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BLOOD TRANSFUSION IS ASSOCIATED WITH PROLONGED DURATION OF MECHANICAL VENTILATION IN INFANTS UNDERGOING REPARATIVE CARDIAC SURGERY

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Abstract

Objective—Perioperative transfusion has adverse effects in adults undergoing cardiac surgery. We sought to investigate whether greater use of blood and blood products might be an independent predictor of prolonged postoperative recovery, indicated by duration of mechanical ventilation (DMV), after reparative infant heart surgery.

Design and Patients—Prospectively collected data on 270 infants from two randomized trials of hematocrit strategy during cardiopulmonary bypass in infant heart surgery were analyzed to explore the association of DMV with perioperative transfusion and other variables.

Measurements and Main Results—In univariable analyses, longer DMV was associated with younger age and lower weight at surgery, diagnostic group, and higher intraoperative and postoperative blood product transfusion (each $p < 0.001$). In multivariable proportional hazard regression, longer total support time and greater intraoperative and early postoperative blood products per kg were the strongest predictors of longer DMV. Patients in the highest tertile of intraoperative blood products per kg had an instantaneous risk of being extubated approximately half that of patients in the lowest tertile (hazard ratio=0.51, 95% CI 0.35, 0.73). Patients who received any blood products postoperative day 1, compared to those who did not, had a hazard ratio for extubation of 0.65 (95% CI 0.50, 0.85).

Conclusions—In this exploratory secondary analysis of infants undergoing two ventricular repair of congenital heart disease without aortic arch obstruction, greater intraoperative and early postoperative blood transfusion emerged as potential important risk factors for longer DMV. Future prospective clinical trials are needed to determine whether reduction in blood product administration hastens postoperative recovery after infant heart surgery.

Keywords

Pediatric; Cardiac surgery; Blood transfusion; Ventilation; Tetralogy of Fallot; Transposition; Ventricular septal defect

As contemporary mortality rates have declined for complete congenital heart repair in infancy, research aimed at decreasing perioperative morbidity has assumed greater importance. Early extubation and “fast-tracking” are goals of postoperative care in the current era (1), and most children are successfully extubated within 12 to 48 hours of admission to the intensive care unit (ICU). A small subset, however, remain ventilator dependent for days to weeks. Previous studies of diverse patient populations have linked longer duration of mechanical ventilation (DMV) to gestational age under 36 weeks (1), younger age at surgery (1, 2), duration of operative support (1–3), postoperative arterial oxygen tension ($\text{PaO}_2/\text{FiO}_2$), fluid intake on the first postoperative day, and preoperative intubation (3). Regardless of its etiology, prolonged DMV is associated with longer recovery times, major complications and mortality, increased hospital costs, and worse long-term neurodevelopmental outcome (2, 4, 5). Knowledge of modifiable factors associated with prolonged DMV is limited (4, 6). Further study of risk factors for prolonged DMV in children following cardiac surgery may help guide strategies to reduce length of ventilation, thus decreasing morbidity and associated health care costs.

Recent studies have suggested that perioperative transfusion has adverse effects in adults undergoing cardiac surgery (7, 8). Because transfusion strategy is a modifiable parameter, we sought to explore whether greater use of blood and blood products might have independent adverse effects on DMV after reparative infant heart surgery. Our goal was pursued using the database of two prospective clinical trials on intraoperative hematocrit strategy in a homogeneous population of infants undergoing two ventricular repairs without aortic arch obstruction.

METHODS

Patients

Data were obtained from 270 infants participating in two consecutive randomized, controlled trials evaluating outcomes following different hematocrit strategies during cardiopulmonary bypass in infants undergoing corrective cardiac surgery (9, 10). Patients were enrolled at a single center between November 1996 and July 2004. Eligibility criteria and recruitment strategies, conduct of the hematocrit trials, and outcomes have been previously described (9, 10). Briefly, inclusion criteria included infants <9 months of age from one of the following diagnostic groups: (1) ventricular septal defect (VSD) or complete common atrioventricular canal defect (“VSD group”), (2) D-transposition of the great arteries (TGA) with or without intact ventricular septum (“TGA group”), and (3) a conotruncal group including tetralogy of Fallot with or without pulmonary atresia and truncus arteriosus (“TOF group”). Patients with a birth weight under 2.3 kg, congenital anomalies consistent with a specific syndrome, significant extracardiac anomalies (defined as those needing treatment or that affect functional status), and previous cardiac operations were excluded. Both trials were approved by the Institutional Review Board, and informed consent was obtained prior to subject participation.

Perioperative data

Preoperative, anesthetic, and operative management for these infants has been described in detail previously (9, 10). Study nurses recorded daily events, respiratory status, medications,

laboratory studies, fluid inputs and outputs, and use of blood products. Although there was no formalized protocol to judge readiness for extubation and thus DMV is subject to practice variability, most patients in our ICU are weaned to a low ventilator rate, typically 4 breaths/minute with a pressure support level appropriate to the size of the endotracheal tube (e.g. usually 10 cm H₂O for endotracheal tube sizes of 3 or 4 French) and are extubated when the level of sedation is judged to be appropriate. DMV was defined as the time from exiting the operating room to extubation. In patients requiring reintubation, the duration of this second intubation was added. We measured serum lactate 60 minutes after cessation of CPB. Inotrope scores, modified from Wernovsky *et al.*, were calculated for the first 24 postoperative hours (11).

Statistical analyses

Data are presented as medians and interquartile ranges for continuous data and as counts and proportions for categorical data. To minimize the effect of outliers, we analyzed data using tertiles. As more than one third of patients had no early postoperative blood product transfusion, we also analyzed early postoperative transfusion as a dichotomous variable. Percents of patients ventilated over time by tertile of intraoperative blood products were estimated through Kaplan-Meier survival curves. DMV across intraoperative blood exposure groups were compared with the Kruskal-Wallis test. We used Spearman correlation coefficients to assess univariable associations of perioperative data with DMV. Cox proportional hazards regression analyses were used to assess factors associated with DMV in multivariable models. We adjusted for age at surgery < 30 days versus > 30 days in the TOF group only. We were unable to adjust for the effects of age at surgery in the other diagnosis groups, because almost all (98%) infants with TGA underwent surgery at age < 30 days at surgery, and nearly all (97%) subjects in the VSD group were > 30 days at surgery. Due to one death in a TOF patient, our DMV analyses are on the 269 surviving patients.

Transfusion variables considered for the multivariable regression model included intraoperative blood products per kg and postoperative blood products per kg administered during the initial postoperative period, defined as the time from admission to the ICU until 8 AM the following morning. Blood products were analyzed both as total blood products and as categories of red cells (whole blood plus packed cells) versus other products (platelets, fresh frozen plasma, plus cryoprecipitate). Albumin was not considered a blood product and was excluded. Additional variables considered for the multivariable regression model included diagnosis group, gender, birth weight, gestational age, race, age at surgery, surgeon, year of surgery, hematocrit randomization group, preoperative intubation status, intraoperative support times (bypass, cross-clamp, circulatory arrest, and total), intraoperative fluid balance, lactate values at 60 minutes post-bypass, chest tube output per kg during the initial postoperative period, and 24-hour inotrope score. Candidate variables were retained if they were significantly associated with DMV at a p value <0.05 in the multivariable analysis.

RESULTS

The demographic characteristics of the 270 patients are summarized according to tertile of intraoperative blood products in Table 1. Infants with lower birth weight and earlier gestational age received more intraoperative blood products. Patients in the highest tertile received 68–364 mL blood products per kg compared to 4–34 mL per kg in the lowest tertile. Older age at surgery was associated with lower total intraoperative blood products administered per kg; mean age at surgery among patients in the highest tertile of administered blood products, compared to the lowest tertile, was 21 days vs. 128 days (Table 1). Longer intraoperative support times (including total bypass, cross-clamp, circulatory arrest, and total support times), as well as greater intraoperative fluid balance

were each significantly associated with administration of more intraoperative blood products (Table 1). There was a single death in a TOF with pulmonary atresia patient who underwent surgery on day of life 16 and died on postoperative day 12.

DMV was highly associated with length of stay in the ICU ($r=0.86$, $p<0.001$) and hospital ($r=0.78$, $p<0.001$). Because DMV is collinear with ICU and hospital length of stay, we focused the analyses on the association of blood product transfusion with DMV as an indicator of postoperative recovery.

DMV according to blood product tertile is shown in Figure 1. The DMV was longest in patients in the highest tertile of intraoperative blood products (median 2.6 days, range 1.7 to 18.7 days), intermediate in the middle tertile (median 1.9 days, range 0.5 to 8.1 days), and shortest in the lowest tertile (median 1.1 day, range 0.3 to 11.9 days), ($p<0.001$; Table 2). Patients receiving more intraoperative blood products per kg had higher lactate levels 60 minutes post bypass and increased 24-hour inotrope score post-bypass (each $p<0.001$; Table 2). Chest tube output per kg during the initial postoperative period and transfusion of blood products in the post operative period were not associated with intraoperative transfusion tertile.

We explored variables other than intraoperative blood product tertile that were associated with longer DMV. In univariable proportional hazards regression analyses, longer DMV was significantly associated with younger age at surgery, lower weight at surgery, and diagnostic group (longest for TGA, intermediate for TOF, and shortest for VSD), (each $p<0.001$). In contrast, surgeon, year of surgery, hematocrit randomization group, birth weight, and gender were not correlated with DMV.

In stepwise multivariable regression, independent predictors of longer DMV included greater intraoperative blood products administered per kg, longer total support time, diagnostic group, and younger age at surgery within the TOF diagnostic group. For ease of interpretation and to avoid nonlinear effects, indicator variables based on tertiles of their distributions were used in reporting regression results (Table 3). Patients in the highest tertile of intraoperative blood products administered per kg had a hazard (or instantaneous risk) of endotracheal extubation that was approximately half that of patients in the lowest tertile (hazard ratio = 0.51, 95% CI 0.35, 0.73; $p<0.001$; Table 3). A similar dose-response relationship was preserved when blood products were classified as red cells and other blood products. For intraoperative red cell administration, the hazard ratio of highest tertile, compared to the lowest tertile, was 0.60 (95% CI, 0.43, 0.84; $p=0.002$); for other intraoperative blood products, this hazard ratio was 0.67 (95% CI, 0.46, 0.98; $p=0.04$).

We also explored the effect of early postoperative blood product transfusions on DMV by performing stepwise multivariable regressions, adjusting for diagnosis group, age at surgery for the TOF patients, intraoperative transfusion tertiles, and total support time tertiles. Patients who received any blood products on postoperative day 1, compared to those who did not, had a hazard ratio for extubation of 0.65 (95% CI 0.50, 0.85, $p=0.001$). However, we did not observe a dose response during this initial postoperative period for higher volume of blood products administered per kg and hazard for longer DMV (Table 3).

Finally, we explored the influence on DMV of the volume of red blood cell products and other products administered during the initial postoperative period. Among the 189 patients who received any postoperative red blood cell products, a mean of 65% of the total postoperative red cell products was given prior to 8 AM on the first postoperative day. Patients who received any early post-operative red blood cells, compared to those who did not receive any, had a hazard ratio of 0.71 (95% CI 0.54, 0.92; $p=0.009$). Although greater initial postoperative chest tube output per kg was significantly correlated with the quantity

of early postoperative red cell transfusion ($r=0.25$, $p<0.001$), chest tube output itself was not an independent predictor of DMV. Only 52 patients received other blood products in the first postoperative day and there was no statistically significant difference in DMV among those patients who received these non-red cell products compared to those who did not (hazard ratio 0.8, 95% CI 0.57, 1.12, $p=0.189$).

DISCUSSION

In this exploratory secondary analysis of a homogeneous group of infants undergoing reparative open heart surgery with two ventricles and without coarctation of the aorta, intraoperative and early postoperative blood transfusion emerged as powerful independent predictors of DMV. In proportional hazards regression analyses, infants in the highest tertile of volume of administered intraoperative blood products per kg had a hazard of remaining intubated that was twice as high as that of infants in the lowest tertile. Furthermore, after controlling for the amount of intraoperative transfusion and other predictors of DMV, patients who got any blood products on the first postoperative day, compared to those who did not, had a hazard of remaining intubated that was approximately twice as great.

We were able to identify procedure-specific variables (arterial switch operation for TGA), patient-specific variables (young age at surgery, lower weight at surgery, and younger gestational age), and surgeon-specific variables (longer support times), which were independent predictors of longer DMV. Operations that involve long suture lines and great vessel surgery such as the arterial switch procedure are likely to generate increased postoperative bleeding. Indeed, 69% of patients in the highest intraoperative blood product tertile had an arterial switch operation. In contrast, only 12% of patients in this tertile were in the neonatal TOF group. Younger age, lower weight at surgery, and prematurity are known risk factors for prolonged ventilation after pediatric cardiac surgery (1–3). The present study was able to associate those risk factors with increased intraoperative transfusion, and illuminate a potential etiology of the increased DMV observed in these patients (2, 4, 10). In contrast to other studies (12), individual surgeons were not associated with increased transfusions or DMV. However, longer intraoperative support times were highly correlated with DMV. Longer intraoperative support times can be due to technical performance or case complexity within specific diagnostic groups, such as complex coronary transfer in arterial switch operation or pulmonary artery reconstruction in TOF with pulmonary atresia. The design of this study did not allow us to differentiate between these two factors or their interaction.

In adults undergoing coronary artery bypass surgery and/or valve operations, perioperative transfusion has been associated with increased postoperative complications including longer DMV, longer LOS, and higher perioperative mortality (13). As in our study, perioperative transfusion was related to longer cross-clamp and perfusion times (13). Cislighi *et al.* found that intraoperative transfusions of greater than 4 units of red blood cells or fresh frozen plasma and cardiopulmonary bypass time over 91 minutes independently predicted DMV longer than 12 hours in patients following coronary artery bypass graft surgery (14). In a study of coronary artery bypass patients, risk factors differed for low intraoperative hematocrit level and excessive postoperative bleeding (12). As both situations increased blood product use, this study highlighted the variability in triggers for transfusion apart from excessive postoperative bleeding and suboptimal surgical hemostasis (12). To date, no prospective clinical trials have tested whether blood conservation protocols in the cardiac operating room and ICU can decrease ventilation time or other postoperative complications.

Recent studies, including those in children, have explored the risks and benefits of blood transfusions in other populations. In the CRIT study of adult patients in intensive care, after

adjusting for factors including the propensity for receiving a transfusion, administration of red cells was associated with increased mortality (15). The risk of postoperative infection increased with total amount of intraoperative and postoperative blood product administration, after adjusting for perioperative risk factors and the propensity to receive transfusions, in a heterogeneous population of pediatric open heart surgical patients (16). In a study of critically ill pediatric patients, Kneyber *et al.* found an independent association between red cell transfusion and increased mortality (16% vs. 2.6%), prolonged DMV, longer infusion of vasoactive medicines, and longer ICU stay after adjusting for age, sepsis, and severity scores (17). Goodman *et al.* found that blood transfusions were associated with longer DMV in a retrospective evaluation of five pediatric ICUs (18). Stricter transfusion guidelines studied in non-cardiac patients do not appear to adversely affect patients (19–21).

This exploratory study should be viewed in light of its limitations. Secondary analyses of data from a relatively homogeneous, lower-risk surgical group, collected at a single center, may limit the generalizability of the findings. In particular, single ventricle patients in whom hemoglobin level is a more critical factor in oxygen delivery were excluded. We presume that our findings may be amplified in this patient group. Although this group is relatively homogeneous in that all surgeries were in the RACHS 2–4 category, we did not collect a severity of illness indicator (e.g. PRISM) in all patients. Thus we cannot exclude the possibility that sicker patients were more likely to be resuscitated with blood products (i.e. confounding by indication) (22). Children with genetic syndromes, including Down's syndrome, in whom there is a known risk for prolonged DMV were also excluded (3, 4, 6). Transfusion practices were left to the judgment of the anesthesiologist and cardiac intensivist. Thus we could not determine the impact of practice variability on the association of blood transfusion and DMV. We do not have data on the length of storage of the red cells used for transfusions, a factor associated in adult studies with perioperative morbidity (23). Most importantly, our study design did not permit us to assess the causality of the association of blood product usage and longer DMV; rather, our analyses are hypothesis generating.

In conclusion, in infants undergoing reparative heart surgery, greater administration of intraoperative and postoperative blood products emerged as an important risk factor for longer DMV in analyses adjusting for diagnostic group, age at surgery, and greater total support time. Blood product use may be reduced by careful attention to surgical hemostasis, expeditious management of bleeding in the immediate post-operative period, and institution of more conservative postoperative transfusion guidelines. Future prospective studies are needed to determine whether it is possible to reduce intraoperative and early postoperative transfusions, and if so, whether this hastens postoperative recovery after infant heart surgery.

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References

1. Davis S, Worley S, Mee RB, Harrison AM. Factors associated with early extubation after cardiac surgery in young children. *Pediatr Crit Care Med.* 2004; 5:63–68. [PubMed: 14697111]
2. Kanter RK, Bove EL, Tobin JR, Zimmerman JJ. Prolonged mechanical ventilation of infants after open heart surgery. *Crit Care Med.* 1986; 14:211–214. [PubMed: 3943337]

3. Szekely A, Sapi E, Kiraly L, Szatmari A, Dinya E. Intraoperative and postoperative risk factors for prolonged mechanical ventilation after pediatric cardiac surgery. *Paediatr Anaesth*. 2006; 16:1166–1175. [PubMed: 17040306]
4. Ip P, Chiu CS, Cheung YF. Risk factors prolonging ventilation in young children after cardiac surgery: Impact of noninfectious pulmonary complications. *Pediatr Crit Care Med*. 2002; 3:269–274. [PubMed: 12780968]
5. Newburger JW, Wypij D, Bellinger DC, et al. Length of stay after infant heart surgery is related to cognitive outcome at age 8 years. *J Pediatr*. 2003; 143:67–73. [PubMed: 12915826]
6. Harrison AM, Cox AC, Davis S, Piedmonte M, Drummond-Webb JJ, Mee RB. Failed extubation after cardiac surgery in young children: Prevalence, pathogenesis, and risk factors. *Pediatr Crit Care Med*. 2002; 3:148–152. [PubMed: 12780985]
7. Koch CG, Li L, Duncan AI, et al. Morbidity and mortality risk associated with red blood cell and blood-component transfusion in isolated coronary artery bypass grafting. *Crit Care Med*. 2006; 34:1608–1616. [PubMed: 16607235]
8. Engoren MC, Habib RH, Zacharias A, Schwann TA, Riordan CJ, Durham SJ. Effect of blood transfusion on long-term survival after cardiac operation. *Ann Thorac Surg*. 2002; 74:1180–1186. [PubMed: 12400765]
9. Jonas RA, Wypij D, Roth SJ, et al. The influence of hemodilution on outcome after hypothermic cardiopulmonary bypass: results of a randomized trial in infants. *J Thorac Cardiovasc Surg*. 2003; 126:1765–1774. [PubMed: 14688685]
10. Newburger JW, Jonas RA, Soul J, et al. Randomized trial of hematocrit 25% versus 35% during hypothermic cardiopulmonary bypass in infant heart surgery. *J Thorac Cardiovasc Surg*. 2008; 135:347–354. [PubMed: 18242267]
11. Wernovsky G, Wypij D, Jonas RA, et al. Postoperative course and hemodynamic profile after the arterial switch operation in neonates and infants. A comparison of low-flow cardiopulmonary bypass and circulatory arrest. *Circulation*. 1995; 92:2226–2235. [PubMed: 7554206]
12. Dial S, Delabays E, Albert M, et al. Hemodilution and surgical hemostasis contribute significantly to transfusion requirements in patients undergoing coronary artery bypass. *J Thorac Cardiovasc Surg*. 2005; 130:654–661. [PubMed: 16153909]
13. Whitson BA, Huddleston SJ, Savik K, Shumway SJ. Bloodless cardiac surgery is associated with decreased morbidity and mortality. *J Card Surg*. 2007; 22:373–8. [PubMed: 17803571]
14. Cislighi F, Condemi AM, Corona A. Predictors of prolonged mechanical ventilation in a cohort of 3,269 CABG patients. *Minerva Anesthesiol*. 2007; 73:615–621. [PubMed: 18046291]
15. Corwin HL, Gettinger A, Pearl RG. The CRIT Study: Anemia and blood transfusion in the critically ill—current clinical practice in the United States. *Crit Care Med*. 2004; 32:39–52. [PubMed: 14707558]
16. Szekely A, Cserep Z, Sapi E, et al. Risks and predictors of blood transfusion in pediatric patients undergoing open heart operations. *Ann Thorac Surg*. 2009; 87:187–97. [PubMed: 19101294]
17. Kneyber MC, Hersi MI, Twisk JW, Markhorst DG, Plotz FB. Red blood cell transfusion in critically ill children is independently associated with increased mortality. *Intensive Care Med*. 2007; 33:1414–1422. [PubMed: 17572875]
18. Goodman AM, Pollack MM, Patel KM, Luban NL. Pediatric red blood cell transfusions increase resource use. *J Pediatr*. 2003; 142:123–7. [PubMed: 12584531]
19. Hebert PC, Wells G, Blajchman MA, et al. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion requirements in critical care investigators, Canadian Critical Care Trials Group. *N Engl J Med*. 1999; 11(340):409–417. [PubMed: 9971864]
20. Lacroix J, Hebert PC, Hutchison JS, et al. Transfusion strategies for patients in pediatric intensive care units. *N Engl J Med*. 2007; 356:1609–1619. [PubMed: 17442904]
21. Hebert PC, Yetisir E, Martin C, et al. Is a low transfusion threshold safe in critically ill patients with cardiovascular diseases? *Crit Care Med*. 2001; 29:227–234. [PubMed: 11246298]
22. Jenkins KJ, Gauvreau K, Newburger JW, Spray TL, Moller JH, Iezzoni LI. Consensus-based method for risk adjustment for surgery for congenital heart disease. *J Thorac Cardiovasc Surg*. 2002; 123:110–118. [PubMed: 11782764]

23. Koch CG, Li L, Sessler DI, et al. Duration of red-cell storage and complications after cardiac surgery. *N Engl J Med*. 2008; 358:1229–1239. [PubMed: 18354101]

FIGURE 1.

Percent of patients ventilated over time by intraoperative blood product tertile, estimated through Kaplan-Meier survival curves. P-value comparing intraoperative blood product tertiles was based on the Kruskal-Wallis test.

Table 1

Preoperative and intraoperative characteristics of 270 patients

	Intraoperative Blood Product Tertiles			
Variable	Low 4–34 mL/kg (N=89)	Middle 35–67 mL/kg (N=91)	High 68–364 mL/kg (N=90)	P-value ^I
Preoperative				
	Number (column %)			
Diagnosis group				<0.001
VSD group (n=71)	45 (51)	21 (23)	5 (6%)	
TGA group (n=108)	7 (8)	39 (43)	62 (69%)	
TOF group > 30 days (n=69)	36 (40)	21 (23)	12 (13%)	
TOF group 30 days (n=22)	1 (1)	10 (11)	11 (12%)	
	Median (interquartile range)			
Birth weight (kg)	3.4 (3.2, 3.8)	3.4 (3.1, 3.8)	3.3 (2.9, 3.6)	0.02
Gestational age (weeks)	40 (38, 40)	39 (38, 40)	39 (38, 40)	0.01
Age at surgery (days)	120 (80, 175)	12 (4, 82)	6 (4,16)	<0.001
Intraoperative				
Total support time (min)	76 (67, 101)	104 (81, 127)	127 (108, 149)	<0.001
Total bypass time (min)	76 (67, 99)	97 (75, 119)	114 (101, 131)	<0.001
Aortic cross-clamp time (min)	44 (38, 57)	63 (44, 79)	81 (66, 93)	<0.001
Duration of circulatory arrest (min)	0 (0, 0)	0 (0, 11)	9 (0, 18)	<0.001
Intraoperative fluid balance (mL)	299 (176, 464)	380 (227, 492)	604 (450, 771)	<0.001

^I P-values comparing intraoperative blood product tertiles were based on Fisher's exact tests for categorical variables and Kruskal-Wallis tests for continuous variables.

VSD, ventricular septal defect

TGA, dextro-transposition of the great arteries

TOF, tetralogy of Fallot

Table 2Postoperative characteristics of 270 patients ^a

Variable	Intraoperative Blood Product Tertiles			P-value ^b
	Low 4–34 mL/kg (N=89)	Middle 35–67 mL/kg (N=91)	High 68–364 mL/kg (N=90)	
	<i>Median (interquartile range)</i>			
Duration of mechanical ventilation (days)	1.1 (0.8, 1.2)	1.9 (1.2, 2.9)	2.6 (1.7, 3.9)	< 0.001
Lactate 60 minutes post bypass (mmol/L)	1.5 (1.3, 1.9)	2.9 (1.9, 4.4)	3.8 (2.4, 5.0)	< 0.001
Chest tube output in 1 st postoperative day ^c (mL/kg)	19 (13,23)	16 (11,23)	16 (10,22)	0.06
24-hour inotrope score	8 (3,11)	13 (9,17)	11 (6,16)	< 0.001
Blood products in 1 st postoperative day ^c (mL/ kg)	9 (0, 15)	9 (0, 15)	9 (0, 21)	0.66
Total postoperative blood products (mL/kg)	14 (4,21)	15 (0, 24)	16 (0, 46)	0.17
ICU LOS (days)	2 (2,3)	3 (3,5)	4 (3,6)	< 0.001
Hospital LOS (days)	5 (4,6)	7 (6,9)	8 (7,10)	< 0.001

^aFor the 1 death, duration of mechanical ventilation, postoperative events, postoperative blood products, and LOS not calculated.^bP-values comparing diagnostic groups were based on Fisher's exact tests for categorical variables and Kruskal-Wallis tests for continuous variables.^cTime from admission to ICU to 8 AM on postoperative day 1.

Table 3
Multivariable proportional hazards regression models for predictors of duration of mechanical ventilation

Variable	Preoperative and Intraoperative Factors Model				Preoperative, Intraoperative, and Postoperative Factors Model			
	Hazard Ratio	95% CI	P-value	Hazard Ratio	95% CI	P-value	Hazard Ratio	P-value
VSD group	1			1				
TGA group	0.57	(0.36, 0.89)	0.01	0.60	(0.38, 0.95)	0.03		
TOF group 30 days	0.44	(0.26, 0.74)	0.002	0.47	(0.27, 0.80)	0.006		
TOF group > 30 days	0.72	(0.51, 1.02)	0.06	0.84	(0.59, 1.20)	0.33		
Intraoperative blood products (tertiles)								
4–34 mL/kg	1			1				
35–67 mL/kg	0.68	(0.50, 0.93)	0.02	0.64	(0.47, 0.88)	0.006		
68–364 mL/kg	0.51	(0.35, 0.73)	<0.001	0.45	(0.30, 0.65)	<0.001		
Total support time (tertiles)								
49–82 min	1			1				
83–121 min	0.52	(0.37, 0.74)	<0.001	0.51	(0.37, 0.72)	<0.001		
122–302 min	0.55	(0.34, 0.90)	0.02	0.56	(0.35, 0.92)	0.02		
Postoperative day 1 blood products (tertiles)	N/A							
0 mL/kg				1				
3–15 mL/kg				0.60	(0.44, 0.81)	<0.001		
16–399 mL/kg				0.73	(0.53, 1.01)	.006		

Hazard Ratio < 1 implies longer duration of mechanical ventilation compared to baseline category

CI, confidence interval

TGA, dextro-transposition of the great arteries

VSD, ventricular septal defect

TOF, tetralogy of Fallot