A Population-Based Study of the Association of Prenatal Diagnosis With Survival Rate for Infants With Congenital Heart Defects

Matthew E. Oster, MD, MPH[a,b,*], Christopher H. Kim, MD, MPH[a,b], Aaron S. Kusano, MD[a,c], Janet D. Cragan, MD, MPH[a], Paul Dressler, MD[a,b], Alice R. Hales, MD[b], William T. Mahle, MD[b], and Adolfo Correa, MD, PhD[a,d]

Prenatal diagnosis has been shown to improve preoperative morbidity in newborns with congenital heart defects (CHDs), but there are conflicting data as to the association with mortality. We performed a population-based, retrospective, cohort study of infants with prenatally versus postnatally diagnosed CHDs from 1994 to 2005 as ascertained by the Metropolitan Atlanta Congenital Defects Program. Among infants with isolated CHDs, we estimated 1-year Kaplan-Meier survival probabilities for prenatal versus postnatal diagnosis and estimated Cox proportional hazard ratios adjusted for critical CHD status, gestational age, and maternal race/ethnicity. Of 539,519 live births, 4,348 infants had CHDs (411 prenatally diagnosed). Compared with those with noncritical defects, those with critical defects were more likely to be prenatally diagnosed (58% vs 20%, respectively, p <0.001). Of the 3,146 infants with isolated CHDs, 1-year survival rate was 77% for those prenatally diagnosed (n = 207) versus 96% for those postnatally diagnosed (n = 2,939, p <0.001). Comparing 1-year survival rate among those with noncritical CHDs alone (n = 2,455) showed no difference between prenatal and postnatal diagnoses (96% vs 98%, respectively, p = 0.26), whereas among those with critical CHDs (n = 691), prenatally diagnosed infants had significantly lower survival rate (71% vs 86%, respectively, p <0.001). Among infants with critical CHDs, the adjusted hazard ratio for 1-year mortality rate for those prenatally versus postnatally (reference) diagnosed was 2.51 (95% confidence interval 1.72 to 3.66). In conclusion, prenatal diagnosis is associated with lower 1-year survival rate for infants with isolated critical CHDs but shows no change for those with isolated noncritical CHDs. More severe disease among the critical CHD subtypes diagnosed prenatally might explain these findings. Published by Elsevier Inc. (Am J Cardiol 2014;113:1036−1040)

Conflicting results as to whether prenatal diagnosis leads to decreased preoperative and postoperative mortalities have been reported in studies examining hypoplastic left heart syndrome (HLHS)[1−3] and transposition of the great arteries.[1,4] A lack of definitive evidence regarding mortality outcomes may be due in part to the difficulties in obtaining adequate patient numbers when examining specific defects at a single center.[5] In addition, few studies have examined survival beyond the perioperative period. The objective of our study was to examine the 1-year survival rate of infants with prenatally versus postnatally diagnosed congenital heart defects (CHDs) in a large population-based cohort. We hypothesized that prenatal diagnosis would be associated with improved long-term survival rate.

Methods

Established in 1967, the Centers for Disease Control and Prevention's Metropolitan Atlanta Congenital Defects Program (MACDP) is an active population-based surveillance system for major birth defects among infants, fetuses, and children born to residents of the 5 central counties of metropolitan Atlanta.[6] The MACDP operates in collaboration with the Georgia Department of Public Health and has approval of the Centers for Disease Control and Prevention's Institutional Review Board. Trained abstractors visit area birth and pediatric hospitals, maternal-fetal medicine departments, and outpatient perinatal offices to identify affected pregnancies and children in whom a birth defect is diagnosed before 6 years of age. Their medical records are reviewed, and demographic and clinical information collected. Cases in the MACDP are coded using a modified British Pediatric Association code. All cases with CHDs undergo review and classification by clinical experts in pediatric cardiology according to a standard nomenclature adopted from the Society of Thoracic Surgeons and based on current understanding of development morphogenesis.[7]

For this analysis, prenatal echocardiographic records were obtained from metropolitan Atlanta area pediatric

[a]National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, Georgia; [b]Children's Healthcare of Atlanta, Emory University, Atlanta, Georgia; [c]Department of Radiation Oncology, University of Washington, Seattle, Washington; and [d]Department of Medicine, University of Mississippi Medical Center, Jackson, Mississippi. Manuscript received September 16, 2013; revised manuscript received and accepted November 18, 2013.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

See page 1040 for disclosure information.

*Corresponding author: Tel: (404) 256-2593; fax: (770) 488-9477.
E-mail address: osterm@kidsheart.com (M.E. Oster).

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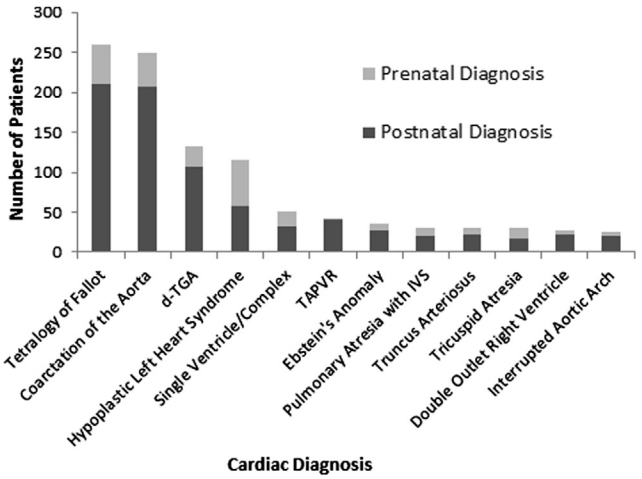

Figure 1. Detection of CCHDs by prenatal echocardiography in Atlanta, Georgia, 1994 to 2005. IVS = intact ventricular septum; TAPVR = total anomalous pulmonary venous return; TGA = transposition of the great arteries.

cardiology clinics and were matched to cases in the MACDP. Cases for which no documented prenatal diagnosis existed were assumed to have been diagnosed postnatally. Survival status for live born infants was determined through a review of available clinical records, linkage with death certificates from the Office of Vital Records, Georgia Department of Public Health, or linkage with the National Death Index. Echocardiographic records were available starting from 1994, and National Death Index records available through 2006. With 1-year mortality rate as the primary outcome, the birth cohort was limited to infants born from January 1, 1994, to December 31, 2005.

Potential covariates for the association between timing of diagnosis (prenatal vs postnatal) and 1-year mortality rate included critical CHD (CCHD) status (critical vs noncritical), gestational age at birth ($\leq$36 vs >36 weeks), neighborhood poverty level (<20% of population in census tract living in poverty vs $\geq$20%), birth weight (<2,500 vs $\geq$2,500 g), maternal race/ethnicity (white non-Hispanic vs all others), and maternal age.

For this study, we defined CCHDs as 12 defects that are likely to require intervention within the first year of life and are likely to present postnatally with hypoxemia some or most of the time.[8] These 12 defects consisted of 7 primary targets of pulse oximetry screening (HLHS, pulmonary atresia, tetralogy of Fallot, transposition of the great arteries, tricuspid atresia, truncus arteriosus, and total anomalous pulmonary venous return) and 5 secondary targets (coarctation of the aorta, double-outlet right ventricle, Ebstein's anomaly, interrupted aortic arch, and single ventricle). As disease severity is not routinely collected by the MACDP, defects such as critical pulmonary stenosis and critical aortic stenosis were not considered as CCHDs.

Chi-square analyses were performed to compare baseline characteristics of each covariate between the prenatally and postnatally diagnosed cohorts. Survival probabilities were estimated using Kaplan-Meier methods, and the log-rank test was used to determine significance ($p < 0.05$). All infants in the MACDP identified with a CHD were included in the baseline statistical summary, but only infants with isolated CHDs (those without chromosomal abnormalities or noncardiac defects) were included in the Kaplan-Meier survival curves or proportional hazards analyses. Covariates were also analyzed using univariate logistic regression modeling, with death at 1 year as the outcome. Covariates that were significantly different between prenatal and postnatal cohorts and were also significantly associated with 1-year mortality rate ($p < 0.05$) were identified as potential confounders and included in Cox proportional hazards models to obtain adjusted hazard ratios for mortality. Finally, a separate Kaplan-Meier curve was constructed to compare 1-year survival rate based on timing of diagnosis for those with isolated CCHDs: prenatal diagnosis versus early postnatal diagnosis ($\leq$1 day of age) versus late postnatal diagnosis (>1 day of age). All analyses were performed in SAS, version 9.3 (Cary, North Carolina).

Table 1
Baseline characteristics for prenatally versus postnatally diagnosed congenital heart defects (CHDs) in metropolitan Atlanta, Georgia: 1994 to 2005

Variable	Prenatally Diagnosed, n = 411 (%)*	Postnatally Diagnosed, n = 3,937 (%)*	p Value
CCHD†	238 (58)	769 (20)	<0.001
Associated defects			
None (isolated)	207 (50)	2,939 (75)	<0.001
Multiple CHD	70 (17)	453 (12)	0.001
Laterality defects	33 (8)	47 (1)	<0.001
Chromosomal abnormality	101 (25)	498 (13)	<0.001
Gestational age (weeks)			
<36	107 (27)	989 (27)	<0.001
37–38	146 (37)	955 (26)	
39–40	126 (32)	1,404 (39)	
>40	12 (3)	280 (8)	
Neighborhood poverty level‡			
0–4.9%	127 (32)	1,287 (34)	0.66
5.0–9.9%	113 (28)	1,056 (28)	
10.0–19.9%	100 (25)	964 (26)	
≥20%	56 (14)	459 (12)	
Low birth weight, <2,500 g	120 (29)	988 (25)	0.07
Race/ethnicity			
White, non-Hispanic	177 (43)	1,757 (45)	0.002
Black, non-Hispanic	170 (41)	1,360 (35)	
Hispanic	38 (9)	609 (15)	
Others	26 (6)	211 (5)	
Maternal age (yrs)			
<20	37 (9)	325 (8)	0.14
20–24	76 (18)	727 (18)	
25–29	82 (20)	984 (25)	
≥30	216 (53)	1,901 (48)	
1-yr mortality rate	137 (33)	345 (9)	<0.001

* Not all subcategories sum to total n because of missing values.

† Defined as 7 primary CHD targets for pulse oximetry screening (HLHS, truncus arteriosus, tricuspid atresia, total anomalous pulmonary venous return, pulmonary atresia, tetralogy of Fallot, and transposition of the great arteries) plus 5 secondary targets for pulse oximetry screening (interrupted aortic arch, coarctation of the aorta, Ebstein's anomaly, single ventricle, and double-outlet right ventricle).

‡ Defined by the percentage of residents below the poverty level in census tract associated with the maternal address at the time of the child's birth.