate (i.e., the presence or absence of the infusion). Pre-ECMO vasopressor and inotrope infusions were employed for at least 6 h within 24 h of the start of ECMO cannulation.

Single-lumen cannulation involves placement in two vascular access sites and double-lumen cannulation involves placement of a cannula in single vascular access site. Definitions for on-ECMO complications are provided in the eMethods.

Race/ethnicity was coded per patient as one of Asian, Black, Hispanic, Middle Eastern or North African, Native American, Native Pacific Islander, Multiple, Other, Unknown, and White. We restricted our primary analysis to Asian, Black, Hispanic, and White patients. White patients were chosen as the reference comparator based on previous literature showing the first pulse oximeters were calibrated to this race/ethnicity. [13]

Outcomes

Occult hypoxemia was defined as $SaO_2 \leq 88\%$ with a time-matched $SpO_2 \geq 92\%$ [2]. The primary outcomes were the occult hypoxemia (binary variable) and SpO_2-SaO_2 discrepancy (continuous variable), which were compared between different races/ethnicities. We also assessed the accuracy and precision for SpO_2 to predict SaO_2.

Statistical Analysis

Continuous variables were assessed for normality with the Kolmogorov–Smirnov test, and all were determined to be not normally distributed. Therefore, these variables are denoted as median with interquartile range (IQR). Categorical variables are represented as frequency with percentages. The Kruskal–Wallis, Wilcoxon rank-sum, and Pearson chi-square tests were utilized to compare continuous and categorical variables, respectively. SpO_2–SaO_2

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differences were compared with Kruskal–Wallis and Wilcoxon rank-sum tests. A P value < 0.05 was considered statistically significant (eMethods contain more details).

Bland–Altman analyses were used to assess agreement between SpO_2 and the gold standard, SaO_2, by calculating the difference between SpO_2 and SaO_2, the mean of SpO_2 and SaO_2, the estimated bias (median difference), and limits of agreement (median and 95% limits of agreement at 2.5th and 97.5th percentiles) using a nonparametric method to estimate the limits given the non-normality of the differences between SpO_2 and SaO_2. The one-sample Wilcoxon signed-rank test was used to compare the median difference between SpO_2 and SaO_2 (estimated bias) for Asian, Black, and Hispanic patient groups as compared to the median value for White patients (hypothetical value set at 0). Boxplots were performed to visually assess the SpO_2–SaO_2 discrepancy, while scatterplots were used to visually assess the correlation between SpO_2 and SaO_2. Spearman correlations were conducted for pre-ECMO and on-ECMO SpO_2 and SaO_2 by race/ethnicity.

Multivariable logistic regressions were performed to examine whether race/ethnicity was associated with occult hypoxemia in pre-ECMO and on-ECMO measurements. One pre-ECMO SpO_2–SaO_2 pair and a corresponding on-ECMO SpO_2–SaO_2 pair were measured from the same patient for adequate comparison. We selected covariates a priori that were hypothesized to be associated with the SpO_2–SaO_2 discrepancy based on clinical judgment and prior data. Covariates in both the pre-ECMO and on-ECMO models included age, sex, presence of pre-ECMO temporary mechanical circulatory support (tMCS), and presence of pre-ECMO vasopressor and inotrope infusions. The on-ECMO model also included hemolysis, hyperbilirubinemia, cannulation strategy (single- versus double lumen), ECMO pump flow rate, and on-ECMO serum lactate value. Adjusted odds ratios (OR) are presented with 95% confidence intervals (CIs).

Receiver-operating characteristic curve (ROC) analyses were performed to determine the accuracy of on-ECMO SpO_2 in predicting SaO_2. Based on previous literature [14–17], the following on-ECMO SaO_2 thresholds were tested: 88%, 92%, and 95%. All SpO_2 values were tested to detect the specific SaO_2 threshold at or below its value. Area under the receiver-operating characteristic curve (AUC), sensitivity, and specificity were calculated. In addition, the AUC for each SaO_2 threshold was compared by race/ethnicity groups. All statistical analyses were performed using R Studio (R 4.1.2, www.r-project.org) or IBM SPSS Statistics for Windows, Version 28.0 (IBM Corp, Armonk, NY).

Results

Study Population

Of 30,407 VV-ECMO patients, we included 13,171 patients for our study after applying the inclusion and exclusion criteria (Fig. 1). Of 13,171 VV-ECMO patients (median age = 48.6 years, 66% male), 7772 (59%) were White, 2114 (16%) were Hispanic, 1777 (14%) were Black, and 1,508 (11%) were Asian (Table 1). Of 9851 patients with valid COVID-19 data, 59% (N = 5830) had a diagnosis of SARS CoV-2 and COVID-19. The median ECMO duration was 11.4 days (IQR = 5.7–22.9). Of patients with complete cannulation information (N = 12,966), 9,833 (76%) received single-lumen VV-ECMO versus 3133 (24%) received

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double-lumen VV-ECMO. Black patients were less likely to have single-lumen cannulation (N = 1206, 69%) compared to other races/ethnicities.

Occult Hypoxemia

Overall, on-ECMO occult hypoxemia was observed in 2.0% of patients (233 of 11,709). On-ECMO occult hypoxemia was more common in Black (3.1% vs 1.7%, $P < 0.001$) and Hispanic (2.5% vs 1.7%, $P = 0.025$) patients *versus* White patients. The proportion of on-ECMO occult hypoxemia was similar between Asian and White patients (1.6%% vs 1.7%, $P = 0.787$).

In a multivariable logistic regression, Black patients were at higher risk of pre-ECMO occult hypoxemia *versus* White patients (aOR = 1.55, 95% CI = 1.18–2.02, $P = 0.001$; Fig. 2A, eTable 1). No other race/ethnicity group differences were found.

For on-ECMO occult hypoxemia, multivariable logistic regression analysis found that Black patients (aOR = 1.79, $P = 0.008$) and Hispanic patients (aOR = 1.71, $P = 0.008$) had greater risk *versus* White patients (Table 2, Fig. 2B). Other significant risk factors included pump flow rate at 24 h on ECMO (aOR = 1.29, $P = 0.005$) and on-ECMO lactate (aOR = 1.06, $P < 0.001$; Table 2).

SpO_2–SaO_2 Discrepancy

Figure 3 depicts boxplots of the on-ECMO SpO_2–SaO_2 difference for each race/ethnicity. The overall on-ECMO estimated bias for the entire cohort was 1.0 (median difference between SpO_2 and SaO_2) with 95% limits of agreement at −6.0 and 7.0 (2.5th and 97.5th percentiles). In Bland–Altman plots, the limits of agreement for Asian, Black, and Hispanic patients were wider as compared to White patients (eFig. 1). In addition, the median difference of the SpO_2-SaO_2 difference for Asian, Black, and Hispanic patients was significantly higher than the hypothetical value set at the median for White patients. The overall Spearman correlation coefficient comparing on-ECMO SpO_2 with SaO_2 was moderate ($r_s = 0.69$, $P < 0.001$). The Spearman correlation coefficients comparing on-ECMO SpO_2 with SaO_2 were relatively comparable in magnitude across the race/ethnicity groups, and all were significant ($P < 0.001$): Asian patients ($r_s = 0.69$), Black patients ($r_s = 0.67$), Hispanic patients ($r_s = 0.72$), and White patients ($r_s = 0.68$), but Fisher r-to-z transformation did find a significant difference in r_s between White and Hispanic patients ($z = -2.84$, $P = 0.005$). Each race/ethnicity group was found to have greater on-ECMO discrepancies as a continuous variable *versus* White patients after adjustment (eTable 2). Supplementary analysis of other races/ethnicities (Middle Eastern or North African, Multiple, Native American, Native Pacific Islander, and Other) was also conducted. The overall on-ECMO estimated bias for additional races/ethnicities was 1.1%. The on-ECMO estimated biases for Middle Eastern or North African, Multiple, Native American, Native Pacific Islander, and Other was 3.0%, 1.0%, 0.64%, − 1.1%, 0.47%, and 0.63%, respectively.

On-ECMO Receiver-Operating Characteristic Curve Analyses

At an 88% SaO_2 threshold, SpO_2 predicted hypoxemia with an AUC of 0.89 (95% CI = 0.88–0.90), at a 92% threshold, SpO_2 predicted hypoxemia with an AUC of 0.87 (95% CI =

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0.86–0.88), and at a 95% threshold, SpO_2 predicted hypoxemia with an AUC of 0.83 (95% CI = 0.83–0.84; eFig. 2, eResults), sensitivity of 0%, and specificity of 100%.

Exploratory Analysis: Single Lumen Versus Double Lumen

There was no difference in the incidence of on-ECMO occult hypoxemia for single-lumen *versus* dual-lumen cannulation (2% vs 2%, $P = 0.527$). However, the correlation between on-ECMO SpO_2 and SaO_2 was weaker for single lumen ($r_s = 0.68$, $P < 0.001$) *versus* double lumen ($r_s = 0.72$, $P < 0.001$) using Fisher *r*-to-*z* transformation to compare r_s values ($z = -3.45$, $P < 0.001$). In patients with confirmed hemolysis, there was no difference in the incidence of on-ECMO occult hypoxemia for single-lumen versus double-lumen cannulation (6% vs 4%, $P = 0.463$). The correlation between on-ECMO SpO_2 and SaO_2 was weaker for single lumen ($r_s = 0.67$, $P < 0.001$) *versus* double lumen ($r_s = 0.83$, $P < 0.001$) using Fisher r-to-z transformation to compare r_s values ($z = -4.28$, $P < 0.001$).

Exploratory Analysis: COVID-19 vs Non-COVID-19

In those with COVID-19 (N = 5,830, 59%), the incidence of pre-ECMO occult hypoxemia did not differ for patients with and without COVID-19 (4% vs 4% $P = 0.993$), but the incidence of on-ECMO occult hypoxemia was significantly greater for patients with COVID-19 (2.4% vs 1.5%, $P = 0.003$).

Sensitivity Analyses

To reduce heterogeneity, subgroup analysis was performed between different primary indications for VV-ECMO. The frequency of occult hypoxemia in the subset of VV-ECMO patients with a primary indication of ARDS was similar to that of COPD or asthma patients (2.8% vs. 0%, $P = 0.31$; 2.7% vs. 2.1%, $P = 0.53$). The frequency of hemolysis in ARDS patients was similar to that of COPD patients (5.4% vs. 2.8%, $P = 0.49$) but greater than that of asthma patients (5.4% vs. 1%, $P = 0.008$).

In sensitivity analysis of only $SpO_2 < 90\%$ datapoints, the overall on-ECMO estimated bias was − 2.68%. The on-ECMO estimated bias within this subgroup was − 2.92%, − 2.96%, − 3.65%, and − 1.39% for White, Black, Asian, and Hispanic VV-ECMO patients, respectively. The frequency of occult hypoxemia was higher in older patients (≥ 48.6 years, median age) versus younger patients (< 48.6 years, 2.7% vs. 1.8%, $P < 0.001$). The frequency of occult hypoxemia was greater in patients with higher 4-h pump flows (≥ 4.100 L/min, median pump flow rate) versus patients with lower 4-h pump flows (< 4.100 L/min, 2.8% vs. 1.8%, $P < 0.001$). The frequency of occult hypoxemia was greater in patients with higher 24-h pump flows (≥ 4.15 L/min, median pump flow rate) versus patients with lower 24-h pump flows (< 4.15 L/min, 2.8% vs. 2.1%, $P = 0.016$).

Comment

In this retrospective observational analysis of the international multicenter ELSO Registry, we found that the frequency of unadjusted and adjusted occult hypoxemia in VV-ECMO patients was higher in Black and Hispanic patients *versus* White patients. After adjusting for clinically relevant risk factors, we found that ECMO support exacerbated occult hypoxemia

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(compared to pre-ECMO). This finding suggests that, in addition to race/ethnicity, being supported by VV-ECMO may lead to more inaccurate pulse oximetry measurements likely mediated by greater ECMO pump flow and corresponding associated hemolysis.

Pre-ECMO vs On-ECMO Occult Hypoxemia

While a previous ELSO Registry study using solely pre-ECMO SpO_2 and SaO_2 measurements found a similar frequency of occult hypoxemia in Hispanic patients compared to White patients [2], we found a higher frequency of occult hypoxemia in Hispanic versus White patients in "*on*-ECMO" SpO_2 and SaO_2 values. This finding suggests the SpO_2-SaO_2 discrepancy is worse during the time that patients were supported with ECMO. Besides one single-center study analyzing this discrepancy in 57 VV-ECMO patients [17], which found the unadjusted frequency of occult hypoxemia to be greater in Black *versus* White patients but not in Hispanic or Asian versus White patients, no other literature exists pertaining to this discrepancy directly for patients supported on ECMO.

Undetected hypoxemia during cannulation is important as ECMO patients are already at high risk for many complications, such as acute brain injury from inadequate oxygen delivery [18], which increases mortality [19, 20]. Occult hypoxemia may increase in-hospital mortality due to increased risk of organ dysfunction [21, 22], lung injury [23], and worse neurocognition [24]. Accordingly, monitoring for occult hypoxemia in patients with such risk factors (Black and Hispanic race/ethnicity, high pump flow, and lactate) in ECMO is extremely important.

Additionally, compared to this pre-ECMO ELSO study, our study has several strengths including (1) having a larger sample size (N = 13,171 versus N = 1562), (2) the use of methodically rigorous statistical methods such as the Kolmogorov–Smirnov test to assess for non-normality and nonparametric analyses when comparing the SpO_2–SaO_2 discrepancy, and (3) the adjustment of more clinically relevant and ECMO-specific covariates *versus* only adjusting for measured SpO_2 and sex as was done in this prior study.

Cannulation Strategy, ECMO Pump Flow Rate, and Hemolysis

In contrast to previous data [6], we found no differences in the SpO_2–SaO_2 discrepancy between patients with single-lumen *versus* double-lumen, perhaps because the rates of hemolysis in our population were similar (5.5% versus 5.4%) which may be the primary driver of increased SpO_2–SaO_2 discrepancy via carbon monoxide production increasing carboxyhemoglobin. However, we still observed the correlation between SpO_2 versus SaO_2 was weaker in single lumen *versus* double lumen, with and without confirmed hemolysis. However, relative to single lumen, the double-lumen cannula enhanced the SpO_2–SaO_2 discrepancy in our multivariable linear regression analysis. Overall, further research is warranted to investigate the association between cannulation strategy and the SpO_2–SaO_2 discrepancy.

Although "ELSO-defined" hemolysis during ECMO was not independently associated with occult hypoxemia, higher ECMO pump flow rates were associated with higher occurrence of occult hypoxemia. This finding may indicate varying degree of hemolysis is occurring with high ECMO pump flow rates [6, 7, 25]. Due to shear mechanical

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stress that is produced by high pump flow rates in combination with large cannula sizes [7] throughout the ECMO circuit and oxygenator, ECMO-associated hemolysis can occur [26]. Furthermore, intravascular hemolysis, which has been reported to occur in 18% of ECMO-supported patients, can increase plasma hemoglobin [27]. This hemoglobin can then scavenge endothelial-derived nitric oxide, which causes oxidative stress and triggers inflammatory signaling pathways that can potentially worsen the discrepancy as well. [25, 28]

Limitations

In line with previous studies [2, 3, 29, 30], we duly note that race/ethnicity was used as a substitute for skin tone as clinicians do not obtain this information and this data was not available in the ELSO Registry. However, future studies examining the relationship between skin tone and the SpO_2–SaO_2 discrepancy are needed to confirm our results, ideally using dermatology scales, such as the Fitzpatrick skin type or Monk Skin Tone Scale. The ELSO Registry is an international consortium of over 500 ECMO centers; therefore, heterogeneity in data collection and the patient cohort inherently exists [31]. However, this diversity in sampling may be offset by the large sample size of our study. Frequency of occult hypoxemia was relatively low in our cohort; however, it was measured at a single timepoint during ECMO cannulation and may not reflect the SpO_2–SaO_2 discrepancy throughout the entire ECMO run, as observed in previous studies [6, 17]. Furthermore, center volume may be an important explanatory variable in our analysis but this variable was not available in this study. Additionally, there are several other limitations with the ELSO Registry including lack of granular data on skin perfusion (e.g., perfusion index, mottling score, or recapillarization time), Vasopressor Dose Equivalence scores which have previously confounded the SpO_2–SaO_2 discrepancy in ECMO patients [6], timestamps for when SpO_2 and SaO_2 data were collected, or specific markers for hemolysis, such as haptoglobin, lactate dehydrogenase, or free hemoglobin. Information regarding bridge to transplantation as an indication for VV-ECMO was also not available in this study, which could confound our results as these patients may be able to better tolerate hypoxemia. Outcome data such as mortality was also not available, but is likely important for future studies to determine if occult hypoxemia in ECMO patients is associated with worse clinical outcomes. Finally, prospective observational studies are needed to assess causation effects and appropriately suggest a correction factor by race/ethnicity for pulse oximeters.

Conclusion

Black and Hispanic VV-ECMO patients are at higher risk for occult hypoxemia and overestimated true oxygen saturation measurements compared to White patients. Patients who were supported with ECMO had an increased risk of the SpO_2–SaO_2 discrepancy compared to the pre-ECMO SpO_2–SaO_2 discrepancy, which was greater in non-White patients. As occult hypoxemia and SpO_2–SaO_2 discrepancy may worsen in patients with ECMO support, clinicians should carefully monitor ABGs during ECMO support for those with such risk factors.

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Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Declarations

Conflict of Interest Dr. Tonna is supported by a Career Development Award from the National Institutes of Health/ National Heart, Lung, And Blood Institute (K23HL141596). Dr. Tonna is the Chair of the Registry Committee of the Extracorporeal Life Support Organization (ELSO). Dr. Brodie receives research support from and consults for LivaNova. He has been on the medical advisory boards for Abiomed, Xenios, Medtronic, Inspira, and Cellenkos. He is the President-elect of the Extracorporeal Life Support Organization (ELSO) and the Chair of the Executive Committee of the International ECMO Network (ECMONet) and he writes for UpToDate. Dr. Lorusso is a consultant for Medtronic, LivaNova, Getinge, and ASbiomed and Member of the Medical Advisory Board of Eurosets and Xenios. He is the ELSO Research Committee Chair, and Honorary Secretary of EuroELSO. The authors do not have any additional conflicts of interest to declare.

Abbreviations

ABG	Arterial blood gas
aOR	Adjusted odds ratio
AUC	Area under the receiver-operating characteristic curve
CI	Confidence interval
COVID-19	Coronavirus Disease 19
ECMO	Extracorporeal membrane oxygenation
ELSO	Extracorporeal Life Support Organization
IQR	Interquartile range
PaO_2	Partial pressure of oxygen
ROC	Receiver-operating characteristic
SaO_2	Oxygen saturation measured by arterial blood gas
SpO_2	Oxygen saturation measured by pulse oximetry
SD	Standard deviation
tMCS	Temporary mechanical circulatory support
VV-ECMO	Venovenous ECMO

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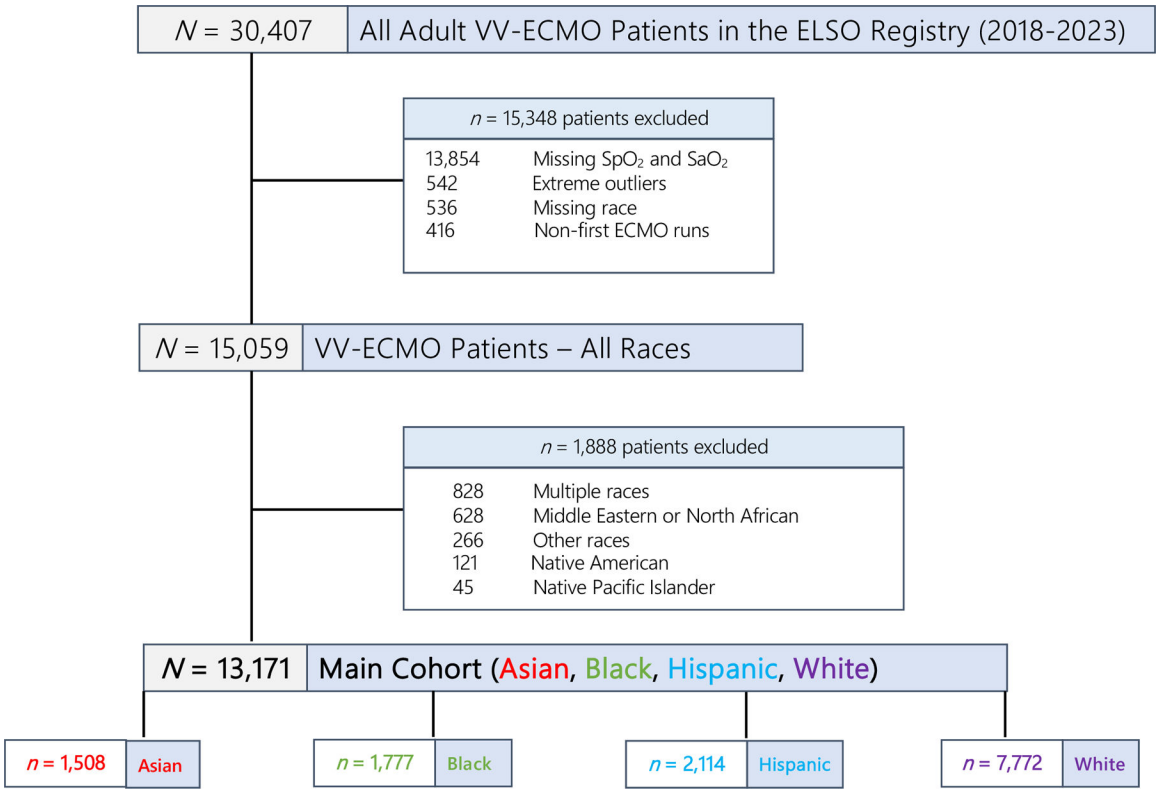

Fig. 1.
Creation of study cohort from the ELSO Registry (1/2018–5/2023)

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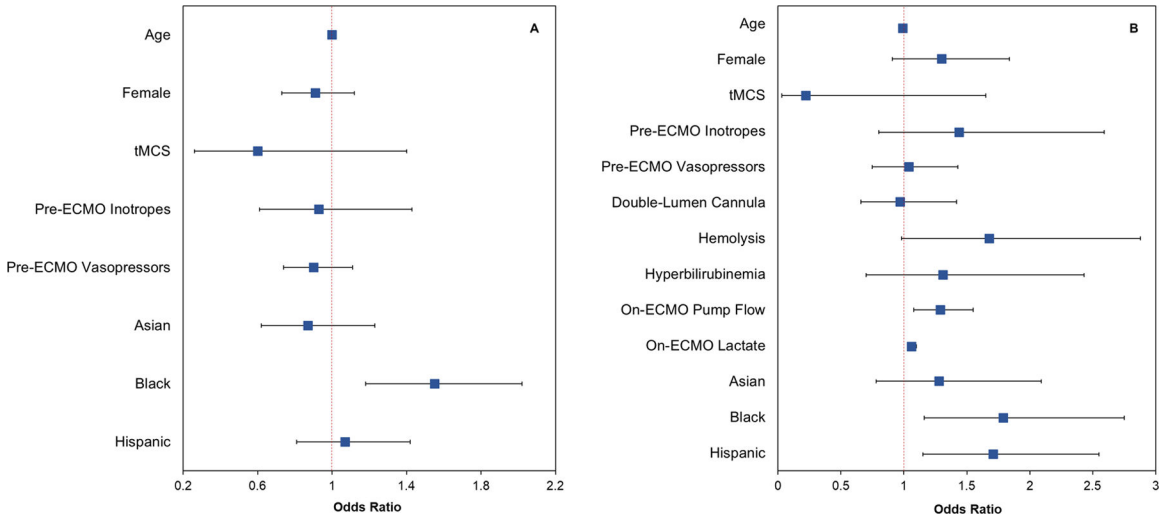

Fig. 2.

Forest plots of odds ratios and 95% confidence intervals from the multivariable logistic regression for occult hypoxemia in **A** pre-ECMO SpO_2-SaO_2 and **B** on-ECMO SpO_2-SaO_2 pairs. Pre-ECMO and on-ECMO SpO_2-SaO_2 measurements were extracted from the same patient

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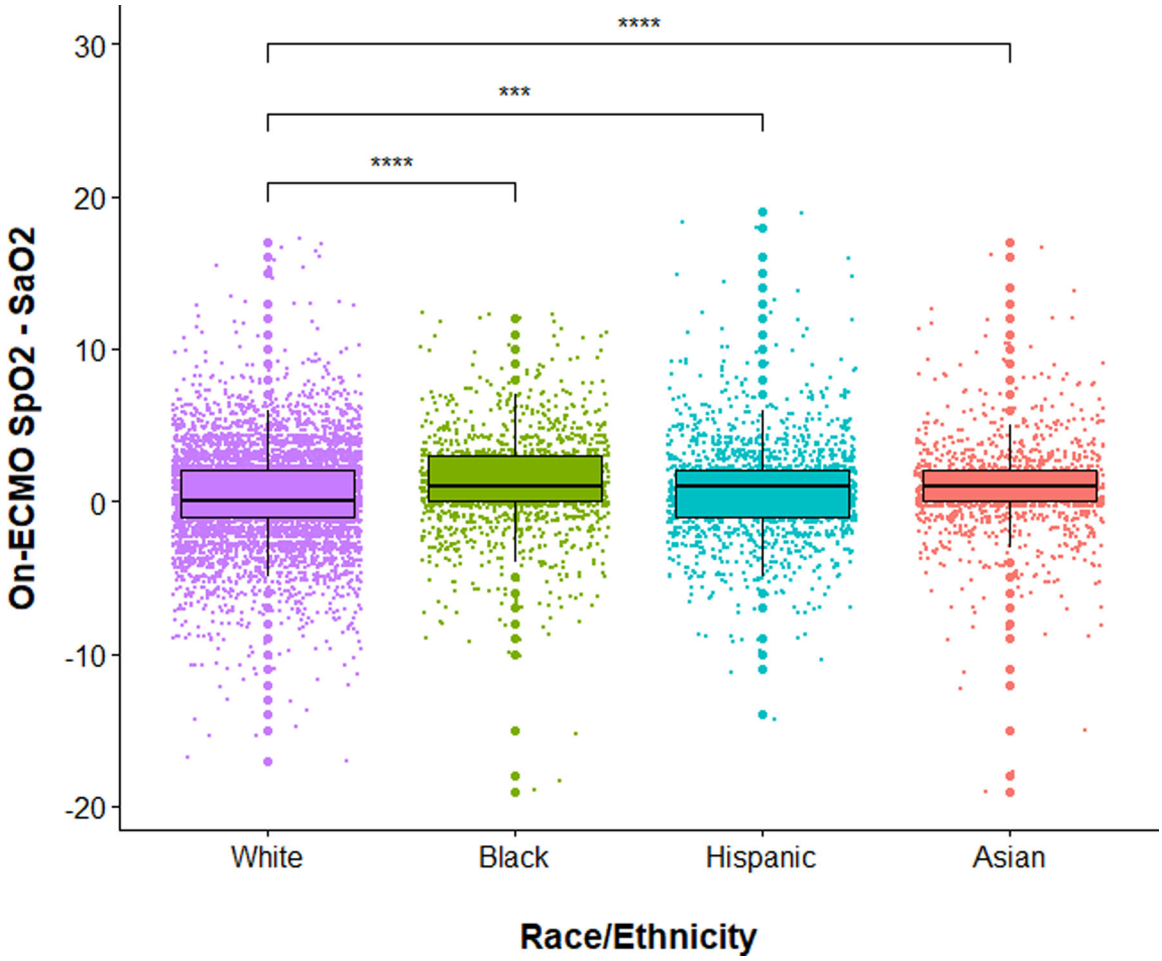

Fig. 3.

Boxplots showing pulse oximetry (SpO_2) overestimates arterial blood gas (SaO_2) in Black, Asian, and Hispanic venovenous (VV)-extracorporeal membrane oxygenation (ECMO) patients, compared to White VV-ECMO patients. Purple color = White patients. Green color = Black patients. Turquoise color = Hispanic patients. Red color = Asian patients. Solid black line represents the median value while the upper and lower limits of the boxes represent the 75% and 25% quartiles, respectively. White patients were used as the reference comparator. **** and *** represent *P* values < 0.0001 and < 0.001, respectively

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Table 1

Baseline characteristics and clinical variables of VV-ECMO patients stratified by race/ethnicity

	Total (*N* = 13,171)	**Asian (*n* = 1508, 11%)**	**Black (*n* = 1777, 14%)**	**Hispanic (*n* = 2114, 16%)**	**White (*n* = 7772, 59%)**
Demographics					
Age (years)	48.6 (37.0–58.3)	49.8 (38.7–60.7)	44.3 (32.4–55.0)	44.9 (35.4–54.5)	50.2 (38.3–59.5)
Male	8675 (66)	1029 (68)	1021 (58)	1519 (72)	5106 (66)
Body mass index, kg/m^2	30.7 (26.0–36.4)	25.6 (22.9–29.7)	32.5 (26.5–38.7)	31.1 (27.1–36.2)	31.1 (26.5–36.9)
Year ECLS					
2018	1626 (12)	217 (14)	197 (11)	120 (6)	1092 (14)
2019	2096 (16)	296 (20)	250 (14)	198 (9)	1352 (17)
2020	3756 (29)	472 (31)	537 (30)	881 (42)	1866 (24)
2021	3909 (30)	377 (25)	514 (29)	683 (32)	2335 (30)
2022	1576 (12)	137 (9)	250 (14)	206 (10)	983 (13)
2023	208 (2)	9 (1)	29 (2)	26 (1)	144 (2)
Past medical history					
Diabetes	1372 (10)	96 (6)	242 (14)	316 (15)	718 (9)
Hypertension	1873 (14)	112 (7)	331 (19)	285 (13)	1145 (15)
Atrial fibrillation	845 (6)	36 (2)	108 (6)	94 (4)	607 (8)
Cardiomyopathy	177 (1)	10 (1)	40 (2)	27 (1%)	100 (1)
COPD	478 (4)	20 (1)	46 (3)	21 (1)	391 (5)
COVID-19 status (*N* = 9851)	5830 (59)	621 (59)	722 (53)	1433 (79)	3054 (54)
Pre-ECMO support					
tMCS	310 (2)	23 (2)	71 (4)	17 (1)	199 (3)
Vasopressor infusions	8119 (62)	992 (66)	1059 (60)	1194 (57)	4874 (63)
Inotrope infusions	870 (7)	82 (5)	144 (8)	113 (5)	531 (7)
Pre-ECMO mean blood pressure (mm Hg)	77 (69–88)	78 (69–90)	78 (69–90)	80 (71–89)	76 (68–87)
Pre-ECMO ABG					
pH	7.28 (7.19–7.36)	7.28 (7.19–7.36)	7.27 (7.17–7.35)	7.29 (7.20–7.37)	7.28 (7.18–7.36)
HCO_3-(mEq/L)	26.6 (22.1–31.4)	25.0 (21.0–29.6)	26 (22.1–30.2)	28.0 (24.0–34.0)	26.6 (22.0–31.2)
PaO_2	67 (56–84)	65 (56–80)	68 (53–87)	68 (57–84)	68 (56–84)
$PaCO_2$	59 (48–74)	58 (46–74)	59 (47–74)	60 (49–75)	59 (48–73)

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	Total (*N* = 13,171)	Asian (*n* = 1508, 11%)	Black (*n* = 1777, 14%)	Hispanic (*n* = 2114, 16%)	White (*n* = 7772, 59%)
Lactate (mmol/L)	1.8 (1.2–3.0)	1.9 (1.2–3.2)	1.8 (1.2–3.4)	1.6 (1.2–2.4)	1.7 (1.2–3.0)
SpO_2	91 (85–95)	90 (84–94)	91 (84–96)	91 (86–95)	91 (86–95)
SaO_2	91 (85–95)	90 (84–94)	90 (83–95)	91 (85–95)	91 (85–95)
On-ECMO mean blood pressure (mm Hg)	76 (70–85)	79 (71–88)	77 (71–86)	77 (70–85)	75 (69–83)
On-ECMO pulse pressure (mm Hg)	55 (46–66)	52 (43–63)	55 (45–68)	56 (47–67)	56 (46–67)
On-ECMO ABG					
pH	7.40 (7.36–7.44)	7.40 (7.36–7.46)	7.40 (7.36–7.44)	7.41 (7.37–7.45)	7.40 (7.36–7.44)
HCO_3-(mEq/L)	27 (24–31)	26 (23–29)	26 (23–29)	28 (24–32)	27 (24–31)
PaO_2	78 (66–100)	83 (68–107)	80 (67–109)	75 (63–94)	78 (66–98)
$PaCO_2$	44 (38–50)	42 (36–48)	43 (38–48)	44 (39–51)	44 (39–50)
Lactate (mmol/L)	1.5 (1.1–2.2)	1.6 (1.2–2.4)	1.5 (1.1–2.2)	1.4 (1.1–2.0)	1.5 (1.0–2.2)
SpO_2	96 (93–98)	97 (94–99)	97 (93–99)	95 (92–98)	96 (93–98)
SaO_2	95 (92–98)	96 (93–98)	96 (93–98)	95 (91–97)	95 (93–97)
Pump flow (4 h)	4.10 (3.60–4.65)	3.95 (3.40–4.36)	4.15 (3.65–4.70)	4.13 (3.68–4.70)	4.15 (3.60–4.70)
Pump flow (24 h)	4.14 (3.60–4.72)	3.95 (3.40–4.42)	4.12 (3.60–4.72)	4.20 (3.70–4.79)	4.20 (3.65–4.80)
Cannulation strategy (*N* = 12,966)					
Single lumen (two sites)	9,833 (76)	1,279 (88)	1,206 (69)	1,572 (75)	5,776 (75)
Double lumen (one site)	3,133 (24)	169 (12)	545 (31)	525 (25)	1,894 (25)
Days on ECMO support	11.4 (5.7–22.9)	11.3 (5.8–23.2)	10.1 (5.3–21.2)	15.8 (7.6–30.2)	10.7 (5.3–21.0)
ECMO complications					
ECMO circuit mechanical failure	1224 (9)	138 (9)	156 (9)	237 (11)	693 (9)
Renal replacement therapy	3419 (26)	368 (24)	483 (27)	490 (23)	2078 (27)
Hemolysis	659 (5)	44 (3)	80 (5)	155 (7)	380 (5)
Hyperbilirubinemia	534 (4)	56 (4)	69 (4)	114 (5)	295 (4)
Cardiac arrhythmia	1202 (9)	93 (6)	156 (9)	165 (8)	788 (10)
Gastrointestinal hemorrhage	790 (6)	92 (6)	112 (6)	156 (7)	430 (6)

ECMO extracorporeal oxygenation membrane, *tMCS* temporary mechanical circulatory support, *VV* venovenous

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Table 2

Factors associated with on-ECMO occult hypoxemia frequencies in multivariable logistic regression analysis

	OR	95% CI	*P* value
Age	0.99	0.98–1.00	0.069
Female sex	1.30	0.91–1.84	0.147
Race/ethnicity			
White	Reference		
Black	1.79	1.16–2.75	0.008
Asian	1.28	0.78–2.09	0.332
Hispanic	1.71	1.15–2.55	0.008
Pre-ECMO support			
Pre-ECMO tMCS	0.22	0.03–1.65	0.142
Pre-ECMO inotrope infusions	1.44	0.80–2.59	0.228
Pre-ECMO vasopressor infusions	1.04	0.75–1.43	0.830
ECMO physiology			
Double-lumen cannula (one-site)	0.97	0.66–1.42	0.874
Hemolysis	1.68	0.98–2.88	0.060
Hyperbilirubinemia	1.31	0.70–2.43	0.402
Pump flow at 24 h on-ECMO	1.29	1.08–1.55	0.005
On-ECMO lactate	1.06	1.03–1.10	< 0.001

CI confidence interval, *ECMO* extracorporeal membrane oxygenation, *OR* odds ratio, *tMCS* temporary mechanical circulatory support