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ORIGINAL RESEARCH

CRITICAL CARE CARDIOLOGY

Racial and Ethnic Variation in ECMO Utilization and Outcomes in Pediatric Cardiac ICU Patients

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ABSTRACT

BACKGROUND Previous studies have reported racial disparities in extracorporeal membrane oxygenation (ECMO) utilization in pediatric cardiac patients.

OBJECTIVES The objective of this study was to determine if there was racial/ethnic variation in ECMO utilization and, if so, whether mortality was mediated by differences in ECMO utilization.

METHODS This is a multicenter, retrospective cohort study of the Pediatric Cardiac Critical Care Consortium clinical registry. Analyses were stratified by hospitalization type (medical vs surgical). Logistic regression models were adjusted for confounders and evaluated the association between race/ethnicity with ECMO utilization and mortality. Secondary analyses explored interactions between race/ethnicity, insurance, and socioeconomic status with ECMO utilization and mortality.

RESULTS A total of 50,552 hospitalizations from 34 hospitals were studied. Across all hospitalizations, 2.9% (N = 1,467) included ECMO. In medical and surgical hospitalizations, Black race and Hispanic ethnicity were associated with severity of illness proxies. In medical hospitalizations, race/ethnicity was not associated with the odds of ECMO utilization. Hospitalizations of other race had higher odds of mortality (adjusted odds ratio [aOR]: 1.61; 95% CI: 1.22-2.12; $P = 0.001$). For surgical hospitalizations, Black (aOR: 1.24; 95% CI: 1.02-1.50; $P = 0.03$) and other race (aOR: 1.50; 95% CI: 1.17-1.93; $P = 0.001$) were associated with higher odds of ECMO utilization. Hospitalizations of Hispanic patients had higher odds of mortality (aOR: 1.31; 95% CI: 1.03-1.68; $P = 0.03$). No significant interactions were demonstrated between race/ethnicity and socioeconomic status indicators with ECMO utilization or mortality.

CONCLUSIONS Black and other races were associated with increased ECMO utilization during surgical hospitalizations. There were racial/ethnic disparities in outcomes not explained by differences in ECMO utilization. Efforts to mitigate these important disparities should include other aspects of care. (JACC Adv 2023;2:100634) © 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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ABBREVIATIONS AND ACRONYMS

ACS = American Community Survey

aOR = adjusted odds ratio

CICU = cardiac intensive care unit

CPB = cardiopulmonary bypass

DHCA = deep hypothermic circulatory arrest

ECMO = extracorporeal membrane oxygenation

ECPR = extracorporeal cardiopulmonary resuscitation

IQR = interquartile range

PC4 = Pediatric Cardiac Critical Care Consortium

PICU = pediatric intensive care unit

SES = socioeconomic status

SOI = severity of illness

VIS = vasoactive-inotropic score

Extracorporeal membrane oxygenation (ECMO) is the most common form of mechanical circulatory support for children with congenital and acquired heart disease, used in 4.1% of surgical cardiac admissions and 2.4% of medical cardiac admissions in the United States.[1] ECMO provides a vital opportunity to identify residual lesions and to support end organs, while the heart recovers. Timely and appropriate ECMO utilization is vital to achieving optimal outcomes in this vulnerable population.

In the past several years, disparities in both health services and outcomes have been described in pediatric cardiac patients.[2-7] In contrast, studies of critically ill children in the pediatric intensive care unit (PICU) that adjusted for severity of illness (SOI) have not demonstrated differences in care processes and outcomes based on race or ethnicity.[8,9] A critical factor in addressing disparities is identifying modifiable aspects of care. A recent study, using administrative data from the Pediatric Health Information Systems database, demonstrated associations between Black race, patients of other race, and public insurance with increased odds of postcardiac surgical mortality and attributed this association to increased likelihood of dying without ECMO support.[10] If this observation is correct, ECMO access could be a powerful lever to improve outcomes in racial and ethnic minorities. An inherent limitation of administrative databases is unmeasured confounding with limited clinical details that are imperative for accurate risk adjustment.

We sought to overcome the above limitations by leveraging the clinical data available in the Pediatric Cardiac Critical Care Consortium (PC^4) registry to perform a multicenter cohort study to determine whether race and ethnicity influence ECMO utilization in surgical and medical cardiac patients after adjusting for measurable confounders. We also sought to explore whether race and ethnicity were associated with in-hospital mortality and whether this was mediated by ECMO utilization.

METHODS

DATA SOURCE. The PC^4 data registry collects data on patients with cardiac disease admitted to the cardiac intensive care unit (CICU) of participating hospitals. At the time of this analysis, 34 hospitals were submitting cases to the registry. Each participating center has a trained data manager who has completed a certification examination and collects and enters data in accordance with the standardized PC^4 Data Definitions Manual.[11] Participating centers are audited on a regular schedule and audit results suggest complete, accurate, and timely submission of data.[12,13] The University of Michigan Institutional Review Board provides oversight for the PC^4 Data Coordinating Center; this study was approved with waiver of informed consent. This study was also reviewed by the Institutional Review Board at Children's Hospital of Philadelphia and deemed not human subjects' research. Due to the individual data-use agreements of PC^4 member institutions, patient identifiers were not shared. Data were provided by PC^4 with assistance from their Data Coordinating Center. Statistical

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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analyses were performed by the Children's Hospital of Philadelphia Cardiac Center Clinical Research Core.

STUDY POPULATION. All consecutive medical and surgical CICU admissions at participating hospitals from 1 August 2014 to 31 January 2019 were studied. A subject could have multiple hospitalizations during the study period, and each hospitalization could include multiple CICU encounters. Surgical and medical hospitalizations were considered separately because the clinical scenarios, including risk factors associated with ECMO, and outcomes are qualitatively different. Hospitalizations were defined as surgical if they included a Society of Thoracic Surgeons-defined cardiothoracic surgical procedure with or without cardiopulmonary bypass during the hospitalization. Surgical data from the index procedure were included. The remaining CICU hospitalizations were considered medical hospitalizations. Hospitalizations were excluded if the patient was admitted to a CICU without a diagnosis of heart disease (eg, noncardiac patient on ECMO for acute respiratory distress syndrome). Hospitalizations including multiple ECMO runs were analyzed with data from the first ECMO run. If a subject had more than one hospitalization where he/she received ECMO support, the first hospitalization was included and subsequent hospitalizations were excluded. Hospitalizations were excluded if ECMO was initiated at a referring hospital prior to CICU admission since patient data prior to ECMO cannulation were not available. For surgical subjects, recipients of preoperative ECMO were excluded since they had a probability of receiving postoperative ECMO qualitatively different from other surgical patients. ECMO initiated in the operating room during the index procedure or anytime thereafter was included. Patients with missing demographic, clinical data, or outcomes were excluded (<5% of the total sample).

STUDY MEASURES. All variables included in this analysis are defined in the PC[4] Data Definitions Manual. The primary exposure was race and ethnicity as reported by the patient or family, which were combined to form the following categories: Hispanic; non-Hispanic Black race; non-Hispanic White race; Asian race; other race/ethnicity which included Native American, Pacific Islander, and multirace; and unknown race/ethnicity. The primary outcome of interest was receipt of ECMO support. Data collected included demographics, noncardiac comorbid conditions, and pre-ECMO status, such as use of mechanical ventilation and vasoactive medications, for each hospitalization.

The indication for ECMO was recorded to provide context. We combined the indications of low cardiac output syndrome, ventricular dysfunction, and cardiac failure to create a composite category of systemic circulatory failure. If the patient was placed on ECMO during active cardiopulmonary resuscitation (ECPR), this was designated as the indication regardless of the underlying etiology leading to cardiopulmonary arrest.

The secondary outcome measured was in-hospital mortality. The major and minor complications reported as tertiary outcomes are listed in Supplemental Table 2. Complications were included if they occurred during or after the first ECMO run of a hospitalization.

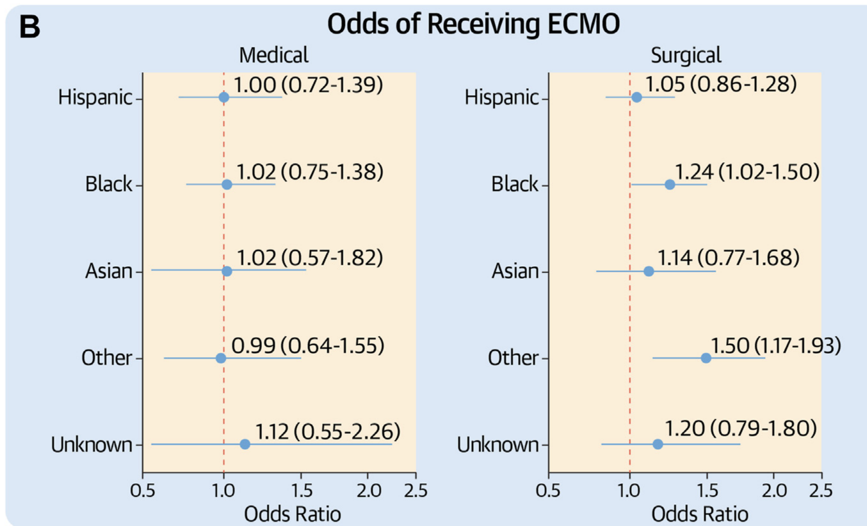
Age categories were defined as follows: preterm neonate, <30 days old and <37 weeks' gestation; full-term neonate, <30 days old and ≥37 weeks' gestation; infant, 30 days up to 1 year; child, 1 year up to 18 years; adult, >18 years. Weight categories were created based on body mass index percentiles as previously described.[14] Surgical complexity was characterized using Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery mortality categories.[15] For medical hospitalization indications, we created a composite "heart failure" category consisting of cardiomyopathy, myocarditis, acute decompensated, or chronic heart failure regardless of underlying structural cardiac diagnosis. Vasoactive-inotropic score (VIS) was calculated as previously described.[16,17] For analysis, the VIS within 2 hours of admission to the CICU for medical admissions and within 2 hours of admission from the operating room for surgical admissions was used. For VIS at the time of surgery, the VIS was categorized as 0 or >0, that is, on vasoactive medications entering the operating room or not. Preoperative high-risk factors included any of the following before the index operation: cardiopulmonary resuscitation, shock at the time of surgery, hepatic dysfunction, neurologic injury within 48 hours prior to surgery, or renal failure requiring dialysis. We created the composite "neurologic injury" category for cerebrovascular accident or intracranial hemorrhage grade >2. For the postoperative variables of mechanical ventilation and arrhythmia, these were assessed as present or absent 2 hours after CICU admission from the operating room.

We also sought to measure socioeconomic status (SES) as another potential factor influencing ECMO utilization or outcomes independently or in concert with race and ethnicity. Since there was no direct way to measure patient SES, we used the characteristics of the patient's home zip code as a proxy. Patient home zip code at the time of CICU admission, when available, was linked to measures of SES from the 5-year American Community Survey (ACS) based on

CENTRAL ILLUSTRATION Racial and Ethnic Variation in ECMO Utilization in Pediatric Cardiac ICU Patients

A

- Multicenter, retrospective cohort study of extracorporeal membrane oxygenation (ECMO) utilization in pediatric cardiac patients using the Pediatric Cardiac Critical Care Consortium clinical registry
- Analyses stratified by medical vs surgical hospitalization type
- 50,552 hospitalizations at 34 hospitals
- 2.9% of hospitalizations included ECMO



C **RESULTS**

- No group had lower odds of ECMO utilization
- Black and Other race were associated with higher odds of ECMO utilization during pediatric cardiac surgical hospitalizations

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(A) Study population. (B) Forest plot of ECMO utilization in pediatric cardiac patients across racial and ethnic groups by surgical or medical hospitalization type. (C) Summary points. Data presented as odds ratios (circles) with 95% CIs (horizontal line). Referent is white race. Footnotes: Covariates adjusted for: race/ethnicity category, insurance type, sex, age category, weight category, unplanned initial CICU admission, extracardiac anomaly, chromosomal anomaly or syndrome. Additional covariates in medical cohort: transplant rejection, pulmonary hypertension, acute or chronic heart failure, mechanical ventilation within 2 hours of CICU admission, VIS within 2 hours of CICU admission. Additional covariates in surgical cohort: pre-operative high-risk factors present, VIS at time of surgery, STAT category, presence of cardiopulmonary bypass, mechanical ventilation at time of admission from operating room. CICU = cardiac intensive care unit; STAT = STS-European Association for Cardio-Thoracic Surgery; VIS = vasoactive-inotropic score.

hospital admission year (admissions during 2018 and 2019 were linked to 2017 ACS data based on availability at the time of data receipt).[18] SES measures were percent of adults with a high school degree or less, median household income, percent unemployed, and percent of residents with income below 150% of the poverty line. An SES index was created by dichotomizing each ACS variable to yes (1) if the hospitalization zip code variable was in the most favorable quartile (top 25th percentile for median household income, bottom 25th percentile for high school degree or less, percent unemployment, and percent below poverty level); no (0) if not.[19] The 4 dichotomized variables were summed to form an index ranging from 0 to 4, with 4 indicating all 4 ACS variables were in the most preferable quartile.

STATISTICAL ANALYSIS. Hospitalization was the primary unit of analysis, with analyses stratified by hospitalization type (medical or surgical). Patient demographic and clinical characteristics, primary indication of the first ECMO run, complications, outcomes, and SES characteristics are presented stratified by race and ethnicity groups using count/percentage of total for categorical variables and median (IQR) for continuous variables. Comparisons between baseline characteristics among race and ethnicity groups were performed using chi-square, Fisher exact, and Kruskal-Wallis tests.

The primary aim of the study was to evaluate the association between race and ethnicity and ECMO utilization. The unadjusted likelihood of receiving ECMO by race and ethnicity was measured by chi-square test. Adjustment for measurable confounders was performed by calculating mixed-effects multivariable logistic regression models. Covariates included as fixed effects are listed in the Central Illustration and were included based on clinical suspicion and inclusion in previous studies.[1,20-22] A random intercept for hospital was included to account for within hospital clustering of each outcome.

All analyses were performed separately for surgical and medical hospitalizations.

Secondary analyses were performed to determine: 1) whether the risk of in-hospital mortality was associated with race and ethnicity; and 2) whether those associations were mediated by differential ECMO utilization. For the former, multivariable models were calculated for the secondary outcome along with ECMO utilization as listed in Figure 2. For the latter, a propensity score for receipt of ECMO was calculated and a propensity-score adjusted model was calculated for mortality. This approach was taken as a supplement to multivariable analyses, in that the propensity score reduces the potential bias in the treatment estimates (ECMO) in nonrandomized studies. Confounders are reduced into a single dimension via the propensity score that balances between non-ECMO and ECMO hospitalization groups. The propensity score was created via logistic regression with ECMO as the outcome and demographic and clinical characteristics as covariates (omitting race and ethnicity and insurance status). From this model, each hospitalization is assigned a propensity score for ECMO utilization, which is the probability of ECMO utilization conditional on demographic and clinical characteristics. This score was included in the mortality model, along with race and ethnicity and insurance status. If the odds of mortality were influenced by ECMO access, inclusion of this measure of propensity to receive ECMO should result in significant changes in the measured associations. If no change is seen in the associations, it suggests that ECMO access does not influence the odds of outcome.

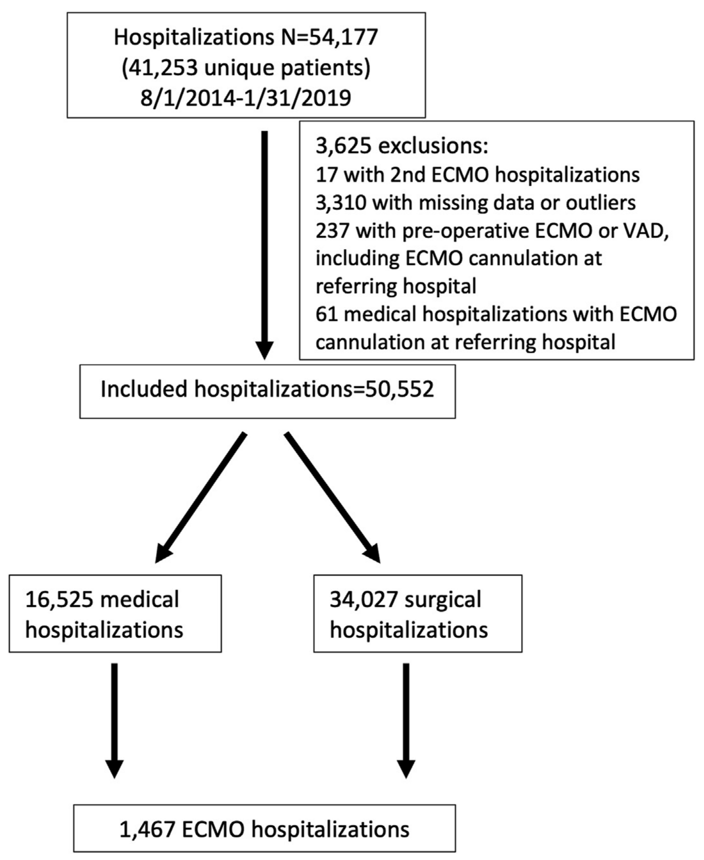
To explore another secondary aim of the study, the degree to which the associations between race and ethnicity, ECMO utilization, and mortality were influenced by SES, 2 additional sets of models were explored: an interaction of race and ethnicity and insurance status and an interaction of race and ethnicity and SES index. Due to the small sample size when interacting race and ethnicity and SES index, only Hispanic, non-Hispanic White, and non-Hispanic Black categories were included for these models. Interaction terms were assessed via Wald tests.

To avoid bias, for each model, identified covariates were included without a bivariable screen and no additional refinements were made to models. ORs and 95% CIs are reported. Analyses were conducted in STATA version 16.1 and SAS version 9.4.

RESULTS

STUDY POPULATION. There were 54,177 eligible hospitalizations from 34 hospitals (Figure 1). A total of 3,625 hospitalizations were excluded, mostly for missing data. There were 167 (0.5%) surgical hospitalizations excluded for preoperative ECMO runs. Seventeen hospitalizations were excluded for a patient having >1 hospitalization with an ECMO run. Of the 50,552 included hospitalizations, 34,027 (67.3%) were surgical hospitalizations. Across all included hospitalizations, 1,467 (2.9%) contained ECMO. Hospital characteristics included 353 median CICU admissions/y (IQR: 57-527), 242 median surgical cases/y (IQR: 34-328), and 10 median ECMO runs/y (IQR: 2-20).

FIGURE 1 Eligible and Included Hospitalizations



Flow chart of eligible patients, exclusions, and included patients in each cohort.

DEMOGRAPHICS AND PREHOSPITAL STATUS. Overall distribution of hospitalizations by patient race and ethnicity were White 53.0%, Hispanic 17.7%, Black 14.4%, other races 8.0%, and Asian 3.7%. Table 1 summarizes patient and admission characteristics. In general, measures of prehospitalization status suggested a greater SOI in hospitalizations of non-White patients. Hospitalizations of Black and

TABLE 1 Patient Characteristics by Race and Ethnicity, All Hospitalizations

Medical Hospitalizations (N = 16,525)	Hispanic (n = 3,049)	Black (n = 2,669)	White (n = 8,681)	Asian (n = 586)	Other (n = 1,174)	Unknown (n = 366)	P Value
Male	1,696 (55.62)	1,388 (52.00)	5,006 (57.67)	301 (51.37)	675 (57.50)	218 (59.56)	<0.0001
Antenatal diagnosis	1,002 (38.78)	865 (38.55)	3,052 (41.73)	135 (27.16)	368 (41.72)	134 (55.37)	<0.0001
Extracardiac anomaly	629 (20.63)	557 (20.87)	1,965 (22.64)	121 (20.65)	161 (13.71)	55 (15.03)	<0.0001
Chromosomal abnormality/syndrome	785 (25.75)	657 (24.62)	1,941 (22.36)	128 (21.84)	226 (19.25)	86 (23.50)	<0.0001
Insurance status							
Public/other	2,295 (75.27)	2,028 (75.98)	3,764 (43.36)	261 (44.54)	709 (60.39)	262 (71.58)	<0.0001
Private	754 (24.73)	641 (24.02)	4,917 (56.64)	325 (55.46)	465 (39.61)	104 (28.42)	
Age group at initial hospital admission							
Preterm neonate	108 (3.54)	101 (3.78)	280 (3.23)	18 (3.07)	83 (7.07)	16 (4.37)	<0.0001
Full-term neonate	350 (11.48)	320 (11.99)	1,169 (13.47)	58 (9.90)	303 (25.81)	90 (24.59)	
Infant	746 (24.47)	585 (21.92)	1,974 (22.74)	108 (18.43)	268 (22.83)	98 (26.78)	
Child	1,610 (52.80)	1,368 (51.26)	4,039 (46.53)	348 (59.39)	463 (39.44)	149 (40.71)	
Adult	235 (7.71)	295 (11.05)	1,219 (14.04)	54 (9.22)	57 (4.86)	13 (3.55)	
Weight status at hospital admission							
Severely underweight	690 (22.63)	762 (28.55)	2,582 (29.74)	184 (31.40)	325 (27.68)	88 (24.04)	<0.0001
Underweight	245 (8.04)	210 (7.87)	689 (7.94)	75 (12.80)	113 (9.63)	30 (8.20)	
Normal	1,324 (43.42)	1,074 (40.24)	3,597 (41.44)	225 (38.40)	487 (41.48)	156 (42.62)	
Overweight	325 (10.66)	241 (9.03)	742 (8.55)	51 (8.70)	108 (9.20)	35 (9.56)	
Obese	465 (15.25)	382 (14.31)	1,071 (12.34)	51 (8.70)	141 (12.01)	57 (15.57)	
Unplanned initial CICU admission	1,930 (63.30)	1,747 (65.46)	5,005 (57.65)	313 (53.41)	638 (54.34)	161 (43.99)	<0.0001
Acute and chronic heart failure	626 (20.53)	728 (27.28)	1,477 (17.01)	122 (20.82)	206 (17.55)	63 (17.21)	<0.0001
Transplant rejection	65 (2.13)	115 (4.31)	200 (2.30)	9 (1.54)	11 (0.94)	3 (0.82)	<0.0001
Pulmonary hypertension	292 (9.58)	326 (12.21)	897 (10.33)	97 (16.55)	141 (12.01)	33 (9.02)	<0.0001
Mechanical ventilation within 2 h of CICU admission	601 (19.71)	610 (22.86)	1,725 (19.87)	107 (18.26)	301 (25.64)	108 (29.51)	<0.0001
VIS within 2 h of CICU admission	0.0 (0, 100)	0.0 (0, 220)	0.0 (0, 200)	(0, 100)	0.0 (0, 105)	0.0 (0, 62)	<0.0001
ECMO during the hospitalization	64 (2.10)	74 (2.77)	187 (2.15)	15 (2.56)	30 (2.56)	10 (2.73)	0.435

Continued on the next page

Hispanic patients had higher rates of unplanned CICU admission in both medical and surgical groups. For medical hospitalizations, hospitalizations of Black patients had higher rates of heart failure and transplant rejection. Hospitalizations of Black and other race patients had higher rates of mechanical ventilation within 2 hours of CICU admission. For the surgical cohort, hospitalizations of Black patients had higher rates of mechanical ventilation at admission from the operating room.

For both the medical and surgical groups, hospitalizations of Black and Hispanic patients had the highest rates of public insurance. Hospitalizations of Hispanic and Black patients had higher rates of chromosomal anomalies and genetic syndromes. For surgical hospitalizations, antenatal diagnosis was highest in hospitalizations of other race patients, lowest in hospitalizations of Asian patients, and similar across hospitalizations of Hispanic, Black, and White patients.

Systemic circulatory failure and ECPR were the most common ECMO indications across racial and ethnic groups in both medical and surgical hospitalizations (Table 2). For medical hospitalizations, ECPR rates were similar across Hispanic, Black, and White patients. For surgical hospitalizations, hospitalizations of Hispanic patients had higher ECPR rates.

ASSOCIATION OF RACE AND ETHNICITY WITH ECMO UTILIZATION. The overall rate of ECMO utilization in the medical cohort was 2.3%. There was no significant difference in ECMO utilization among racial and ethnic groups ($P = 0.435$) (Table 1). In adjusted analyses, no significant association was seen between race and ethnicity and the odds of receiving ECMO (Central Illustration).

In surgical hospitalizations, the overall rate of ECMO utilization was 3.2%. Black (3.79%) and other race (4.42%) were associated with higher rates of ECMO utilization ($P < 0.0001$) (Table 1). Adjusted analyses confirmed this finding, demonstrating that Black (adjusted odds ratio [aOR]: 1.24; 95% CI: 1.02-1.50; $P = 0.03$) and other race (aOR: 1.50; 95% CI: 1.17-1.93; $P = 0.001$) (Central Illustration) were associated with higher odds of ECMO.

IN-HOSPITAL MORTALITY. Overall mortality rates by race and ethnicity were Hispanic 3.9%, Black 4.6%, White 3.1%, Asian 2.9%, other race 4.7%, and

TABLE 1 Continued

Surgical Hospitalizations (N = 34,027)	Hispanic (n = 5,874)	Black (n = 4,614)	White (n = 18,101)	Asian (n = 1,285)	Other (n = 2,872)	Unknown (n = 1,281)	*P* Value
Male	3,152 (53.66)	2,449 (53.08)	10,124 (55.93)	667 (51.91)	1,561 (54.35)	699 (54.57)	<0.0001
Antenatal diagnosis	2,153 (38.93)	1,719 (39.44)	6,759 (41.25)	349 (30.48)	984 (45.05)	315 (49.53)	<0.0001
Extra-cardiac anomaly	1,098 (18.69)	878 (19.03)	3,357 (18.55)	199 (15.49)	354 (12.33)	162 (12.65)	<0.0001
Chromosomal abnormality/syndrome	1,569 (26.71)	1,189 (25.77)	3,922 (21.67)	244 (18.99)	567 (19.74)	270 (21.08)	<0.0001
Insurance status							
Public/other	4,379 (74.55)	3,479 (75.40)	7,553 (41.73)	497 (38.68)	1,955 (68.07)	979 (76.42)	<0.0001
Private	1,495 (25.45)	1,135 (24.60)	10,548 (58.27)	788 (61.32)	917 (31.93)	302 (23.58)	
Age group at initial hospital admission							
Preterm neonate	262 (4.46)	210 (4.55)	657 (3.63)	36 (2.80)	127 (4.42)	47 (3.67)	<0.0001
Full-term neonate	1,046 (17.81)	710 (15.39)	3,284 (18.14)	156 (12.14)	587 (20.44)	224 (17.49)	
Infant	1,845 (31.41)	1,640 (35.54)	5,521 (30.50)	372 (28.95)	1,034 (36.00)	424 (33.10)	
Child	2,469 (42.03)	1,879 (40.72)	7,361 (40.67)	649 (50.51)	1,052 (36.63)	527 (41.14)	
Adult	252 (4.29)	175 (3.79)	1,278 (7.06)	72 (5.60)	72 (2.51)	59 (4.61)	
Weight status at hospital admit							
Severely underweight	1,444 (24.58)	1,358 (29.43)	4,898 (27.06)	431 (33.54)	831 (28.93)	362 (28.26)	<0.0001
Underweight	601 (10.23)	525 (11.38)	1,905 (10.52)	174 (13.54)	361 (12.57)	140 (10.93)	
Normal	2,772 (47.19)	1,983 (42.98)	8,430 (46.57)	530 (41.25)	1,263 (43.98)	591 (46.14)	
Overweight	469 (7.98)	356 (7.72)	1,385 (7.65)	71 (5.53)	222 (7.73)	88 (6.87)	
Obese	588 (10.01)	392 (8.50)	1,483 (8.19)	79 (6.15)	195 (6.79)	100 (7.81)	
Unplanned initial CICU admission	1,085 (18.47)	852 (18.47)	2,733 (15.10)	152 (11.83)	459 (15.98)	10(8.43)	<0.0001
Preoperative high risk factors present[a]	143 (2.43)	117 (2.54)	470 (2.60)	21 (1.63)	60 (2.09)	19 (1.48)	0.035
VIS at time of surgery							
0	5,346 (91.01)	4,312 (93.45)	16,770 (92.65)	1,132 (88.09)	2,656 (92.48)	1,221 (95.32)	<0.0001
>0	528 (8.99)	302 (6.55)	1,331 (7.35)	153 (11.91)	216 (7.52)	60 (4.68)	
STAT categories							
1	1,699 (28.92)	1,318 (28.57)	4,956 (27.38)	442 (34.40)	726 (25.28)	357 (27.87)	<0.0001
2	1,868 (31.80)	1,461 (31.66)	5,800 (32.04)	393 (30.58)	921 (32.07)	394 (30.76)	
3	658 (11.20)	565 (12.25)	2,411 (13.32)	149 (11.60)	419 (14.59)	165 (12.88)	
4	1,417 (24.12)	1,046 (22.67)	4,050 (22.37)	282 (21.95)	690 (24.03)	298 (23.26)	
5	232 (3.95)	224 (4.85)	884 (4.88)	19 (1.48)	116 (4.04)	67 (5.23)	
CPB present	4,974 (84.68)	3,968 (86.00)	15,368 (84.90)	1,123 (87.39)	2,488 (86.63)	1,133 (88.45)	<0.0001
CPB time (min)	107.0 (73.0-161.0)	101.5 (69.0-150.0)	102.0 (67.0-153.0)	103.0 (71.0-158.0)	102.0 (70.0-149.0)	109.0 (73.0-162.0)	<0.0001
Aortic cross clamp time (min)	62.0 (37.0-99.0)	58.0 (36.0-90.0)	56.0 (32.0-90.0)	57.0 (35.0-90.0)	62.0 (36.0-98.0)	70.0 (41.0-102.0)	<0.0001
DHCA time (min)	21.0 (8.0-36.0)	24.0 (9.0-41.0)	23.0 (9.0-36.0)	23.0 (7.5-38.0)	26.0 (14.0-39.0)	11.0 (3.0-29.0)	<0.0001
Mechanical ventilation at admission from operating room	4,097 (69.75)	3,428 (74.30)	11,922 (65.86)	884 (68.79)	1,967 (68.49)	994 (77.60)	<0.0001
VIS in the first 2 postoperative h in the CICU	5.0 (0-240)	5.0 (0-210)	5.0 (0-271)	5.0 (0-108)	5.0 (2-100)	3.0 (0-60)	<0.0001
ECMO during the hospitalization	173 (2.95)	175 (3.79)	549 (3.03)	30 (2.33)	127 (4.42)	33 (2.58)	<0.0001

Values are n (%) or median (IQR). [a]Preoperative high risk factors: Cardiopulmonary resuscitation; shock at time of surgery; hepatic dysfunction; neurologic injury within 48 h prior to surgery; renal failure requiring dialysis

CICU = cardiac intensive care unit; CPB = cardiopulmonary bypass; DHCA = deep hypothermic circulatory arrest; ECMO = extracorporeal membrane oxygenation; STAT = STS-European Association for Cardio-thoracic Surgery; VIS = vasoactive-inotropic score.

unknown 3.3%. Table 3 summarizes unadjusted comparisons of mortality across race and ethnicity, stratified by hospitalization type, and ECMO utilization.

For medical hospitalizations, the unadjusted in-hospital mortality rate for ECMO hospitalizations was 49.21% with no significant differences across racial and ethnic groups ($P = 0.887$) (Table 3). On adjusted analyses, hospitalizations of other race patients had higher odds of mortality (aOR: 1.61; 95% CI: 1.22-2.12; $P = 0.001$) (Figure 2).

For surgical hospitalizations, the unadjusted in-hospital mortality rate for ECMO hospitalizations was 42.4% with no significant differences across racial and ethnic groups ($P = 0.249$) (Table 3). On adjusted analyses, hospitalizations of Hispanic patients had higher odds of mortality than those of White patients (aOR: 1.31; 95% CI: 1.03-1.68; $P = 0.03$) (Figure 2).

As a sensitivity analysis to further isolate the association between race and ethnicity and outcome independent of differential ECMO utilization rates,

TABLE 2 Indications for Initial ECMO Run

Medical Hospitalizations (N = 380)	Hispanic (n = 64)	Black (n = 74)	White (n = 187)	Asian (n = 15)	Other (n = 30)	Unknown (n = 10)
Systemic circulatory failure	19 (29.69)	29 (39.19)	64 (34.22)	3 (20.00)	10 (33.33)	3 (30.00)
ECPR	28 (43.75)	34 (45.95)	78 (41.71)	5 (33.33)	12 (40.00)	6 (60.00)
Hypoxemia/hypercarbia or shunt occlusion	8 (12.50)	7 (9.46)	20 (10.70)	3 (20.00)	3 (10.00)	1 (10.00)
Arrythmia	3 (4.69)	2 (2.70)	10 (5.35)	1 (6.67)	4 (13.33)	0 (0.00)
Bleeding	1 (1.56)	0 (0.00)	2 (1.07)	0 (0.00)	0 (0.00)	0 (0.00)
Multisystem organ failure	4 (6.25)	2 (2.70)	9 (4.81)	2 (13.33)	1 (3.33)	0 (0.00)
Missing	1 (1.56)	0 (0.00)	4 (2.14)	1 (6.67)	0 (0.00)	0 (0.00)
Surgical Hospitalizations (N = 1,087)	**Hispanic (n = 173)**	**Black (n = 175)**	**White (n = 549)**	**Asian (n = 30)**	**Other (n = 127)**	**Unknown (n = 33)**
Systemic circulatory failure	65 (37.57)	86 (49.14)	272 (49.54)	10 (33.33)	67 (52.76)	14 (42.42)
ECPR	67 (38.73)	52 (29.71)	163 (29.69)	10 (33.33)	33 (25.98)	13 (39.39)
Hypoxemia/hypercarbia or shunt occlusion	22 (12.72)	21 (12.00)	77 (14.03)	7 (23.33)	17 (13.39)	3 (9.09)
Arrythmia	8 (4.62)	6 (3.43)	15 (2.73)	2 (6.67)	5 (3.94)	2 (6.06)
Bleeding	8 (4.62)	6 (3.43)	13 (2.37)	1 (3.33)	3 (2.36)	0 (0.00)
Multisystem organ failure	2 (1.16)	1 (0.57)	5 (0.91)	0 (0.00)	1 (0.79)	0 (0.00)
Missing	1 (0.58)	3 (1.71)	4 (0.73)	0 (0.00)	1 (0.79)	1 (3.03)

Values are n (%).
ECPR = extracorporeal cardiopulmonary resuscitation.

models were created adjusting for the propensity of requiring ECMO. In these models (Supplemental Table 1), inclusion of the propensity score did not significantly alter the point-estimates of associations between race and ethnicity and in-hospital mortality. This suggests that the observed associations were not the result of differential ECMO utilization.

Complications are detailed in Supplemental Table 2. Tertiary outcomes, such as duration of ECMO support and lengths of stay, are shown in Supplemental Table 3.

ASSOCIATIONS BETWEEN SOCIOECONOMIC STATUS AND OUTCOMES. Sixteen hospitals reported home zip code for each hospitalization, accounting for 60% of hospitalizations. Zip codes were used to determine SES variables, which are summarized in **Table 4**. Hospitalizations of Hispanic and Black patients had the highest rates of high school education or less, families living below poverty level, unemployment, and the lowest median household incomes, resulting in the lowest SES indices. When an interaction term between race and ethnicity and insurance type was included in the ECMO utilization model, the interaction term was not significant, and the observed associations described were unchanged (data not shown.) When a term for overall interaction between race and ethnicity and insurance type was included in the mortality model, the interaction term was

TABLE 3 Unadjusted Comparisons of In-Hospital Mortality Across Race/Ethnicity Groups by Hospitalization Type

Medical ECMO Hospitalizations	Hispanic (n = 64)	Black (n = 74)	White (n = 187)	Asian (n = 15)	Other (n = 30)	Unknown (n = 10)	*P* Value
Overall mortality	34 (53.13)	36 (48.65)	92 (49.20)	6 (40.00)	13 (43.33)	6 (60.00)	0.887
Medical Non-ECMO Hospitalizations	**Hispanic (n = 2,985)**	**Black (n = 2,595)**	**White (n = 8,494)**	**Asian (n = 571)**	**Other (n = 1,144)**	**Unknown (n = 356)**	
Overall mortality	155 (5.19)	160 (6.17)	354 (4.17)	22 (3.85)	88 (7.69)	16 (4.49)	<0.001
Surgical ECMO Hospitalizations	**Hispanic (n = 173)**	**Black (n = 175)**	**White (n = 549)**	**Asian (n = 30)**	**Other (n = 127)**	**Unknown (n = 33)**	
Overall mortality	85 (49.13)	79 (45.14)	215 (39.16)	13 (43.33)	53 (41.73)	16 (48.48)	0.249
Surgical Non-ECMO Hospitalizations	**Hispanic (n = 5,701)**	**Black (n = 4,439)**	**White (n = 17,552)**	**Asian (n = 1,255)**	**Other (n = 2,745)**	**Unknown (n = 1,248)**	
Overall mortality	75 (1.32)	59 (1.33)	165 (0.94)	14 (1.12)	35 (1.28)	16 (1.28)	0.081

Values are n (%).

significant in both medical and surgical cohorts but with further analysis, no significant findings were found (Supplemental Table 4). There was no evidence of interaction with SES index in models for ECMO utilization or mortality and inclusion of the SES index did not affect the previously reported associations (data not shown).

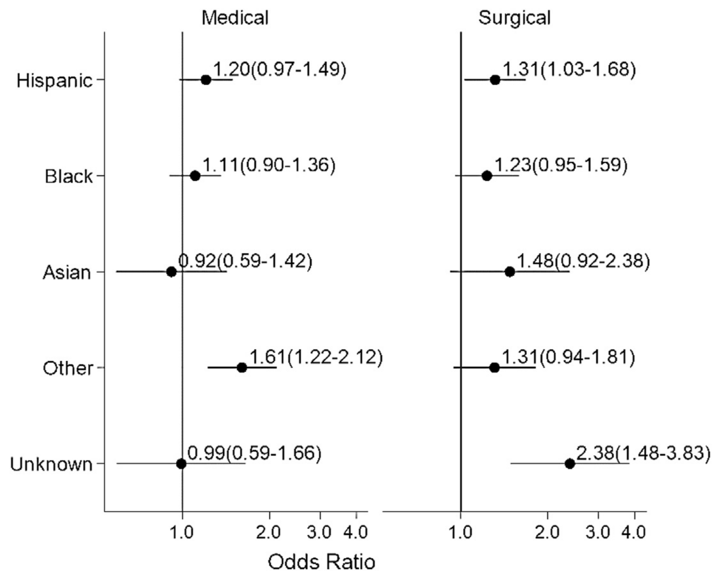
DISCUSSION

In this large, multicenter cohort study, we studied the association between race and ethnicity and ECMO utilization in critically ill young patients with cardiac disease. Black and other race were associated with higher odds of receiving ECMO during surgical hospitalizations despite adjustment for patient complexity. The etiology for increased ECMO utilization after cardiac surgery in these populations is unclear and may reflect unmeasured differences in SOI, patient complexity, or pre-ECMO management. Importantly, race and ethnicity were associated with outcome, yet mortality was not mediated by differences in ECMO utilization.

Our report provides important direction to efforts to mitigate racial and ethnic disparities in children with congenital heart disease requiring advanced mechanical support therapies. It is noteworthy that diagnoses and clinical factors consistent with worse SOI were higher in minority groups. Tjoeng et al[23] recently reported on the association of race and ethnicity and mortality for pediatric cardiac surgical patients. They found that Black patients had higher odds of mortality after postoperative admission. However, after adjusting for SOI, the increased odds of mortality were eliminated. Furthermore, black and other race patients had higher SOI scores for those requiring preoperative admission, but there was no difference in mortality possibly because they were able to be stabilized before going to the operating room. It is also noteworthy that pediatric critical care studies which adjust for SOI have not found disparities in outcomes.[8,9] These early reports of differences in SOI highlight possible disparity in access to care, including primary care, specialty care, and emergency care, and create system-level targets for efforts to reduce health care inequity.

There are increasing data on disparities in health care. It is notable that our data show worse outcomes for hospitalizations of other race and Hispanic patients. Studies have shown worse outcomes for Hispanic children with cardiac and noncardiac conditions.[24-30] The other race group included Native Americans, Pacific Islanders, and mixed-race patients, and although literature is more limited on Native American and Pacific Island populations, there are data that outcomes are worse for patients in these groups.[31-34] Although there are certainly data supporting health care disparities for minority groups, including outcomes in this study, our multicenter data showed that no group was deprived of the critical resource of ECMO for pediatric cardiac disease.

FIGURE 2 **Forest Plot of In-Hospital Mortality Across Hospitalization Types and Racial and Ethnic Groups Adjusted for ECMO Utilization**



Data presented as ORs (circles) with 95% CIs (horizontal line). Referent is white race. Footnotes: Covariates adjusted for: ECMO utilization, race/ethnicity category, insurance type, sex, age category, weight category, unplanned initial CICU admission, extracardiac anomaly, chromosomal anomaly or syndrome. Additional covariates in medical cohort: transplant rejection, pulmonary hypertension, acute or chronic heart failure, mechanical ventilation within 2 hours of CICU admission, VIS within 2 hours of CICU admission. Additional covariates in surgical cohort: preoperative high-risk factors present, VIS at time of surgery, STAT category, presence of cardiopulmonary bypass, mechanical ventilation at operating room admission. CICU = cardiac intensive care unit; STAT = STS-European Association for Cardio-Thoracic Surgery; VIS = vasoactive-inotropic score.

Chan et al[10,35] have published the most pediatric data on racial variation in ECMO utilization. In their first study, the authors looked at the association of race and ethnicity with mortality in children with heart disease undergoing ECMO support.[35] Using clinical data from the Extracorporeal Life Support Organization registry, Black and Hispanic ECMO patients had a higher risk of mortality. In a second study using the Pediatric Health Information Systems database, the authors queried whether there was variation in ECMO utilization and hospital survival in children after congenital heart surgery.[10] Black patients were found to be more likely to die and this was

TABLE 4 American Community Survey Characteristics and SES Index by Race/Ethnicity

Medical Hospitalizations (N = 10,264)	Hispanic (n = 1,597)	Black (n = 1,867)	White (n = 5,655)	Asian (n = 316)	Other (n = 548)	Unknown (n = 281)
Percent of population aged 18+ y with a high school education or less	48.6 (37.0-59.9)	46.8 (37.6-54.6)	42.8 (31.9-52.5)	34.9 (22.9-45.85)	40.7 (30.8-50.15)	40.7 (31.3-49.9)
Percent of families below poverty	17.1 (11.1-25.4)	20.2 (13.1-28.6)	11.6 (7.0-17.9)	11.1 (6.0-18.8)	11.8 (6.4-18.75)	11.9 (7.2-18.6)
Percent unemployed	7.8 (5.7-10.8)	9.9 (6.9-13.4)	6.2 (4.6-8.2)	6.3 (4.8-8.1)	6.9 (5.2-9.0)	6.2 (4.5-9.0)
Median household income	49,945.0 (38,798.0-62,734.0)	43,608.5 (33,757.0-56,145.0)	56,142.0 (44,836.0-72,326.0)	65,850.5 (48,915.0-90,396.0)	59,404.0 (45,165.0-77,324.0)	59,694.0 (44,586.0-76,150.0)
SES index						
0	1,091 (68.3)	1,393 (74.6)	2,757 (48.8)	128 (40.5)	285 (52.0)	132 (47.0)
1	184 (11.5)	223 (11.9)	957 (16.9)	40 (12.7)	59 (10.8)	43 (15.3)
2	131 (8.2)	102 (5.5)	666 (11.8)	41 (13.0)	62 (11.3)	27 (9.6)
3	116 (7.3)	81 (4.3)	597 (10.6)	56 (17.7)	70 (12.8)	35 (12.5)
4	75 (4.7)	68 (3.6)	678 (12.0)	51 (16.1)	72 (13.1)	44 (15.7)
Surgical Hospitalizations (N = 20,983)	**Hispanic (n = 3,042)**	**Black (n = 3,234)**	**White (n = 11,846)**	**Asian (n = 708)**	**Other (n = 1,107)**	**Unknown (n = 1,046)**
Percent of population aged 18+ y with a high school education or less	47.9 (37.0-58.0)	47.0 (37.7-55.1)	43.4 (32.1-53.2)	34.1 (23.7-46.4)	40.7 (30.1-50.4)	38.8 (26.8-49.2)
Percent of families below poverty	16.3 (10.7-23.9)	20.3 (13.4-29.0)	11.9 (7.1-17.8)	10.0 (6.2-16.8)	11.9 (7.0-19.6)	10.9 (5.8-18.6)
Percent unemployed	7.4 (5.5-10.15)	9.5 (6.8-13.1)	6.2 (4.7-8.2)	5.9 (4.5-7.85)	7.0 (5.3-9.2)	5.9 (4.4-8.0)
Median household income	50,755.5 (40,078.5-63,333.0)	43,112.0 (33,550.5-54,472.0)	54,846.0 (44,158.0-71,798.0)	65,591.5 (49,545.5-87,350.0)	57,336.0 (44,153.0-75,885.0)	61,566.0 (46,742.0-84,784.0)
SES index						
0	2,027 (66.6)	2,479 (76.7)	5,934 (50.1)	249 (35.2)	563 (50.9)	453 (43.3)
1	439 (14.4)	387 (12.0)	2,060 (17.4)	111 (15.7)	166 (15.0)	140 (13.4)
2	248 (8.2)	152 (4.7)	1,281 (10.8)	95 (13.4)	140 (12.6)	119 (11.4)
3	183 (6.0)	130 (4.0)	1,312 (11.1)	129 (18.2)	145 (13.1)	159 (15.2)
4	145 (4.8)	86 (2.7)	1,259 (10.6)	124 (17.5)	93 (8.4)	175 (16.7)

Values are median (IQR) or n (%).
SES = socioeconomic status.

attributed to less ECMO access. Adjusting for the relatively limited number of clinical covariates in this data set, it was found that non-White patients were more likely to receive pre-op mechanical ventilation, vasoactive medications, antiarrhythmic medications, pulmonary vasodilators, and both preoperative and postoperative CPR suggesting SOI differences. Pasquali et al[36,37] have previously reported on limitations in conclusions from administrative databases including misclassification of diagnoses, procedures, and outcomes. In contrast, PC[4] is a clinical registry with granular data abstracted from the medical record in proximity to the clinical events. Patient characteristics, ICU therapies, procedural data, laboratory test results, risk factors for adverse outcomes, and timestamps which allow timing of the patient's course, such as complications that occurred on or after ECMO, are provided by PC[4] and likely explain the differential outcomes.

Although there are data on how SES impacts children with congenital heart disease, data are scant on the relationship of SES with critical illness in children and there are no data on whether SES influences care or outcomes of children in the CICU.[19,26,38-43] To explore this, we performed additional analyses that included SES data from a subgroup of the study population. We did not find additional influence on ECMO utilization or outcome by including SES or insurance type. Other studies have found a link between pediatric outcomes and SES; however, most studies look at outcomes resulting from outpatient care.[26,38,39] SES certainly impacts access to care in these situations. Using zip codes, we were able to investigate environmental SES more fully, which showed it not to be a factor in ECMO support or outcome. In a single-center retrospective study, Epstein et al[42] investigated the impact of SES and home geographic location on SOI at PICU admission and mortality. They found that Hispanic children and those with government insurance had higher SOI at PICU presentation but there was no effect on PICU mortality. In the only published study to look at in-hospital care and SES status, Zheng et al[43] studied SES and bronchiolitis severity among hospitalized infants as measured by admission to the PICU and/or mechanical ventilation. They found that those with the highest median household income were more likely to be admitted to the PICU compared to those in the intermediate median household income despite adjustment for disease severity and hospital center. Additionally, the higher-income group did not receive more mechanical ventilation or have longer lengths of stay suggesting that SOI was similar. Further study is needed on how SES affects children in hospital-based settings.

STUDY LIMITATIONS. The optimal data source for understanding the decision to pursue ECMO would contain detailed clinical information, such as physiologic markers and therapies, to track the progress of patients toward ECMO. These data are not available in any available multicenter dataset; therefore, we were limited by the variables available. SOI scores are also not available in PC^4, so we used proxies for SOI. Subjects of unknown race are also a limitation of any data set. Although unknowns were reported from the majority of sites, approximately half came from one site which may introduce bias. Unmeasured confounding is inevitable in observational studies. For the SES analyses, not all centers reported zip code data, which may have resulted in selection bias. Also, since patient addresses were not available, zip codes were a proxy for more granular SES measurements and may have biased our results. In the propensity score analyses, there was a >10% change in the point estimates for mortality in Black and other race hospitalizations. Though this did not change the direction of the association, it suggests unexplained variations that deserve further attention in a follow-up study. Finally, no long-term data are available, limiting the scope of this investigation.

CONCLUSIONS

Race and ethnicity were not associated with reduced access to ECMO, with hospitalizations of Black and other race patients having higher odds of ECMO utilization during pediatric cardiac surgical hospitalizations. Simultaneously and importantly, race and ethnicity were associated with increased risk of in-hospital mortality, but there was no evidence that these differences were mediated through differential ECMO access. Of note, pretreatment markers of SOI differed across groups. Efforts to mitigate racial and ethnic disparities in young patients with cardiac disease should include identifying other modifiable factors such as access to care.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE: Non-White pediatric patients with cardiac disease have worse markers of SOI early in their CICU course, have increased odds of being placed on ECMO, and have increased odds of in-hospital mortality.

TRANSITIONAL OUTLOOK: Additional research is needed to identify the factors that lead to disparities in critically ill pediatric cardiac patients. Access to care is an important factor that would affect critical illness severity and requires further study.

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APPENDIX For supplemental tables, please see the online version of this paper.