Acute kidney injury following cardiopulmonary bypass in Jamaica

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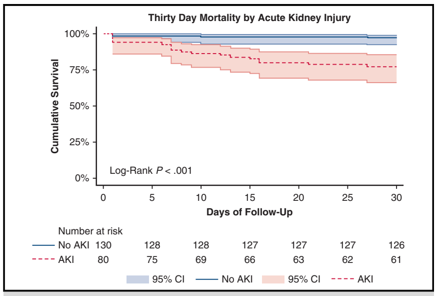
ABSTRACT

Objectives: The study objectives were to describe the incidence, risk factors, and outcomes of acute kidney injury after cardiopulmonary bypass in Jamaica.

Method: We performed a review of the medical records of adult patients (aged ≥ 18 years) with no prior dialysis requirement undergoing cardiopulmonary bypass at the University Hospital of the West Indies, Mona, between January 1, 2016, and June 30, 2019. Demographic, preoperative, intraoperative, and postoperative data were abstracted. Acute kidney injury was defined using Kidney Disease Improving Global Outcomes criteria. The primary outcomes were acute kidney injury incidence and all-cause 30-day mortality. Multivariable logistic regression and Cox proportional analyses were used to examine the association between the acute kidney injury risk factors and the primary outcome.

Results: Data for 210 patients (58% men, mean age 58.1 ± 12.9 years) were analyzed. Acute kidney injury occurred in 80 patients (38.1%), 44% with Kidney Disease Improving Global Outcomes I, 33% with Kidney Disease Improving Global Outcomes II, and 24% with Kidney Disease Improving Global Outcomes III. From multivariable logistic regression models, European System for Cardiac Operative Risk Evaluation II (odds ratio, 1.19; 95% confidence interval, 1.01-1.39 per unit), bypass time (odds ratio, 1.94; 95% confidence interval, 1.40-2.67 per hour), perioperative red cell transfusion (odds ratio, 3.03; 95% confidence interval, 1.36-6.76), and postoperative neutrophil lymphocyte ratio (odds ratio, 1.65; 95% confidence interval, 1.01-2.68 per 10-unit difference) were positively associated with acute kidney injury. Acute kidney injury resulted in greater median hospital stay (18 vs 11 days, $P < .001$) and intensive care unit stay (5 vs 3 days, $P < .001$), and an 8-fold increase in 30-day mortality (hazard ratio, 8.15; 95% confidence interval, 2.76-24.06, $P < .001$).

Conclusions: Acute kidney injury after cardiopulmonary bypass surgery occurs frequently in Jamaica and results in poor short-term outcomes. Further studies coupled with quality interventions to reduce the mortality of those with acute kidney injury are needed in the Caribbean. (JTCVS Open 2022;11:161-75)



Kaplan–Meier survival graph stratified by AKI.

CENTRAL MESSAGE

AKI incidence after bypass surgery in Jamaica is high and associated with adverse perioperative outcomes. Interventions to reduce AKI incidence can impact hospital stay and all-cause mortality.

PERSPECTIVE

AKI occurs in 38% of patients after bypass surgery in Jamaica and is associated with increased healthcare burden and 30-day mortality. High bypass time, euroSCORE II, postoperative NLR, and red cell transfusion were independent AKI risk factors. Further studies should validate these factors and evaluate interventions to reduce AKI in the Caribbean.

▶ Video clip is available online.

Forty-four million persons reside in the Caribbean, composed of predominantly high- and middle-income countries with a significant burden of cardiovascular disease, the leading cause of death and disability in the region.[1-3] Despite the apparent high-income sociodemographic index, lack of

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Abbreviations and Acronyms

AKI	= acute kidney injury
BMI	= body mass index
CABG	= coronary artery bypass grafting
CI	= confidence interval
CKD	= chronic kidney disease
eGFR	= estimated glomerular filtration rate
euroSCORE	= European System for Cardiac Operative Risk Evaluation
HR	= hazard ratio
ICU	= intensive care unit
IQR	= interquartile range
KDIGO	= Kidney Disease Improving Global Outcomes
NLR	= neutrophil lymphocyte ratio
OR	= odds ratio
RBC	= red blood cell
SCr	= serum creatinine

healthcare resources, and subspeciality care contribute to inequity in access to cardiovascular surgical care,[2] with an estimated 14 million of the Caribbean inhabitants having no direct access to cardiothoracic surgical services.[2,4,5] Jamaica, considered an upper middle–income Caribbean country by the 2020 World Bank Classification (US $8950.00 gross national income per capita)[5] has 1 of 10 regional Caribbean facilities for cardiopulmonary bypass surgery and the only such institution on the island.[6,7]

Acute kidney injury (AKI) is a common and resource-intensive complication of cardiac surgery, occurring in up to one-third of patients in high-income countries.[8] AKI increases the risk of death by 3 to 8 times, with the highest mortality in the 2% to 6% of patients who will require renal replacement therapy.[9,10] Survivors of AKI-complicating bypass surgery have a higher risk of chronic kidney disease (CKD), lower quality of life, and higher mortality and healthcare use in the subsequent years to surgery.[9-12]

There is a paucity of data on the epidemiology and outcomes of AKI-complicating bypass in the Caribbean. Smith and colleagues[13] reviewed 62 patients undergoing coronary artery bypass grafting (CABG) in Jamaica over a 10-year period. The incidence of AKI was 5%.[13] However, in this study AKI was defined as a creatinine increase of 89 μmol/L underestimating AKI based on current definitions.[13]

Given the high observed mortality of AKI and lack of dialysis resources in many middle-income countries,[14] establishing perioperative clinical AKI risk factors in a high-risk group and low-resource environment can prompt cost-effective regional measures to reduce risk and help identify timely quality care interventions to improve outcomes and ensure the appropriate allocation of resources.[15]

In this study, we determined the incidence of AKI after cardiopulmonary bypass surgery in Jamaica and examined risk factors for this outcome and the impact of AKI on hospital stay and all-cause mortality at a single-center tertiary referral unit.

MATERIALS AND METHODS

Study Population and Design

A retrospective cohort study of patients aged more than 18 years undergoing cardiopulmonary bypass surgery at the University Hospital of the West Indies, in Kingston, Jamaica, from January 1, 2016, to June 30, 2019, was performed. Patients with end-stage renal disease or dialysis dependence preoperatively, aged less than 18 years, or who died intraoperatively or who had no preoperative serum creatinine (SCr) measurements were excluded from this study.

Ethics approval was obtained by the University of the West Indies Ethics Committee- Approval Number: ECP 155, 17/18 on August 28, 2019. Informed consent was waived. Data abstracted from medical records included patient demographics (date of birth, date of admission), baseline hemoglobin, and renal function (as defined as preoperative hemoglobin and creatinine), baseline absolute neutrophil and lymphocyte count, type and indication for surgery, time on cardiopulmonary bypass, crossclamp time, intraoperative and bypass fluid balance, chronic medical illness (presence of hypertension, diabetes mellitus, or on preoperative medications for these conditions), preoperative left ventricular function, laboratory values for renal function (SCr), and hemoglobin in the first 72 hours postoperatively, immediate or day 0 postoperative neutrophil and lymphocyte count (first blood draw on day 0 of surgery), perioperative blood transfusion (defined as the need for red blood cell [RBC] transfusion intraoperatively or within 48 hours postoperatively), need for renal replacement therapy, duration on mechanical ventilation, length of intensive care unit (ICU) and hospital stay, and death from any cause. The 30-day survival was determined from outpatient records encounters postsurgery and validated through the Hospital's Births and Deaths Registry for the National Registrar General's Department from January 1, 2016, to April 30, 2020.

Measurements

All laboratory measurements were obtained from the University Hospital of the West Indies Laboratories. Samples for creatinine were analyzed using a Cobas c111 Analyzer (Roche). Estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease-Epidemiology Collaboration equation for black individuals.

$$\text{Female}: \ \text{SCr} \leq 61.9\ \mu\text{mol}/\text{L},\ \text{GFR} = 166 \times (\text{SCr}/61.9)^{-0.329} \times (0.993)^{\text{Age}}$$

$$\text{Female}: \ \text{SCr} > 61.9\ \mu\text{mol}/\text{L},\ \text{GFR} = 166 \times (\text{SCr}/61.9)^{-1.209} \times (0.993)^{\text{Age}}$$

$$\text{Male}: \ \text{SCr} \leq 79.6\ \mu\text{mol}/\text{L},\ \text{GFR} = 163 \times (\text{SCr}/79.6)^{-0.411} \times (0.993)^{\text{Age}}$$

$$\text{Male}: \ \text{SCr} > 79.6\ \mu\text{mol}/\text{L},\ \text{GFR} = 163 \times (\text{SCr}/79.6)^{-1.209} \times (0.993)^{\text{Age}}$$

Where SCr = Serum creatinine.[16]

Blood counts and automated differentials were obtained from output from a Cell-Dyne Ruby-Hematology Analyzer. Preoperative anemia was defined on the basis of the World Health Organization definition (hemoglobin <12 g/dL in women and <13 g/dL in men). Neutrophil/lymphocyte ratio was defined as the absolute neutrophil count divided by the lymphocyte count.

European System for Cardiac Operative Risk Evaluation (euroSCORE) risk model II was calculated using review of the preoperative medical record and preoperative laboratory values with the variables defined on the basis of euroSCORE II definitions.[17]

Study Outcomes

AKI was defined by Kidney Disease Improving Global Outcomes (KDIGO) criteria as an increase in SCr 26.5 μmol/L or greater or SCr 1.5 times or greater baseline from baseline SCr. Table E1 shows the details of KDIGO staging.

According to these criteria, patients were assigned to KDIGO stage 0 (no AKI) or KDIGO stages 1, 2, or 3 based on peak creatinine in the first 72 hours postoperatively compared with the baseline creatinine. This was defined as the preoperative creatinine in the electronic medical record. Primary outcomes were AKI incidence and 30-day mortality. The latter was defined as death by any cause during within 30 days of surgery.

Statistical Analysis

Study data were collected and managed using Research Electronic Data Capture electronic data capture tools hosted on the Caribbean Institute for Health Research's Health Insurance Portability and Accountability–compliant server.[18] Data were de-identified before export and analysis using STATA software (version SE 16.1; StataCorp LP).

The assumption for normality was assessed using skewness and kurtosis tests for continuous variables. The chi-square test for proportions or *t* tests and Wilcoxon rank-sum tests were used to assess differences in patient baseline characteristics by AKI.

Logistic regression models were also used to determine the effect of these factors on AKI incidence. Table E2 shows the details of the univariable analyses of the variables considered in the model development. All exposure variables with *P* values .20 or less or a prior known association with AKI regardless of *P* value were included in the multivariable analyses, and a backwards model building approach was used to develop the final logistic model. Variables were checked for collinearity and excluded in the final model if the correlation coefficient was 0.7 or more. Correlation matrices for the variables included in the final model are presented in Table E3. Hosmer–Lemeshow goodness-of-fit testing was done to assess differences between observed and expected results in the subgroups of the model population.

A Cox proportional analysis was performed to determine the association of AKI with 30-day mortality and produce Kaplan–Meier survival curves. We investigated proportional hazards assumption by tests and graphical diagnostics based on scaled Schoenfeld residuals.

Missing Data

Forty-three percent of the sample had missing data on independent variables on the outcome of interest (AKI). Details of the imputed variables are presented in the Supplemental Material (Table E4 shows percentages and number of imputed variables, and Table E5 shows variables with no missing data). Table E6 shows the details of the descriptive characteristics of the imputed dataset. Multiple chained imputation equations were used to impute the missing data. Univariable and multivariable logistic regression was used with the outcome of interest on those with complete data and then with imputed data. Standardized differences between the imputed and non-imputed dataset were performed (Table E7).

RESULTS

Of 259 patients (259) who underwent bypass surgery by local surgeons in the study period, 8 patients were excluded because of the presence of baseline end-stage renal disease or dialysis requirement preoperatively, 30 patients were pediatric patients (age <18 years), and 11 patients died intraoperatively or had no baseline creatinine (Figure 1: Study Cohort diagram).

Baseline Characteristics

Characteristics of the 210 patients are presented in Table 1. More than half (59%) were male with a mean age 57.6 $\pm$ 12.6 years, with women being older than men (60.1 $\pm$ 12.4 years vs 56 $\pm$ 12.9 years, respectively, $P = .023$). More than half (63%) of the participants were overweight or obese with mean body mass index (BMI) of 27.2 kg/m^2. Women had a higher mean BMI than men, and a higher proportion of women were obese. As expected, women had lower hemoglobin and serum creatinine, but there was no difference in anemia prevalence or baseline eGFR. Table E8 shows the sex-based differences in baseline characteristics.

Hypertension was present in 77%, with one-third of the population having diabetes mellitus. One-third of patients had reduced left ventricular ejection fraction (EF < 50%) or preoperative myocardial infarction. CKD (eGFR <60 mL/min/1.73 m^2) was present in 13%.

More than half of the patients received isolated coronary bypass grafting (CABG). Isolated valve replacement surgery (mitral or aortic valve) was performed in one-third of cases, and combined valve surgery and CABG were performed in 4% of cases. Median bypass time and crossclamp time were 168 and 96 minutes, respectively. More than half of patients (54%) required red cell transfusion intraoperatively, and 37.1% had postoperative red cell transfusion within 48 hours of surgery.

Acute Kidney Injury Incidence and Determinants

AKI occurred in 38.3% of patients (80), with 43.8% (35) KDIGO I, 32.5% (26) KDIGO II, and 23.7% (19) KDIGO III. Renal replacement therapy was required in 3.2% (7) of patients. Intermittent hemodialysis was performed in all patients requiring renal replacement therapy (Figure 2).

Differences in baseline characteristics according to AKI are presented in Table 1. Patients who developed AKI had lower baseline renal function with a higher prevalence of CKD and a higher euroSCORE II. These patients were also more likely to have a myocardial infarction within 90 days of surgery or preoperative diabetes.

In terms of surgical factors, a higher proportion of persons undergoing elective procedures did not have AKI; however, a higher proportion who underwent isolated valve replacement surgery developed AKI. Bypass and aortic crossclamp times were higher in AKI versus non-AKI groups. Despite no difference in bypass fluid balance between the AKI and non-AKI groups, bypass urine output was lower in the AKI group than in the non-AKI group. A higher proportion of participants with AKI had intraoperative and 48-hour

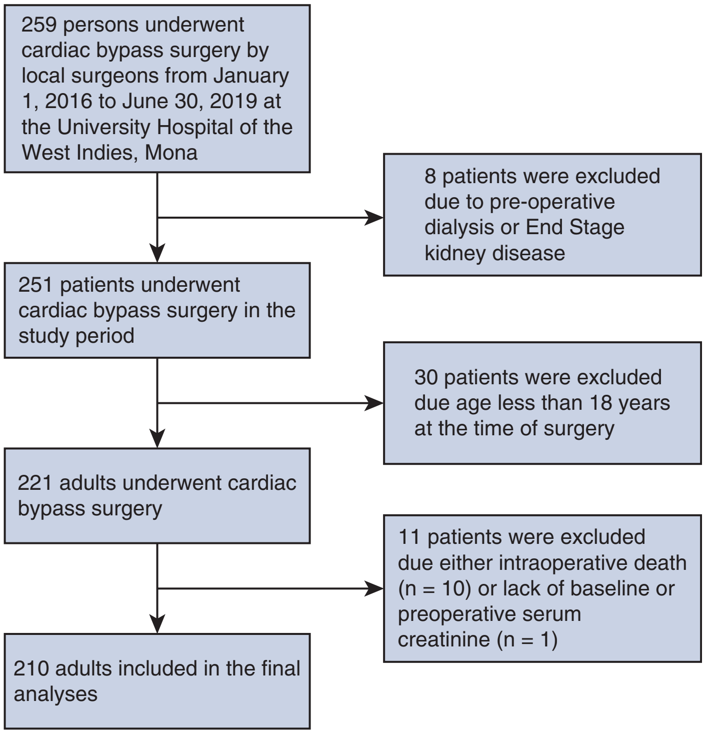


FIGURE 1. Study cohort description. A total of 259 patients underwent surgery in the study time period, and 8 were excluded because of end-stage renal disease. Thirty patients were aged less than 18 years, and 11 died intraoperatively or had no baseline creatinine, leaving a final cohort sample size of 210.

postoperative red cell transfusion. Preoperative and postoperative neutrophil lymphocyte ratio (NLR) was higher in the AKI group than in the non-AKI group.

euroSCORE II, BMI, preoperative and postoperative NLR, bypass time, perioperative RBC transfusion (red cell transfusion intraoperatively or within 48 hours postoperatively), preoperative hemoglobin, and preoperative hypertension were retained in the final model.

In this model, using the imputed dataset, euroSCORE II (odds ratio [OR], 1.19; 95% confidence interval [CI], 1.01-1.39) bypass time per hour (OR, 1.94; 95% CI, 1.40-2.67), perioperative RBC transfusion (OR, 3.03; 95% CI, 1.36-6.76), and postoperative NLR per 10-unit increase (OR, 1.65; 95% CI, 1.01-2.68) were associated with an increased risk of AKI. Preoperative BMI, preoperative hypertension, and hemoglobin were not associated with AKI in our model. Table 2 shows univariable and multivariable analyses for risk factors for AKI. Our model area under the receiver curve was 0.773, with a sensitivity of 53.1% and specificity of 90.0%. Hosmer–Lemeshow goodness-of-fit for the model chi-square was 5.3 ($P = .50$).

Secondary Analyses: Missing Data

Participants with missing data were older, with a higher preoperative creatinine, and a higher proportion requiring intraoperative red cell transfusion and undergoing isolated CABG surgery. There were no other significant differences in the known baseline characteristics between those with no missing data and those with missing data (Table E9). Multivariable logistic regression was performed in the complete dataset (no missing variables) and the imputed dataset. The results of the complete dataset regression model are highlighted in Table E10. There were no differences in the strengths in the associations of AKI; however, only bypass time, euroSCORE II, and perioperative blood transfusion remained statistically significant in the complete dataset.

Standardized differences between the variables of the imputed dataset and the complete dataset are presented in Table E7. There were no differences between the imputed variables and the nonimputed variables on secondary analyses.

Acute Kidney Injury Mortality and Outcomes

Overall, the 30-day mortality for the entire cohort was 11.0%; those with AKI had a 30-day mortality of 23.9%. AKI was associated with an approximately 9-fold increased risk for 30-day mortality (unadjusted hazard ratio [HR], 8.56, 95% CI, 2.91-25.17, $P < .001$). Figure 3 shows the Kaplan–Meier survival estimates. The estimate was only slightly attenuated after adjusting for age and sex (HR, 8.15, 95% CI, 2.76-24.06, $P < .001$). Risk of death at

TABLE 1. Baseline characteristics of the study population

Variable	All (n = 210)	AKI (n = 80)	No AKI (n = 130)	*P* value
Demographics				
Age (y) mean ± SD	57.6 ± 12.8	59.7 ± 12.5	56.4 ± 12.9	.075
Male n (%)	123 (58.6)	46 (57.5)	77 (59.2)	.805
BMI (kg/m^2) mean ± SD	27.2 ± 5.6	27.9 ± 5.8	26.7 ± 5.5	.162
Overweight n (%)	76 (36.2)	34 (42.5)	42 (32.3)	.349
Obese n (%)	56 (26.7)	21 (26.3)	35 (26.9)	.349
Baseline preoperative				
Preoperative Creatinine (μmol/L) mean ± SD	88.8 ± 46.8	99.8 ± 61.8	82.1 ± 32.9	**<.001**
Preoperative hemoglobin (g/dL) mean ± SD	13.1 ± 1.9	12.7 ± 2.1	13.3 ± 1.7	**.036**
Preoperative eGFR (mL/min/1.73 m^2) mean ± SD	94.9 ± 29.0	85.7 ± 30.5	100.6 ± 26.6	**<.001**
Preoperative NLR median (IQR)	2.0 (1.3-3.2)	2.4 (1.6-3.8)	1.8 (1.2-2.8)	.033
CKD (eGFR <60 mL/min/1.73 m^2) n (%)	27 (12.9)	19 (23.8)	8 (6.1)	**.001**
Preoperative anemia† n (%)	72 (34.8)	33 (41.3)	39 (30.7)	.121
Diabetes mellitus n (%)	57 (34.8%)	27 (45%)	30 (28.9%)	**.036**
Hypertension n (%)	127 (77.4%)	49 (80.3%)	78 (75.7%)	.496
euroSCORE II (%) median (IQR)	1.4 (0.9-2.3)	1.9 (1.3-3.6)	1.2 (0.8-1.8)	**<.001**
MI within 90 d, n (%)	47 (30.9)	24 (47.1)	23 (22.8)	**.002**
Preoperative LV dysfunction (EF <50%) n (%)	51 (33.8)	19 (33.9)	32 (33.7)	.976
Preoperative statin therapy n (%)	83 (55.0)	29 (54.7)	54 (55.1)	.964
Preoperative beta-blocker n (%)	98 (64.9)	35 (66.0)	63 (64.3)	.830
NYHA III or IV n (%)	48 (31.0)	20 (37.0)	28 (27.7)	.232
Intraoperative				
Elective surgery n (%)	130 (61.9)	38 (47.5)	92 (70.8)	**.001**
Isolated CABG n (%)	122 (58.1)	42 (52.5)	80 (61.5)	.197
Isolated valve replacement surgery n (%)	73 (34.7)	35 (43.8)	38 (29.2)	**.032**
Bypass time (min) median (IQR)	168 (131-211)	189 (159.5-259)	153.5 (126-193)	**<.001**
Aortic crossclamp time (min) median (IQR)	96 (75-120)	101 (83-139)	89.5 (70-116)	**.008**
Intraoperative RBC transfusion n (%)	112 (53.3)	53 (66.3)	59 (45.4)	**.003**
Bypass urine output (mL) median (IQR)	700 (500-1150)	671.5 (437.5-1015)	733 (550-1350)	**.048**
Bypass fluid balance (+mL) median (IQR)	1334.5 (690-1985)	1350 (555-2180)	1332 (810-1900)	.818
Postoperative				
Postoperative RBC transfusion*	78 (37.1)	41 (51.3)	37 (28.5)	**.001**
Postoperative NLR median (IQR)	9.4 (6.6-14)	10.5 (7.1-15.5)	8.7 (6.3-12.9)	**.038**

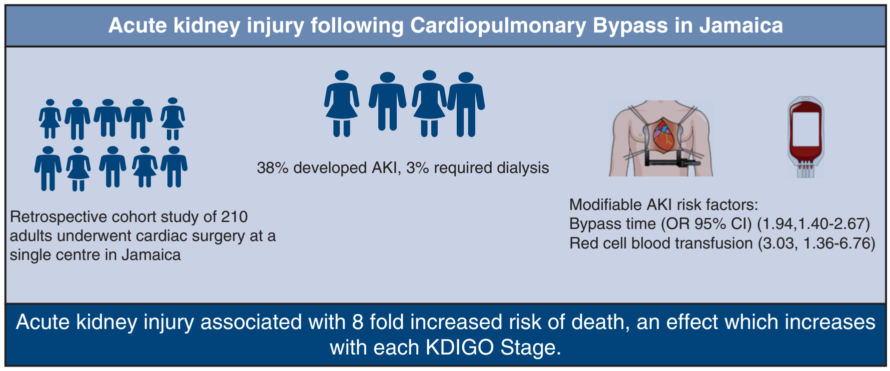
Bold values refer to statistical significance *P* values <.05. *AKI*, Acute kidney injury; *SD*, standard deviation; *BMI*, body mass index; *eGFR*, estimated glomerular filtration rate; *NLR*, neutrophil lymphocyte ratio; *CKD*, chronic kidney disease (preoperative eGFR <60 mL/min/m^2); *IQR*, interquartile range; *MI*, myocardial infarction; *LV*, left ventricle; *EF*, ejection fraction; *NYHA*, New York Heart Association; *CABG*, coronary artery bypass grafting; *RBC*, red blood cell. *Postoperative RBC, red cell transfusion within 48 hours postoperatively. †Preoperative anemia (hemoglobin <13 g/dL in men and 12 g/dL in women).

30 days was higher with increasing KDIGO stage: KDIGO stage I (unadjusted HR, 3.91; 95% CI, 1.00-15.63), KDIGO stage II (unadjusted HR, 9.9, 95% CI, 2.91-34.00), and KDIGO stage III (unadjusted HR, 16.46, 95% CI, 4.94-54.87). This effect was similar when adjusting for age and sex. The need for renal replacement therapy (dialysis) increased the risk of death by 20 times (adjusted HR, 19.54; 95% CI, 7.19-53.13).

Median length of hospital stay was 13 (interquartile range [IQR], 9-20) days. The median length of ICU stay was 3 (IQR, 2-5) days (Video Abstract). Patients with AKI had a longer median length of hospitalization (18 vs 11 days, $P < .001$) and ICU stay (5 vs 3 days, $P < .001$) compared with non-AKI patients. Table 3 shows details of length of stay by KDIGO stage.

DISCUSSION

This is the largest cohort study describing the epidemiology, risk factors, and outcomes of AKI after cardiac bypass surgery in the Caribbean that we are aware of. AKI occurred in 38.1% of persons after bypass, with 3% requiring renal replacement. This is significantly higher than the global reported incidence of AKI after cardiac surgery of 22%,[19] with the range reported in several observational studies of 5%-30%.[3,10,20-23] In a recent retrospective multicenter review of more than 6000 cardiac surgeries in North America, the incidence of AKI using KDIGO-based creatinine definitions was 39%.[24] The majority of AKI was KDIGO stage I (82%) compared with our cohort, which had a higher rate of stage II and III AKI.[24] This has implications for mortality, healthcare costs, and use because



AKI: Acute kidney injury, KDIGO: Kidney Disease Improving Global Outcomes, CI: Confidence Interval, OR: Odds Ratio

FIGURE 2. AKI after cardiopulmonary bypass surgery in Jamaica. Of 210 persons undergoing bypass surgery in Jamaica, 38.1% developed AKI with 3% requiring dialysis. Modifiable risk factors include prolonged bypass time, per 1-hour increase, perioperative red cell transfusion. AKI was associated with an 8-fold increase in mortality, an effect that increases with increasing KDIGO AKI stage. *AKI*, Acute kidney injury; *OR*, odds ratio; *CI*, confidence interval; *KDIGO*, Kidney Disease Improving Disease Outcomes.

stage II and III AKI are associated with a significantly higher morbidity and mortality compared with stage I AKI.[4-6,25]

Prolonged bypass time, elevated postoperative NLR and euroSCORE II, and RBC transfusion perioperatively were risk factors identified for the development of AKI, whereas baseline hemoglobin, BMI, hypertension, and preoperative NLR were not associated with cardiac surgery–associated AKI.

Day 0 postoperative NLR was associated with an approximately 2-fold increased risk of AKI in our cohort. This is in congruence with prior observational studies reporting an association with postoperative NLR and perioperative AKI[26,27] and supports an inflammatory host response after bypass and surgery contributing to its pathogenesis. Our data may suggest that this effect is independent of bypass time, because day 0 remained a factor associated with AKI on multivariable analysis. Although we did not measure kidney injury biomarkers, which have been reported as determinants of AKI and AKI outcomes with varying predictive power in large prospective cohorts,[15-17] the applicability and feasibility of these biomarkers in the Caribbean population are restricted by cost and accessibility.[18] The clinical utility of NLR may be an early predictor of AKI because creatinine-based measurements are influenced by immediate perioperative fluid balance and is a late marker of renal dysfunction.[25] NLR is also inexpensive and readily accessible in resource-poor settings. Our study did not have a validation cohort; therefore, further studies validating this marker and identifying optimal cutoff points for AKI prediction are needed.

Both anemia and RBC transfusion may increase the risk of perioperative AKI. Anemia causes increased renal hypoxic stress and RBC transfusion by increased inflammatory response and free radical–related injury.[28] Observational data also suggest that both preoperative anemia and perioperative RBC increase the risk of AKI and morbidity in CABG surgery. Based on multivariable analyses, however, RBC transfusion intraoperatively or within the first 48 hours postoperatively was associated with a 3-fold increased risk for AKI even when adjusting for baseline or preoperative hemoglobin. Garg and colleagues,[20] in their randomized

TABLE 2. Univariable and multivariable logistic regression analysis for acute kidney injury

Risk factors	Univariable Odds ratio (95% CI)	*P* value	Multivariable Odds ratio (95% CI)	*P* value
BMI (per 1 increase)	1.04 (0.98-1.10)	.164	1.04 (0.98-1.10)	.248
euroSCORE II	1.18 (1.00-1.38)	.044	1.19 (1.01-1.39)	**.040**
Hypertension	1.32 (0.62-2.83)	.470	1.27 (0.51-3.20)	.604
Baseline hemoglobin	0.85 (0.73-0.99)	.042	0.96 (0.79-1.16)	.680
CPB time (per hour)	1.94 (1.45-2.60)	<.001	1.94 (1.40-2.67)	**<.001**
Preoperative NLR (per 10 increase)	1.43 (0.52-3.91)	.491	1.19 (0.36-3.90)	.771
Perioperative PRBC transfusion	2.45 (1.30-4.60)	.005	3.03 (1.36-6.76)	**.007**
Postoperative NLR (per 10 increase)	1.54 (1.04-2.29)	.033	1.65 (1.01-2.68)	**.046**

Bold values refer to statistical significance *P* values <.05. *CI*, Confidence interval; *BMI*, body mass index (kg/m^2); *euroSCORE*, European System for Cardiac Operative Risk Evaluation; *CPB*, cardiopulmonary bypass; *NLR*, neutrophil lymphocyte ratio; *PRBC*, packed red blood cell.

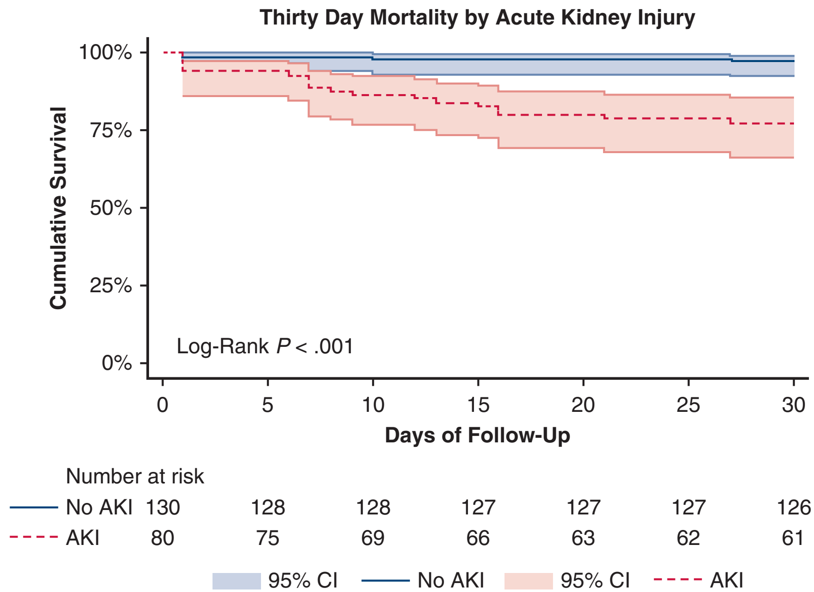


FIGURE 3. Kaplan–Meier survival curves. Kaplan–Meier 30-day survival stratified by AKI. Shading corresponds to 95% CI. *AKI*, Acute kidney injury; *CI*, confidence interval.

control trial comparing a restrictive with a liberal regimen (transfusion threshold of <7.5 vs 9.5 g/dL), reported no increased risk in RBC restrictive transfusion practice and development of postoperative AKI. There was a 38% reduction in blood transfusion requirements in the restrictive group.[20] There is a lack of availability of blood products locally, and institutional practice uses preoperative donation from relatives. The association of blood transfusion with AKI may reflect perioperative transfusion practices at the institution and highlights the need for quality improvement with measures aimed at a more restrictive transfusion threshold to improve outcomes.

Bypass time was another modifiable factor identified in our analyses as a risk factor for AKI, with bypass time per hour increase associated with a 2-fold increase in AKI. Mean bypass time in our study was 2 times higher compared with that reported in the literature.[21] This may reflect operator experience because this center is a low-volume center performing approximately 70 to 80 bypass surgeries annually, divided among 4 locally trained cardiothoracic surgeons and limited trained supporting staff inclusive of perfusionists, specialized cardiothoracic nurses, intensivists, and cardiac anesthesiologists. Table 4 shows details of the capacity and resources at the University Hospital of the West Indies, Jamaica. Measures to reduce the bypass time may be needed to mitigate AKI risk. Off-pump bypass surgery is associated with significantly less risk of AKI than bypass surgery, with a reported incidence of 4% globally.[22] In Trinidad and Tobago, another cardiac surgical center in the Caribbean, which performs mainly off-pump cardiac surgery (99%), reported an incidence of AKI of 2% from a retrospective cohort of 205 participants.[23] Given the reduced frequency of AKI after off-pump surgery reported, considerations for development of an off-pump cardiac program in small island states like Jamaica may be made.

euroSCORE II was an independent risk factor of AKI in our cohort, with each 1% increase the risk of AKI by 19%. euroSCORE II is a widely used preoperative clinical risk score validated in large studies to predict 30-day mortality after surgery.[26,29] Several observational studies report euroSCORE II as an independent predictor of renal replacement therapy and severity of AKI.[5] Based on our data, preoperative euroSCORE II may be a useful clinical score in identifying those persons at high risk for AKI. Contrary to prior reports, hypertension and BMI were also not associated with development of AKI in our cohort.

TABLE 3. Outcomes for acute kidney injury by Kidney Disease Improving Global Outcomes stage

Outcome	Stage 0 KDIGO (no AKI)	Stage 1 KDIGO	Stage 2 KDIGO	Stage 3 KDIGO
30-d mortality n (%)	4 (17.4)	4 (17.4)	7 (30.4)	8 (34.8)
Dialysis n (%)	0	0	1 (14.3)	6 (85.7)
Length of stay ICU (d), median (IQR)	3 (2-4)	3 (2-6)	6 (3-8)	13.5 (5-23)
Length of stay hospital (d), median (IQR)	11 (8-15.5)	15 (11-24)	20 (15-26)	39 (13-98)

KDIGO, Kidney Disease Improving Global Outcomes; *AKI*, acute kidney injury; *ICU*, intensive care unit; *IQR*, interquartile range.

TABLE 4. Available resources at the University Hospital of the West Indies and Jamaica for cardiac surgery

	Jamaica	University hospital of the West Indies
No. of perfusionists	1	1
No. of cardiothoracic surgeons	6	4
No. of cardiac anaesthesiologists	2	2
No. of nephrologists	12	4
Residency program in cardiothoracic surgery	Yes since 1994	Yes
Year of onset of cardiac surgery	1968	1968
ICU beds	30	21

ICU, Intensive care unit.

We also found a significant increased correlation of AKI with 30-day mortality and length of ICU and hospital stay. Furthermore, length of stay in hospital was significantly higher in our entire cohort than that reported globally for bypass surgery.[10] This may be related to limitations in ICU space, availability of operation time, or blood products that may delay surgery and add to length of stay. The impact of AKI on length of ICU and hospital stay is of clinical significance in resource-poor settings, because cost increases as hospital and ICU stay increase.[5,18] Additionally, ICU capacity per population is lower in low- and middle-income versus high-income countries, with Jamaica having an ICU capacity of 1 bed per 100,000 population.[30] Measures to reduce AKI may improve healthcare costs and mortality after cardiac surgery.

Study Limitations

Our study had several limitations. The sample size was small; therefore, associations may have been underestimated. We had to impute some of the explanatory variables using multiple imputation, potentially further underestimating the associations. The study was also underpowered to perform some subgroup analyses. There were no data on postoperative urine output; therefore, correlation with prevalence of AKI based on KDIGO definitions may be limited. Prior studies in AKI suggested a higher incidence of AKI when urine-output criteria are used.[24] The study was retrospective; therefore, other risk factors for AKI development may have not been identified in the data collected.

CONCLUSIONS

AKI frequently complicates bypass surgery in Jamaica and is associated with an 8-fold increase in 30-day mortality and increases in length of ICU and hospital stay, with an effect that increases with increasing KDIGO stage. Potential modifiable risk factors for AKI identified in this study include bypass time and RBC transfusion. Immediate postoperative NLR was an identified risk factor for AKI, and further studies are needed to validate this marker and identify optimal cutoff points for AKI prediction. This study provides the basis for implementation studies that could target surgical time and optimal transfusion thresholds to mitigate AKI risk and improve patient outcomes. This may guide policy in resource allocation to improve the capacity of cardiopulmonary bypass programs in the Caribbean.

Conflict of Interest Statement

The authors reported no conflicts of interest.

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

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Key Words: acute kidney injury, cardiopulmonary bypass, Caribbean, euroSCORE II, neutrophil lymphocyte ratio

TABLE E1. Kidney Disease Improving Global Outcomes stages of acute kidney injury

Stage	Serum creatinine criteria
I	≥26.5 μmol/L increase from baseline OR 1.5-1.9 times baseline creatinine
II	2-2.9 times baseline
III	3 times baseline OR ≥353.6 μmol/L OR Initiation of renal replacement therapy

TABLE E2. Univariable and multivariable analyses for acute kidney injury

	Univariable		Multivariable	
Risk factors	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value
Age (per 10-y increase)	1.23 (0.98-1.54)	.076		
Female sex	1.07 (0.61-1.89)	.805		
BMI (per 1 increase)	1.04 (0.98-1.10)	.164	1.04 (0.98-1.10)	.248
Elective surgery	0.37 (0.21-0.67)	.001		
euroSCORE II	1.18 (1.00-1.38)	.044	1.19 (1.01-1.39)	**.040**
Diabetes mellitus	1.86 (0.98-3.53)	.057		
Hypertension	1.31 (0.62-2.84)	.47	1.27 (0.51-3.20)	.604
Baseline creatinine	1.01 (1.00-1.02)	.018		
Chronic kidney disease*	4.75 (1.97-11.47)	.038		
Baseline hemoglobin	0.85 (0.73-0.99)	.038	0.96 (0.79-1.16)	.680
NYHA category 3 and 4	1.67 (0.95-2.95)	.074		
Preoperative MI	2.29 (1.11-4.73)	.025		
Bypass time (per hour)	1.94 (1.45-2.60)	<.001	1.94 (1.40-2.67)	**<.001**
Isolated valve replacement	1.63 (0.89-2.96)	.109		
Preoperative NLR (per 10 increase)	1.46 (0.53-4.00)	.459	1.19 (0.36-3.90)	.771
Perioperative RBC transfusion	2.45 (1.30-4.60)	.005	3.03 (1.36-6.76)	**.007**
Postoperative NLR (per 10 increase)	1.53 (1.04-2.29)	.033	1.65 (1.01-2.68)	**.046**
Bypass urine output per kg per hour	0.79 (0.70-0.90)	<.001		

Bold values refer to statistical significance *P* values <.05. *CI*, Confidence interval; *BMI*, body mass index; *euroSCORE*, European System for Cardiac Operative Risk Evaluation; *NYHA*, New York Heart Association; *MI*, myocardial infarction; *NLR*, neutrophil lymphocyte ratio; *RBC*, red blood cell. *Chronic kidney disease was defined as a preoperative eGFR less than 60 mL/min/m^2.

TABLE E3. Covariance matrix of coefficients of the final logistic model

	Baseline hemoglobin	Postoperative NLR	Bypass time	RBC transfusion	euroSCORE II	BMI	Hypertension	Preoperative NLR
Baseline hemoglobin	1.0							
Postoperative NLR	0.15	1.0						
Bypass time	−0.03	0.03	1.0					
RBC transfusion	0.40	0.25	0.02	1.0				
euroSCORE II	0.11	0.03	−0.02	0.08	1.0			
BMI	0.01	0.05	−0.02	0.05	0.08	1.0		
Hypertension	0.1	0.07	0.21	−0.05	−0.06	−0.25	1.0	
Preoperative NLR	−0.04	−0.28	0.04	−0.03	−0.03	0.02	−0.09	1.0

Baseline hemoglobin (defined as baseline or preoperative hemoglobin). *NLR*, Neutrophil lymphocyte ratio; *euroSCORE*, European System for Cardiac Operative Risk Evaluation; *RBC*, red blood cell; *BMI*, body mass index.

TABLE E4. Variables with missing data

Variables	No. of observations with missing data n (%)
Preoperative hemoglobin	3 (1.4)
Hypertension	46 (21)
Diabetes	46 (21)
NYHA stage	55 (26)
Preoperative EF	58 (28)
MI at 90 d	58 (28)
Preoperative beta-blocker	59 (28)
Preoperative statin therapy	59 (28)
euroSCORE II	67 (32)
Urine output on bypass	1 (0.5)
Preoperative NLR	16 (8)
Aortic crossclamp time	1 (0.5)
Hospital LOS	73 (35)
ICU LOS	15 (7)

NYHA, New York Heart Association; *EF*, ejection fraction; *MI*, myocardial infarction; *euroSCORE*, European System for Cardiac Operative Risk Evaluation; *NLR*, neutrophil lymphocyte ratio; *LOS*, length of stay; *ICU*, intensive care unit.

TABLE E5. Variables with no missing data

Variables
Preoperative creatinine
Bypass time
Intraoperative RBC transfusion
Postoperative RBC transfusion*
Age
Sex
Weight
Height
Postoperative NLR
AKI (outcome of interest)
Death (outcome of interest)
Type of surgery performed

AKI, Acute kidney injury; *NLR*, neutrophil-lymphocyte ratio; *RBC*, red blood cell; *PRBC*, packed red blood cell. *Postoperative RBC: red cell transfusion within 48 hours postoperatively.

TABLE E6. Descriptive statistics for imputed dataset

Variable	All (n = 210)	AKI (n = 80)	No AKI (n = 130)
euroSCORE II (%) mean ± SE	2.2 ± 0.247	2.9 ± 0.489	1.7 ± 0.252
Urine output on bypass (mL/kg/h) mean ± SE	4.4 ± 0.236	3.2 ± 0.250	5.1 ± 0.335
Preoperative NLR mean ± SE	2.8 ± 0.205	3.0 ± 0.280	2.7 ± 0.284
Baseline hemoglobin (g/dL) mean ± SE	13.1 ± 0.131	12.7 ± 0.236	13.3 ± 0.153
Hypertension (%) ± SE	77.5 ± 3.179	80.4 ± 4.964	75.7 ± 4.108
Diabetes (%) ± SE	35.3 ± 3.688	44.2 ± 6.131	29.8 ± 4.483
NYHA stage III/IV (%) ± SE	32.2 ± 3.816	36.7 ± 6.845	29.4 ± 4.447
Preoperative MI (%) ± SE	31.4 ± 0.390	42.6 ± 7.058	24.5 ± 4.323

AKI, Acute kidney injury; *euroSCORE*, European System for Cardiac Operative Risk Evaluation; *SE*, standard error; *NLR*, neutrophil lymphocyte ratio; *NYHA*, New York Heart Association; *MI*, myocardial infarction.

TABLE E7. Standardized differences between imputed dataset and complete dataset

euroSCORE II	−0.005
Urine output on bypass (mL/kg/h)	0.000
Preoperative NLR mean	−0.005
Baseline hemoglobin (g/dL)	0.001
Hypertension (%)	0.000
NYHA stage III/IV	0.000
Preoperative MI	0.250

euroSCORE, European System for Cardiac Operative Risk Evaluation; *NLR*, neutrophil lymphocyte ratio; *NYHA*, New York Heart Association; *MI*, myocardial infarction.

TABLE E8. Baseline characteristics of the study population

Variable	All (n = 210)	Male (n = 123)	Female (n = 87)	*P* value
Demographics				
Age (y) mean ± SD	57.6 ± 12.9	56.0 ± 12.9	60.1 ± 12.4	**.023**
BMI (kg/m^2) mean ± SD	27.2 ± 5.6	26.2 ± 4.8	28.6 ± 6.4	**.003**
Overweight n (%)	76 (36.2)	46 (37.4)	30 (34.5)	**.010**
Obese n (%)	56 (26.7)	23 (18.7)	33 (37.9)	**.010**
Baseline preoperative				
Preoperative creatinine (μmol/L) mean ± SD	88.8 ± 46.8	97.0 ± 47.0	77.2 ± 44.2	**.002**
Preoperative hemoglobin (g/dL) mean ± SD	13.1 ± 1.9	13.5 ± 1.9	12.5 ± 1.8	**<.001**
Preoperative eGFR (mL/min/1.73 m^2) mean ± SD	94.9 ± 29.0	95.1 ± 28.6	94.7 ± 29.8	.932
Preoperative NLR median (IQR)	2.0 (1.3-3.2)	2.2 (1.6-3.2)	1.6 (1.2-2.5)	.005
CKD (eGFR < 60 mL/min/1.73 m^2) n (%)	27 (12.9)	17 (13.8)	10 (11.5)	.620
Preoperative anemia† n (%)	72 (34.8)	43 (35.5)	29 (33.7)	.787
Diabetes mellitus n (%)	57 (34.8)	30 (31.9)	27 (38.6)	.376
Hypertension n (%)	127 (77.4)	68 (72.3)	59 (84.3)	.070
euroSCORE II (%) median (IQR)	1.4 (0.9-2.3)	1.9 (1.3-3.6)	1.3 (0.8-1.8)	.331
MI within 90 d n (%)	47 (30.9)	28 (32.6)	19 (28.8)	.618
Preoperative LV dysfunction (EF <50%) n (%)	51 (33.8)	32 (38.1)	19 (28.4)	.209
Preoperative statin therapy n (%)	83 (55.0)	47 (54.0)	36 (56.3)	.786
Preoperative beta-blocker n (%)	98 (64.9)	54 (62.1)	44 (68.8)	.395
NYHA III or IV n (%)	48 (31.0)	26 (29.2)	22 (33.3)	.232
Intraoperative				
Elective surgery n (%)	130 (61.9)	74 (60.2)	56 (64.4)	.536
Isolated CABG n (%)	122 (58.1)	74 (60.2)	48 (55.2)	.470
Isolated valve replacement surgery n (%)	73 (34.7)	39 (31.7)	34 (39.1)	.269
CPB time (min) median (IQR)	168 (131-211)	171 (136-215)	154 (128-211)	.125
Aortic crossclamp time (min) median (IQR)	96 (75-120)	100 (76-126)	92 (69-113)	.137
Intraoperative RBC transfusion n (%)	112 (53.3)	53 (43.1)	59 (67.8)	**<.001**
Bypass urine output (mL) median (IQR)	700 (500-1150)	703 (500-1100)	700 (450-1330)	.710
Bypass fluid balance (+mL) median (IQR)	1334.5 (690-1985)	1325 (630-1900)	1375 (810-2170)	.242
Postoperative				
Postoperative RBC transfusion*	78 (37.1)	44 (35.8)	34 (39.1)	.625
Postoperative NLR median (IQR)	9.4 (6.6-14)	10.0 (7.0-14.1)	8.5 (5.8-14)	.100

Bold values refer to statistical significance *P* values <.05. *SD*, Standard deviation; *BMI*, body mass index; *CKD*, chronic kidney disease; *eGFR*, estimated glomerular filtration rate; *euroSCORE*, European System for Cardiac Operative Risk Evaluation; *MI*, myocardial infarction; *LV*, left ventricle; *EF*, ejection fraction; *NYHA*, New York Heart Association; *CABG*, coronary artery bypass grafting; *CPB*, cardiopulmonary bypass; *IQR*, interquartile range; *RBC*, red blood cell; *NLR*, neutrophil lymphocyte ratio. *Postoperative RBC: red cell transfusion within 48 hours postoperatively. †Preoperative anemia: Hemoglobin less than 13 g/dL in men and 12 g/dL in women.

TABLE E9. Differences between complete dataset (no missing variables) and dataset with missing variables

	Data set with no missing data (n = 120)	Data set with missing data* (n = 90)	*P* value
Age (y) mean ± SD	55.7 ± 14.1	60.3 ± 10.5	.010
BMI (kg/m^2) mean ± SD	26.7 ± 5.6	27.8 ± 5.7	.188
Female, n (%)	50 (41.7)	37 (41.1)	.936
Preoperative creatinine (μmol/L) mean ± SD	85.0 ± 46.3	94.0 ± 47.2	.050
Elective surgery n (%)	75 (61.5)	55 (62.5)	.880
Isolated CABG n (%)	58 (48.3)	56 (62.2)	.046
Isolated valve replacement surgery n (%)	41 (34.2)	24 (26.7)	.245
CPB time (min) mean ± SD	184.2 ± 71.9	178.6 ± 76.7	.284
Intraoperative RBC transfusion n (%)	35 (35.7)	55 (49.1)	.050
Postoperative RBC transfusion*	59 (44.7)	31 (39.7)	.483
Postoperative NLR mean ± SD	10.6 ± 5.9	12.2 ± 8.5	.428

BMI, Body mass index; *SD*, standard deviation; *CABG*, coronary artery bypass grafting; *CPB*, cardiopulmonary bypass; *RBC*, red blood cell; *NLR*, neutrophil lymphocyte ratio. *Post operative RBC transfusion was defined as transfusion of blood within 48 hours of surgery.

TABLE E10. Univariable and multivariable logistic regression for complete data set (n = 120)

Risk factors	Univariable Odds ratio (95% CI)	*P* value	Multivariable Odds ratio (95% CI)	*P* value
BMI (per 1 increase)	1.04 (0.99-1.09)	.164	1.09 (0.99-1.18)	.059
euroSCORE II	1.47 (1.14-1.89)	.003	1.39 (1.09-1.77)	**.008**
Hypertension	1.31 (0.60-2.84)	.496	1.05 (0.35-3.17)	.930
Baseline hemoglobin	0.85 (0.73-0.99)	.038	1.17 (0.88-1.56)	.290
Bypass time (per hour)	1.94 (1.45-2.60)	<.001	1.89 (1.17-3.07)	**.010**
Preoperative NLR (per 10 increase)	1.46 (0.53-4.00)	.459	0.86 (0.16-4.79)	.867
Perioperative RBC transfusion	2.45 (1.30-4.60)	.005	3.40 (1.17-9.83)	**.024**
Postoperative NLR (per 10 increase)	1.54 (1.04-2.29)	.033	1.57 (0.73-3.35)	.243

Bold values refer to statistical significance *P* values <.05. *CI*, Confidence interval; *BMI*, body mass index; *euroSCORE*, European System for Cardiac Operative Risk Evaluation; *NLR*, neutrophil lymphocyte ratio; *RBC*, red blood cell.