Outcomes of cardiac surgery in patients weighing <2.5 kg: Affect of patient-dependent and -independent variables

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Objective: A recent Society of Thoracic Surgeons database study showed that low weight (<2.5 kg) at surgery was associated with high operative mortality (16%). We sought to assess the outcomes after cardiac repair in patients weighing <2.5 kg versus 2.5 to 4.5 kg in an institution with a dedicated neonatal cardiac program and to determine the potential role played by prematurity, the Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery (STAT) risk categories, uni/biventricular pathway, and surgical timing.

Methods: We analyzed the outcomes (hospital mortality, early reintervention, postoperative length of stay, mortality [at the last follow-up point]) in patients weighing <2.5 kg at surgery (n = 146; group 1) and 2.5 to 4.5 kg (n = 622; group 2), who had undergone open or closed cardiac repairs from January 2006 to December 2012 at our institution. The statistical analysis was stratified by prematurity, STAT risk category, uni/biventricular pathway, and usual versus delayed surgical timing. Univariate versus multivariate risk analysis was performed. The mean follow-up was 21.6 ± 25.6 months.

Results: Hospital mortality in group 1 was 10.9% (n = 16) versus 4.8% (n = 30) in group 2 ($P = .007$). The postoperative length of stay and early unplanned reintervention rate were similar between the 2 groups. Late mortality in group 1 was 0.7% (n = 1). In group 1, early outcomes were independent of the STAT risk category, uni/biventricular pathway, or surgical timing compared with group 2. A lower gestational age at birth was an independent risk factor for early mortality in group 1.

Conclusions: A dedicated multidisciplinary neonatal cardiac program can yield good outcomes for neonates and infants weighing <2.5 kg independently of the STAT risk category and uni/biventricular pathway. A lower gestational age at birth was an independent risk factor for hospital mortality. (J Thorac Cardiovasc Surg 2014;148:2499-506)

See related commentary on pages 2506-7.

Supplemental material is available online.

Despite improvements in the outcomes in neonatal cardiac surgery during the past 20 years, low weight remains a risk factor for increased mortality in neonates and infants undergoing cardiac surgery.[1] A Society of Thoracic Surgeons (STS) Congenital Heart Surgery Database study, with 32 participating centers, recently demonstrated that the average operative mortality rate in patients with a low weight (≤2.5 kg) at surgery was as high as 16%.[2] Moreover, the risk factors for mortality and reintervention in that specific population are still controversial.[3-10] To our knowledge, the potential role played by the Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery (STAT) risk categories, the uni/biventricular pathway, timing of surgery, and gestational age were never investigated in a study directly comparing 2 groups of patients (those weighing ≤2.5 kg and those weighing >2.5 kg). Thus, the objectives of our study were to (1) assess the early and mid-term outcomes of cardiac repair in patients weighing ≤2.5 kg in an institution with a dedicated neonatal cardiac program; (2) compare these results with those of patients weighing 2.5 to 4.5 kg undergoing surgery at the same institution; (3) determine the potential role played by gestational age, STAT risk category, uni/biventricular pathway, and timing of surgery; and (4) perform univariate and multivariate risk analysis of the group weighing ≤2.5 kg.

METHODS

The present retrospective single-center study included patients who had undergone open or closed cardiac surgery at the New York-Presbyterian Morgan

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Abbreviations and Acronyms
ANOVA = analysis of variance
STAT = Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery
STS = Society of Thoracic Surgeons
TOF = tetralogy of Fallot

Stanley Children's Hospital, Columbia University Medical Center, from January 2006 to December 2012 with a weight of ≤2.5 kg at surgery (group 1) or 2.5 to 4.5 kg (group 2). The patients who underwent ductus arteriosus closure alone were not included in the present study. The perioperative data were retrospectively collected by reviewing the hospital records and the computerized database of our department. Follow-up data were obtained from the institution outpatient records and the same computerized database.

The dedicated neonatal cardiac program offers care to neonates or young infants with congenital heart disease from birth to discharge. A dedicated medical and nursing team staff this program and included members from the neonatal intensive care, pediatric cardiology, and pediatric cardiac surgery divisions. The practitioners on this team had either received advanced training in pediatric cardiac intensive care and/or had an advanced understanding and were skilled in the management of newborn infants with congenital heart disease. Dedicated neonatal cardiac intensive care nurses and neonatal nurse practitioners, neonatal respiratory therapists, and neonatal nutritionists and feeding specialists staffed the neonatal cardiac intensive care unit. Patients who were born at our institution or transferred from outside medical centers with known or suspected congenital heart disease were admitted to the neonatal cardiac intensive care unit of the neonatal intensive care unit. Although no clear cut restrictions to admission to the neonatal cardiac intensive care unit were in place, infants >6 to 8 weeks of age at transfer or admission were preferably admitted to our pediatric cardiac intensive care unit.

The STAT risk categories, uni/biventricular pathway, and timing of surgery were assigned for each patient included in the present study. The STAT risk categories were determined from the definition of the categories established by O'Brien and colleagues.[11] The surgical pathway was defined as "univentricular" (Norwood procedure, aortopulmonary shunt, pulmonary artery band, and/or atrial septectomy performed for single ventricle disease), "biventricular" (primary biventricular complete repair), or "palliation toward biventricular" (systemic-pulmonary shunt, pulmonary artery band, unifocalization, and/or transannular patch as a first step before biventricular repair). The timing of surgery was defined as "usual" (determined from usual divisional management paradigms for infants of normal weight) or "delayed" (intentional delay of early intervention or unusual choice of a palliative approach to permit growth or maturation), as previously described by Hickey and colleagues.[12] This adjudication of the surgical timing was determined from an accurate and precise retrospective medical record review by the senior coauthors (D.K., E.B.). The mean age at surgery for patients with the usual timing of surgery was 10.9 ± 11.9 days versus 50.6 ± 36 days for those with delayed surgery.

The primary endpoint was mortality occurring before hospital discharge or within 30 days postoperatively. The secondary endpoints were the postoperative hospital length of stay (LOS), unplanned early reintervention (during the same hospital stay), and late mortality. The institutional review board of Columbia University Medical Center approved the study.

Population

A total of 146 and 622 patients were included in groups 1 and 2, respectively. The demographic and surgical characteristics, cardiac diagnoses, STAT categories, surgical pathway, and timing of surgery of both groups are listed in Table 1. Of the patients in group 1, 70% (n = 102) had a STAT 4 or 5 risk category, 63% (n = 92) a biventricular pathway, and 18.5% (n = 27) delayed timing. Compared with group 2, group 1 was characterized by a statistically significant lower male/female ratio ($P = .01$), older age at surgery ($P < .001$), more patients with tetralogy of Fallot (TOF) ($P = .006$), and more with an aortopulmonary window ($P = .02$) but fewer with simple transposition of the great arteries ($P = .04$), more with STAT 2 category ($P = .01$), and a shorter bypass time ($P = .01$). Single ventricles, right-side heart lesions, aortic arch lesions, and transposition of the great arteries were the most frequent group of diseases in both groups. Patients in group 1 had extracardiac malformations and a genetic syndrome in 18.4% and 13% of cases, respectively. The mean gestational age at birth for patients in group 1 was 35.5 ± 2.8 weeks. In group 1, 56% of the patients (n = 82) were premature (<37 weeks) and 42% (n = 61) had a gestational age of <36 weeks. Also, 42% were small for their gestational age (defined as <10th percentile). In group 1, 41% (n = 33) of the STAT 4 patients had a gestational age of <36 weeks compared with 25% (n = 6) of the STAT 5 patients ($P = .15$). Of the patients who underwent a univentricular pathway in group 1, 22% (n = 9) had a gestational age of <36 weeks versus 48% (n = 44) of those with a biventricular pathway ($P = .007$) and 61% (n = 8) of those with palliation toward biventricular repair ($P = .014$).

The frequencies of the main procedures in groups 1 and 2 are listed in Table E1. The 4 most frequent procedures performed in group 1 were the Norwood procedure (n = 25; 17%), the arterial switch operation (n = 13; 8.9%), primary repair of TOF (n = 12; 8.2%), and shunt palliation or unifocalization for TOF or pulmonary atresia with a ventricular septal defect (n = 12; 8.2%). The latter procedure was performed more frequently in group 1 (8.2%; n = 12) than in group 2 (3.2%; n = 20; $P = .01$). The frequency of all other procedures was not significantly different between the 2 groups. Of the patients who underwent a Norwood procedure in group 1, 20% (n = 5) had a gestational age of <36 weeks versus 62% (n = 5) of those who underwent hypoplastic aortic arch repair ($P = .036$).

Statistical Analysis

Descriptive statistics were performed and stratified by weight of ≤2.5 kg versus >2.5 kg. Bivariate testing by weight category for demographic and surgical characteristics and for the outcomes of hospital mortality, postoperative hospital LOS, early unplanned reintervention, and late mortality was performed for categorical variables using Fisher's exact test or the chi-square test and for continuous variables using the Student *t* test, the Wilcoxon rank sum test, analysis of variance (ANOVA), or the Kruskal-Wallis test. Multiple comparisons were explored using Tukey's test. Trends for ordinal independent variables were performed using *P* for trend (ANOVA) or the Cochran-Armitage test for trend. Comparisons between the endpoints and demographic and surgical characteristics between the weight categories were performed using the Cochran Mantel-Haenszel or 2-way ANOVA, first testing for interaction with the Breslow-Day test or by creating interaction terms in 2-way ANOVA. The statistical analysis was stratified by the STAT risk categories, surgical pathway, and timing of surgery.

A risk analysis was performed for the endpoints of early mortality and early unplanned reintervention in group 1. Univariate analysis was performed for the categorical variables using Fischer's exact test or the chi-square test and for continuous variables using the Student *t* test or Mann-Whitney *U* test. Multivariate analysis was performed using a logistic regression model to estimate the risk factors for early mortality and early unplanned reintervention. Variables were included into the model by backward elimination if $P < .05$. The adjustment factors for multivariate analysis were the surgeon, STAT score, procedure type (uni/biventricular), and gestational age at birth. Postoperative complications were defined as ≥1 of the following postoperative major events: cardiac arrest, extracorporeal membrane oxygenation, arrhythmia, atrioventricular block requiring a pacemaker, diaphragm paralysis, atelectasis, pleural effusion requiring thoracocentesis, respiratory failure, seizure, cerebrovascular event, renal failure requiring dialysis, necrotizing enterocolitis, mediastinitis, or any septic syndrome. Statistical Analysis Systems, version 9.3 (SAS Institute, Cary, NC), was used for data analysis.