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Self-reported Race/Ethnicity and Intraoperative Occult Hypoxemia: A Retrospective Cohort Study

Garrett W. Burnett, M.D., Blaine Stannard, M.D., David B. Wax, M.D., Hung-Mo Lin, Sc.D., Chantal Pyram-Vincent, M.D., M.P.H., Samuel DeMaria, Jr., M.D., Matthew A. Levin, M.D.

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Pulse oximetry is part of the American Society of Anesthesiologists' Standards for Basic Anesthetic Monitoring
- Pigmentation in dark skin has been associated with overestimation of pulse oximeter values
- Recent critical care literature has renewed concerns regarding the accuracy of pulse oximetry in detecting hypoxemia in Black *versus* White patients

What This Article Tells Us That Is New

- Among 46,523 patients with 151,070 paired arterial oxygen saturation (Sao_2)–oxygen saturation measured by pulse oximetry (Spo_2) intraoperative readings at a single center, the prevalence of occult hypoxemia (Sao_2 less than 88% despite concurrent Spo_2 greater than 92%) was significantly increased in patients self-reporting Black (2.1%) and Hispanic (1.8%) race/ethnicity compared with patients self-reporting White (1.1%) race/ethnicity
- After adjusting for other clinical factors, Black or Hispanic race/ethnicity was independently associated with occult hypoxemia

ABSTRACT

Background: Pulse oximetry is ubiquitous in anesthesia and is generally a reliable noninvasive measure of arterial oxygen saturation. Concerns regarding the impact of skin pigmentation and race/ethnicity on the accuracy of pulse oximeter accuracy exist. The authors hypothesized a greater prevalence of occult hypoxemia (arterial oxygen saturation [Sao_2] less than 88% despite oxygen saturation measured by pulse oximetry [Spo_2] greater than 92%) in patients undergoing anesthesia who self-reported a race/ethnicity other than White.

Methods: Demographic and physiologic data, including self-reported race/ethnicity, were extracted from a departmental data warehouse for patients receiving an anesthetic that included at least one arterial blood gas between January 2008 and December 2019. Calculated Sao_2 values were paired with concurrent Spo_2 values for each patient. Analysis to determine whether Black, Hispanic, Asian, or Other race/ethnicities were associated with occult hypoxemia relative to White race/ethnicity within the Spo_2 range of 92 to 100% was completed.

Results: In total, 151,070 paired Sao_2–Spo_2 readings (70,722 White; 16,011 Black; 21,223 Hispanic; 8,121 Asian; 34,993 Other) from 46,253 unique patients were analyzed. The prevalence of occult hypoxemia was significantly higher in Black (339 of 16,011 [2.1%]) and Hispanic (383 of 21,223 [1.8%]) *versus* White (791 of 70,722 [1.1%]) paired Sao_2–Spo_2 readings ($P < 0.001$ for both). In the multivariable analysis, Black (odds ratio, 1.44 [95% CI, 1.11 to 1.87]; $P = 0.006$) and Hispanic (odds ratio, 1.31 [95% CI, 1.03 to 1.68]; $P = 0.031$) race/ethnicity were associated with occult hypoxemia. Asian and Other race/ethnicity were not associated with occult hypoxemia.

Conclusions: Self-reported Black and Hispanic race/ethnicity are associated with a greater prevalence of intraoperative occult hypoxemia in the Spo_2 range of 92 to 100% when compared with self-reported White race/ethnicity.

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In 1986, the American Society of Anesthesiologists (ASA; Schaumburg, Illinois) adopted the Standards for Basic Intra-Operative Monitoring, which stated, "During all anesthetics, a quantitative method of assessing oxygenation such as pulse oximetry shall be employed."[1] Since that time, pulse oximetry has become ubiquitous in health care and is an important component of the World Health Organization's (Geneva, Switzerland) Safe Surgery Checklist.[2] The addition of widespread pulse oximetry use, in combination with additional perioperative safety initiatives, has coincided

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Garrett W. Burnett, M.D.: Department of Anesthesiology, Perioperative and Pain Medicine, Icahn School of Medicine at Mount Sinai, New York, New York.

Blaine Stannard, M.D.: Department of Anesthesiology, Perioperative and Pain Medicine, Icahn School of Medicine at Mount Sinai, New York, New York.

David B. Wax, M.D.: Department of Anesthesiology, Perioperative and Pain Medicine, Icahn School of Medicine at Mount Sinai, New York, New York.

Hung-Mo Lin, Sc.D.: Department of Population Health Science and Policy, Icahn School of Medicine at Mount Sinai, New York, New York.

Chantal Pyram-Vincent, M.D., M.P.H.: Department of Anesthesiology, Perioperative and Pain Medicine, Icahn School of Medicine at Mount Sinai, New York, New York.

Samuel DeMaria, Jr., M.D.: Department of Anesthesiology, Perioperative and Pain Medicine, Icahn School of Medicine at Mount Sinai, New York, New York.

Matthew A. Levin, M.D.: Department of Anesthesiology, Perioperative and Pain Medicine and Department of Genetics and Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, New York.

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with a 90% reduction in anesthesia-related fatalities[3]; its use in postanesthesia care units has likely contributed to the significant reduction in need for patient rescue or intensive care unit admissions.[3,4]

While the measurement of oxygen saturation by pulse oximetry (Spo_2) is generally a reliable noninvasive measure of a patient's true arterial oxygen saturation (Sao_2), several factors may interfere with the accuracy of pulse oximetry measurement.[5] These include inadequate waveform capture from hypotension; motion artifact or hypoperfusion; falsely elevated values due to ambient light or carboxyhemoglobin; or falsely low values from severe anemia, nail polish, or vital dyes.[5–7] Skin pigmentation is another potential source of inaccuracy, and studies have demonstrated conflicting data regarding the impact of skin pigmentation on the difference between Sao_2 concentrations and Spo_2 values (*i.e.*, Spo_2 device bias). Overestimation of Spo_2 (positive device bias) in patients with dark skin pigmentation has been shown to be as high as 5%, although some studies have demonstrated no evidence of Spo_2 device bias.[8–13] More recent studies evaluating modern pulse oximeters have evaluated Spo_2 device bias in hypoxic patients with and without dark skin pigmentation.[14,15] Positive Spo_2 device bias was noted in patients with deeply pigmented skin at Sao_2 concentrations less than 80%, but this discrepancy did not persist at Sao_2 concentrations greater than 80%.

Most recently, Sjoding *et al.* compared pulse oximetry use in Black and White patients in the critical care setting, demonstrating approximately three times the frequency of clinically significant occult hypoxemia (*i.e.*, Sao_2 less than 88% despite Spo_2 greater than 92 to 96%) in Black (11.4%) *versus* White (3.6%) patients.[16] These findings demonstrated Sao_2 and Spo_2 discrepancies in Black patients at much higher Spo_2 values than previously described.[14,15] These are important and concerning findings, but may not be applicable to a population of patients undergoing anesthetic care.

The aim of this retrospective study was to determine if self-reported race/ethnicity, as a surrogate for skin pigmentation, was associated with greater prevalence of occult hypoxemia in a cohort of patients undergoing general anesthesia, regional anesthesia, or monitored anesthesia care. We hypothesized a greater prevalence of occult hypoxemia in those who self-reported a race/ethnicity other than White.

Materials and Methods

After receiving Institutional Review Board approval from the Icahn School of Medicine at Mount Sinai (New York, New York), data were extracted from our departmental data warehouse for all adult patients (older than 18 yr) who received an anesthetic that included at least one arterial blood gas (ABG) sample between January 2008 and December 2019. Our departmental data warehouse is a unified data source that contains data from both our historical anesthesia information management system (CompuRecord; Philips Medical Systems, USA) as well as our electronic health record (Epic; Epic Systems, USA). Matching of historical intraoperative anesthesia information management system data to additional demographics from the electronic health record, and import of these additional data into our departmental data warehouse, is done *via* an automated process and was not specifically undertaken for this project. Informed consent was waived by the institutional review board because of the retrospective nature of the study.

For each Sao_2 concentration calculated by ABG (GEMStat Premier 3000; Instrumentation Laboratory, USA), the corresponding Spo_2 was found by calculating the mean Spo_2 during a 5-min interval starting 10 min before the ABG time (interval ended at 5 min before the ABG time). This interval was chosen to represent the prevailing Spo_2 values at the time the laboratory specimen was likely drawn, as well as to account for specimen transport time before logging/processing of the specimen using point-of-care ABG analyzers. ABG data were excluded if there were no comparative Spo_2 values available during this interval, or if Sao_2 or Spo_2 values were greater than 100% and deemed to be device error. Spo_2 values were captured every 15 s for all cases. The calculated Sao_2 value and calculated Spo_2 value were then linked to one another as a "paired Sao_2–Spo_2 reading" for the purpose of data analyses.

Pulse oximeter device bias was calculated as the difference between the averaged Spo_2 and Sao_2 values. Occult hypoxemia was defined as Sao_2 less than 88% despite a Spo_2 of greater than 92%, based on previously published parameters.[16] Our analysis included the full range of Spo_2 values between 92 to 100%.

Patient- and case-level data extracted included basic patient demographics (age, sex, body mass index, self-identified race, self-identified ethnicity); smoking status at time of surgery (current, previous, or never smoker); year of procedure as a categorical variable; ASA Physical Status; history of relevant comorbidities (hypertension, chronic pulmonary disease, congestive heart failure, coronary artery disease, valvular heart disease, diabetes, peripheral vascular disease, renal failure); anesthesia type (general, monitored anesthesia care, regional anesthesia); use of volatile anesthetic agent (yes/no); use of vasoactive infusion (yes/no [for use of a phenylephrine, norepinephrine, epinephrine, or vasopressin infusion at any time during the portion of the anesthetic]); mean arterial pressure (MAP); hematocrit value as reported at the time of the associated ABG; and set ventilator parameters (fraction of inspired oxygen [Fio_2], tidal volume, positive end-expiratory pressure [PEEP]). Measured ventilatory parameters were not recorded or saved to the departmental data warehouse. For each case, we calculated the mean Fio_2, tidal volume, and PEEP for the same interval that was used to calculate mean Spo_2. The year of procedure was included to account for changes in pulse oximeters used at our institution (primarily Nellcor [Medtronic, USA] before 2011 and Masimo [Masimo, USA] thereafter). Comorbidities were calculated from

International Classification of Diseases, Ninth Revision and Tenth Revision codes using the icd package[17] in R (R Foundation for Statistical Computing, Vienna, Austria). This is an open-source, validated package that assigns comorbidities using the methods of Elixhauser *et al.*[18] and Quan *et al.*[19]

Self-reported race and ethnicity data collected at time of admission were used for our analyses. Options for self-reported race and ethnicity varied during the time of the study period but were cross-referenced for agreement. Race and ethnicity data were classified into a synthetic race/ethnicity variable according to a previously described method.[20] Specifically, we modified the U.S. Census Bureau/Office of Management and Budget (Washington, D.C.) standards for classification of race/ethnicity to assign each patient to one of the following groups: White (European, North African, Middle Eastern, non-Hispanic), Black (African American, sub-Saharan African, non-Hispanic), Hispanic/Latinx, Asian, or Other race/ethnicity.[21,22] Race/ethnicity was synthesized into a single variable in order to include Hispanic/Latinx patients who may be difficult to categorize using standard U.S. Census guidelines, as a growing percentage of these patients identify race as "Other"[23]; thus, all patients who self-identified as Hispanic ethnicity were categorized into the Hispanic race/ethnicity group. Patients self-identifying as Native American/Alaskan Native, Indian/South Asian, and Pacific Islander were grouped into the Other race/ethnicity group due to an extremely low number of these patients in our dataset, which caused instability of the multivariable model during preliminary analysis. The full process used to assign self-reported race/ethnicity responses to the single synthetic race/ethnicity variable is outlined in Supplemental Digital Content 1 (http://links.lww.com/ALN/C797).

Statistical Analysis

No statistical power calculation was conducted before the study since the sample size was based on available data in our data warehouse. The statistical and data analysis plans were defined before accessing the data and were finalized after the data were accessed, with additional statistical analysis completed after peer review. Patient and case characteristics were compared across self-reported race/ethnicity using one-way ANOVA for continuous variables that met parametric assumptions. Continuous variables that did not meet parametric assumptions, including nonnormal distributions as assessed by histograms, were analyzed using Kruskal–Wallis tests. The chi-square test was utilized for categorical variables. Two-tailed testing was used for all statistical tests. The reference group for race/ethnicity was White; the reference group for sex was female. For ASA Physical Status, ASA Physical Status I and II were grouped together because of the small number of ASA Physical Status I patients (less than 1.5%); this combined ASA Physical Status I and II group was used as the reference.

Generalized estimating equations modeling was utilized to determine if any race/ethnicity was an independent predictor of occult hypoxemia relative to White race/ethnicity within the study Spo_2 range of 92 to 100%. A Poisson regression model with logarithmic link was used because of the low prevalence of occult hypoxemia. Multiple paired Sao_2–Spo_2 readings for each patient were accounted for by clustering within patients using independent working correlation structure; however, sandwich estimators were utilized for standard errors. The model was first run without controlling for confounders in order to assess for significant differences in unadjusted prevalence of occult hypoxemia across race/ethnicity groups. A multivariable model was then created to control for all of the collected demographic, comorbidity, and operative variables. A continuous Spo_2 variable was included as a fixed effect, and an interaction term between Spo_2 and race/ethnicity was also assessed for inclusion. Continuous variables (*e.g.*, Fio_2, tidal volume) were entered directly into the model as covariates, without transformation. The year of procedure was assessed as a categorical variable; 2011 was used as the reference level (since this was the approximate year that the pulse oximeter device type changed). All covariates included were assessed as confounding variables rather than effect modifiers. An additional model focusing on 92 to 96% Spo_2 was created as a supplemental analysis, as this was the range focused on in the analysis of occult hypoxemia from Sjoding *et al.*[16]

As an exploratory analysis, the optimal threshold for predicting occult hypoxemia based on Spo_2 was assessed using the F_1 score. The F_1 score is the harmonic mean of the precision (positive predictive value) and recall (sensitivity), and is a measure of a test's accuracy.[24] It can be used to determine the threshold at which a test has the best performance, particularly in cases where the outcome (in this case, occult hypoxemia) is rare. F_1 scores were calculated using univariate analysis for the range of Spo_2 between 92 to 100%, stratified by race/ethnicity, and then plotted. This allowed for visual identification of the best Spo_2 cutoff to identify occult hypoxemia.

The overall design of the analysis and threshold for statistical significance ($P < 0.05$) were established *a priori*. After reviewing our findings, several *post hoc* sensitivity analyses were performed to further elucidate the relationship between race/ethnicity, occult hypoxemia, and comorbid risk factors.

All statistical analysis was performed in R version 3.5.0 (R Foundation for Statistical Computing).

Results

Readings from 47,067 unique patients were collected, totaling 157,482 Sao_2–Spo_2 pairs. Before data analysis, 17 paired Sao_2–Spo_2 readings were excluded because of missing Sao_2 data, and an additional 28 paired Sao_2–Spo_2 readings were excluded for Sao_2 values greater than 100, deemed to be device error. There were 11,232 paired Sao_2–Spo_2 readings

Table 1. Patient Demographics

	Overall	White	Black	Asian	Hispanic	Other	*P* Value
Paired Sa_{O_2}–Sp_{O_2} readings, No.	151,070	70,722	16,011	8,121	21,223	34,993	
Patients, No.	46,253	22,089	5,177	2,612	6,304	10,071	
Age, yr (mean ± SD)	57 ± 21	61 ± 19	54 ± 19	55 ± 21	52 ± 23	54 ± 22	< 0.001
Male sex	25,226 (54.5%)	12,530 (56.7%)	2,381 (46.0%)	1,526 (58.4%)	3,220 (51.1%)	5,569 (55.3%)	< 0.001
Body mass index, kg/m^2, median [interquartile range]	26 [23–30]	27 [23–30]	27 [23–32]	24 [21–27]	27 [23–31]	26 [22–30]	< 0.001
ASA Physical Status							< 0.001
I	688 (1.5%)	329 (1.5%)	75 (1.4%)	49 (1.9%)	102 (1.6%)	133 (1.3%)	
II	6,603 (14.3%)	3,250 (14.7%)	671 (13.0%)	527 (20.2%)	880 (14.0%)	1,275 (12.7%)	
III	19,892 (43.0%)	10,080 (45.6%)	2,198 (42.5%)	1,219 (46.7%)	2,518 (40.0%)	3,877 (38.5%)	
IV	18,232 (39.4%)	8,168 (37.0%)	2,117 (40.9%)	780 (29.9%)	2,664 (42.3%)	4,503 (44.8%)	
V	818 (1.8%)	258 (1.2%)	115 (2.2%)	37 (1.4%)	136 (2.2%)	272 (2.7%)	
Hypertension	12,469 (27.0%)	5,342 (24.2%)	1,254 (24.2%)	581 (22.2%)	1,784 (28.3%)	3,508 (34.8%)	< 0.001
Congestive heart failure	2,805 (6.1%)	1,280 (5.8%)	312 (6.0%)	89 (3.4%)	362 (5.7%)	762 (7.6%)	< 0.001
Valvular heart disease	4,103 (8.9%)	2,428 (11.0%)	233 (4.5%)	127 (4.9%)	396 (6.3%)	919 (9.1%)	< 0.001
Chronic pulmonary disease	3,134 (6.8%)	1,414 (6.4%)	344 (6.6%)	84 (3.2%)	451 (7.2%)	841 (8.4%)	< 0.001
Diabetes	5,409 (11.7%)	1,762 (8.0%)	583 (11.3%)	296 (11.3%)	975 (15.5%)	1,793 (17.8%)	< 0.001
Renal failure	2,246 (4.9%)	729 (3.3%)	315 (6.1%)	85 (3.3%)	395 (6.3%)	722 (7.2%)	< 0.001
Peripheral vascular disease	2,344 (5.1%)	1,067 (4.8%)	243 (4.7%)	103 (3.9%)	336 (5.3%)	595 (5.9%)	< 0.001
Coronary artery disease	5,353 (11.6%)	2,415 (10.9%)	460 (8.9%)	215 (8.2%)	746 (11.8%)	1,517 (15.1%)	< 0.001
Smoking status							< 0.001
Never	31,756 (77.9%)	14,567 (76.3%)	3,465 (74.6%)	1,957 (86.9%)	4,542 (80.2%)	7,225 (79.4%)	
Current	2,913 (7.1%)	1,189 (6.2%)	511 (11.0%)	106 (4.7%)	406 (7.2%)	701 (7.7%)	
Prior	6,082 (14.9%)	3,331 (17.5%)	666 (14.3%)	190 (8.4%)	716 (12.6%)	1,179 (12.9%)	
Anesthesia type							< 0.001
General	43,061 (93.2%)	20,503 (92.9%)	4,802 (92.8%)	2,473 (94.8%)	5,825 (92.5%)	9,458 (94.0%)	
Monitored anesthesia care	1,506 (3.3%)	781 (3.5%)	119 (2.3%)	34 (1.3%)	196 (3.1%)	376 (3.7%)	
Regional	1,643 (3.6%)	785 (3.6%)	252 (4.9%)	103 (3.9%)	273 (4.3%)	230 (2.3%)	
Volatile anesthetic	32,214 (69.6%)	15,126 (68.5%)	3,737 (72.2%)	1,882 (72.1%)	4,460 (70.7%)	7,009 (69.6%)	< 0.001
Vasoactive infusion used	21,158 (45.7%)	10,415 (47.2%)	1,878 (36.3%)	945 (36.2%)	2,746 (43.6%)	5,174 (51.4%)	< 0.001
Tidal volume, ml (mean ± SD)	460 ± 153	477 ± 146	472 ± 151	440 ± 142	438 ± 163	437 ± 159	< 0.001
F_{IO_2}, %, median [interquartile range]	85 [72–97]	85 [73–97]	84 [73–97]	81 [72–97]	86 [72–97]	85 [71–97]	< 0.001
PEEP, cm H_2O, median [interquartile range]	5 [3–5]	5 [3–5]	5 [3–5]	5 [3–5]	5 [3–5]	5 [3–5]	< 0.001
MAP (mean ± SD)	83 ± 17	83 ± 16	85 ± 18	83 ± 16	82 ± 17	82 ± 17	< 0.001
Hematocrit (mean ± SD)	33 ± 6	33 ± 6	33 ± 6	34 ± 6	33 ± 7	33 ± 7	< 0.001
Year of procedure							< 0.001
2008	2,905 (6.3%)	1,574 (7.1%)	372 (7.2%)	157 (6.0%)	468 (7.4%)	334 (3.3%)	
2009	3,692 (8.0%)	1,930 (8.7%)	528 (10.2%)	230 (8.8%)	547 (8.7%)	457 (4.5%)	
2010	3,889 (8.4%)	1,967 (8.9%)	578 (11.2%)	267 (10.2%)	587 (9.3%)	490 (4.9%)	
2011	4,184 (9.0%)	2,137 (9.7%)	548 (10.6%)	284 (10.9%)	635 (10.1%)	580 (5.8%)	
2012	4,673 (10.1%)	2,313 (10.5%)	641 (12.4%)	272 (10.4%)	627 (9.9%)	820 (8.1%)	
2013	4,875 (10.5%)	2,381 (10.8%)	689 (13.3%)	329 (12.6%)	626 (9.9%)	850 (8.4%)	
2014	4,481 (9.7%)	2,036 (9.2%)	544 (10.5%)	288 (11.0%)	540 (8.6%)	1,073 (10.7%)	
2015	5,256 (11.4%)	2,169 (9.8%)	676 (13.1%)	308 (11.8%)	609 (9.7%)	1,494 (14.8%)	
2016	3,071 (6.6%)	1,333 (6.0%)	188 (3.6%)	53 (2.0%)	346 (5.5%)	1,151 (11.4%)	
2017	3,553 (7.7%)	1,690 (7.7%)	265 (5.1%)	152 (5.8%)	466 (7.4%)	980 (9.7%)	
2018	3,099 (6.7%)	1,354 (6.1%)	88 (1.7%)	135 (5.2%)	513 (8.1%)	1,009 (10.0%)	
2019	2,575 (5.6%)	1,205 (5.5%)	60 (1.2%)	137 (5.2%)	340 (5.4%)	833 (8.3%)	

Data are n (%) unless otherwise noted.

ASA, American Society of Anesthesiologists; F_{IO_2}, fraction of inspired oxygen; PEEP, positive end-expiratory pressure; Sa_{O_2}, arterial oxygen saturation; Sp_{O_2}, oxygen saturation measured by pulse oximetry.

for patients whose race was recorded as "Unknown," who were grouped into the Other race/ethnicity group. We then isolated paired Sa_{O_2}–Sp_{O_2} readings to the Sp_{O_2} 92 to 100% range, which left a total of 151,070 paired Sa_{O_2}–Sp_{O_2} readings for 46,253 unique patients. Demographics for the cohort for data analysis are listed in table 1. The most represented race/ethnicity groups by number of unique patients were White (22,089 of 46,253 [47.8%]), Other (10,071 of 46,253 [21.8%]), Hispanic (6,304 of 46,253 [13.6%]), and Black (5,177/46,253 [11.2%]). The White cohort was older (61 *vs.* 52 to 54 yr) than the non-White groups on average, and had a greater proportion of male sex (12,530 of 22,089 [56.7%]) compared to the Black (2,381 of 5,177 [46%]) and Hispanic (3,220 of 6,304 [51.1%]) cohorts. The proportions

of male sex in the Asian (1,526 of 2,612 [58.4%]) and Other (5,569 of 10,071 [55.3%]) cohorts were similar to the White cohort. The Black, Hispanic, and Other cohorts had greater proportions of ASA Physical Status IV and V, diabetes, and renal failure compared with the White and Asian cohorts. Rates of congestive heart failure, hypertension, and chronic pulmonary disease were similar between the White, Black, and Hispanic cohorts, greater in the Other cohort, and lesser in the Asian cohort. Rates of general anesthesia were high across all groups, with few study patients having received monitored anesthesia care or regional anesthesia. The median Spo_2 was 100% (interquartile range, 99 to 100) and median calculated Sao_2 was 100% (interquartile range, 100 to 100) for the overall cohort as well as for each race/ethnicity group.

Prevalence of Occult Hypoxemia and Spo_2 Device Bias by Self-reported Race/Ethnicity (Univariate Analysis)

The prevalence of occult hypoxemia in the Spo_2 study range for each self-reported race/ethnicity group is listed in table 2 and illustrated in figure 1. Overall, occult hypoxemia was present in 1.3% (2,016 of 151,070) of paired Sao_2–Spo_2 readings. The prevalence of occult hypoxemia in Black patients was 2.1% (339 of 16,011 paired Sao_2–Spo_2 readings) *versus* 1.1% (791 of 70,722 paired Sao_2–Spo_2 readings) in White patients ($P < 0.001$). Hispanic patients also had a significantly greater prevalence of 1.8% (383 of 21,223 paired Sao_2–Spo_2 readings; $P < 0.001$). Asian and Other race/ethnicity had a similar prevalence to White race.

The overall Spo_2 device bias was $0.0 \pm 6.8\%$ (mean ± SD). White race/ethnicity was the only group that demonstrated a negative Spo_2 device bias ($-0.2 \pm 6.3\%$). Positive Spo_2 device bias was observed for Black ($0.6 \pm 9.1\%$), Hispanic ($0.5 \pm 7.9\%$), Asian ($0.2 \pm 6.5\%$), and Other ($0.1 \pm 5.9\%$) patients.

Multivariable Analysis Results

Factors associated with occult hypoxemia in the multivariable analysis for the Spo_2 study range are shown in table 3. Black (odds ratio, 1.44 [95% CI, 1.11 to 1.87]; $P = 0.006$) and Hispanic (odds ratio, 1.31 [95% CI, 1.03 to 1.68]; $P = 0.031$) race/ethnicity were associated with significantly greater odds of occult hypoxemia relative to White race/ethnicity. Higher Spo_2 was associated with decreased risk of occult hypoxemia (odds ratio, 0.71 [95% CI, 0.69 to 0.73]; $P < 0.001$). The overall interaction term between race/ethnicity and Spo_2 was not significant ($P = 0.948$) and was thus not included in the final model. ASA Physical Status V was an independent risk factor for occult hypoxemia (odds ratio, 1.83 [95% CI, 1.16 to 2.88]; $P = 0.009$). Higher PEEP (odds ratio, 1.10 [95% CI, 1.06 to 1.13]; $P < 0.001$) and higher hematocrit (odds ratio, 1.05 [95% CI, 1.03 to 1.06]; $P < 0.001$) were also associated with a significantly greater risk of occult hypoxemia. In contrast, higher tidal volume (odds ratio, 0.80, [95% CI, 0.75 to 0.84]; $P < 0.001$) and higher MAP (odds ratio, 0.89 [95% CI, 0.84 to 0.95]; $P < 0.001$) were associated with significantly lower risk of occult hypoxemia. Older age was associated with lower odds of occult hypoxemia (odds ratio, 0.94 [95% CI, 0.89 to 0.99]; $P = 0.012$). A more recent year of procedure (2015 to 2019) was also associated with decreased odds of occult hypoxemia compared with the reference year (2011; table 3).

Several *post hoc* sensitivity analyses were performed based on the results of the multivariable analysis. Specifically, because of the strong association between ASA Physical Status V and occult hypoxemia, as well as the greater proportion of ASA Physical Status V patients in the Black, Hispanic, and Other groups, multivariable analyses were repeated while excluding ASA Physical Status V patients. The association between Black (odds ratio, 1.40 [95% CI, 1.08 to 1.82]; $P = 0.011$) and Hispanic (odds ratio, 1.29 [95% CI 1.01 to 1.64]; $P = 0.039$) race/ethnicity and occult hypoxemia was still significant with comparable odds ratios. Full results of this sensitivity analysis are shown in Supplemental Digital Content 2 (http://links.lww.com/ALN/C797). We also performed a sensitivity analysis limited to the 92 to 96% Spo_2 range, as per Sjoding *et al.*[16] Results were consistent with our primary analysis. Black race/ethnicity was significantly associated with occult hypoxemia (odds ratio, 1.80 [95% CI, 1.10 to 2.94]; $P = 0.020$) *versus* White race/ethnicity, with a greater odds ratio than in the full 92 to 100% Spo_2 model. The association

Table 2. Prevalence of Occult Hypoxemia* Stratified by Self-reported Race/Ethnicity (Univariate Analysis)

Race/Ethnicity	Number of Paired Sao_2–Spo_2 Readings	Prevalence of Occult Hypoxemia (Paired Readings)	Patients, No.	Prevalence of Occult Hypoxemia (Number of Patients)	*P* Value†
Overall	151,070	2,016 (1.3%)	46,253	1,855 (4.0%)	—
White‡	70,722	791 (1.1%)	22,089	731 (3.3%)	—
Black	16,011	339 (2.1%)	5,177	319 (6.2%)	< 0.001
Asian	8,121	92 (1.1%)	2,612	85 (3.3%)	0.865
Hispanic	21,223	383 (1.8%)	6,304	348 (5.5%)	< 0.001
Other	34,993	411 (1.2%)	10,071	372 (3.7%)	0.594

*Occult hypoxemia is defined as Sao_2 at less than 88% despite Spo_2 being greater than 92%. †*P* value calculated for paired readings using generalized estimating equations modeling (with clustering within patients) without controlling for confounders. ‡Reference group.

Sao_2, arterial oxygen saturation; Spo_2, oxygen saturation measured by pulse oximetry.

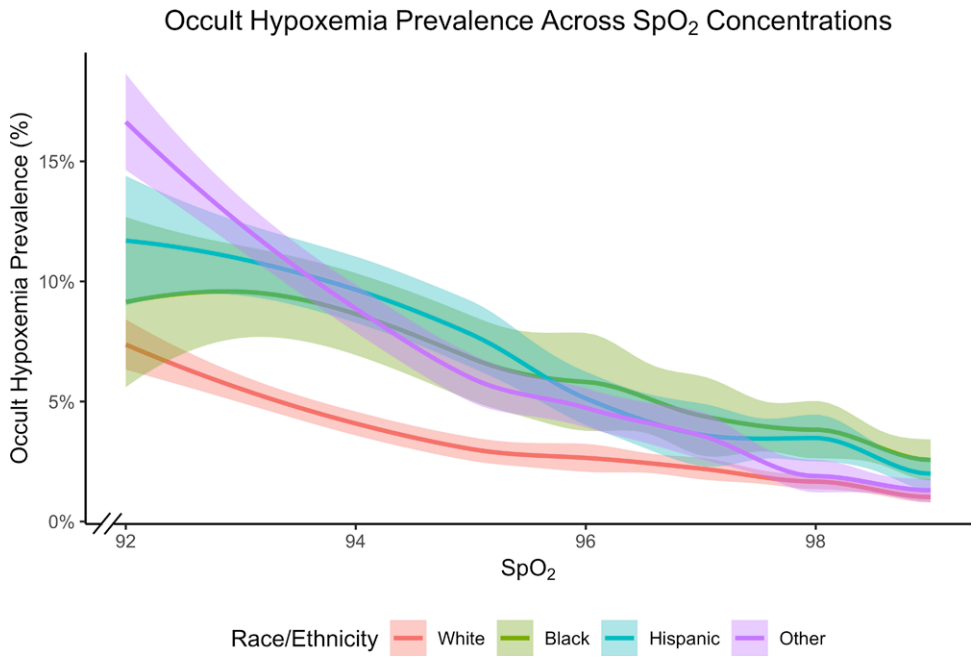

Fig. 1. Prevalence of occult hypoxemia (arterial oxygen saturation at less than 88% despite oxygen saturation measured by pulse oximetry [Spo_2] being greater than 92%) by self-reported race/ethnicity between mean Spo_2 values of 92 to 100%. The curve was generated using the locally weighted scatterplot smoothing method with 50% smoothing to predict the hypoxemia prevalence at a given Spo_2 value. Each prediction is derived from fitting a locally linear regression from the neighboring 50% data points. The shading represents the 95% CI of the locally weighted scatterplot smoothing curve.

of occult hypoxemia in Hispanic patients no longer reached significance using the Spo_2 range of 92 to 96% (odds ratio, 1.46 [95% CI, 0.95 to 2.25]; $P = 0.082$). The full results of this analysis can be found in Supplemental Digital Content 3 (http://links.lww.com/ALN/C797).

Identification of Optimal Spo_2 Threshold for Predicting Occult Hypoxemia (Univariate Analysis)

The F_1 score was calculated for White, Black, and Hispanic patients. F_1 scores for Asian and Other race/ethnicity were not calculated given the lack of significant difference in occult hypoxemia prevalence relative to the White reference group. Supplemental Digital Content 4 (http://links.lww.com/ALN/C797) includes a figure with graphic representation of the calculated F_1 scores. The peak F_1 score for White patients was at Spo_2 94% (F_1 score, 0.08), meaning that Spo_2 values less than 94% were most associated with occult hypoxemia. The F_1 score for Black race/ethnicity peaked at 96% (F_1 score, 0.11). The peak F_1 score was at 95% for Hispanic race/ethnicity (F_1 score, 0.13).

Discussion

In this large, retrospective, single-center analysis, we found that self-reported Black race/ethnicity (339 of 16,011 paired Sao_2–Spo_2 readings [2.1%]; odds ratio, 1.44 [95% CI, 1.11 to 1.87]) and Hispanic race/ethnicity (383 of 21,223 paired Sao_2–Spo_2 readings [1.8%]; odds ratio, 1.31 [95% CI, 1.03 to 1.68]) were significantly associated with occult hypoxemia in the 92 to 100% Spo_2 range compared with White race/ethnicity (791 of 70,222 paired Sao_2–Spo_2 readings [1.1%]). The interaction between Spo_2 and race/ethnicity was not significant, supporting our finding that race/ethnicity is associated with occult hypoxemia independent of Spo_2. These findings are consistent with recent descriptions of occult hypoxemia in the critical care population,[16] but contrary to previous studies suggesting racial discrepancies exist at Spo_2 values less than 80% and are minimal at more commonly encountered Spo_2 values.[14,15] The sensitivity analysis of the 92 to 96% Spo_2 range ([Black race/ethnicity] odds ratio, 1.80 [95% CI, 1.10 to 2.94]) is consistent with the findings of Sjoding *et al.* The lack of statistical significance of Hispanic race/ethnicity *versus* White race/ethnicity in the 92 to 96% analysis is likely attributed to underpowered analyses.

Patients with ASA Physical Status V also demonstrated a significant association with occult hypoxemia (odds ratio, 1.83 [95% CI, 1.16 to 2.88]) across all race/ethnicity groups, potentially because of derangements in physiology or therapeutic interventions associated with patients of ASA Physical Status V. Although a larger percentage of ASA

Table 3. Factors Associated with Occult Hypoxemia*

Perioperative Variable	Odds Ratio	95% CI	*P* Value
Race/ethnicity			
White†	—	—	—
Black	1.44	1.11–1.87	0.006
Asian	0.77	0.51–1.17	0.223
Hispanic	1.31	1.03–1.68	0.031
Other	1.24	1.00–1.53	0.052
Spo_2	0.71	0.69–0.73	< 0.001
ASA Physical Status			
I–II†	—	—	—
III	0.74	0.55–1.01	0.056
IV	1.00	0.74–1.35	0.996
V	1.83	1.16–2.88	0.009
Age, yr‡	0.94	0.89–0.99	0.012
Body mass index, kg/m²‡	0.97	0.91–01.03	0.332
Sex			
Female†	—	—	—
Male	0.89	0.75–1.06	0.189
Fio_2, %‡	0.99	0.95–1.03	0.644
Tidal volume, ml‡	0.80	0.75–0.84	< 0.001
PEEP, cm H_2O‡	1.10	1.06–1.13	< 0.001
MAP, mmHg‡	0.89	0.84–0.95	< 0.001
Hematocrit‡	1.05	1.03–1.06	< 0.001
Volatile anesthetic use	0.87	0.69–1.10	0.248
Vasoactive infusion use	1.08	0.89–1.30	0.445
Diabetes	0.99	0.72–1.35	0.931
Peripheral vascular disease	0.89	0.56–1.41	0.624
Hypertension	0.78	0.59–1.04	0.090
Congestive heart failure	1.29	0.94–1.78	0.118
Chronic pulmonary disease	1.01	0.68–1.51	0.960
Smoking status			
Never†	—	—	—
Current	1.06	0.75–1.50	0.742
Prior	0.88	0.68–1.15	0.343
$ETco_2$‡	0.99	0.98–1.01	0.352
Renal failure	1.14	0.69–1.88	0.611
Year of procedure			
2008	0.97	0.62–1.50	0.877
2009	0.80	0.53–1.21	0.290
2010	0.48	0.31–0.75	0.001
2011†	—	—	—
2012	1.01	0.74–1.36	0.960
2013	0.85	0.62–1.16	0.306
2014	0.76	0.54–1.06	0.106
2015	0.55	0.39–0.78	0.001
2016	0.57	0.38–0.86	0.007
2017	0.58	0.40–0.86	0.006
2018	0.54	0.35–0.86	0.009
2019	0.50	0.30–0.83	0.008

*Occult hypoxemia is defined as Sao_2% at less than 88% despite Spo_2 being greater than 92%. †Reference group. ‡For continuous variables, the odds ratio is calculated per 1-unit increase. Scaled continuous variables were used as follows: age, per 10 yr; body mass index, per 5 kg/m²; Fio_2, per 10%; tidal volume, per 100 ml; and MAP, per 10 mmHg.

ASA, American Society of Anesthesiologists; $ETco_2$, end-tidal carbon dioxide; Fio_2, fraction of inspired oxygen; MAP, mean arterial pressure; PEEP, positive end-expiratory pressure; Sao_2, arterial oxygen saturation; Spo_2, oxygen saturation measured by pulse oximetry.

Physical Status V patients were in the Black and Hispanic groups, sensitivity analyses demonstrated this relationship remained significant with the exclusion of ASA Physical Status V patients in both Black (odds ratio, 1.40 [95% CI, 1.08 to 1.82]) and Hispanic (odds ratio, 1.29 [95% CI, 1.01 to 1.64]) groups.

Surprisingly, neither the use of vasoactive infusions nor the diagnoses of peripheral vascular disease or diabetes were associated with occult hypoxemia despite previous literature indicating an association.[25–27] Sjoding *et al.* excluded diabetic patients from their analysis, so there is no recent and direct comparison to our study available.[16] The associations between age, ventilatory parameters, MAP, and hematocrit with occult hypoxemia were all statistically significant; however, associations were hard to interpret clinically since the magnitude of the effect size was generally very small and often in a contradictory direction (*e.g.*, higher PEEP appeared to be associated with more occult hypoxemia; table 3). Further evaluation of the impact of these covariates is required across all populations and is beyond the scope of this work. There is no clear explanation as to why year was significantly associated with occult hypoxemia, as it does not correspond to the change in pulse oximeter manufacturers in 2011.

Despite our primary findings, the overall Spo_2 device bias in White patients compared to non-White patients was not as striking on univariate analysis, with a difference of less than 1.0% across all groups. The pulse oximeter slightly underestimated Sao_2 in White patients and slightly overestimated Sao_2 in non-White patients. It is likely that Spo_2 device bias does not occur in all non-White patients, which may explain the discrepancy between the increased prevalence of occult hypoxemia in the Black and Hispanic self-reported populations, but more similar prevalence of overall Spo_2 device bias. This discrepancy may be attributed to the wide range of skin pigmentations in patients who self-identify as Black and Hispanic, including multiracial individuals who self-identify as Black or Hispanic because of historical racial integrity laws.[28,29]

As shown in our primary analysis, lower Spo_2 (evaluated as a continuous variable) is significantly associated with a increased risk of occult hypoxemia. The univariate F_1 scores presented in Supplemental Digital Content 4 (http://links.lww.com/ALN/C797) were calculated to explore if there are optimal Spo_2 thresholds for predicting occult hypoxemia. Based on our findings, it may be prudent to have a greater index of suspicion for occult hypoxemia if Spo_2 is less than 96% for Black patients and 95% for Hispanic patients (compared with 94% for White patients). The magnitude of the F_1 scores was not high regardless of race/ethnicity (range, 0.08 to 0.16), indicating the ability of Spo_2 in the 92 to 100% range to reflect hypoxemia is low. This is not surprising since the overall prevalence of hypoxemia in that range is very low and occult hypoxemia is an unexpected event. Thus, the difference in peak F_1 scores between each race/ethnicity should not be overinterpreted.

Limitations of this study are important to consider, given the potential clinical impact of our findings. The retrospective nature of the study contributes to several

limitations including lack of specific self-reported race/ethnicity (hence, the Other race/ethnicity group) for a large portion of our sample and the use of two different manufacturers' pulse oximeters during the study period, as well as other unknown patient-specific confounding factors such as jaundice, presence of nail polish, skin thickness, probe placement, and probe location. The large sample size of this study likely limits the impact of most individual patient factors, but the overall small number of patients found to have occult hypoxemia should be considered a limitation. Additionally, the contribution of each race/ethnicity to the overall number of paired Sao_2–Spo_2 readings compared with the number of patients is slightly different, which potentially indicates selection bias due to repeated values for the same individual. However, this risk for selection bias is limited because of the very small differences in these populations (table 1). To help account for differences in the number of paired Sao_2–Spo_2 readings per patient, we utilized a generalized estimating equations model with clustering within patients. Additionally, we must recognize our use of "race/ethnicity" is a surrogate measurement for skin pigmentation. There is likely wide variation in skin pigmentation among the races/ethnicities represented in our data that cannot be addressed given the retrospective nature of the study.

The variety of pulse oximeters used at our institution during the study period (primarily Nellcor before 2011; Masimo thereafter) was controlled for using the year of procedure as a covariate in the multivariable analysis—although this is an imperfect proxy. It is possible that pulse oximeters from other manufacturers have better or worse performance with differing skin pigmentations, thus limiting the generalizability of our study. Additionally, unknown concentrations of carboxyhemoglobin may exist in this population, but we believe this risk is mitigated by demonstrating a lack of association between smoking status and occult hypoxemia in the multivariable model, as well as the fact that patients suffering from thermal injury are not cared for at our institution. The risk of carboxyhemoglobinemia is also likely mitigated given our institution's adherence to Anesthesia Patient Safety Foundation (Rochester, Minnesota) guidelines on the use of modern carbon dioxide absorbents.[30] Calculated—rather than measured—Sao_2 presents a potential limitation and may limit comparisons to the Sjoding *et al.* study in which cooximetry was used to directly measure Sao_2.

Despite this, previous studies evaluating the ABG analyzer used during the duration of the study demonstrate accuracy of the Sao_2 calculation.[31,32] Body temperature could potentially affect pulse oximetry data and has not been included as a covariate, which must be recognized as a limitation of this study. The clinical indication for ABG sampling is also unknown given the retrospective nature of this study. Finally, anesthesia type may affect our findings: because of the low sample size of the regional anesthesia and monitored anesthesia care cases compared with general anesthesia cases, our model was unable to adjust for anesthesia type as a covariate.

In conclusion, we have found evidence that Black and Hispanic race/ethnicity are significantly associated with occult hypoxemia in the 92 to 100% Spo_2 range in anesthetized patients. Although the lack of objective skin pigmentation information and the retrospective nature of this study may limit the strength of our findings, we believe it is important to recognize the limitations of monitoring devices and maintain vigilance to avoid unrecognized hypoxemia.

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Competing Interests

The authors declare no competing interests.

Correspondence

Address correspondence to Dr. Burnett: 1 Gustave Levy Place, Klingenstein Clinical Center 8th Floor, Box 411, New York, New York 10029. garrett.burnett@mountsinai.org. This article may be accessed for personal use at no charge through the Journal Web site, www.anesthesiology.org.

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