Racial and ethnical discrepancy in hypoxemia detection in patients on extracorporeal membrane oxygenation

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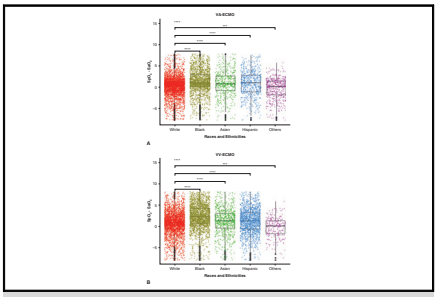
ABSTRACT

Objective: To determine whether there is racial/ethnical discrepancy between pulse oximetry (SpO_2) and oxygen saturation (SaO_2) in patients receiving extracorporeal membrane oxygenation (ECMO).

Methods: This was a retrospective observational study at a tertiary academic ECMO center with adults (>18 years) on venoarterial (VA) or venovenous (VV) ECMO. Datapoints were excluded if oxygen saturation ≤70% or SpO_2–SaO_2 pairs were not measured within 10 minutes. The primary outcome was the presence of a SpO_2–SaO_2 discrepancy between different races/ethnicities. Bland–Altman analyses and linear mixed-effects modeling, adjusting for prespecified covariates, were used to assess the SpO_2–SaO_2 discrepancy between races/ethnicities. Occult hypoxemia was defined as SaO_2 <88% with a time-matched SpO_2 ≥92%.

Results: Of 139 patients receiving VA-ECMO and 57 patients receiving VV-ECMO, we examined 16,252 SpO_2–SaO_2 pairs. The SpO_2–SaO_2 discrepancy was greater in VV-ECMO (1.4%) versus VA-ECMO (0.15%). In VA-ECMO, SpO_2 overestimated SaO_2 in Asian (0.2%), Black (0.94%), and Hispanic (0.03%) patients and underestimated SaO_2 in White (−0.06%) and nonspecified race (−0.80%) patients. The proportion of SpO_2–SaO_2 measurements considered occult hypoxemia was 70% from Black compared to 27% from White patients ($P < .0001$). In VV-ECMO, SpO_2 overestimated SaO_2 in Asian (1.0%), Black (2.9%), Hispanic (1.1%), and White (0.50%) patients and underestimated SaO_2 in nonspecified race patients (−0.53%). In linear mixed-effects modeling, SpO_2 overestimated SaO_2 by 0.19% in Black patients (95% confidence interval, 0.045%-0.33%, $P = .023$). The proportion of SpO_2–SaO_2 measurements considered occult hypoxemia was 66% from Black compared with 16% from White patients ($P < .0001$).

Conclusions: SpO_2 overestimates SaO_2 in Asian, Black, and Hispanic versus White patients, and this discrepancy was greater in VV-ECMO versus VA-ECMO, suggesting the need for physiological studies. (JTCVS Open 2023;14:145-70)



SpO_2 overestimates SaO_2 in Black ECMO patients compared with White ECMO patients.

CENTRAL MESSAGE

Race/ethnicity biases pulse oximetry measurements in ECMO patients, leading to occult hypoxemia in Black ECMO patients. There may be further physiological explanations for this SpO_2–SaO_2 discrepancy.

PERSPECTIVE

Considering the severity of illness of ECMO patients and ECMO's increasing popularity, accurate and precise oxygen saturation measurements for ECMO patients are crucial, particularly at hypoxemic levels. Black ECMO patients seem to be at greatest risk for occult hypoxemia, and clinicians should note for this SpO_2–SaO_2 discrepancy when monitoring pulse oximetry and treating these patients.

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Abbreviations and Acronyms

ABG = arterial blood gas
CI = confidence interval
ECMO = extracorporeal membrane oxygenation
ICU = intensive care unit
IQR = interquartile range
LDH = lactate dehydrogenase
LMM = linear mixed-effects modeling
ROC = receiver-operating characteristic
SaO_2 = oxygen saturation measured by arterial blood gas
SpO_2 = oxygen saturation measured by pulse oximetry
VA = venoarterial
VV = venovenous

Oxygen saturation measured by pulse oximetry (SpO_2) is a noninvasive method to continuously monitor oxygenation in place of arterial gas oxygen saturation (SaO_2). SpO_2 has been known to inaccurately predict SaO_2 readings, especially in the intensive care unit (ICU),[1] both overestimating[2-4] and underestimating[5-7] the true SaO_2 value. Importantly, this SpO_2–SaO_2 discrepancy originates from differences in race and ethnicity[3,4,8-13] As pulse oximetry works by spectrophotometry, such inaccuracy in SpO_2 measurements in predicting SaO_2 has been attributed to skin color among other physiological reasons such as dyshemoglobinemia interference, low perfusion, and sickle cell anemia.[14,15] The first calibrations of pulse oximeters used White patients, possibly further contributing to the SpO_2–SaO_2 discrepancy.[16]

Use of venoarterial (VA) and venovenous (VV) extracorporeal membrane oxygenation (ECMO) for heart and/or lung support has increased.[17,18] Currently, sparse data exist on the SpO_2 and SaO_2 discrepancy between racial/ethnical groups in VA- and VV-ECMO populations. We hypothesized that this discrepancy would be heightened in patients receiving ECMO, as the result of their critical illness, and complex physiology such as differential hypoxia. We also hypothesized that different cannulation strategies in patients receiving VA- and VV-ECMO would affect this discrepancy in addition to race/ethnicity.

METHODS

Study Design

This study was approved on October 22, 2019, by the Johns Hopkins Hospital Institutional Review Board with a waiver of informed consent, as this was a retrospective observational study (IRB00216321) entitled "Retrospective Analysis of Outcomes of Patients on Extracorporeal Membrane Oxygenation," in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975. A retrospective analysis of a database containing patients undergoing ECMO at a tertiary care center between June 2016 and April 2021 was performed. All patients were managed in the Cardiovascular Surgery Intensive Care Unit, Cardiac Critical Care Unit and obtained neurocritical care consultations based on our standardized neuromonitoring protocol.[19] The on-call ECMO attending physician rounded for all ECMO patients on both ICUs.

Participants

We included all adult patients (age $\geq$18 years) who received VA-ECMO and VV-ECMO. Patients without race/ethnicity or SpO_2 and SaO_2 information were excluded.

Data Collection

For all study patients, we collected SaO_2 measured by arterial blood gas (ABG), SpO_2 measured by pulse oximetry during ECMO support, and ECMO cannulation strategy extracted from electronic medical records. Precannulation characteristics included demographics, medical history, and on-ECMO physiological and laboratory values. Postcannulation characteristics such as discharge location, ECMO duration, mortality, neurological outcome, and the number of SpO_2 measurements per individual were also acquired. ABGs were collected every 2 to 4 hours during ECMO support, and SpO_2 was recorded every 15 minutes, according to the standard clinical protocol at Johns Hopkins Hospital with more recurrent collections if clinically indicated. All patients with VA-ECMO had a right radial arterial line for accurate and recurrent ABG measurements and as a sensitive marker of differential hypoxia. Baseline ABGs before ECMO cannulation and serial ABGs after ECMO cannulation were collected. SaO_2 from ABG was calculated based on the partial pressure of oxygen. Vital signs were also collected at least every 15 minutes pre- and postcannulation. SpO_2 and SaO_2 measurements were recorded as a single reading at a particular time and date. For patients receiving VA-ECMO, the pulse oximeter probe was placed on the right finger or right earlobe. For patients receiving VV-ECMO, the pulse oximeter probe was placed on the right or left hand. All SpO_2 and SaO_2 measurements that were recorded outside of ECMO duration were excluded.

Definitions

SpO_2 was defined as peripheral oxygen saturation measured by pulse oximetry, whereas SaO_2 was defined as arterial oxygen saturation measured by ABG. SpO_2 and SaO_2 values of less than 70% were excluded from analysis, because these were determined to likely be from erroneous measurements. SpO_2–SaO_2 pairs were matched by time-only values that were measured $\leq$10 minutes apart and were used for the analysis to control for fluctuations over time. Our data contained one entry for each race/ethnicity: Asian, Black, Hispanic, Others, and White. "Others" denoted races/ethnicities that were not specified in the previously aforementioned entries (ie, "nonspecified races"). Occult hypoxemia was defined as SaO_2 <88% with a time-matched SpO_2 $\geq$92%.

Outcomes

The primary outcome was the presence of a SpO_2–SaO_2 discrepancy between patients of different races and ethnicities. White race/ethnicity was used as the reference comparator. Our secondary outcome was the presence of a SpO_2–SaO_2 discrepancy between different cannulation strategies in patients with VA- and VV-ECMO. In addition, we assessed the accuracy and precision of SpO_2 in predicting SaO_2 in patients with VA-ECMO and VV-ECMO support.

Statistical Analysis

Median data were presented (interquartile range [IQR]) for continuous variables and absolute numbers with percentages for binary/categorical variables. Wilcoxon rank-sum test was used for comparing data with continuous variables and Pearson χ^2 test for binary/categorical variables. Differences between SpO_2–SaO_2 pairs across different individuals were compared using the Wilcoxon rank-sum and Kruskal–Wallis tests. Bland–Altman analyses were conducted through the following: mean difference (estimated bias) = the average of SpO_2 and SaO_2 and then subtracting SaO_2 from SpO_2, precision = the standard deviation of the mean difference, limits of agreement = mean difference +/− 1.96*precision, and root mean square error = sqrt(((mean difference – precision)^2)), as described in previous studies.[6,11]

The relationship between race/ethnicity and the difference between SpO_2 and SaO_2 measurements were analyzed first using unadjusted linear mixed-effects modeling (LMM), with the individual patient as a random effect. This LMM was then adjusted for preselected covariates posited to be associated with pulse oximetry accuracy, including demographics and time-dependent clinical and laboratory variables.[15] Covariates were age, sex, vasopressor or inotrope requirement during ECMO, and cannulation strategy. Time-dependent clinical and laboratory variables included pH, temperature, lactate dehydrogenase (LDH), and hemoglobin. Time-independent and -dependent covariates were included as fixed and random effects, respectively, in the LMM. Patients receiving VA- and VV-ECMO were analyzed separately.

Three different thresholds of SaO_2 were selected as 88%, 92%, and 95%, based on previous literature[1,20,21] to determine the sensitivity and specificity of SpO_2 to predict SaO_2 accurately. For each SaO_2 threshold, we tested all SpO_2 values acquired in the study and calculated sensitivities and specificities for the cut-off point of SpO_2 to detect SaO_2 at the threshold or below. We also determined an "optimal" SpO_2 using the receiver-operating characteristic (ROC) curve and area under the ROC curve analyses, ultimately based on Youden's[22] index. Moreover, we determined the median sensitivity, specificity, positive predictive value, and negative predictive value for each SaO_2 threshold and corresponding SpO_2 cut-off value.

All statistical analyses were performed using R Studio (R 4.1.2, 2022). LMM was fitted using the lme4 package, and ROC analyses were conducted using the pROC package.

RESULTS

Of 196 patients (139 patients receiving VA-ECMO; 57 patients receiving VV-ECMO), we collected 37,514 SaO_2 and 164,212 SpO_2 data points. A total of 16,252 SpO_2–SaO_2 pairs were used in our final analysis, as they were measured 10 minutes or less between each other and had 70% or greater oxygen saturation (Figure 1).

Our demographics and clinical characteristics information, stratified by race and ethnicity within each ECMO type (VA- and VV-ECMO), are presented in Tables 1 and 2. Of 139 VA-ECMO (median age, 60 years, 63% male) and 57 VV-ECMO (median age, 47 years, 56% male) patients, 5 underwent both VA-ECMO and VV-ECMO support and were accounted for in both analyses. Overall, patients receiving VV-ECMO were cannulated over 4 times longer (median, 348.98 hours; IQR, 151.42-605.58 hours) than patients receiving VA-ECMO (median, 95.88 hours; IQR, 58.32-191.62 hours). Black patients receiving VA-ECMO had the greatest number of SpO_2 measurements recorded per patient (median, 61; IQR, 21.5-91.75), and a correspondingly longer ECMO duration time (median, 93.9 hours; IQR, 58.3-150.9 hours) compared with other races/ethnicities. In addition, Hispanic patients receiving VA-ECMO had a 100% mortality and a correspondingly high median BMI (median, 36.50 kg/m^2; IQR, 36.45-36.55 kg/m^2) and significantly shorter ECMO duration time (median, 27.52 hours; IQR, 24.98-40.77 hours). Asian VA-ECMO patients also had a 100% mortality rate and the greatest median age (70 years; IQR, 58-78 years). Table E1 summarizes VA- and VV-ECMO patient analyses by race and ethnicity. The overall estimated bias (mean difference) was greater for patients receiving VV-ECMO (1.4%) than patients receiving VA-ECMO (0.15%).

VA-ECMO

Figure 2, *A*, depicts SpO_2–SaO_2 for each race/ethnicity, with Black patients receiving VA-ECMO having the greatest discrepancy. White patients had minimal bias (mean difference) at –0.06%, whereas Black, Asian, Hispanic, and nonspecified race patients had estimated biases of 0.94%, 0.2%, 0.03%, and –0.80%, respectively ($P < .001$ for all, Table E1, Figure E1). Overall, SpO_2–SaO_2 correlation coefficients were weak for all races/ethnicities (all $R < 0.50$), with Hispanic patients having the worst overall SpO_2–SaO_2 correlation ($R = 0.39$, Table E1, Figure E2). Notably, patients with peripherally cannulated VA-ECMO had a positive estimated bias (0.3%) and stronger SpO_2–SaO_2 correlation ($R = 0.51$), whereas centrally cannulated patients had a bias close to zero (0.004%) and worse correlation ($R = 0.44$, Figure E3, Table E2).

There were a total of 422 SpO_2–SaO_2 pairs where SpO_2 overestimated SaO_2 by ≥4%. Of these pairs, 40% occurred in White patients, 55% in Black patients ($P = .002$), 0% in Hispanic patients ($P < .001$), 2% in Asian patients ($P < .001$), and 2% in "Others" patients ($P < .001$). The proportion of matched SpO_2–SaO_2 measurement pairs in patients receiving VA-ECMO with occult hypoxemia (88 total pairs) from White patients was 27%, whereas this rate was 70% from Black patients, 0% from Hispanics patients, and 1% from both Asian and nonspecified race patients ($P < .001$ for all).

In unadjusted LMM, compared with White patients, SpO_2 overestimated SaO_2 by 1.02% for Black patients (95% confidence interval [CI], 0.30%-1.74%, $P = .007$, Table E3). In our adjusted VA-ECMO LMM, adjusting for age, sex, vasopressor/inotrope usage, central cannulation strategy, pH, temperature, and hemoglobin, SpO_2 underestimated SaO_2 by −11.38% in nonspecified race patients (95% CI, −22.4% to −0.37%, $P = .043$), and SpO_2 underestimated SaO_2 by −3.8% in centrally-cannulated non-specified race patients (95% CI, −7.4% to −0.21%, $P = .038$, Figure 3, *A*, Table E4). Other race/ethnicity comparisons were not statistically significant, although the method for evaluating statistical significance in LMM is not entirely clear and thus should be interpreted cautiously.[23]

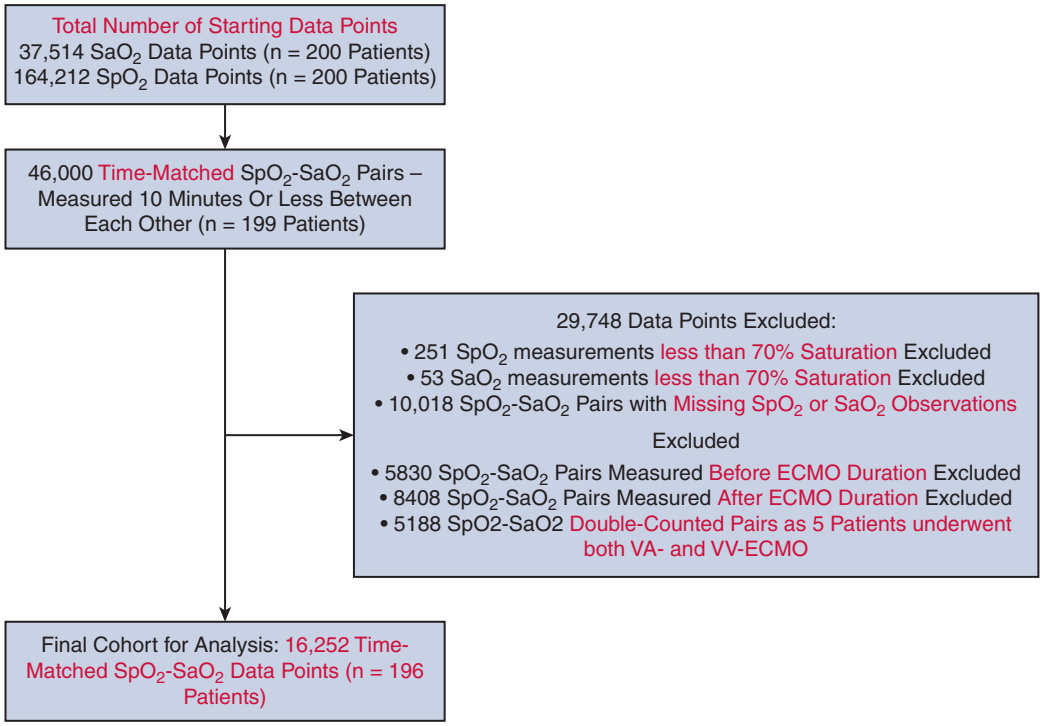


FIGURE 1. Flow diagram of creation of study cohort with time-matched SpO_2-SaO_2 data points that are at least 70% saturation. *SaO_2*, Oxygen saturation measured by arterial gas; *SpO_2*, oxygen saturation measured by pulse oximetry; *ECMO*, extracorporeal membrane oxygenation; *VA*, venoarterial; *VV*, venovenous.

Comparing the SpO_2–SaO_2 difference between different cannulation strategies within VA-ECMO patients through boxplot analyses (Figure E4, *A*), we found that peripherally cannulated patients had a greater SpO_2–SaO_2 discrepancy compared with centrally cannulated patients ($P < .0001$).

In patients receiving VA-ECMO, the 88% SaO_2 threshold had the greatest sensitivity (98%), and the 95% SaO_2 threshold had the greatest specificity (100%) for SpO_2 reliably predicting SaO_2 (Figure 4, *B*, Table E5). The optimal SpO_2 value (97%) was greatest for the 88% SaO_2 threshold, which was the lowest threshold we assessed (Table E6).

VV-ECMO

Figure 2, *B*, depicts SpO_2–SaO_2 for each race/ethnicity, with Black patients receiving VV-ECMO having the greatest discrepancy. Similar to VA-ECMO, White, Black, Asian, Hispanic, and nonspecified race patients had estimated bias (mean difference) values of 0.50%, 2.9%, 1.0%, 1.1%, and −0.53%, respectively (Figure E5, Table E1). Comparing different cannulation strategies, patients with single-lumen cannula had a greater estimated bias (1.8%) and worse SpO_2–SaO_2 correlation ($R = 0.62$) than those with double-lumen (1.1% and $R = 0.73$, Figure E6, Table E2). Overall, correlation coefficients varied by race/ethnicity, with Asians having the worst overall SpO_2–SaO_2 correlation ($R = 0.46$, Figure E7).

There were a total of 1706 SpO_2–SaO_2 pairs where SpO_2 overestimated SaO_2 by ≥4%. Of these pairs, 19% occurred in White patients, 55% in Black patients ($P < .001$), 16% in Hispanic patients ($P = .06$), 9% in Asian patients ($P < .001$), and 0.4% in "Others" patients ($P < .001$). The proportion of matched SpO_2–SaO_2 measurement pairs in patients receiving VV-ECMO with occult hypoxemia (385 total pairs) from White patients was 16%, whereas this rate was 66% from Black ($P < .001$), 11% from Hispanic ($P = .09$), 6% from Asian ($P < .001$), and 1% from nonspecified race patients ($P < .001$).

In unadjusted LMM, compared with White patients, SpO_2 overestimated SaO_2 by 2.77% in Black patients (95% CI, 1.57%-3.96%, $P < .001$, Table E7), and this discrepancy persisted after we adjusted for age, sex, cannulation strategy, LDH, pH, and temperature, as SpO_2 still overestimated SaO_2 by 0.19% in Black patients (95% CI, 0.045%-0.33%, $P = .023$, Figure 3, *B*, Table E8).

Comparing the SpO_2–SpO_2 difference between different cannulation strategies within patients receiving VV-ECMO through boxplot analyses (Figure E4, *B*), single-lumen cannulated patients had a greater SpO_2–SaO_2 discrepancy, compared with double-lumen cannulated patients ($P < .0001$).

In VV-ECMO, the 88% SaO_2 threshold had the greatest sensitivity (76%), and the 95% SaO_2 threshold had the

TABLE 1. Baseline characteristics and clinical variables of patients receiving venoarterial extracorporeal oxygenation membrane (VA-ECMO)

	Total (n = 139)	White (n = 91, 65%)	Black (n = 27, 19%)	Asian (n = 9, 6%)	Hispanic (n = 3, 2%)	Others (n = 9, 6%)
Demographics						
Age, y	60 (48.5-68)	62 (52.25-68)	49.5 (40-60)	70 (58-78)	46 (37.5-47)	62 (52-72)
Male	87 (63%)	58 (64%)	13 (48%)	8 (89%)	1 (33%)	7 (78%)
Female	52 (37%)	33 (36%)	14 (52%)	1 (11%)	2 (67%)	2 (22%)
Body mass index, kg/m^2	29.15 (25.50-35.05)	29.25 (25.52-33.67)	31.00 (25.40-35.60)	26.20 (24.25-27.20)	36.50 (36.45-36.55)	27.90 (27.80-30.25)
Medical history						
Ischemic stroke	11 (8%)	8 (9%)	2 (7%)	0 (0%)	0 (0%)	1 (11%)
Intracranial hemorrhage	1 (1%)	1 (1%)	0 (5%)	0 (0%)	0 (0%)	0 (0%)
Hypertension	71 (51%)	43 (47%)	18 (67%)	3 (33%)	1 (33%)	6 (66%)
Hyperlipidemia	54 (39%)	34 (37%)	11 (41%)	3 (33%)	1 (33%)	5 (56%)
Diabetes	33 (24%)	16 (18%)	8 (30%)	2 (22%)	1 (33%)	6 (66%)
Congestive heart failure	37 (27%)	26 (29%)	5 (19%)	3 (33%)	1 (33%)	2 (22%)
Chronic kidney disease	33 (24%)	16 (18%)	8 (30%)	2 (22%)	1 (33%)	6 (66%)
Atrial fibrillation	32 (23%)	22 (24%)	5 (19%)	4 (44%)	0 (0%)	1 (11%)
Antiplatelet therapy before index hospitalization	45 (32%)	26 (29%)	9 (33%)	3 (33%)	2 (66%)	5 (56%)
Anticoagulation before index hospitalization	27 (19%)	19 (21%)	4 (15%)	3 (33%)	0 (0%)	1 (11%)
Precannulation variables						
Glasgow coma scale	15 (6.5-15)	15 (5-15)	15 (8.5-15)	15 (6.5-15)	15 (10.5-15)	14 (8-15)
Cardiac arrest	63 (45%)	36 (40%)	15 (56%)	4 (44%)	1 (33%)	7 (78%)
Inotrope or vasopressor support	109 (78%)	71 (78%)	22 (81%)	7 (78%)	2 (66%)	7 (78%)
Arterial blood gas						
pH	7 (7-7)	7 (7-7)	7 (7-7)	7 (7-7)	7 (7-7)	7 (7-7)
$PacO_2$, mm Hg	40 (33.5-48)	42 (37-49)	37 (29.5-49.5)	35 (34-43)	43 (38.5-43.5)	38 (37-45)
PaO_2, mm Hg	161 (89-306.5)	210 (93-298)	199 (97.5-329)	164 (105-293)	230 (172-321.5)	86 (66-98)
HCO_3^-, mEq/L	20 (16-22)	20 (18-23)	20 (16-22.5)	19 (18-21)	15 (12-16.5)	20 (17-22)
SaO_2, %	99 (95-100)	99 (96-100)	99 (97-100)	98 (98-99)	100 (97-100)	97 (89-97)
ECMO day 1 variables*						
Creatinine, mg/dL	1 (1-2)	1 (1-2)	2 (1-2)	2 (1-2)	2 (1.5-6.5)	1 (1-2)
Platelet, units in thousands/μL	83.0 (52.0-116.2)	93.0 (77-120)	67 (53-138)	79 (71-99)	49 (48.5-55.5)	50 (35-57)
Lactate, mmol/L	6 (3-10)	5 (2-9)	5 (3-11)	6 (4-9)	10 (8.5-11)	4 (3-6)
AST, units/L	168 (71-757.5)	160 (60-697)	131 (65.5-625)	138 (126-185)	56 (48.5-366)	314 (95-851)
ALT, IU/L	74 (24-396.5)	45 (26-288.8)	47 (20.5-285)	31 (25-103)	15 (14.5-146.5)	114 (24-386)
SOFA score	11 (10-13)	11 (9-13)	11 (9.5-14)	12 (10-13)	9 (8-10.5)	13 (9-15)
LDH, units/L	876 (562-1929.5)	1114 (532.5-1729.5)	1794 (655.5-5091)	626 (415.5-731)	NA	1698 (1287-2109)
Hemoglobin, g/dL	8.6 (7.6-10.2)	8.75 (7.65-10.18)	7.9 (6.95-9.7)	9.25 (8.275-10.375)	8.3 (7.75-8.85)	9.6 (8.175-11.125)
VA-ECMO indications						
Cardiogenic shock	48 (35%)	31 (34%)	11 (41%)	2 (22%)	0 (0%)	4 (44%)
ECPR	25 (18%)	16 (18%)	6 (22%)	0 (0%)	0 (0%)	3 (33%)
Postcardiotomy shock	25 (18%)	14 (15%)	5 (19%)	3 (33%)	1 (33%)	2 (22%)

(Continued)

TABLE 1. Continued

	Total (n = 139)	White (n = 91, 65%)	Black (n = 27, 19%)	Asian (n = 9, 6%)	Hispanic (n = 3, 2%)	Others (n = 9, 6%)
Cannulation strategy						
Central	69 (50%)	46 (51%)	10 (37%)	7 (78%)	1 (33%)	5 (56%)
Peripheral	70 (50%)	45 (49%)	17 (63%)	2 (22%)	2 (66%)	4 (44%)
Discharge location						
Home	19 (14%)	14 (15%)	5 (19%)	0 (0%)	0 (0%)	0 (0%)
Acute rehabilitation	12 (9%)	11 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (11%)
Long-term facility	2 (1%)	1 (0%)	1 (4%)	0 (0%)	0 (0%)	0 (0%)
Skilled nursing facility	6 (4%)	6 (7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
ECMO duration, h	95.9 (58.3-191.6)	110.8 (59.2-209.7)	93.9 (58.3-150.9)	95.88 (58.32-191.62)	27.52 (24.98-40.77)	83.78 (59.17-143.83)
Mortality	100 (72%)	59 (65%)	21 (78%)	9 (100%)	3 (100%)	8 (89%)
Good neurological outcome, mRS $\leq$3	23 (17%)	15 (16%)	6 (22%)	0 (0%)	0 (0%)	2 (22%)
Number of SpO_2 measurements per patient	36 (18.5-74)	36 (19-72.5)	61(21.5-91.75)	36 (13-50)	5 (3.50-28)	28 (23-45)

$PaCO_2$, Partial pressure of carbon dioxide; *PaO_2*, partial pressure of oxygen; *HCO_3-*, bicarbonate ion; *SaO_2*, arterial gas oxygen saturation; *ECMO*, extracorporeal membrane oxygenation; *AST*, aspartate transaminase; *ALT*, alanine transaminase; *SOFA*, sequential organ failure assessment score; *LDH*, lactate dehydrogenase; *NA*, not available; *VA*, venoarterial; *ECPR*, extracorporeal cardiopulmonary resuscitation; *mRS*, modified Rankin Scale; *SpO_2*, peripheral oxygen saturation. *Variables were collected within the first 12 h of ECMO initiation; creatinine, platelet, lactate, AST, ALT, LDH, and hemoglobin measurements, and SOFA score represent the worst value collected in the first 12 h of ECMO.

greatest specificity (100%) for SpO_2 reliably predicting SaO_2 (Table E5 and Figure 4, *C*). The optimal SpO_2 value (85%) was greatest for the 88% SaO_2 threshold, which was the lowest threshold we assessed (Table E6).

Exploratory Analysis

When analyzing the SpO_2–SpO_2 discrepancy in both VA and VV-ECMO populations, we found that lower arterial gas oxygen saturation values were correlated with a greater difference between SpO_2 and SaO_2 (Figure E8). Notably, SpO_2 tended to overestimate SaO_2 at lower SaO_2 values in the VV-ECMO population more frequently than in VA-ECMO; conversely, SpO_2 underestimated SaO_2 at greater SaO_2 values in the VA-ECMO population more frequently than in VV-ECMO.

DISCUSSION

Race/Ethnicity Discrepancy

Herein, we demonstrated that pulse oximetry consistently overestimated SaO_2 in both VA- and VV-ECMO populations with a greater SpO_2_SaO_2 discrepancy in patients receiving VV-ECMO versus VA-ECMO (Figure 5). Furthermore, the discrepancy was increased in Asian, Black, and Hispanic patients receiving ECMO compared with White patients, with Black patients having the greatest overestimation, and therefore, inaccuracy, of their true oxygen levels. Our analysis is clinically important and novel, as we present a detailed racial/ethnical discrepancy in oxygen levels in patients receiving ECMO with rich SpO_2 and SaO_2 data from a single tertiary academic ECMO center. In addition, our results are particularly clinically significant, as we show a much greater degree of occult hypoxemia occurring in Black patients receiving ECMO as compared with other races/ethnicities, potentially suggesting specific medical management changes unique to these patients, as greater rates of undetected hypoxemia in severely ill patients have been shown to lead to poorer rates of survival.[9]

A recent report by Valbuena and colleagues[11] showed that SpO_2 overestimated SaO_2 in Black compared with White patients in adults with respiratory failure, placing Black patients at risk for occult hypoxemia. However, this study was conducted using only a single timepoint of oxygen saturation data inconsistently measured approximately 6 hours before ECMO cannulation. They found a comparable risk of occult hypoxemia in Asian and Hispanic patients compared with White patients, similar to what Wong and colleagues[9] reported in patients in the ICU. Both studies are in line with our study's findings concerning occult hypoxemia in Asian and Hispanic patients receiving ECMO. However, our study reported greater overall SpO_2–SaO_2 mean differences in Asian and Hispanic patients receiving ECMO, which may be partly explained due to the severity of illness of these patients, coupled with vasopressor/inotrope usage, different blood flow due to ECMO cannulation,

TABLE 2. Baseline characteristics and clinical variables of patients receiving venovenous extracorporeal oxygenation membrane (VV-ECMO)

	Total (n = 57)	White (n = 20, 35%)	Black (n = 19, 33%)	Asian (n = 3, 5%)	Hispanic (n = 13, 23%)	Others (n = 2, 4%)
Demographics						
Age, y	47 (36-57)	44.5 (39.8-60.0)	53 (39-59)	60.0 (54.0-60.0)	39.0 (30.0-47.0)	43.5 (41.3-45.8)
Male	32 (56%)	10 (50%)	7 (37%)	3 (100%)	11 (85%)	1 (50%)
Female	25 (44%)	10 (50%)	12 (63%)	0 (0%)	2 (15%)	1 (50%)
Body mass index, kg/m^2	30.76 (28.23-35.59)	30.90 (29.85-35.40)	32.20 (27.50-35.69)	23.30 (23.15-23.46)	31.52 (29.39-35.40)	31.52 (29.39-32.77)
Medical history						
Ischemic stroke	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Intracranial hemorrhage	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Hypertension	15 (26%)	3 (15%)	9 (47%)	0 (0%)	3 (23%)	0 (0%)
Hyperlipidemia	15 (26%)	6 (30%)	8 (42%)	0 (0%)	1 (8%)	0 (0%)
Diabetes	9 (16%)	3 (15%)	4 (21%)	0 (0%)	2 (15%)	0 (0%)
Congestive heart failure	1 (2%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Chronic kidney disease	9 (16%)	3 (15%)	4 (21%)	0 (0%)	2 (15%)	0 (0%)
Atrial fibrillation	1 (2%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Antiplatelet therapy before index hospitalization	5 (9%)	3 (15%)	2 (11%)	0 (0%)	0 (0%)	0 (0%)
Anticoagulation before index hospitalization	3 (5%)	2 (10%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)
Precannulation variables						
Glasgow coma scale	11 (3-15)	11 (3-15)	11 (7-15)	11 (9-13)	3 (3-13)	12.50 (11.25-13.75)
Cardiac arrest	6 (11%)	1 (5%)	3 (16%)	1 (33%)	1 (8%)	0 (0%)
Inotrope or vasopressor support	24 (42%)	12 (45%)	5 (26%)	2 (66%)	4 (31%)	1 (50%)
Arterial blood gas						
pH	7 (7-7)	7 (7-7)	7 (7-7)	7 (7-7)	7 (7-7)	7 (7-7)
$PaCO_2$, mm Hg	63.5 (53-73.8)	62.0 (54.0-74.0)	64.0 (53.0-77.0)	74.5 (67.3-81.8)	63.0 (52.8-68.0)	88 (88-108)
PaO_2, mm Hg	75.5 (65.3-98.3)	82.0 (65.0-74.0)	72.0 (67.0-81.0)	85.5 (78.8-92.3)	76.5 (66.3-32.8)	169.5 (117.8-221.2)
HCO_3^-, mEq/L	25 (23-32)	25.0 (21.0-32.0)	25.0 (24.0-28.0)	28.0 (26.0-30.0)	27.0. (23.8-32.8)	26 (16-36)
SaO_2, %	92 (88-97)	93.0 (87.8-99.0)	92.0 (86.0-94.0)	93.5 (92.3-94.8)	93.0 (88.8-97.8)	94 (91-97)
ECMO day 1 variables*						
Creatinine, mg/dL	1 (1-2)	1 (1-2)	2 (1-2)	1.5 (1.25-1.75)	1 (1-1)	1 (0.5-1.5)
Platelet, units in thousands/μL	176.5 (100.0-260.0)	132.0. (87.0-254.0)	156.0 (110.0-183.0)	112.5 (73.3-151.8)	222.0 (163.8-280.8)	170.5 (125.8-215.2)
Lactate, mmol/L	3 (1-4)	3 (1-7)	3 (2-4)	2.5 (2.3-2.5)	1.5 (1.0-3.3)	6.5 (4.8-8.3)
AST, units/L	58.0 (36.0-100.2)	42.0 (21.0-79.0)	86.0 (61.0-143.0)	89.5 (73.3-105.8)	46.5 (40.5-80.0)	461.5 (247.8-675.2)
ALT, IU/L	42.5 (22.3-61.8)	19.0 (14.0-48.0)	51.0 (41.0-80.0)	28.0 (21.0-35.0)	44.0 (32.5-71.8)	162.0. (93.0-231.0)
LDH, units/L	515.0 (318.8-686.5)	555.0 (407.5-641.0)	1686 (1686-1686)	N/A	348 (282-414)	N/A
Hemoglobin, g/dL	9.1 (7.9-9.8)	9.1 (8.7-10.3)	8.6 (7.6-9.6)	8.6 (8.6-8.6)	10.5 (10.2-10.9)	6.1 (6.1-6.1)
SOFA score	11 (8-13)	11.0 (9.8-14.0)	11 (8-13)	12 (9.5-13.5)	9 (8-11)	12.5 (11.3-13.8)
VV-ECMO indication						
ARDS	25 (44%)	7 (35%)	10 (53%)	1 (33%)	7 (54%)	0 (0%)
Cannulation strategy						
Single lumen	25 (44%)	9 (45%)	10 (53%)	1 (33%)	4 (31%)	1 (50%)
Double lumen	32 (56%)	11 (55%)	9 (47%)	2 (67%)	9 (69%)	1 (50%)

(Continued)

TABLE 2. Continued

	Total (n = 57)	White (n = 20, 35%)	Black (n = 19, 33%)	Asian (n = 3, 5%)	Hispanic (n = 13, 23%)	Others (n = 2, 4%)
Discharge location						
Home	16 (28%)	5 (25%)	4 (21%)	0 (0%)	7 (54%)	0 (0%)
Acute rehabilitation	10 (18%)	3 (15%)	5 (26%)	0 (0%)	2 (15%)	0 (0%)
Long-term facility	1 (2%)	0 (0%)	1 (5%)	0 (0%)	0 (0%)	0 (0%)
Skilled nursing facility	1 (2%)	0 (0%)	0 (0%)	0 (0%)	1 (8%)	0 (0%)
ECMO duration, h	349.0 (151.4-605.6)	210.2 (104-464.3)	345.4 (95.7-612.2)	402.6 (360.9-1122.2)	427.7 (282.4-602.5)	363.6 (325.2-401.3)
Mortality	29 (51%)	12 (60%)	9 (47%)	3 (100%)	3 (23%)	2 (100%)
Good neurological outcome, mRS ≤ 3	22 (39%)	5 (25%)	6 (32%)	1 (33%)	10 (77%)	0 (0%)
Number of SpO_2 measurements per patient	112 (48-182.5)	92 (45.3-193.5)	115 (74-146)	333.0 (247.5-338.5)	70.0 (47.0-167.0)	127.5 (115.2-139.8)

$PaCO_2$, Partial pressure of carbon dioxide; *PaO_2*, partial pressure of oxygen; *HCO_3-*, bicarbonate ion; *SaO_2*, arterial gas oxygen saturation; *ECMO*, extracorporeal membrane oxygenation; *AST*, aspartate transaminase; *ALT*, alanine transaminase; *LDH*, lactate dehydrogenase; *NA*, not available; *SOFA*, sequential organ failure assessment score; *VV*, venovenous; *ARDS*, acute respiratory distress syndrome; *mRS*, modified Rankin Scale; *SpO_2*, peripheral oxygen saturation. *Variables were collected within the first 12 h of ECMO initiation; creatinine, platelet, lactate, aspartate transaminase, alanine transaminase, lactate dehydrogenase, and hemoglobin measurements, and SOFA score represent the worst value collected in the first 12 h of ECMO.

and complex physiology, that may exacerbate the inaccuracy of pulse oximetry measurements compared with non-ECMO patients. Accordingly, the SpO_2–SaO_2 discrepancy in patients receiving ECMO by race/ethnicity is greater because of these factors that underlie ECMO. Furthermore, this exacerbation of SpO_2 overestimating SaO_2 is apparent in Black and Hispanic patients receiving VV-ECMO who had a greater bias (2.9% and 1.1%) than what was found in Valbuena and colleagues' pre-ECMO cohort study[11] (1.7% and 0.8%). Because of this significant SpO_2–SaO_2 discrepancy, ECMO presents a unique challenge in predicting SpO_2 based on SaO_2, which prompted us to analyze the VA- and VV-ECMO populations separately. In addition, as we surmise the SpO_2–SaO_2 discrepancy between different races/ethnicities primarily arises due to measuring specific wavelengths of light and calibration to a White person, other measures that have similar methodologies, such as pulse-wave contour analysis and bioimpedance, may have similar racial discrepancies and thus warrant further investigation.

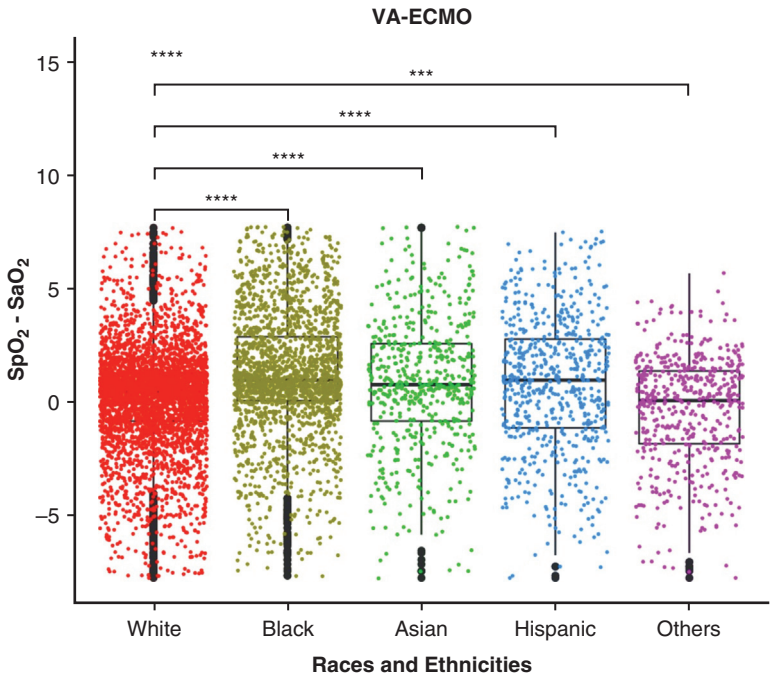
VA-ECMO

To our knowledge, no study has examined the SpO_2–SaO_2 discrepancy by cannulation strategy in patients receiving VA-ECMO. In addition to discrepancies based on race/ethnicity, we found that patients receiving peripherally cannulated VA-ECMO have a greater SpO_2–SaO_2 discrepancy compared with patients receiving centrally cannulated VA-ECMO. One explanation for this discrepancy is due to differential hypoxia, which mainly occurs in peripherally cannulated patients.[24]

In addition, with differential hypoxia, we posit that pulse oximeters are likely not sensitive enough to detect lower oxygen saturation levels.[25] In contrast, in centrally cannulated VA-ECMO, blood is fed immediately into the ascending aorta, and thus no lowly oxygenated blood should be measured by pulse oximetry or arterial blood gas since they are distal to the mixing zone.

Another potential confounding factor is the usage of vasopressors or inotropes during ECMO. If patients receiving VA-ECMO are on vasopressors, vasoconstriction occurs, leading to capillary constriction, and ultimately elevated pulse oximetry levels.[26] If patients are on inotropes, vasodilation may occur, leading to decreased SpO_2 levels. In our LMM, we accounted for usage of vasopressor/inotrope, including norepinephrine, epinephrine, phenylephrine, dopamine, and vasopressin, and this adjustment resolved the SpO_2–SaO_2 difference in patients receiving centrally cannulated VA-ECMO, as expected.

Several studies have also shown SpO_2 to underestimate SaO_2 in critically ill patients,[1,7,16,27] in line with our results of the nonspecified race patients receiving VA- and VV-ECMO, which may be related to sepsis, peripheral vasodilation, severe inflammation, and venous pulsatility.



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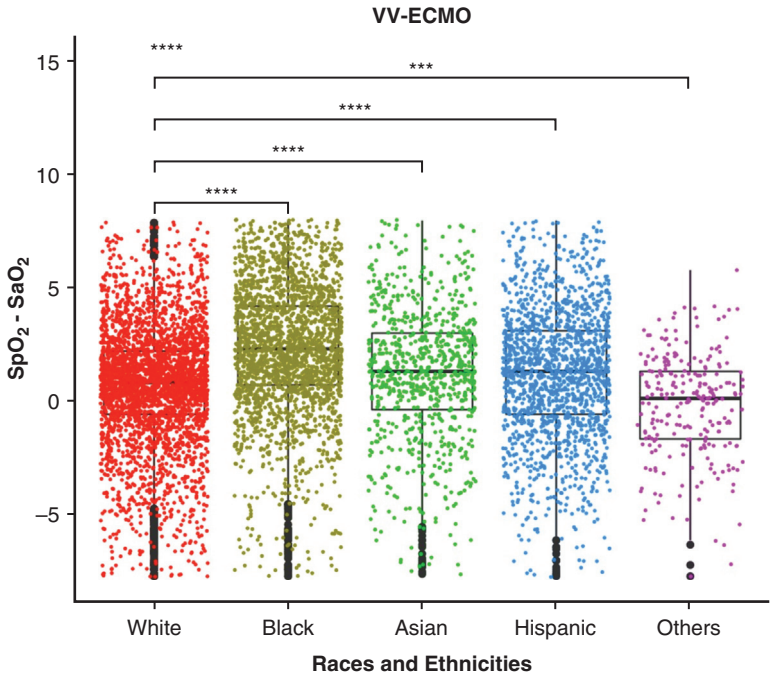
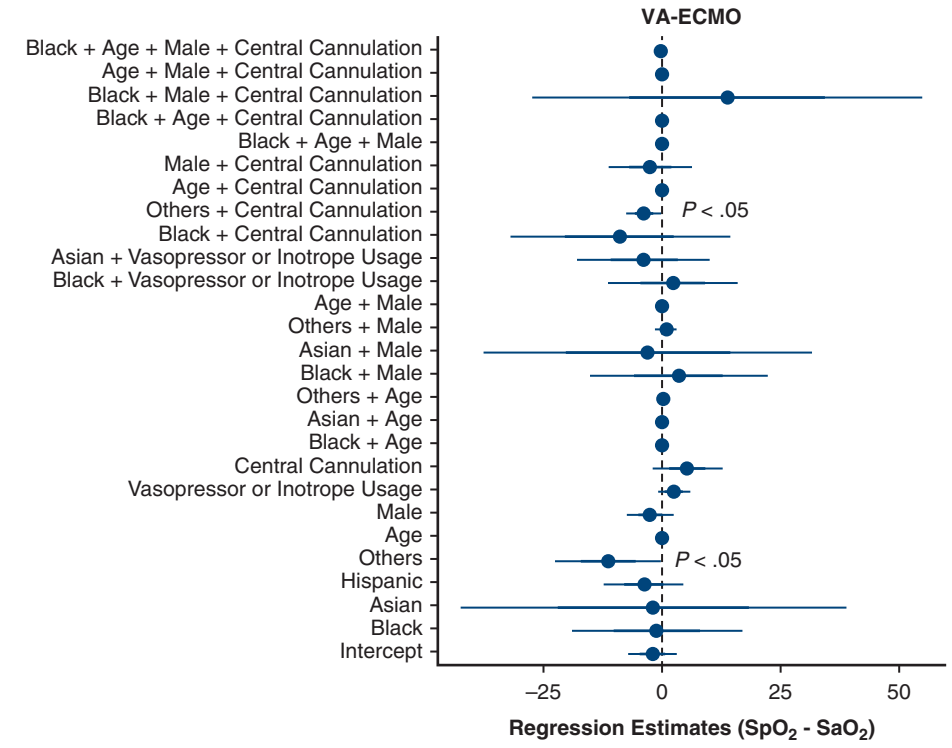


B

FIGURE 2. Boxplots of patients receiving (A) VA-ECMO and (B) VV-ECMO stratified by race/ethnicity. The *horizontal lines* represent the median, and the *top and bottom ends of each box* represent the 75% and 25% limits of the interquartile range, respectively. The *lower and upper whiskers* represent the minimum and maximum values of nonoutliers, whereas the *extra dots* represent outliers. Only data points within 2 standard deviations of the mean are shown. Each *small dot* represents an individual data point (SpO_2–SaO_2 pair), colored by race. *Red*, *dark yellow*, *light green*, *blue*, and *magenta dots* represent White, Black, Asian, Hispanic, and nonspecified race/ethnicity patients, respectively. Wilcoxon rank-sum test was used for comparisons between 2 races. Kruskal–Wallis test was used for a global comparison (significance shown in the *top left corner*). ****Indicates a $P \leq .0001$. ***Indicates $P \leq .001$. *Indicates $P \leq .05$. "Others" refer to nonspecified races (patients who did not identify as Asian, Black, Hispanic, or White). *VA*, Venoarterial; *ECMO*, extracorporeal membrane oxygenation; *SpO_2*, oxygen saturation measured by pulse oximetry; *SaO_2*, oxygen saturation measured by arterial gas; *VV*, venovenous.



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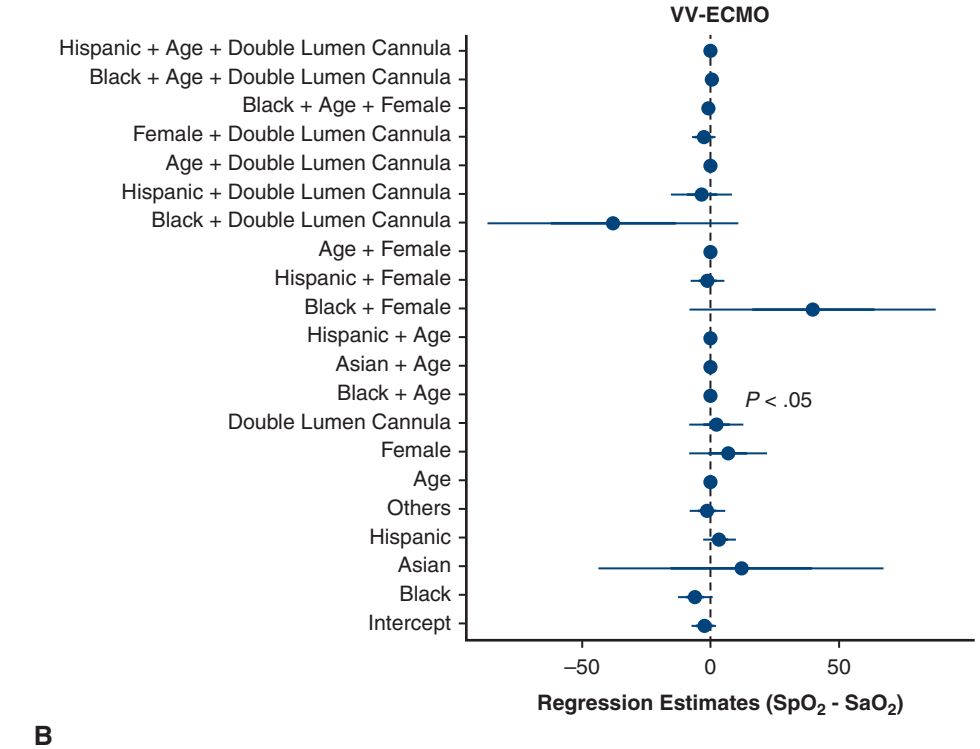

B

FIGURE 3. Coefficient plots of both adjusted linear mixed-effects models for patients receiving (A) VA-ECMO and (B) VV-ECMO. A, Age, sex, usage of vasopressor/inotrope during ECMO, and cannulation strategy (central vs peripheral) were included as fixed-effects, whereas pH, temperature, and hemoglobin were incorporated as random-effects. B, Age, sex, and cannulation strategy (single vs double lumen) were included as fixed-effects, whereas lactate dehydrogenase, pH, and temperature were incorporated as random-effects. "Regression estimates" represent the response variable (SpO_2–SaO_2). "Others" represent nonspecified races (patients who did not identify as Asian, Black, Hispanic, or White). Statistically significant ($P < .05$) regression estimates are labeled on the coefficient plots. *VA*, Venoarterial; *ECMO*, extracorporeal membrane oxygenation; *SpO_2*, oxygen saturation measured by pulse oximetry; *SaO_2*, oxygen saturation measured by arterial gas; *VV*, venovenous.

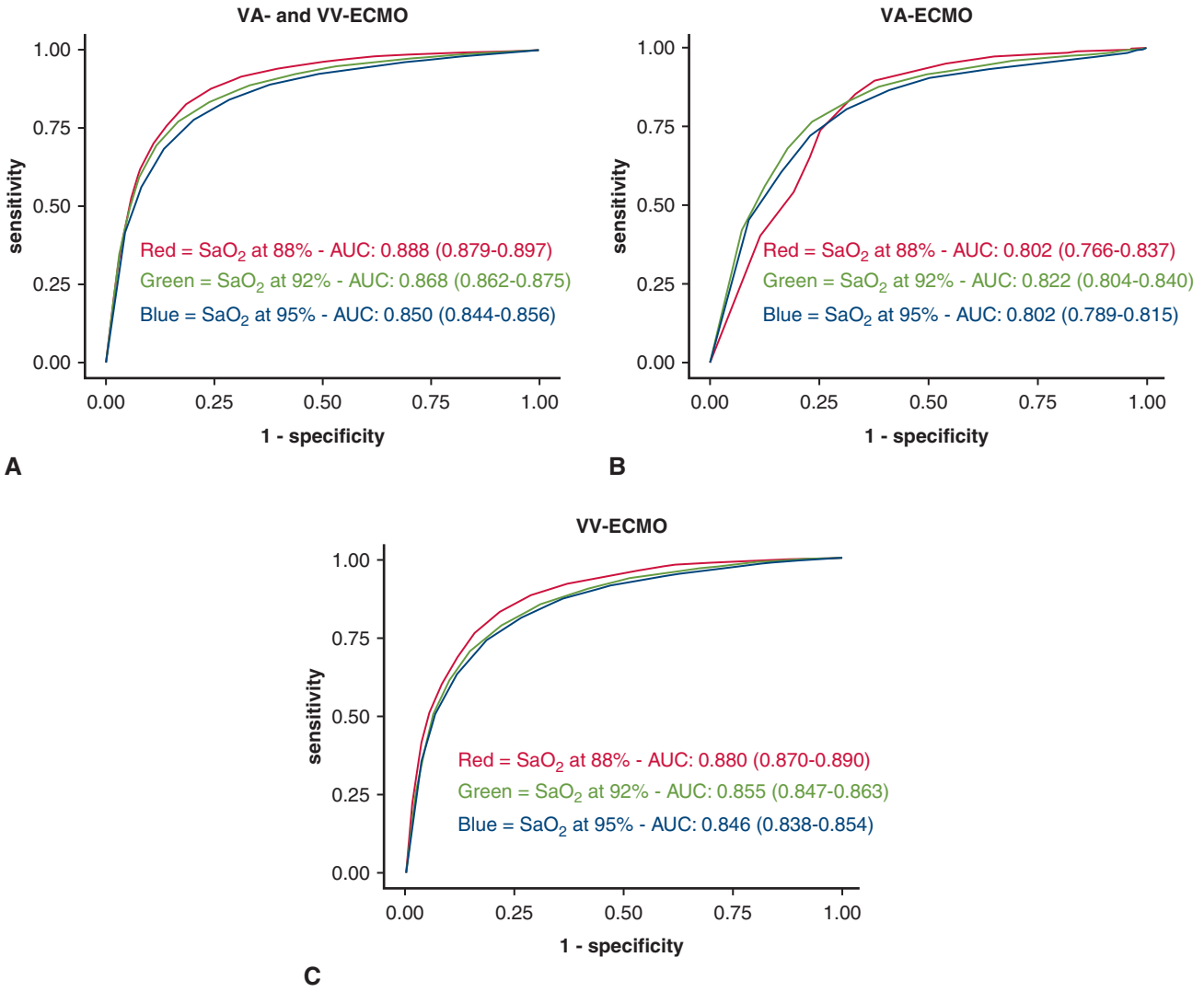

FIGURE 4. Receiver-operating characteristic (*ROC*) curves and area under the ROC curves (*AUCs*) with 95% confidence interval limits for (A) all patients receiving extracorporeal membrane oxygenation (*ECMO*), (B) patients receiving venoarterial (*VA*) ECMO, and (C) patients receiving venovenous (*VV*) ECMO. ROC curves are shown for each SaO_2 threshold. SaO_2 = 88% (*red*), 92% (*green*), and 95% (*blue*), representing the sensitivity (y-axis) and 1—specificity (x-axis) of all cut off points of SpO_2 to accurately detect a SaO_2 at all three of these predefined SaO_2 thresholds. *SaO_2*, Oxygen saturation measured by arterial gas.

VV-ECMO

We demonstrated that patients receiving VV-ECMO who underwent single-lumen cannulation had a greater SpO_2 overestimation of SaO_2 (1.8%) than double-lumen cannulated patients (1.1%). Although further investigation is required, SpO_2 may have overestimated SaO_2 in patients receiving VV-ECMO due to greater carboxyhemoglobin levels.[28,29] Still, no study has analyzed this discrepancy between cannulation strategies within VV-ECMO. The SpO_2–SaO_2 discrepancy may potentially result from varying degrees of hemolysis,[30-32] and single- versus double-lumen cannulation strategy likely has different risks of hemolysis.[33] In addition, recirculation in single-lumen VV-ECMO, shown to be accentuated in greater pump speeds and greater RPM,[34,35] may lead to this greater SpO_2–SaO_2 discrepancy.

We reported the presence of more frequent SpO_2 overestimation of SaO_2 values at lower oxygen saturation levels, especially in the VV-ECMO population, as these patients are at a greater risk for blood gas derangements, given their primary respiratory failure. Accordingly, we hypothesized that the VV-ECMO population had a greater SpO_2–SaO_2 discrepancy than the VA-ECMO population, which was confirmed in our data and consistent with previous data.[16,36,37]

Accuracy, Precision, Sensitivity and Specificity, and Threshold

Overall, the area under the ROC curves for SpO_2 predicting SaO_2 values were lower for patients receiving VA-ECMO than for patients receiving VV-ECMO, although patients receiving VV-ECMO had a greater SpO_2–SaO_2 mean

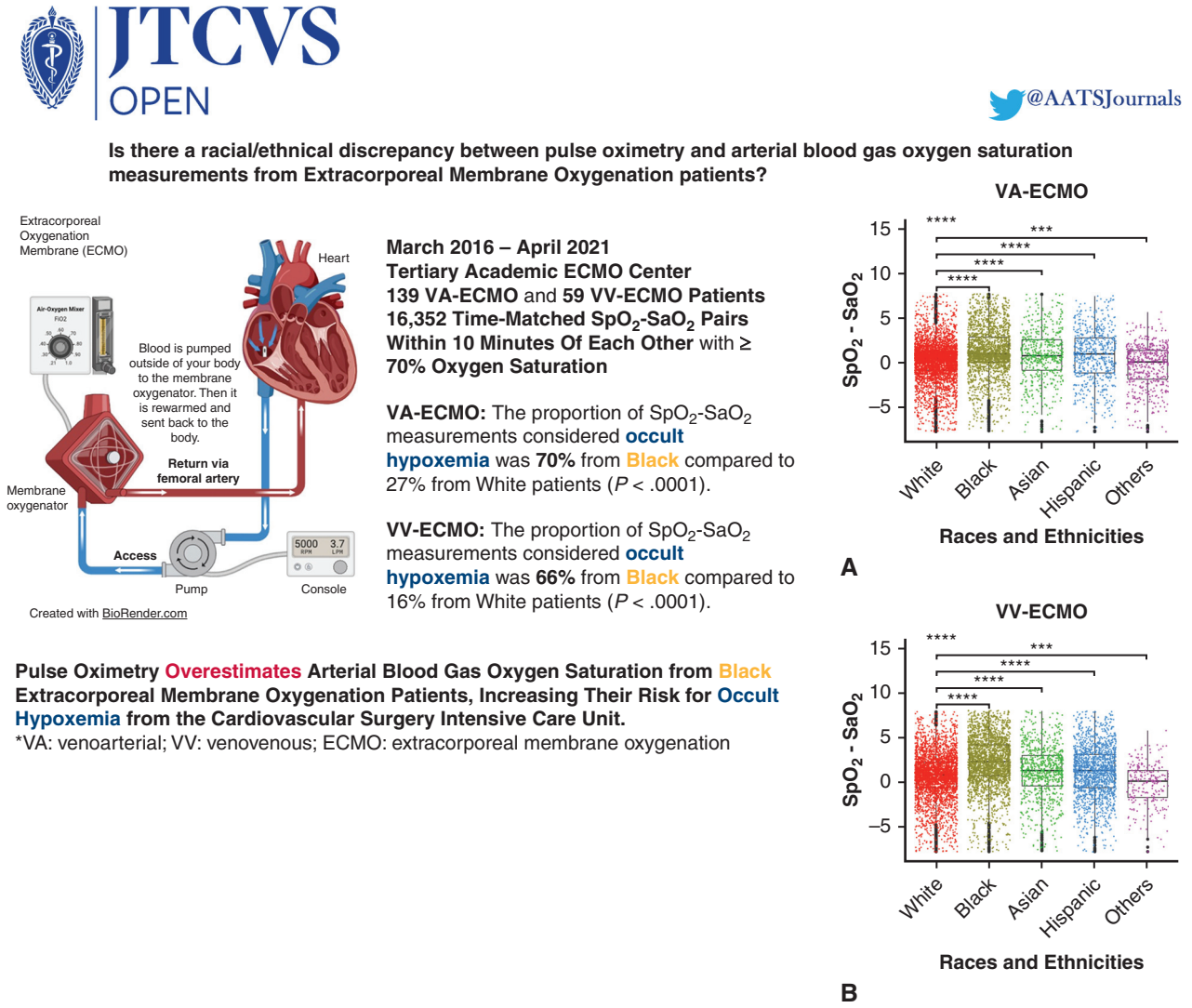

FIGURE 5. Summary of key findings. Pulse oximetry consistently overestimates arterial blood gas oxygen saturation in Black patients undergoing extracorporeal membrane oxygenation (ECMO), compared with White patients undergoing ECMO. This overestimation of their true oxygen saturation places Black patients undergoing ECMO at greater risk of occult hypoxemia (oxygen saturation measured by arterial gas; [SaO_2] <88% with a time-matched oxygen saturation measured by pulse oximetry [SpO_2] ≥92%), and should be noted when monitoring and treating them in the intensive care unit setting. The image of the ECMO circuit was retrieved from BioRender (www.Biorender.com). *VA*, Venoarterial; *VV*, venovenous

difference in our Bland–Altman analyses than patients receiving VA-ECMO. For all ECMO patients together, SpO_2 was less accurate at greater SaO_2 values. These results surprisingly oppose those found in evaluating pulse oximetry in critical care patients in other studies,[1,38] thus raising the need for additional studies regarding pulse oximetry accuracy and thresholds in this unique patient population.

Limitations

Our study is limited by the lack of consistency in the placement (location) of the pulse oximeter probe in both patients undergoing VA-ECMO and VV-ECMO, thus leading to variation in accuracy and bias of the device. Furthermore, exact locations of the probes correlating with each SpO_2 measurement were also not recorded. In addition, other potential confounders such as patient's skin temperature and ECMO flow and sweep should be noted. The majority of patients receiving VA-ECMO were White, and the numbers of non-White and non-Black patients are relatively small and, thus, an external validation is necessary with a larger sample size; however, there was a more equal distribution of each race/ethnicity in the VV-ECMO population, suggesting a more robust generalizability of our results in this cohort. Another limitation in this study and those preceding ours is equalizing race and ethnicity with an individual's skin color. Furthermore, because of the small numbers of patients in this analysis, dividing the Asian racial group between northern and southern Asia, which likely have different skin color

and genetics, was not possible. In addition, as a single-institution and retrospective observational study, prospective multicenter studies are required to validate our findings.

CONCLUSIONS

Pulse oximetry is a widely used, noninvasive method of obtaining a patient's oxygen saturation. We demonstrated that the pulse oximetry and arterial blood gas oxygen saturation discrepancy, between different races, is clinically relevant in patients supported with ECMO. Furthermore, our results imply prospective physiological explanations for this discrepancy; specifically, further analysis of granular data such as vasoactive-inotropic score and LDH should be further examined.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: blood gas analysis, extracorporeal membrane oxygenation, hypoxemia, pulse oximetry, racial groups

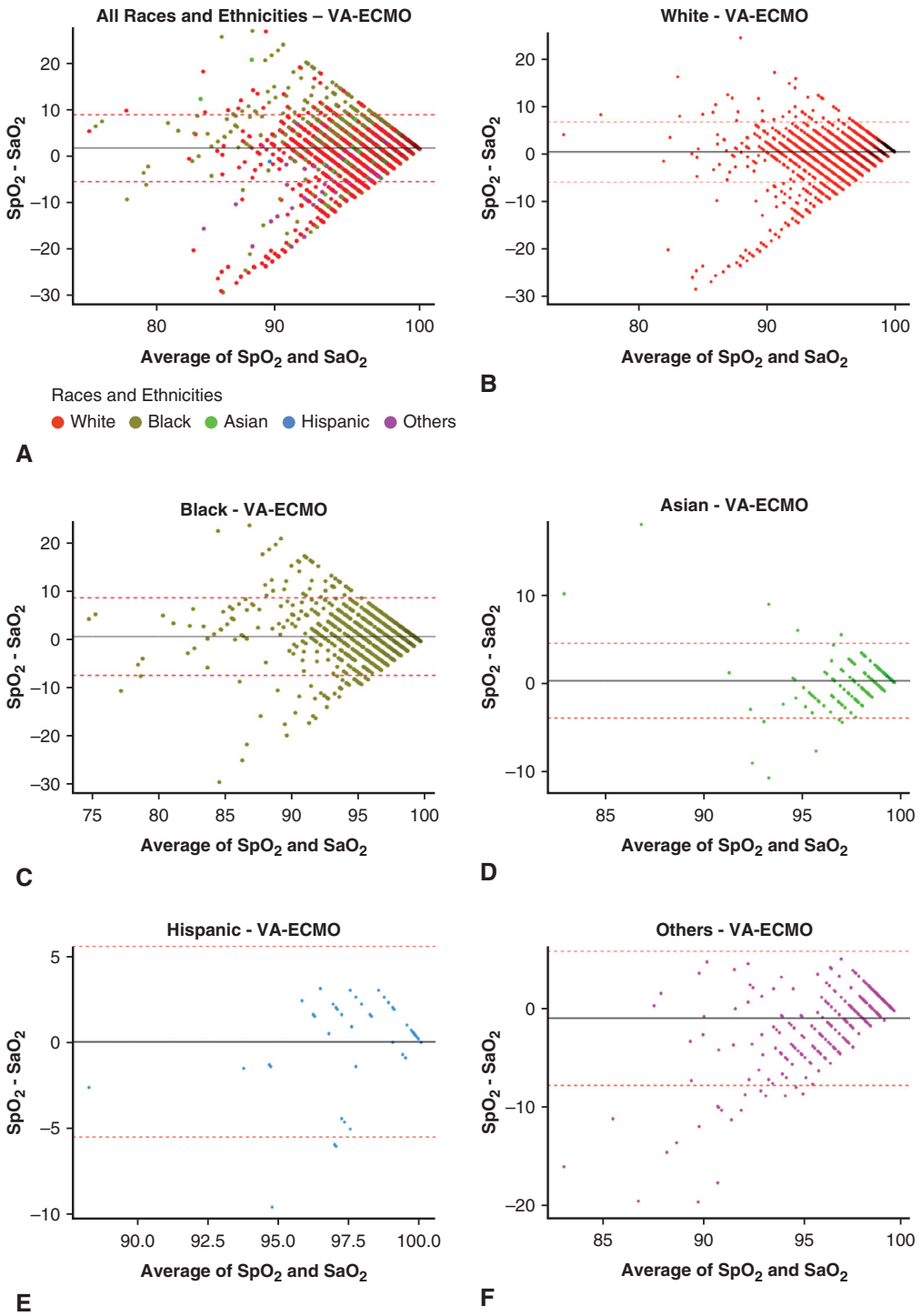


FIGURE E1. Bland–Altman plots of $(SpO_2 + SaO_2)/2$ (x-axis) vs $SpO_2 - SaO_2$ (y-axis), highlighting the discrepancy between SpO_2 and SaO_2 values in patients receiving venoarterial extracorporeal membrane oxygenation (*VA-ECMO*) separated by race and ethnicity. A, *Red*, *yellow–green*, *light green, blue*, and *purple dots* represent White, Black, Asian, Hispanic, and others (nonspecified races) patients receiving VA-ECMO, respectively. The *upper red dashed line* represents the upper 95% confidence interval limit of agreement (7.0%), and the *lower red dashed line* represents the lower 95% confidence interval limit of agreement (–6.7%), within which 95% of the differences between SpO_2 and SaO_2 fall. The *solid black line* represents the mean difference between SpO_2 and SaO_2 (0.15%), calculated by first determining the averages of SpO_2 and SaO_2, individually, and then subtracting the average SaO_2 from the average SpO_2 value. The further away SpO_2 and SaO_2 data points are vertically from the *solid black line*, the more discrepant SpO_2 and SaO_2 are. Data points above the *solid black line* indicate SpO_2 overestimated SaO_2 whereas data points below indicate SpO_2 underestimated SaO_2. Panels B, C, D, E, and F are separate Bland–Altman plots for each race: White, Black, Asian, Hispanic, and others, respectively. *SaO_2*, Oxygen saturation measured by arterial gas; *SpO_2*, oxygen saturation measured by pulse oximetry.

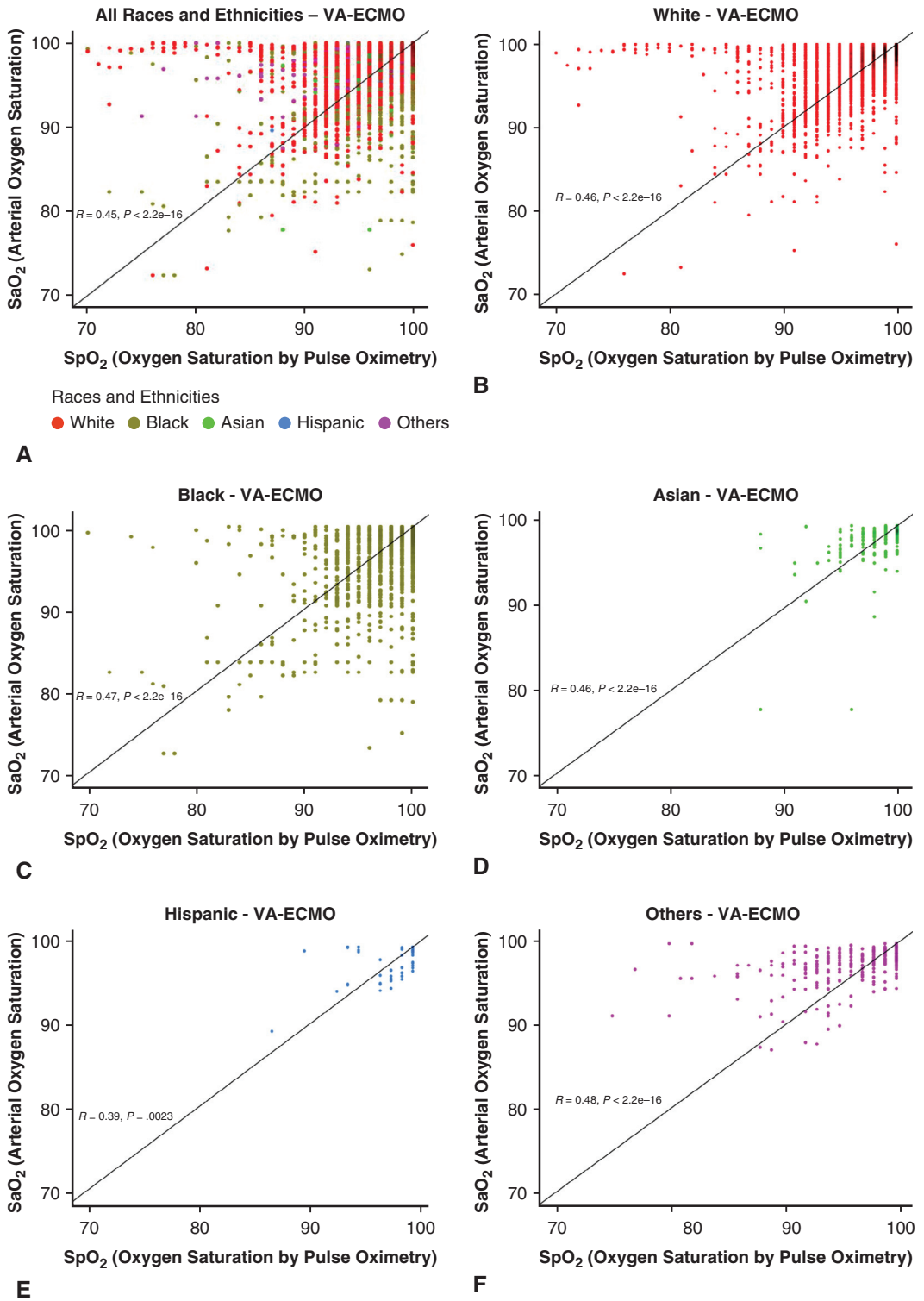


FIGURE E2. Scatterplots of pulse oximetry oxygen saturation levels (SpO_2, x-axis) vs arterial oxygen saturation levels (SaO_2, y-axis) in patients receiving venoarterial extracorporeal membrane oxygenation (*VA-ECMO*) separated by race and ethnicity. *Red*, *yellow–green*, *light green, blue*, and *purple dots* represent White, Black, Asian, Hispanic, and others (nonspecified races) patients receiving VA-ECMO, respectively. A 45-degree line is shown to model the ideal 1:1 ratio of SpO_2 to SaO_2, further highlighting the discrepancy between SpO_2 and SaO_2 values for patients receiving VA-ECMO between different races and ethnicities, as most SpO_2 and SaO_2 points do not fit on this 45-degree line. Pearson correlation coefficients were generated to measure the linear correlation between SpO_2 and SaO_2. Panels B, C, D, E, and F are separate scatterplots for each race: White, Black, Asian, Hispanic, and others, respectively. *SaO_2*, Oxygen saturation measured by arterial gas; *SpO_2*, oxygen saturation measured by pulse oximetry.

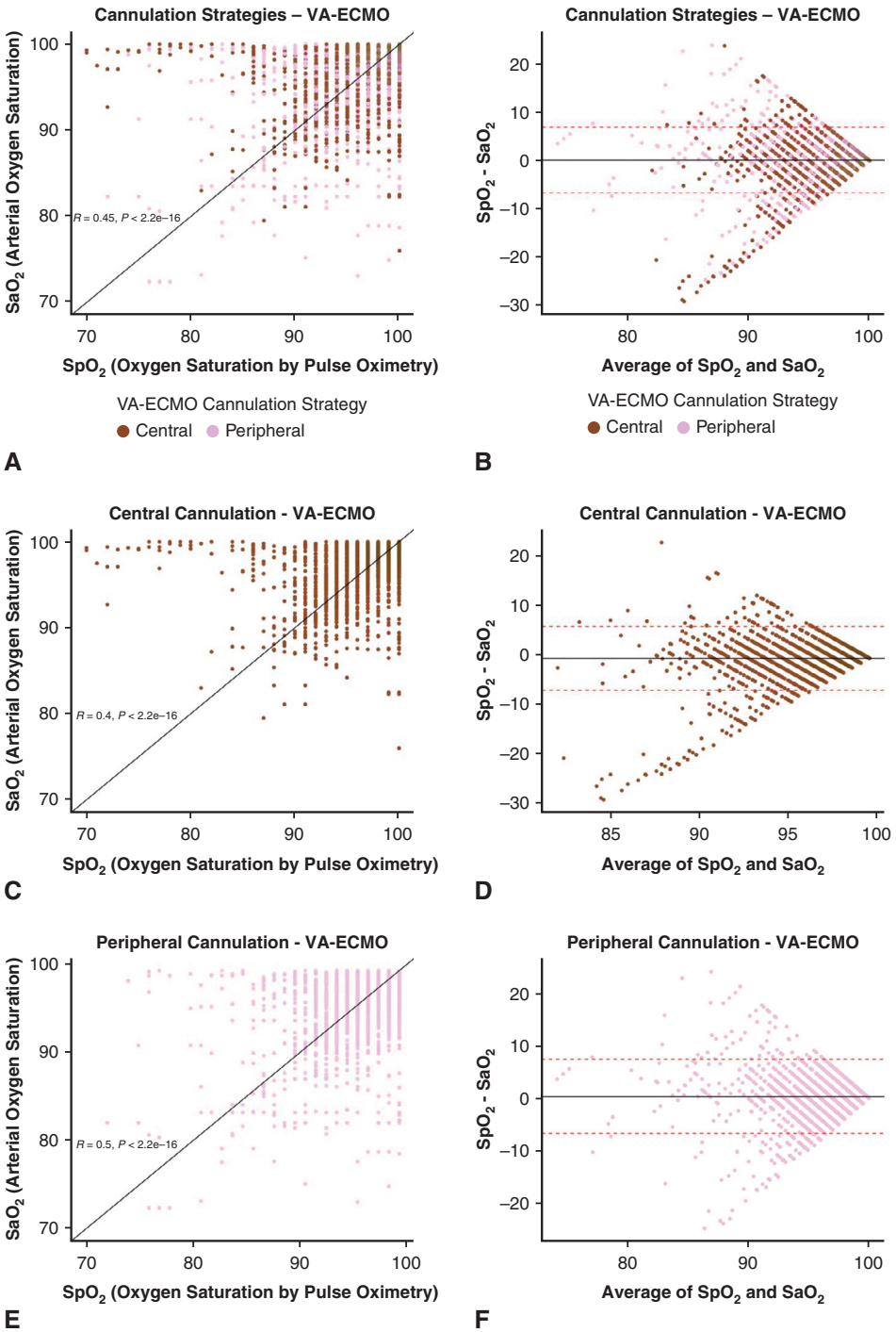
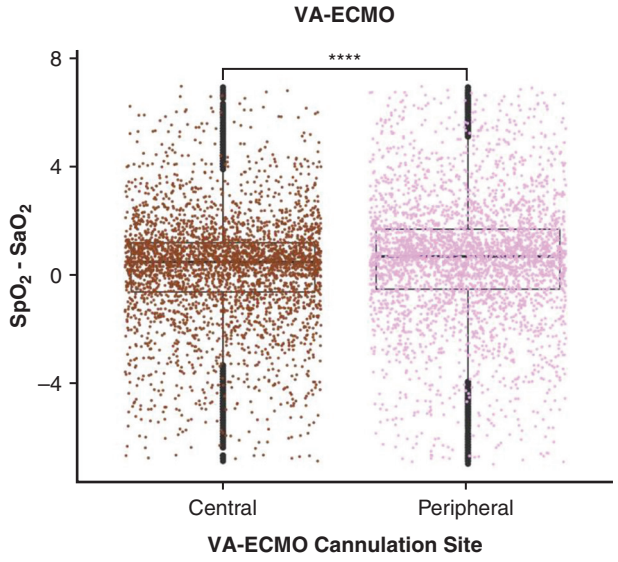
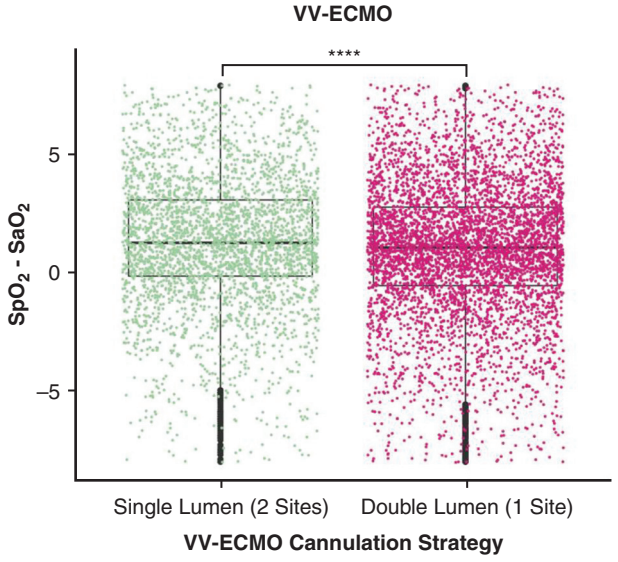


FIGURE E3. Scatterplots of pulse oximetry oxygen saturation levels (SpO_2, x-axis) vs arterial oxygen saturation levels (SaO_2, y-axis) and Bland–Altman plots of $(SpO_2 + SaO_2)/2$ (x-axis) vs $SpO_2 - SaO_2$ (y-axis) in patients receiving venoarterial extracorporeal membrane oxygenation (*VA-ECMO*) stratified by cannulation strategy. A, *Brown* and *pink dots* represent centrally and peripherally cannulated patients receiving VA-ECMO, respectively. A 45-degree line is shown to model the ideal 1:1 ratio of SpO_2 to SaO_2, further highlighting the discrepancy between SpO_2 and SaO_2 values for patients with VA-ECMO that differ by cannulation strategy as most SpO_2 and SaO_2 points do not fit on this 45-degree line. Pearson correlation coefficients were generated to measure the linear correlation between SpO_2 and SaO_2. Panels C and E are separate scatterplots for patients undergoing centrally- and peripherally-cannulated VA-ECMO, respectively. B, The *upper red dashed line* represents the upper 95% confidence interval limit of agreement (7.0%), and the *lower red dashed line* represents the lower 95% confidence interval limit of agreement (–6.7%), within which 95% of the differences between SpO_2 and SaO_2 fall. The *solid black line* represents the mean difference between SpO_2 and SaO_2 (0.15%), calculated by first determining the averages of SpO_2 and SaO_2, individually, and then subtracting the average SaO_2 from the average SpO_2 value. Panels D and F are separate Bland–Altman plots for patients receiving centrally and peripherally cannulated VA-ECMO, respectively. *SaO_2*, Oxygen saturation measured by arterial gas; *SpO_2*, oxygen saturation measured by pulse oximetry.



A



B

FIGURE E4. Boxplots of SpO_2–SaO_2 discrepancy by cannulation strategies in patients receiving venoarterial extracorporeal membrane oxygenation (*VA-ECMO*) and venovenous (*VV*)-ECMO. In these boxplots of VA-ECMO (A) and VV-ECMO (B) patients stratified by cannulation strategy, the *horizontal lines* represent the median, and the *top and bottom ends of each box* represent the 75% and 25% limits of the interquartile range, respectively. Only data points within 2 standard deviations of the mean are shown. Each *small dot* represents an individual data point (SpO_2–SaO_2 pair), colored by cannulation strategy. In (A), *brown* and *pink dots* represent patients receiving centrally and peripherally cannulated VA-ECMO, respectively. In B, *green* and *violet dots* represent single-lumen (two sites) and double-lumen (one site) cannulation strategy patients receiving VV-ECMO. Wilcoxon rank-sum test was used for comparisons between 2 different cannulation strategies. **** indicates a $P \leq .0001$. *SpO_2*, Oxygen saturation measured by pulse oximetry; *SaO_2*, oxygen saturation measured by arterial gas.

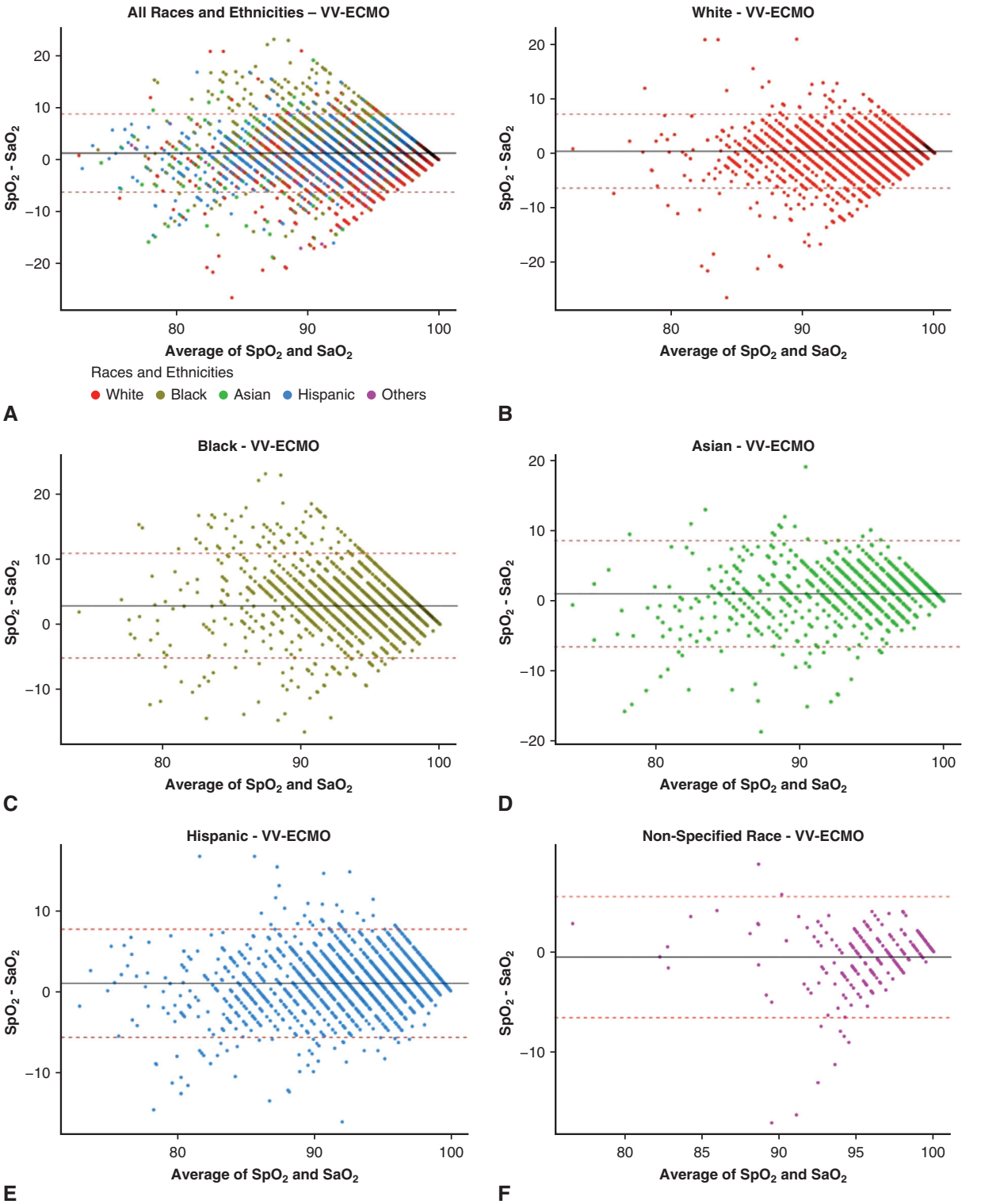


FIGURE E5. Bland–Altman plot of $(SpO_2 + SaO_2)/2$ (x-axis) vs $SpO_2 - SaO_2$ (y-axis), highlighting the discrepancy between SpO_2 and SaO_2 values in patients receiving venovenous extracorporeal membrane oxygenation (*VV-ECMO*) separated by race and ethnicity. A, *Red*, *yellow–green*, *light green*, *blue*, and *purple dots* represent White, Black, Asian, Hispanic, and others (nonspecified races) patients receiving VV-ECMO, respectively. The *upper red dashed line* represents the upper 95% confidence interval limit of agreement (9.2%), and the *lower red dashed line* represents the lower 95% confidence interval limit of agreement (–6.4%), within which 95% of the differences between SpO_2 and SaO_2 fall. The *solid black line* represents the mean difference between SpO_2 and SaO_2 (1.4%), calculated by first determining the averages of SpO_2 and SaO_2, individually, and then subtracting the average SaO_2 from the average SpO_2 value. The further away SpO_2 and SaO_2 data points are vertically from the *solid black line*, the more discrepant SpO_2 and SaO_2 are. Data points above the *solid black line* indicate SpO_2 overestimated SaO_2, whereas data points below indicate SpO_2 underestimated SaO_2. Panels B, C, D, E, and F are separate Bland–Altman plots for each race: White, Black, Asian, Hispanic, and others, respectively. *SaO_2*, Oxygen saturation measured by arterial gas; *SpO_2*, oxygen saturation measured by pulse oximetry.

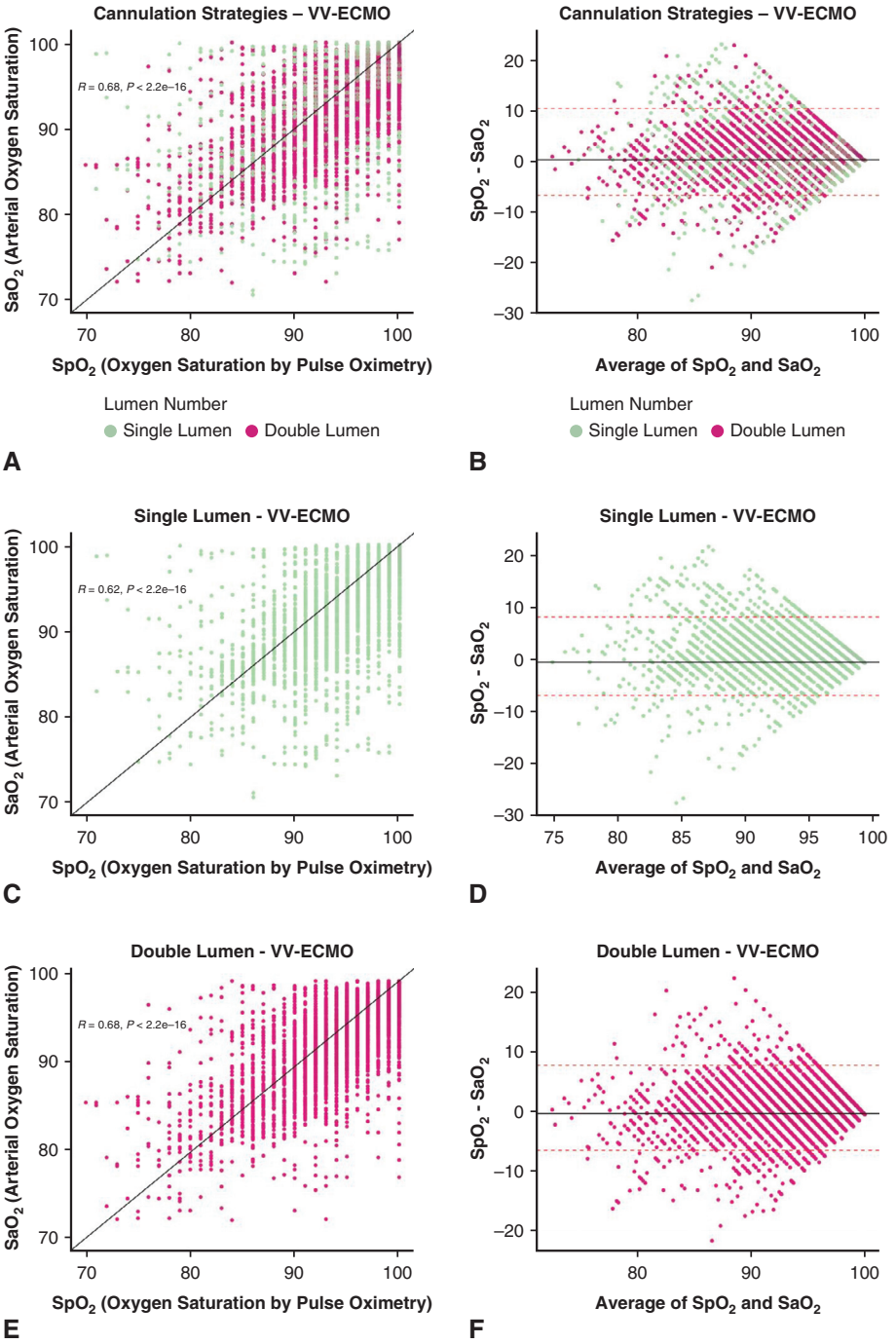


FIGURE E6. Scatterplot of pulse oximetry oxygen saturation levels (SpO_2, x-axis) vs arterial oxygen saturation levels (SaO_2, y-axis) and Bland–Altman plot of ($SpO_2 + SaO_2$)/2 (x-axis) vs $SpO_2 - SaO_2$ (y-axis), in patients receiving venovenous extracorporeal membrane oxygenation (*VV-ECMO*) stratified by cannulation strategy. A, *Green* and *purple dots* represent single- and double-lumen cannulated patients receiving VV-ECMO, respectively. A 45-degree line is shown to model the ideal 1:1 ratio of SpO_2 to SaO_2, further highlighting the discrepancy between SpO_2 and SaO_2 values for patients receiving VV-ECMO that differ by cannulation strategy, as most SpO_2 and SaO_2 points do not fit on this 45-degree line. Pearson correlation coefficients were generated to measure the linear correlation between SpO_2 and SaO_2. C and E are separate scatterplots for single- and double-lumen cannulated VV-ECMO patients, respectively. B, The *upper red dashed line* represents the upper 95% confidence interval limit of agreement (9.2%), and the *lower red dashed line* represents the lower 95% confidence interval limit of agreement (–6.4%), within which 95% of the differences between SpO_2 and SaO_2 fall. The solid black line represents the mean difference between SpO_2 and SaO_2 (1.4%), calculated by first determining the averages of SpO_2 and SaO_2, individually, and then subtracting the average SaO_2 from the average SpO_2 value. D and F are separate Bland–Altman plots for patients receiving single- and double-lumen cannulated VV-ECMO, respectively. *SaO_2*, Oxygen saturation measured by arterial gas; *SpO_2*, oxygen saturation measured by pulse oximetry.

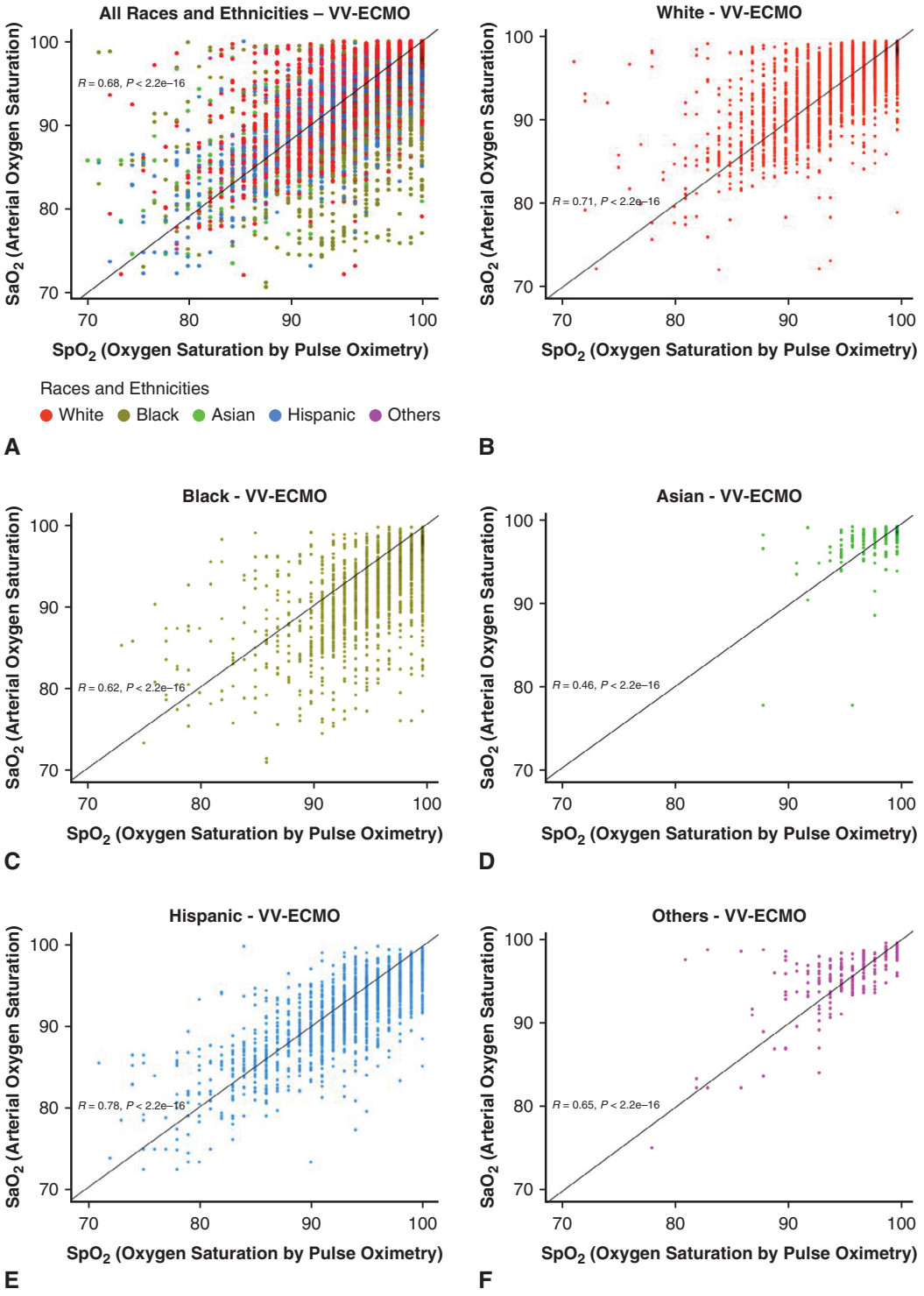


FIGURE E7. Scatterplot of pulse oximetry oxygen saturation levels (SpO_2, x-axis) vs arterial oxygen saturation levels (SaO_2, y-axis) in patients receiving venovenous extracorporeal membrane oxygenation (*VV-ECMO*) separated by race and ethnicity. A, *Red*, *yellow–green*, *light green*, *blue*, and *purple dots* represent White, Black, Asian, Hispanic, and others (nonspecified races). A 45-degree line is shown to model the ideal 1:1 ratio of SpO_2 to SaO_2, further highlighting the discrepancy between SpO_2 and SaO_2 values for VV-ECMO patients between different races and ethnicities as most SpO_2 and SaO_2 points do not fit on this 45-degree line. Pearson correlation coefficients were generated to measure the linear correlation between SpO_2 and SaO_2. B, C, D, E, and F are separate scatterplots for each race: White, Black, Asian, Hispanic, and others, respectively. *SaO_2*, Oxygen saturation measured by arterial gas; *SpO_2*, oxygen saturation measured by pulse oximetry.

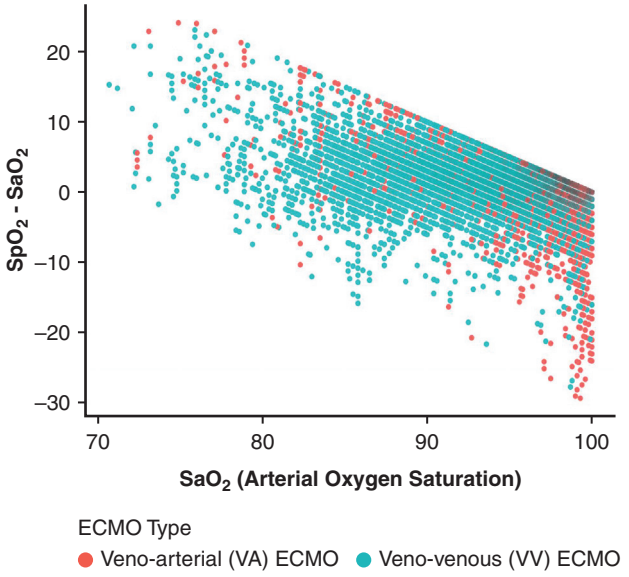


FIGURE E8. Difference between SpO_2 and SaO_2 (y-axis) plotted as a function of SaO_2 (x-axis). As oxygen saturation decreases, SpO_2–SaO_2 increases. There are more SpO_2–SaO_2 pairs at lower saturations with a greater SpO_2–SaO_2 discrepancy (SpO_2 *overestimating* SaO_2) in patients receiving venovenous extracorporeal membrane oxygenation (*VV-ECMO*) patients (*red dots*) versus patients receiving venoarterial extracorporeal membrane oxygenation (*VA-ECMO*) (*turquoise dots*). Conversely, there were more SpO_2–SaO_2 pairs at greater oxygen saturations where SpO_2 *underestimated* SaO_2 in the VA-ECMO population. *SpO_2*, Oxygen saturation measured by pulse oximetry; *SaO_2*, oxygen saturation measured by arterial gas.

TABLE E1. Estimated bias, precision, upper and lower limits of agreement, root mean square error, and Pearson correlation coefficient, stratified by race and ethnicity in patients receiving ECMO in all SpO_2–SaO_2 pairs measured 10 minutes or less between each other

	Venoarterial (VA) ECMO patients						Venovenous (VV) ECMO patients					
	All (139 patients, 7366 pairs)	White (91 patients, 4820 pairs)	Black (27 patients, 1763 pairs)	Asian (9 patients, 320 pairs)	Hispanic (3 patients, 58 pairs)	Nonspecified races (9 patients, 405 pairs)	All (57 patients, 8886 pairs)	White (20 patients, 3357 pairs)	Black (19 patients, 2774 pairs)	Asian (3 patients, 839 pairs)	Hispanic (13 patients, 1661 pairs)	Nonspecified races (2 patients, 255 pairs)
Estimated bias, % (mean difference)	0.15	−0.06	0.94	0.2	0.03	−0.80	1.4	0.5	2.9	1.0	1.1	−0.53
Precision, % (standard deviation)	3.5	3.3	4.1	2.2	2.8	3.6	4.0	3.3	4.6	3.9	3.4	3.1
Upper limit of agreement, % (95% CI limit)	7.0	6.3	9.0	4.5	5.5	6.2	9.2	7.1	11.9	8.6	7.8	5.5
Lower limit of agreement, % (95% CI limit)	−6.7	−6.4	−7.1	−4.1	−5.5	−7.8	−6.4	−6.1	−6.2	−6.6	−5.5	−6.5
Root mean square error, %	3.3	3.3	3.2	2.0	2.8	4.4	2.6	2.9	1.7	2.9	2.3	3.6
Pearson correlation coefficient (P value)	0.45 ($P < .0001$)	0.46 ($P < .0001$)	0.47 ($P < .0001$)	0.46 ($P < .0001$)	0.39 ($P = .002$)	0.48 ($P < .001$)	0.68 ($P < .0001$)	0.71 ($P < .0001$)	0.62 ($P < .0001$)	0.46 ($P < .0001$)	0.78 ($P < .0001$)	0.65 ($P < .0001$)

ECMO, Extracorporeal membrane oxygenation; *CI*, confidence interval.

TABLE E2. Estimated bias, precision, upper and lower limits of agreement, root mean square error, and Pearson correlation coefficient, stratified by cannulation strategy in patients receiving ECMO in all SpO_2–SaO_2 pairs measured 10 minutes or less between each other

	Venoarterial (VA) ECMO			Venovenous (VV) ECMO		
	All with cannulation strategy (139 patients, 7295 pairs)	Central (69 patients, 3924 pairs)	Peripheral (70 patients, 3371 pairs)	All with cannulation strategy (56 patients, 8805 pairs)	Single-lumen (24 patients, 3498 pairs)	Double-lumen (32 patients, 5307 pairs)
Estimated bias, % (mean difference)	0.15	0.004	0.33	1.4	1.8	1.1
Precision, % (standard deviation)	3.5	3.4	3.6	4.0	4.4	3.6
Upper limit of agreement, % (95% CI Limit)	7.0	6.6	7.4	9.2	10.4	8.3
Lower limit of agreement, % (95% CI Limit)	−6.7	−6.6	−6.7	−6.4	−6.8	−6.0
Root mean square error, %	3.3	3.4	3.3	2.6	2.6	2.5
Pearson correlation coefficient (*P* value)	0.45 ($P < .0001$)	0.40 ($P < .0001$)	0.50 ($P < .0001$)	0.68 ($P < .0001$)	0.62 ($P < .0001$)	0.73 ($P < .0001$)

ECMO, Extracorporeal membrane oxygenation; *CI*, confidence interval.

TABLE E3. Unadjusted venoarterial ECMO linear mixed-effects model assessing the relationship between race and SpO_2–SaO_2 for all time-matched and ≥70% oxygen saturation data points

	Estimate	Std. error	df	t value	Pr(>|t|)	2.5% (95% CI limit)	97.5% (95% CI limit)
(Intercept)	−0.3436	0.2130	78.3475	−1.613	0.11072	−0.76115226	0.07386538
Black	1.0187	0.3661	54.2250	2.782	0.00741	0.30106155	1.73633289
Asian	0.6081	0.3180	24.6890	1.912	0.06748	−0.01509709	1.23138934
Hispanic	−1.7411	1.8289	2.3148	−0.952	0.42960	−5.32562468	1.84340491
Others	−0.1400	0.4079	15.3592	−0.343	0.73614	−0.93932560	0.65941719

df, Degrees of freedom; *CI*, confidence interval.

TABLE E4. Adjusted venoarterial ECMO linear mixed-effects model assessing the relationship between race and each covariate as a fixed effect for all SpO_2–SaO_2 time-matched and ≥70% oxygen saturation data points

	Estimate	Std. error	df	t value	Pr(>|t|)	2.5% (95% CI limit)	97.5% (95% CI limit)
(Intercept)	−2.052e+00	2.603e+00	3.521e+01	−0.788	0.4358	−7.15281040	3.049504161
Black	−1.147e+00	8.967e+00	7.155e+00	−0.128	0.9017	−18.72286720	16.428492941
Asian	−1.836e+00	2.027e+01	1.513e-04	−0.091	0.9996	−41.56833197	37.897203047
Hispanic	−3.730e+00	4.220e+00	5.197e-04	−0.884	0.9977	−12.00082634	4.539889436
Others	−1.138e+01	5.617e+00	2.708e+03	−2.026	0.0428	−22.39278325	−0.373532372
Age	−6.918e-04	3.655e-02	2.891e+01	−0.019	0.9850	−0.07232758	0.070943957
Male	−2.482e+00	2.431e+00	2.975e+01	−1.021	0.3154	−7.24667826	2.281791761
Vasopressor/inotrope usage	2.565e+00	1.626e+00	3.652e+01	1.578	0.1232	−0.62136017	5.751468212
Central cannulation	5.394e+00	3.702e+00	2.948e+01	1.457	0.1557	−1.86223834	12.650328636
Black + age	−2.599e-02	1.267e-01	7.040e+00	−0.205	0.8433	−0.27433209	0.222356878
Asian + age	1.213e-01	4.925e-01	1.501e-04	0.246	0.9994	−0.84405529	1.086612868
Others + age	1.995e-01	1.091e-01	3.070e+03	1.829	0.0675	−0.01430126	0.413288675
Black + male	3.593e+00	9.376e+00	6.861e+00	0.383	0.7131	−14.78385109	21.970751286
Asian + male	−3.087e+00	1.725e+01	1.507e-04	−0.179	0.9995	−36.90229359	30.727487802
Others + male	9.399e-01	1.033e+00	1.615e+02	0.910	0.3642	−1.08470386	2.964478446
Age + male	3.560e-02	4.464e-02	3.012e+01	0.798	0.4314	−0.05188553	0.123089242
Black + vasopressor/inotrope usage	2.240e+00	6.826e+00	6.893e+00	0.328	0.7525	−11.13839813	15.619162665
Asian + vasopressor/inotrope usage	−3.875e+00	7.001e+00	1.716e-04	−0.553	0.9992	−17.59691429	9.846908126
Black + central cannulation	−8.958e+00	1.154e+01	7.573e+00	−0.777	0.4610	−31.56927619	13.652853309
Others + central cannulation	−3.811e+00	1.840e+00	2.314e+03	−2.072	0.0384	−7.41673109	−0.205436028
Age + central cannulation	−1.177e-01	6.339e-02	2.958e+01	−1.856	0.0734	−0.24192770	0.006566784
Male + central cannulation	−2.534e+00	4.388e+00	2.908e+01	−0.577	0.5681	−11.13427713	6.066276039
Black + age + male	2.571e-02	1.927e-01	6.670e+00	0.133	0.8978	−0.35193578	0.403347865
Black + age + central cannulation	1.590e-01	2.294e-01	7.067e+00	0.693	0.5103	−0.29051975	0.608533784
Black + male + central cannulation	1.373e+01	2.059e+01	6.559e+00	0.667	0.5278	−26.63638448	54.094041403
Age + male + central cannulation	6.155e-02	7.454e-02	2.937e+01	0.826	0.4156	−0.08454957	0.207646924
Black + age + male + central cannulation	−2.800e-01	3.690e-01	6.496e+00	−0.759	0.4746	−1.00326501	0.443287580

df, Degrees of freedom; *CI*, confidence interval.

TABLE E5. ROC and AUC analyses for SpO_2 to accurately detect 88%, 92%, and 95% SaO_2 thresholds

Patient type	SaO_2 threshold (%)	AUC	Specificity (%)	Sensitivity (%)
All (VA-ECMO + VV-ECMO)	88	0.888 (0.879-0.897)	76	88
	92	0.868 (0.862-0.875)	95	48
	95	0.850 (0.844-0.856)	100	0
VA-ECMO only	88	0.802 (0.766-0.837)	23	98
	92	0.822 (0.804-0.840)	69	83
	95	0.802 (0.789-0.815)	100	0
VV-ECMO only	88	0.880 (0.870-0.890)	84	76
	92	0.855 (0.847-0.863)	98	26
	95	0.846 (0.838-0.854)	100	0

SaO_2, Oxygen saturation measured by arterial gas; *AUC*, area under the receiver-operating characteristic curve; *VA*, venoarterial; *ECMO*, extracorporeal membrane oxygenation; *VV*, venovenous.

TABLE E6. ROC analyses of an "optimal" SpO_2 (based on Youden's index) to accurately detect each SaO_2 threshold

Patient type	SaO_2 threshold (%)	Optimal SpO_2 (%)	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
All (VA + VV-ECMO)	88	90	83	81	98	32
	92	81	77	83	94	50
	95	69	78	80	87	67
VA-ECMO only	88	97	86	66	99	12
	92	93	77	76	98	21
	95	84	80	71	94	39
VV-ECMO only	88	85	83	79	96	44
	92	68	78	78	88	64
	95	56	74	82	78	78

SaO_2, Oxygen saturation measured by arterial gas; *SpO_2*, oxygen saturation measured by pulse oximetry; *VA*, venoarterial; *VV*, venovenous; *ECMO*, extracorporeal membrane oxygenation.

TABLE E7. Unadjusted venovenous ECMO linear mixed-effects model assessing the relationship between race and SpO_2–SaO_2 for all time-matched and ≥70% oxygen saturation data points

	Estimate	Std. error	df	t value	Pr(>|t|)	2.5% (95% CI limit)	97.5% (95% CI limit)
(Intercept)	−0.1855	0.4128	48.4206	−0.449	0.655	−0.9945786	0.6235495
Black	2.7654	0.6089	48.3778	4.541	3.72e-05	1.5719211	3.9588357
Asian	1.4706	1.1250	45.5359	1.307	0.198	−0.7343245	3.6754743
Hispanic	1.0670	0.6569	48.2163	1.624	0.111	−0.2205120	2.3545324
Others	−0.4770	1.3553	46.6053	−0.352	0.726	−3.1333892	2.1793811

df, Degrees of freedom; *CI*, confidence interval.

TABLE E8. Adjusted venovenous ECMO linear mixed-effects model assessing the relationship between race and each covariate as a fixed effect for all SpO_2–SaO_2 time-matched and ≥70% oxygen saturation data points

	Estimate	Std. Error	df	t value	Pr(>|t|)	2.5% (95% CI limit)	97.5% (95% CI limit)
(Intercept)	−2.963e+00	2.350e+00	5.062e+00	−1.261	0.2624	−7.56890474	1.64292640
Black	−4.502e+00	3.258e+00	1.234e+01	−1.382	0.1915	−10.88721046	1.88332055
Asian	1.480e+01	3.121e+01	6.855e-05	0.474	0.9997	−46.37958646	75.97640209
Hispanic	3.777e+00	2.897e+00	6.312e+00	1.304	0.2378	−1.90041771	9.45471651
Others	−7.193e-01	3.978e+00	2.356e-05	−0.181	0.9999	−8.51623638	7.07760379
Age	6.675e-02	4.881e-02	4.751e+00	1.368	0.2326	−0.02891663	0.16242499
Female	1.892e+01	2.326e+01	3.574e+00	0.813	0.4667	−26.67546964	64.51903101
Double-lumen cannula	−1.454e+01	3.131e+01	3.520e+00	−0.464	0.6697	−75.90531006	46.83094777
Black + age	1.856e-01	7.200e-02	1.336e+01	2.578	0.0225	0.04451583	0.32676384
Asian + age	−2.448e-01	5.756e-01	6.910e-05	−0.425	0.9997	−1.37300969	0.88349131
Hispanic + age	−5.460e-02	6.456e-02	5.970e+00	−0.846	0.4303	−0.18112814	0.07193721
Black + female	−2.057e+01	1.135e+02	3.851e+00	−0.181	0.8653	−243.05728004	201.90808294
Hispanic + female	−1.069e+01	1.753e+01	3.718e+00	−0.609	0.5775	−45.04734486	23.67732100
Age + female	−4.045e-01	5.419e-01	3.620e+00	−0.746	0.5010	−1.46663130	0.65763568
Black + double-lumen cannula	2.706e+01	1.130e+02	3.761e+00	0.240	0.8232	−194.36008605	248.48535955
Hispanic + double-lumen cannula	1.315e+01	3.194e+01	3.791e+00	0.412	0.7026	−49.44037080	75.75029352
Age + double-lumen cannula	2.531e-01	5.199e-01	3.447e+00	0.487	0.6557	−0.76590155	1.27206949
Female + double-lumen cannula	2.486e+00	9.239e+00	3.755e+00	0.269	0.8020	−15.62132567	20.59404898
Black + age + female	3.711e-01	2.069e+00	3.837e+00	0.179	0.8667	−3.68388457	4.42599426
Black + age + double-lumen cannula	−5.395e-01	2.058e+00	3.740e+00	−0.262	0.8070	−4.57247794	3.49342111
Hispanic + age + double-lumen cannula	−2.218e-01	5.383e-01	3.945e+00	−0.412	0.7017	−1.27690949	0.83325120

df, Degrees of freedom; *CI*, confidence interval.