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Characteristics and outcomes of children with ductal-dependent congenital heart disease and esophageal atresia/tracheoesophageal fistula: A multi-institutional analysis

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ABSTRACT

Background. Extracardiac birth defects are associated with worse outcomes in congenital heart disease (CHD). The impact of esophageal atresia/trachea-esophageal fistula (EA/TEF) on outcomes after surgery for ductal-dependent CHD is unknown.

Methods. Retrospective matched cohort study using the Pediatric Health Information System database from 07/2004 to 06/2015. Hospitalizations with ductal-dependent CHD and EA/TEF, undergoing CHD surgery were included as cases. Admissions with ductal-dependent CHD without EA/TEF were matched 3:1 for age at admission and Risk Adjustment for Congenital Heart Surgery-1 classification. Comparisons were performed using generalized estimating equations.

Results. There were 124 cases and 372 controls. Cases included 32 (25.8%) low-risk, 86 (69.3%) intermediate-risk, and 6 (4.8%) high-risk patients. Cases had more females compared to controls (53.2% vs 41.1%, $P = .022$). Cases were more likely to be premature (28.2% vs 13.7%, $P = .001$) and low birth weight (29.8% vs 11.8%, $P < .001$). Cases had a similar frequency of Down syndrome, and DiGeorge/Velocardiofacial syndrome, but a higher frequency of anorectal malformations (4.3% vs 2.4%, $P < .001$) and renal anomalies (27.4% vs 9.9%, $P < .001$) than controls. Cases had a higher mortality on univariate (22.0% vs 8.4%, $P < .001$) and multivariable analysis (odds ratio 2.45, 95%, confidence interval 1.34 – 4.49). Prematurity also was significantly associated with mortality on multivariable analysis. Cases had a longer duration of mechanical ventilation, longer hospital duration of stay, and higher total cost than controls (all $P < .001$).

Conclusion. In children with ductal-dependent CHD, EA/TEF is associated with increased morbidity, mortality and resource utilization. A majority of patients undergo EA/TEF repair prior to congenital heart disease surgery. (Surgery 2017;160:XXX-XXX.)

Ductal-dependent congenital heart disease (CHD) necessitates early intervention to establish circulatory stability without prostaglandin (PGE) infusion. The present mortality for the surgical repair of 2-ventricle ductal-dependent lesions (e.g., transposition of the great arteries or coarctation repair) varies between 1% and 3%.[1-4] The mortality after the first stage of surgical palliation for single ventricle (SV) ductal-dependent CHD varies from <10% to 40%.[5-7] Previous studies have shown an association between mortality and extracardiac malformations in patients with CHD.[8-10]

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Congenital airway and gastrointestinal tract anomalies are the second-most common malformations associated with CHD.[11] The reported prevalence of CHD in cases of esophageal atresia/tracheoesophageal fistula (EA/TEF) has ranged from 15% to almost 70%.[12,13] Case series suggest that this combination is associated with mixed outcomes.[14-17] Furthermore, the impact of EA/TEF on outcomes after CHD surgery in different categories of surgical complexity has not been reported previously.

The aim of this study was to describe and compare demographic and clinical characteristics, morbidity and resource utilization, and mortality of infants with ductal-dependent CHD and EA/TEF, with that of infants with ductal-dependent CHD and no EA/TEF, after undergoing CHD surgery during their first hospitalization. We hypothesized that: (1) infants with ductal-dependent CHD-EA/TEF have greater in-hospital mortality after CHD surgery during their first admission than infants with ductal-dependent CHD without EA/TEF; and (2) Infants with ductal-dependent CHD-EA/TEF would have longer total length of stay (LOS), longer duration of mechanical ventilation and requirement for parenteral nutrition (TPN), and higher hospital costs during their first admission than infants with ductal-dependent CHD without EA/TEF.

Methods

We performed a multicenter retrospective matched cohort study, querying the Pediatric Health Information System (PHIS) database. The PHIS is a comparative pediatric database including ICD-9 codes and clinical resource utilization data from 45 US nonprofit children's hospitals.[18] Details of the PHIS have been previously described, and it has been used to study hospital mortality as well as resource utilization particularly for less common or more specialized diagnoses and procedures.[19,20]

We queried all patients admitted between July 2004 and June 2015 that underwent a Risk Adjustment for Congenital Heart Surgery – 1 (RACHS-1) classified CHD surgery at ages <1 year. The age cut-off of 1 year was chosen to allow for inclusion of any patients that may have been on PGE for extended periods of time prior to their RACHS-1 surgery, potentially while awaiting clinical stability or recovery from other procedure. From this pool, patients that met all of the after inclusion criteria were selected as cases: (1) a ductal-dependent cardiac diagnosis, defined as anatomic diagnoses that may be consistent with ductal-dependence (International Classification of Diseases, ICD-9 codes listed in Appendix 1) and administration of PGE infusion continued until the day of CHD surgery (based on days of service for PGE medication and CHD surgery in PHIS); (2) CHD surgery classified RACHS-1 categories 1 to 6, and (3) a diagnosis of EA/TEF confirmed with presence of diagnostic codes for EA/TEF as well as EA/TEF repair during the index admission (previously described methodology, ICD-9 codes listed in Appendix 1).[19]

Controls were infants with ductal-dependent CHD without EA/TEF who underwent CHD surgery, matched exactly for age at admission (±1 day), RACHS-1 classification, and time period of admission (closest matches for date of admission within 6 months of date of index admission to avoid surgical era differences). Three separate controls were matched per case.

Covariates analyzed included sex, race/ethnicity, prematurity (gestational age <37 weeks at birth, defining ICD-9 codes listed in Appendix 1), low birth weight (<2,500 grams, defining ICD-9 codes listed in Appendix 1), and presence of other birth defects/genetic anomalies excluding EA/TEF (defining ICD-9 codes listed in Appendix 1). DiGeorge/Velo-cardiofacial syndrome (ICD-9 code 279.11 or 758.32) and Down syndrome (ICD-9 code 758.0) were analyzed as individual covariates also as they are known to be associated with CHD. VACTERL association (defined as presence of 3 of the 7 components in the association: vertebral, anorectal malformations, cardiac, TEF, renal anomalies, and limb defects) also was assessed as a separate covariate. Anorectal malformations and renal anomalies were individually analyzed for any association with the primary and secondary outcomes, to account for any possible confounding. ICD-9 codes accounting for VACTERL association, anorectal malformations and the renal anomalies associated with VACTERL are detailed in Appendix 1.

The primary outcome was hospital mortality. Secondary outcomes of morbidity and resource utilization included duration of mechanical ventilation, LOS in the intensive care unit, duration of TPN administration, total hospital LOS, total LOS after cardiac surgery, and total cost of services (based on the ratio of cost to charges [RCC] per the insurance). This is determined as a product of the charge reported by each PHIS hospital and their RCC, which is adjusted for geographical location.[21] Charges in the PHIS are adjusted for the wage and price index (published annually in the *Federal Register*).

Statistical analysis

Categorical and continuous variables were compared using χ^2/Fisher exact and nonparametric tests as appropriate. Univariate and multivariable analyses were performed using generalized estimating equations (GEE) for categorical outcomes and mixed modeling for continuous outcomes, to account for clustering within hospitals. Factors with P value ≤0.1 on univariate analysis were included in the initial multivariable analysis models, and factors with P value ≤0.1 were retained in successive models. The results of the initial model (using all variables with P value ≤0.1 on univariate analysis), as well as the final models (retaining only significant covariates) are both shown in the tables. To limit heterogeneity of the sample, we also a performed a subanalysis limiting the case and controls to those who underwent CHD surgery at age <31 days. To examine the association between EA/TEF and mortality by surgical complexity and assess if EA/TEF was a more relevant prognosticator in certain categories of CHD surgery, we also performed the analysis after stratifying by RACHS-1 categories into low-risk (1 and 2), intermediate-risk (3 and 4), and high-risk (5 and 6) groups.

Given the finding of a large proportion of the cases with prematurity compared to controls, a post-hoc secondary matched cohort analysis was also performed, in which a second set of controls were selected matched for prematurity (birth at gestation <37 weeks, defined by ICD-9 codes listed in Appendix 1) in addition to RACHS-1 classification. This was performed to confirm findings of the primary analysis and to estimate the effect size of the association of EA/TEF on surgical mortality without having to adjust for confounding of prematurity. Two controls were selected for each case for this secondary analysis. Outcomes for this analysis included the primary outcome of mortality as well as secondary outcomes of total LOS and total cost of services.

An additional analysis was performed comparing hospital mortality between cases who underwent CHD surgery after, on the same day, or before to the EA/TEF repair. SPSS 22.0 (IBM, Armonk, NY) and SAS version 9.3 (SAS Institute Inc., Cary, NC) were used for data analysis.

Results

The schematic of inclusion of cases and controls is illustrated in Fig. Our initial query on PHIS identified 21,960 patients, and on reviewing patients individually, many of them were on PGE for periods of time that were shorter than the day of service of their CHD surgery (potentially indicating PGE was started initially and then discontinued once diagnosis was known), or did not have cardiac diagnoses consistent with ductal-dependent lesions. Of the 142 unique patients with ductal-dependent CHD and a diagnosis code of EA/TEF (ICD-9 code 750.3) who underwent RACHS-1 classified CHD surgery,

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