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*In neonates undergoing open-heart surgery, numerous factors influence post-operative blood loss. Previous studies have identified prematurity, lower weight, longer cardiopulmonary bypass time, longer aortic cross-clamp time, and longer regional perfusion time or circulatory arrest time to be potentially prognostic.

In this single-centre retrospective cohort study of over 100 neonates undergoing open-heart surgery with cardiopulmonary bypass, after adjustment for other factors, African American race was independently associated with increased post-operative blood loss.

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Post-operative blood loss is higher among African American neonates undergoing open-heart surgery with cardiopulmonary bypass for CHD*

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Abstract

Background: Neonates are at high risk of bleeding after open-heart surgery. We sought to determine pre-operative and intra-operative risk factors for increased bleeding after neonatal open-heart surgery with cardiopulmonary bypass. *Methods:* We conducted a retrospective cohort study of neonates (0–30 days old) who underwent open-heart surgery with cardiopulmonary bypass from January, 2009, to March, 2013. Cardiac diagnosis; demographic and surgical data; and blood products, haemostatic agents, and anti-thrombotic agents administered before, during, and within 24 hours after surgery were abstracted from the electronic health record and anaesthesia records. The outcome of interest was chest tube output (in ml/kg body weight) within 24 hours. Relationships between chest tube output and putative associated factors were evaluated by unadjusted and adjusted linear regression. *Results:* The cohort consisted of 107 neonates, of whom 79% had a Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery (STAT) Mortality Category of 4 or 5. Median chest tube output was 37 ml/kg (range 9–655 ml/kg). Age, African-American race, and longer durations of surgery and cardiopulmonary bypass each had statistically significant associations with increased chest tube output in unadjusted analyses. In multivariable analysis, African-American race retained an independent, statistically significant association with increased chest tube output; the geometric mean of chest tube output among African-American neonates was 71% higher than that of Caucasians (95% confidence interval, 29–125%; $p = 0.001$). *Conclusion:* Among neonates with CHD undergoing open-heart surgery with cardiopulmonary bypass, African-American race is independently associated with greater chest tube output over the first 24 hours post-operatively.

CHD is estimated to occur in nearly 1.0% of live births worldwide.[1] Although CHD contributes significantly to neonatal morbidity and mortality, advances in medical and surgical care have improved survival. Despite the improved survival, many characteristics of neonates, including the immaturity of organ systems, render them especially vulnerable when cardiac surgery is performed.

In comparison to healthy neonates, neonates who undergo cardiac surgery are at increased risk for both bleeding and clotting. Immaturity of the coagulation profile in neonates involves many aspects of the haematologic system. Neonates with CHD who undergo cardiopulmonary bypass have decreased circulating clotting factors, reduced platelet function, and suboptimal fibrin clot formation.[2] Fibrin clot formation in neonates has been shown by microscopic images to be porous after cardiopulmonary bypass and differs from that observed in adults.[3] The cardiopulmonary bypass circuit also elicits an inflammatory response that further disrupts the coagulation profile.[4] These unique challenges add to the difficulty of caring for neonates after separation from cardiopulmonary bypass.

Many neonatal cardiac operations are performed in patients with complex CHDs or in those who require complex surgical repairs with long cardiopulmonary bypass times, and blood

products are paramount. Younger patients with severe pre-operative conditions such as pre-operative mechanical ventilation, functionally univentricular anatomy, and cyanotic cardiac disease are at increased risk for receiving blood transfusions during the first 24 hours post-operatively.[5] An analysis of The Society of Thoracic Surgeons Congenital Heart Surgery Database involving 81 North American centres documented that unlike adults, neonates who undergo open-heart surgery with cardiopulmonary bypass almost always receive packed red blood cells.[6] During cardiopulmonary bypass, despite the use of un-fractionated heparin or other anti-coagulants, fibrinogen levels decline due to consumption; in addition, increased fibrinolysis can persist for up to 6 hours post-operatively.[7] These factors potentiate the risk for bleeding after neonatal cardiopulmonary bypass, and centres have established practices to manage this risk. Additionally, platelet inhibitors, such as aspirin, are often administered to these patients post-operatively and sometimes pre-operatively, further increasing the risk for excessive bleeding.[4] Therefore, it is not unusual to administer other component blood products to these neonates.

Despite this mechanistic understanding, evidence regarding pre-operative and intra-operative risk factors for bleeding derived from clinical research studies remains limited in neonates undergoing surgery with cardiopulmonary bypass. Accordingly, in this single-centre cohort study, we sought to determine pre-operative and intra-operative factors associated with post-operative blood loss among neonates with CHD undergoing cardiopulmonary bypass.

Methods

Patients

After obtaining approval from the Johns Hopkins All Children's Hospital Institutional Review Board, we conducted a retrospective cohort study of all neonates (0–30 days old) who underwent open-heart surgery with cardiopulmonary bypass at the institution from January, 2009, to March, 2013, inclusive. Premature infants were excluded from the cohort by excluding all patients who were less than 35 weeks estimated gestational age at birth. The Institutional Review Board waived written informed consent.

Data collection

Data sources included paper records (anaesthesia, perfusion, and blood bank), electronic medical records, and the institutional CardioAccess Database. (CardioAccess is a registry and database (CardioAccess Inc., St. Petersburg, Florida, United States of America, and Fort Lauderdale, Florida, United States of America: http://www.cardioaccess.com) that has been prospectively maintained on all patients and has been utilised for data collection and analysis, as well as participation in The Society of Thoracic Surgeons Congenital Heart Surgery Database and its Congenital Cardiac Anesthesia Society module.) Data collected included demographics, weight, cardiac diagnosis, surgical procedure, Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery (STAT) Mortality Category, Risk Adjustment for Congenital Heart Surgery-1 (RACHS-1) Category, intra-operative factors, and blood products administered in the operating room. Race was determined by parental report, as documented in the electronic medical record. Intra-operative factors included primary surgeon performing the operation; administration of intra-operative vitamin K, recombinant factor VIIa, ϵ-aminocaproic acid, and un-fractionated heparin; durations of surgery and cardiopulmonary bypass; lowest temperature on cardiopulmonary bypass; aortic cross clamp time; and circulatory arrest time. The primary outcome variable was the estimated blood loss (ml/kg of body weight) over the first 24 hours post-operatively, as defined by the measured chest tube output.

Clinical management

Cardiopulmonary bypass management was standardised for all patients by utilising the same type of circuit, prime components, and weight-based priming volumes. Blood products were no more than 5 days old and in most instances were administered within 3 days of collection. The blood product administration protocol was non-standardised; however, blood product administration data were collected and utilised in the analysis.

Demographic and clinical characteristics were summarised by descriptive statistics. All potential predictors were assessed for association with chest tube output by unadjusted linear regression analysis. Variables with $p \leq 0.15$ in unadjusted analyses were included in an adjusted linear regression model. Given that the outcome variable (chest tube output) was indexed to patient weight (i.e., ml/kg), weight was not included in the model. Owing to non-normality, chest tube output was log-transformed in the model and the estimates were then back-transformed.

In addition to the pre-specified analysis, an exploratory analysis was performed in which the highest quartile post-operative blood loss (4th quartile of chest tube output) was the outcome of interest. Unadjusted and adjusted logistic regression models were used for these analyses. Similar to the pre-specified analysis, variables with $p \leq 0.15$ in univariate analyses were included in the multivariable model.

All statistical analyses were performed with SAS/STAT software version 9.4 of the SAS system for Windows (SAS Institute Inc., Cary, North Carolina, United States of America). All tests were two-sided, and p values <0.05 were considered statistically significant.

Results

The retrospective cohort consisted of 107 neonates with a median age at surgery of 8 days (range 1–29). As shown in Table 1, males represented 53% of the cohort and 71% of patients were Caucasian. The STAT Mortality Category was 4 or 5 in 79%, and the median duration of cardiopulmonary bypass was 2.4 hours (range 0.2–5.7). The median chest tube output in the first 24 hours post-operatively was 37.4 ml/kg (range 8.5–654.6), and 27 patients were in the highest quartile of post-operative blood loss (>55.24 ml/kg). Figure 1 shows the distribution of chest tube output by race category. Chest tube output was significantly higher among African Americans (median, 57 ml/kg; range, 18.8–655 ml/kg) than that among Caucasians (median, 36 ml/kg; range, 9–120 ml/kg; $p = 0.002$).

Table 2 presents the results of unadjusted linear regression analyses for putative associations with chest tube output. Post-conceptional age, race, STAT Mortality Category, operating room time, cardiopulmonary bypass time, and circulatory arrest time each met criteria for inclusion in the adjusted model. As shown in Table 3, after mutual adjustment in a multiple linear regression model, only African-American race retained a statistically significant, independent association with increased chest tube

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Table 1. Demographic and clinical characteristics of the study population stratified by race

Variable	Total, n = 107	African American, n = 19	Other, n = 12	White, n = 76	p-Value
Post-conceptional age (weeks)					0.6671
Mean (SD)	39.3 (1.6)	39.4 (1.9)	39.8 (1.8)	39.2 (1.4)	
Median (range)	39 (35–44)	39.0 (35–43)	39.5 (37–44)	39 (35–42)	
Gender, n (%)					0.2944
Male	56 (52.8)	7 (36.8)	6 (54.6)	43 (56.6)	
Female	50 (47.2)	12 (63.2)	5 (45.4)	33 (43.4)	
Missing	1				
Weight (kg)					0.3143
Mean (SD)	3.3 (0.7)	3.1 (0.5)	3.3 (0.5)	3.3 (0.8)	
Median (range)	3.3 (1.9–8.3)	3.1 (2.2–3.9)	3.5 (2.3–4.1)	3.3 (1.9–8.3)	
Surgeon					0.7006
A	73 (68.9)	12 (63.2)	8 (66.7)	53 (70.7)	
B	11 (10.4)	3 (15.8)	2 (16.7)	6 (8.0)	
C	22 (20.8)	4 (21.1)	2 (16.7)	16 (21.3)	
Missing	1				
STAT Mortality Category, n (%)					0.4036
1	2 (1.9)	1 (5.3)	0 (0)	1 (1.3)	
2	6 (5.6)	1 (5.3)	0 (0)	5 (6.6)	
3	15 (14.0)	0 (0)	2 (16.7)	13 (17.1)	
4	46 (43.0)	9 (47.4)	4 (33.3)	33 (43.4)	
5	38 (35.5)	8 (42.1)	6 (50.0)	24 (31.6)	
RACHS-1 Category, n (%)					0.8465
1	0 (0)	0 (0)	0 (0)	0 (0)	
2	7 (6.7)	1 (5.6)	0 (0)	6 (8.0)	
3	23 (22.1)	3 (16.7)	3 (27.3)	17 (22.7)	
4	34 (32.7)	6 (33.3)	2 (18.2)	26 (34.7)	
5	0 (0)	0 (0)	0 (0)	0 (0)	
6	40 (38.5)	8 (44.4)	6 (54.6)	26 (34.7)	
Missing	3				
Vitamin K/weight, n (%)					1.0000
>0	6 (5.6)	1 (5.3)	0 (0)	5 (6.6)	
0	101 (94.4)	18 (94.7)	12 (100)	71 (93.4)	
Factor VII/weight, n (%)					0.3012
>0	28 (26.4)	6 (31.6)	5 (41.7)	17 (22.7)	
0	78 (73.6)	13 (68.4)	7 (58.3)	58 (77.3)	
Missing	1				
Rewarming time (minutes)					0.8161
Mean (SD)	39.9 (12.9)	41.9 (11.7)	36.2 (15.9)	39.9 (12.7)	
Median (range)	40 (0–70)	44 (25–70)	35 (0–55)	40 (0–70)	
Missing	1				
Lowest CPB temperature, °C					0.9484
Mean (SD)	20.4 (4.6)	20.7 (4.4)	20.5 (5.3)	20.3 (4.6)	
Median (range)	19 (15–37)	18 (16–30)	19 (15–35)	19 (15–37)	

(*Continued*)

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Table 1. (*Continued*)

Variable	Total, n = 107	African American, n = 19	Other, n = 12	White, n = 76	p-Value
OR time (hours)					0.8100
Mean (SD)	6.6 (1.6)	6.9 (2.1)	6.5 (1.4)	6.5 (1.4)	
Median (range)	6.4 (3.5–13.6)	6.8 (4.2–13.6)	6.4 (3.8–9.1)	6.3 (3.5–12.9)	
Missing	1				
CPB time (hours)					0.7772
Mean (SD)	2.4 (0.8)	2.5 (1.0)	2.4 (1.2)	2.4 (0.7)	
Median (range)	2.4 (0.2–5.7)	2.4 (0.7–5.1)	2.3 (0.6–5.7)	2.4 (0.2–3.9)	
Missing	1				
Aortic clamp time, hours					0.5436
Mean (SD)	1.1 (0.4)	1.1 (0.5)	1 (0.3)	1.1 (0.4)	
Median (range)	1.1 (0–2.9)	1.0 (0.5–2.9)	0.9 (0.6–1.6)	1.1 (0–2.4)	
Missing	5				
Circulatory arrest, n (%)					0.2910
Yes	55 (51.4)	13 (68.4)	6 (50.0)	36 (47.4)	
No	52 (48.6)	6 (31.6)	6 (50.0)	40 (52.6)	
EACA/kg					0.2189
Mean (SD)	85.3 (36.8)	68 (41)	85.6 (21.3)	89.7 (36.7)	
Median (range)	99.8 (0–198.8)	91.4 (0–111.1)	99 (53.6–111.1)	100 (0–198.8)	
Missing	3				
Anticoagulation (heparin) at 24 hours (units/kg)					0.1170
Mean (SD)	124.6 (341.7)	124.6 (163.8)	125.8 (134)	124.5 (393.9)	
Median (range)	45.5 (1.2–3389.7)	63.9 (1.2–631.9)	60.8 (39.5–448.8)	44.2 (13.3–3389.7)	
Missing	2				
CTO at 24 hours (ml/kg)					0.0036
Mean (SD)	50.8 (65.5)	97.4 (140.8)	46.3 (36.6)	39.8 (20.7)	
Median (range)	37.4 (8.5–654.6)	57.1 (18.8–654.5)	31.8 (17.3–148.9)	35.5 (8.5–120.4)	

CPB = cardiopulmonary bypass; CTO = chest tube output; EACA = ϵ-aminocaproic acid; OR = operating room; RACHS = Risk Adjustment for Congenital Heart Surgery; SD = standard deviation; STAT = Society of Thoracic Surgeons-European Association of Cardiothoracic Surgery.

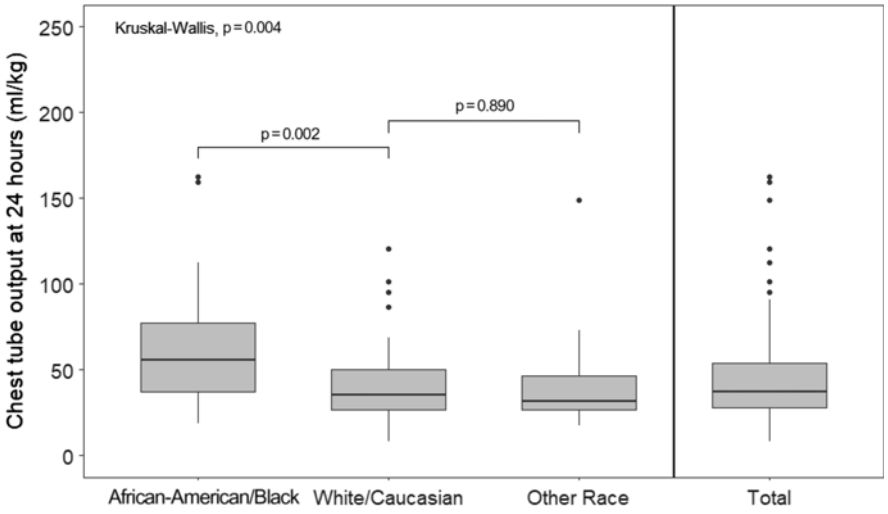

Figure 1. Distribution of chest tube output values 24 hours post-operatively by race. One African-American patient with a chest tube output value of 654.5 ml/kg is omitted.

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Table 2. Unadjusted linear regression for chest tube output per weight at 24 hours

Variable	e^{β}	95% CI	p-Value
Post-conceptional age (weeks)	0.92	0.86–1.00	**0.044**
Gender	1.14	0.90–1.45	0.281
Race			
African American	1.83	1.36–2.45	**<0.001**
Other/missing	1.09	0.76–1.56	0.635
White/Caucasian	*Reference*		
Surgeon			
A	1.10	0.81–1.48	0.551
B	1.19	0.76–1.88	0.452
C	*Reference*		
STAT Mortality Category			
5	1.45	1.05–1.99	**0.025**
4	1.19	0.87–1.61	0.277
<3	*Reference*		
RACHS-1 Category			
≥4	1.15	0.88–1.50	0.304
<4	*Reference*		
Rewarming time (minutes)	1.01	1.00–1.02	0.163
Lowest CPB temperature (°C)	0.99	0.97–1.02	0.543
OR time (hours)	1.15	1.07–1.24	**<0.001**
CPB time (hours)	1.25	1.08–1.45	**0.003**
Aortic clamp time (hours)	1.04	0.78–1.37	0.802
Circulatory arrest			
Yes	1.31	1.09–1.72	**0.009**
No	*Reference*		
EACA (mg/kg)	1.00	0.99–1.00	0.064
Vitamin K (mg/kg)			
>0	1.21	0.72–2.01	0.478
0	*Reference*		
Factor VII administered (μg/kg)			
>0	0.91	0.70–1.20	0.509
0	*Reference*		
Anticoagulation (heparin) at 24 hours, units/kg	1.00	1.00–1.00	0.088

Significant P values < 0.05 in bold.
CI = confidence interval; CPB = cardiopulmonary bypass; EACA = ϵ-aminocaproic acid; OR = operating room; RACHS = Risk Adjustment for Congenital Heart Surgery; STAT = Society of Thoracic Surgeons-European Association of Cardiothoracic Surgery.
Chest tube output per weight at 24 hours was log-transformed for modelling; βs were back-transformed.

output. The geometric mean of chest tube output among African-American neonates was 71% higher than that of Caucasians (95% confidence interval, 29–125%; p = 0.001). Notably, after the removal of a single outlier (chest tube output 645 ml/kg) in a sensitivity analysis, the significant independent association between African-American race and increased chest tube output persisted.

Table 3. Adjusted linear regression for chest tube output per weight at 24 hours

Variable	e^{β}	95% CI	p-Value
Race			
African American	1.71	1.29–2.25	**<0.001**
Other/missing	1.23	0.87–1.74	0.242
White/Caucasian	*Reference*		
Post-conceptional age (weeks)	0.94	0.88–1.01	0.083
OR time (hours)	1.08	0.99–1.18	0.083
CPB time (hours)	1.18	0.96–1.45	0.110
Circulatory arrest			
Yes	1.14	0.84–1.53	0.395
No	*Reference*		
EACA/kg	1.00	1.00–1.00	0.850
Anticoagulation (heparin) at 24 hours, units/kg	1.00	1.00–1.00	0.113

Significant P values < 0.05 in bold.
CI = confidence interval; CPB = cardiopulmonary bypass; EACA = ϵ-aminocaproic acid; OR = operating room.
Chest tube output per weight at 24 hours was log-transformed for modelling and the βs were back-transformed.
Number of observations in the original data set = 107. Number of observations used = 100.

Descriptive statistics and unadjusted logistic regression analysis results for the exploratory analysis of factors associated with the highest quartile of chest tube output are provided in Supplementary Tables 1 and 2, respectively. Race, ϵ-aminocaproic acid total dose (mg/kg body weight), recombinant factor VIIa total dose (mcg/kg body weight), and duration of surgery each met criteria for inclusion in the adjusted logistic regression model. As shown in Table 4, in the adjusted model for the exploratory analysis of factors associated with the highest quartile of chest tube output, only race exhibited a statistically significant independent association with the highest quartile of chest tube output. Specifically, the odds of having post-operative blood loss in the highest quartile were increased more than five-fold among African-American neonates when compared to that of Caucasians (odds ratio = 5.09; 95% confidence interval, 1.47–17.68).

Discussion

In this retrospective cohort study, we evaluated independent pre-operative and intra-operative risk factors for increased bleeding after neonatal cardiopulmonary bypass at one institution. The results from our primary analysis suggest that African-American neonates are at increased risk of bleeding following open-heart surgery for palliation or correction of congenital cardiac defects with cardiopulmonary bypass, after adjustment for other important covariates and potential confounders. Specifically, the geometric mean of chest tube output among African-American neonates was 71% higher than that of Caucasians (p = 0.001). Furthermore, the odds of being in the highest quartile of chest tube output were over 5-fold higher among African Americans than among Caucasians. These findings are consistent with previous analyses that have shown an increased risk of coagulation abnormalities in African-American populations. Our findings suggest evidence for different mechanisms of this coagulation abnormality in African Americans.

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Table 4. Adjusted logistic regression for increased chest tube output per weight at 24 hours (highest quartile post-operative blood loss versus remaining three quartiles)

Covariate	Odds ratio (95% CI)	p-Value
Race		
African American	5.09 (1.47–17.68)	**0.010**
Other/missing	1.86 (0.39–8.93)	0.437
White/Caucasian	*Reference*	–
STAT score		
5	1.43 (0.35–5.86)	0.617
4	0.67 (0.14–3.07)	0.602
<3	*Reference*	
Factor VII administered (μg/kg)		
>0	0.28 (0.07–1.11)	0.069
0	*Reference*	–
OR time (hours)	1.47 (1.02–2.11)	**0.039**
EACA/kg	0.99 (0.98–1.01)	0.208

Significant P values < 0.05 in bold.
CI = confidence interval; CTO = chest tube output; EACA = ϵ-aminocaproic acid; OR = operating room; STAT = Society of Thoracic Surgeons-European Association of Cardiothoracic Surgery.
Number of observations in the original data set = 107. Number of observations used = 102. Highest quartile post-operative blood loss: CTO > 55.24 ml/kg; Remaining three quartiles: CTO ≤ 55.25 ml/kg.

Our findings are consistent with those of previous studies that have shown an increased prevalence of certain disorders of primary haemostasis among African Americans, in particular platelet function defects. In 2003, Phillips and colleagues studied 74 women with unexplained menorrhagia by using platelet aggregometry (the gold standard assay for platelet function) and found that abnormal results were more common among African Americans than among other races in their study population (56 versus 20%).[8] Faraday and co-workers have reported a high prevalence of an abnormal gene for a receptor associated with platelet aggregation among African Americans (genetic variant in PEAR 1).[9] Genotyping studies have also suggested differing expression of platelet receptor glycoprotein (that is, Haplotypes 52C/807T/1648A, or methionine allele -HPA-2) in Africans or other races (Asian, Caucasian, among others), based on single nucleotide polymorphisms, which may confer abnormalities in platelet function and help identify at-risk patients.[10] The findings in our study may be explained by abnormal platelet aggregation in African Americans and might be associated with genomic differences. Thus, future research is needed to identify genomic markers associated with platelet function. Though much of the literature comes from adults, some supporting data have been generated in the paediatric field.

Our findings on the association between African-American race and greater post-operative haemorrhage are supported by several prior studies in the surgical literature. Lam et al[11] reviewed the Health Care Cost and Utilization Project Kids Inpatient Database to search for patient-related risk factors, along with other factors, for blood transfusion in spinal surgery. African-American race, length of hospital stay, and different approaches to fusion were associated with blood transfusions.[11] Maher et al[12] conducted a retrospective review of electronic medical records of paediatric patients undergoing posterior spinal fusions in a tertiary care centre. Charts were reviewed of 74 patients who underwent posterior spinal fusion by one surgeon from June, 2013, to September, 2015. Multiple variables were collected, including self-identified race. African-American race was independently associated with higher blood loss when compared to white race ($p = 0.01$). Additionally African-Americans had higher odds of needing blood transfusion, as well as greater volumes of blood transfused, when compared to Caucasians.[12] Maher et al showed a significantly higher prevalence of type O blood among African-Americans than Caucasians. Consistent with this, Song et al[13] found that African-Americans had a higher incidence of O-type blood, as well as a significantly decreased factor VIII activity. Previous studies have demonstrated that type O blood is associated with reduced levels of factor VIII activity and von Willebrand factor when compared to other ABO types. The higher prevalence of type O blood among African Americans, and associated reduced levels of factor VIII and vWF, could theoretically have contributed to our study's findings, although we did not collect data on ABO blood type.

Although Maher et al[12] found African-American race to be independently associated with bleeding after posterior spinal fusion, other studies suggest socioeconomic status might influence bleeding. Qian et al[14] studied racial disparities using the University Health Consortium system database. After adjusting for levels of insurance, African-American patients had a significantly higher risk of receiving blood transfusion for both coronary artery bypass graft surgery and total hip replacement than did non-African-American patients of comparable insurance coverage. Differences in blood transfusions between African-Americans and Whites were similar before and after controlling for insurance status.[14] This finding might suggest that regardless of socioeconomic status, African-Americans may harbour an additional risk for bleeding. The percentage of patients with low socioeconomic status may be even greater in the neonatal population that requires open-heart surgery, and future analyses might suggest prenatal factors associated with bleeding in these patients. Unfortunately, this information was not collected for this study.

It may not be surprising to find that a greater proportion of African-American patients received factor VIIa when compared to Caucasian or other races. This finding may reflect the increased bleeding in African-Americans, given that factor VIIa has been advocated as a rescue therapy when usual attempts at haemostasis are exhausted.[15] Socioeconomic status may be a confounder in our study model, yet it is not clear if factors such as government-sponsored insurance, poverty, and lack of access to prenatal care play a role in outcomes of neonates undergoing complex congenital heart surgery with cardiopulmonary bypass. The prevailing literature on bleeding after neonatal cardiac surgery does not include pre-operative demographic data such as race.

Others have examined risk factors for bleeding after paediatric cardiac surgery. Guzzetta et al[16] conducted a retrospective review of neonates who underwent complex congenital heart surgery with cardiopulmonary bypass and found significant associations with 24-hour post-operative chest tube output for RACHS-1 Category, cardiopulmonary bypass time, and lowest temperature during cardiopulmonary bypass. Race was not among the data analysed. Savan et al[17], in a retrospective study of 182 children (ages 0–16 years old) who underwent congenital heart surgery, found cyanotic disease and time from cessation of cardiopulmonary bypass to chest closure to be independently associated with post-operative blood loss. In another analysis, Petaja et al[18] found

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that cardiopulmonary bypass time, aortic clamping time, and circulatory arrest time each correlated with red blood cell transfusion among 73 infants between 1 month and 1 year of age.

Our study has several potential limitations worthy of note. First, the single-centre nature of our analysis and the number of patients limit the generalisability of our findings. Additionally, the STAT Mortality Categories are an empirically derived methodology of risk stratification based on the statistical estimation of the risk of mortality prior to discharge from the hospital after paediatric and/or congenital cardiac surgery. In the STAT Mortality Categories, operations are sorted by increasing risk and grouped into five categories that were designed to minimise within-category variation and maximise between-category variation. However, the STAT Mortality categories do not directly estimate the risk for bleeding by incorporating variables such as the length of suture lines or whether or not the operation involved suture lines in high-pressure blood systemic blood vessels versus lower-pressure pulmonary vessels, both of which might also affect bleeding. For example, a longer suture line for aortic reconstruction (as compared to a shorter one used for the same procedure) may pose a greater risk of bleeding post-operatively. A second potential limitation is the outcome variable measured. The assumption made in this study was that in a 24-hour window, chest tube output was primarily a reflection of bleeding; however, chest tube output could consist of serous exudate as well. Alternative options for bleeding outcome measurement include the surrogate markers of post-operative blood transfusion volume (ml/kg) and change in haemoglobin from pre-operative baseline. However, given the variability within and among institutions in regard to blood transfusion thresholds/indications and practices, the diluting effects of fluid management, and fluid shifts in the first 24 hours after surgery, neither blood transfusion nor change in haemoglobin from pre-operative baseline is a reliable measure of post-operative haemorrhage, as indicated by many published studies.[18,19] A third potential limitation is that we were unable to quantify intra-operative bleeding by measuring time from cardiopulmonary bypass separation to chest closure, nor did we weigh sponges and measure suction volumes after separation. The measuring of intra-operative blood loss is not a well-accepted standard across institutions. Lastly, we did not collect data on socioeconomic status. Nevertheless, at the time of data collection, more than 70% of our patient population had indigent care or government-sponsored insurance. Race assignment was determined by the parents of the patient in the demographic information collected; and unfortunately, it was missing from one record. Each of these limitations should be addressed in future prospective multicentre cohort studies designed to substantiate and expand upon the findings of the present study, with the goal of developing a robust risk model for post-operative blood loss among neonates undergoing open-heart surgery with cardiopulmonary bypass for CHD.

Conclusion

Our analysis suggests that African-American neonates experience greater chest tube output over the first 24 hours after open-heart surgery than neonates of other ethnicities. Future prospective multicentre cohort studies or registry-based analyses should be carried out to validate these findings and to investigate potential mechanisms underlying the association between African-American race and greater post-operative bleeding in this population. In particular, the role of platelet function should be investigated, as platelet function defects are known to be more prevalent among African Americans than among Caucasians. Validation of these findings and elucidation of susceptibility traits, as well as the coagulative and fibrinolytic mechanisms that underlie the pre-disposition for post-operative bleeding, will lead to targeted therapies designed to prevent or better treat post-operative bleeding in this vulnerable population of critically ill neonates with CHD.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/S1047951119002683

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