Relation of Prenatal Diagnosis With One-Year Survival Rate for Infants With Congenital Heart Disease

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Prenatal diagnosis of congenital heart defects (CHDs) is increasingly common, but it is still unclear whether it translates to improved postoperative outcomes. We performed a retrospective cohort study of all infants (aged <1 year) who underwent surgery for CHDs from 2006 to 2011 at a single institution. Primary outcomes were in-hospital and 1-year mortality rates. Secondary outcomes were readmission within 30 days of discharge, postoperative length of intensive care unit and hospital stay, unplanned reoperation, and extracorporeal membrane oxygenation use. We used chi-square analyses, Wilcoxon rank-sum tests, Kaplan-Meier survival curves, and adjusted Cox proportional hazards models to compare outcomes. Of the 1,642 patients with CHDs, 539 (33%) were diagnosed prenatally. Patients with prenatal diagnoses were of a younger age and less weight at the time of surgery, had greater Risk Adjustment for Congenital Heart Surgery scores, and were more likely to be white, to have an identified syndrome, or to be born at term. Compared with those diagnosed postnatally, those diagnosed prenatally had a significantly higher unadjusted 1-year mortality rate (11% vs 5.5%, respectively, $p = 0.03$). Controlling for weight, surgical severity, race, age at surgery, prematurity, and the presence or absence of genetic syndrome, patients with prenatal diagnoses had significantly greater mortality at 1 year (adjusted hazard ratio 1.5, $p = 0.03$), as well as significantly longer intensive care unit and hospital stays. Infants with CHDs diagnosed prenatally had worse outcomes compared with those diagnosed postnatally. Prenatal diagnosis likely captures patients with more severe phenotypes within given surgical risk categories and even within diagnoses and thus may be an important prognostic factor when counseling families. **(Am J Cardiol 2014;■:■−■)**

For infants with a congenital heart defect (CHD), prenatal diagnosis can allow for better planning of delivery,[1] better perinatal and preoperative condition,[2] and lower rates of preoperative intubation, antibiotic use, and cardiac catherizations.[3] However, whether improvement in the preoperative state of prenatally diagnosed infants leads to better postoperative outcomes such as mortality is less clear. Decreased mortality rate in infants diagnosed prenatally has been seen in case studies of patients with hypoplastic left heart syndrome (HLHS)[4] and transposition of the great arteries.[5] Other case series and larger studies have failed to demonstrate the same result.[6,7] Several studies have demonstrated improvement in neurocognitive outcomes at up to a year of age in patients with prenatal diagnoses,[8,9] whereas others have shown no effect.[10] We therefore sought to review our experience in outcomes for children with and without prenatal diagnosis. The objective of this study was to understand the relation between the timing of diagnosis of CHDs and postoperative outcomes. We hypothesized that those with a prenatal diagnosis would have better short- and long-term outcomes compared with those with a postnatal diagnosis.

Methods

We performed a retrospective cohort study on all infants (aged <1 year at the time of surgery) who underwent surgery for CHDs from January 2006 to December 2011 at Children's Healthcare of Atlanta at Egleston. Patients were divided into 2 exposure groups: prenatal or postnatal diagnosis. If a patient had >1 surgical hospitalization during the study period, data from the first hospitalization were used.

The primary outcome measure was mortality, both in-hospital and at 1 year of age. Secondary outcome measures were readmission within 30 days of discharge, postoperative hours in the intensive care unit (ICU) and hospital stay, unplanned reoperation, and use of extracorporeal membrane oxygenation. Covariates of interest included age and weight at the time of surgery, surgery performed, cardiac diagnosis, prematurity status, and presence of genetic syndrome as verified by genetic testing or a clinical geneticist. Severity of cardiac lesion was assigned based on the Risk Adjustment for Congenital Heart Surgery (RACHS-1) score (higher number indicates greater risk), an evidence-based risk adjustment tool based on cardiac surgery performed.[11] Patients who underwent cardiac transplantation as their primary surgery were excluded.

For univariate analyses, we used chi-square tests to compare categorical data and Wilcoxon rank-sum tests to

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Table 1
Demographics of infants undergoing congenital heart surgery from 2006 to 2011

Variable	Prenatal Diagnosis (n = 538)	Postnatal Diagnosis (n = 1,104)	p Value*
Male gender	300 (56)	613 (56)	0.96
Race/ethnicity			<0.01
White non-Hispanic	300 (56)	479 (43)	
Black non-Hispanic	143 (27)	358 (32)	
Hispanic	54 (10)	168 (15)	
Asian	8 (1.5)	19 (1.7)	
Others	33 (6.1)	80 (7.3)	
Premature (<37-week gestational age)	59 (11)	169 (15)	0.02
Identified syndrome	59 (11)	61 (6)	<0.01
RACHS-1 score ≥4	199 (37)	197 (18)	<0.01
Age at surgery (days)†	7 (0–285)	77 (0–356)	<0.01
Weight at surgery (kg)†	3.4 (1.4–9.1)	4.1 (4.1–15.0)	<0.01

Data are presented as n (%) or median (range).
* p Values from the chi-square analysis, unless otherwise noted.
† p Values from Wilcoxon rank-sum tests.

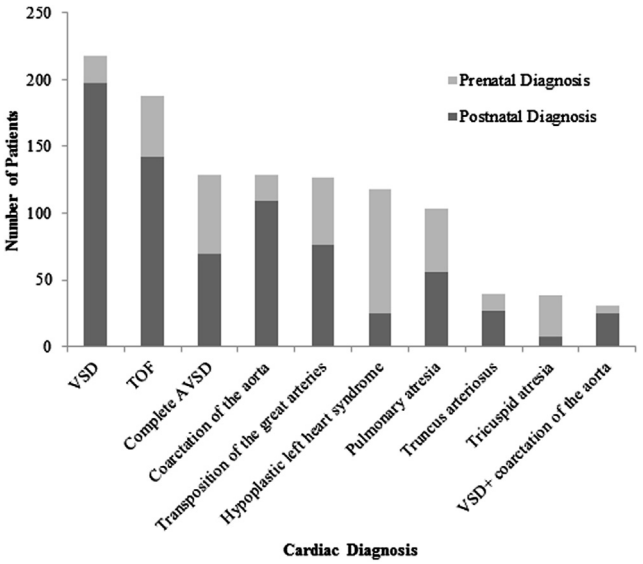

Figure 1. Most common cardiac diagnoses of infants undergoing cardiac surgery from 2006 to 2011. AVSD = atrioventricular septal defect; TOF = tetralogy of Fallot; VSD = ventricular septal defect.

compare continuous data. For our primary outcome of 1-year mortality rate, we created Kaplan-Meier survival curves for those without an identified syndrome. For both our primary and secondary outcome measures, we constructed adjusted Cox proportional hazards models controlling for weight, severity (defined as RACHS-1 score ≥4), race, age at surgery (days), prematurity (<37 weeks), and presence or absence of genetic syndrome. For 1-year mortality rate, we performed additional Cox analyses stratified by the RACHS-1 score. All statistics were performed using SAS, version 9.3 (Cary, North Carolina).

Results

Of the 1,642 patients who met inclusion criteria, 538 (33%) were diagnosed prenatally. Patient characteristics are summarized in Table 1. Infants with prenatal diagnoses were significantly younger and weighed less at the time of surgery than their peers who were diagnosed after birth. African-American and Hispanic patients were more likely to be diagnosed postnatally, whereas white patients were more likely to be prenatally diagnosed. Identified genetic syndromes were significantly more common among patients prenatally diagnosed ($p = 0.02$), although prematurity was significantly less common in this group ($p < 0.01$). Those in the prenatal cohort also had significantly greater RACHS-1 scores; 37% had a score of ≥4 versus 18% in the postnatal group ($p < 0.01$). The most common cardiac diagnoses in both groups are shown in Figure 1. Ventricular septal defects and tetralogy of Fallot were the most frequently seen defects in our cohort.

The prenatal cohort had significantly worse long-term mortality. Although there was no significant difference in the in-hospital mortality rate for the prenatal diagnosis group versus the postnatal diagnosis group, the 1-year mortality rate for the prenatal diagnosis group was double that of the postnatal diagnosis group. Among the secondary outcomes of interest, infants with a prenatal diagnosis had a postoperative ICU stay and total postoperative hospital stay that was approximately 2 days longer than that of infants with a postnatal diagnosis. There was no significant difference between the 2 groups with respect to readmissions, reoperations, or use of extracorporeal membrane oxygenation (Table 2).

In the unadjusted survival analysis for infants without a known syndrome, the 1-year survival rate for those prenatally diagnosed was 88% versus 95% for those postnatally diagnosed (log-rank p value <0.001; Figure 2). In the adjusted Cox proportional hazards model for 1-year mortality rate, there was significantly greater mortality in our prenatally diagnosed cohort when adjusted for weight, severity (RACHS-1 score ≥4), race, age at surgery, prematurity, and presence of syndrome (hazard ratio 1.5, $p = 0.03$; Table 3). This significant difference remained when patients with genetic syndrome were excluded (hazard ratio 1.6, $p = 0.02$). In a subanalysis of our cohort stratified by the RACHS-1 score, there were no significant differences in the 1-year mortality rate between those prenatally diagnosed and those postnatally diagnosed in any of the RACHS-1 categories (Table 3). The greatest differences were seen in RACHS-1 category 6, the highest severity category, which is predominantly comprised of patients having Norwood operations, but this difference did not reach statistical significance.

Discussion

Contrary to our hypothesis, infants with a prenatal diagnosis of a CHD had worse surgical outcomes compared with those with a postnatal diagnosis, both in terms of 1-year mortality rate and postoperative length of ICU and hospital stay. These differences persisted even after controlling for a variety of factors, including surgical risk category. However, although we could account for differences in severity *between* surgical risk categories, we could