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Predictors of Catastrophic Adverse Outcomes in Children With Pulmonary Hypertension Undergoing Cardiac Catheterization

A Multi-Institutional Analysis From the Pediatric Health Information Systems Database

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ABSTRACT

BACKGROUND Cardiac catheterization is the standard of care procedure for diagnosis, choice of therapy, and longitudinal follow-up of children and adults with pulmonary hypertension (PH). However, the procedure is invasive and has risks associated with both the procedure and recovery period.

OBJECTIVES The purpose of this study was to identify risk factors for catastrophic adverse outcomes in children with PH undergoing cardiac catheterization.

METHODS We studied children and young adults up to 21 years of age with PH undergoing 1 or more cardiac catheterization at centers participating in the Pediatric Health Information Systems database between 2007 and 2012. Using mixed-effects multivariable regression, we assessed the association between pre-specified subject- and procedure-level covariates and the risk of the composite outcome of death or initiation of mechanical circulatory support within 1 day of cardiac catheterization after adjustment for patient- and procedure-level factors.

RESULTS A total of 6,339 procedures performed on 4,401 patients with a diagnosis of PH from 38 of 43 centers contributing data to the Pediatric Health Information Systems database were included. The observed risk of composite outcome was 3.5%. In multivariate modeling, the adjusted risk of the composite outcome was 3.3%. Younger age at catheterization, cardiac operation in the same admission as the catheterization, pre-procedural systemic vasodilator infusion, and hemodialysis were independently associated with an increased risk of adverse outcomes. Pre-procedural use of pulmonary vasodilators was associated with reduced risk of composite outcome.

CONCLUSIONS The risk of cardiac catheterization in children and young adults with PH is high relative to previously reported risk in other pediatric populations. The risk is influenced by patient-level factors. Further research is necessary to determine whether knowledge of these factors can be translated into practices that improve outcomes for children with PH. (J Am Coll Cardiol 2015;66:1261–9) © 2015 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

APAH-CHD = pulmonary arterial hypertension associated with congenital heart disease

CCB = calcium-channel blocker

CTEPH = chronic thromboembolic pulmonary hypertension

ERA = endothelin receptor antagonist

ICD-9 = International Classification of Diseases-9th Revision

IPAH = idiopathic pulmonary arterial hypertension

IQR = interquartile range

PDE = phosphodiesterase

PH = pulmonary hypertension

PHIS = Pediatric Health Information Systems

Pulmonary hypertension (PH) affects 2.1 to 3.7 children per million (1–3) but remains an extremely morbid condition, with a 5-year survival of 65% to 75% (1,2,4–6). Right-sided heart catheterization is an important tool in the diagnosis, classification, and longitudinal care of these patients (7,8); however, cardiac catheterization in children with PH carries a risk of cardiac arrest of 4.5 to 5.7 per hundred (9,10), which is >10 times the risk of catheterization in children with other diagnoses and in adults with PH (11–20).

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The determinants of periprocedural morbidity and mortality are not well defined, particularly in children. Relatively small procedural volumes at single centers and differences in practice at different centers are obstacles to the study of outcome in children with PH. Identification of risk factors for adverse outcomes could provide an opportunity to intervene and improve the safety of catheterization in children with PH.

We performed a multicenter retrospective cohort study assessing risk factors for catastrophic adverse events using the Pediatric Health Information Systems (PHIS) database, an administrative database. We hypothesized that patient-level risk factors, such as age, pathogenesis of PH, and indicators of severity of illness, would influence the periprocedural risk of death and catastrophic outcome.

METHODS

DATA SOURCE. The PHIS is an administrative database that contains data from inpatient, emergency department, ambulatory surgery, and observation encounters from 43 nonprofit tertiary care pediatric hospitals affiliated with the Children's Hospital Association (Overland Park, Kansas) in the United States. Encounters in PHIS include inpatient and observation admissions but exclude outpatient procedures (those without overnight observation). Data quality and reliability are ensured through a joint effort between the Children's Hospital Association and participating hospitals. The data warehouse function for the PHIS database is managed by Truven Health Analytics (Ann Arbor, Michigan). For the purposes of external benchmarking, participating hospitals provide discharge/encounter data including demographics, diagnoses, and procedures. Forty-two of these hospitals also submit resource utilization data (e.g., pharmacy products, radiologic studies, and laboratory studies) to the PHIS. Data are deidentified at the time of data submission and are subjected to a number of reliability and validity checks before being included in the database. A data-use agreement was signed between study investigators and the Children's Hospital Association. The institutional review board of The Children's Hospital of Philadelphia reviewed the proposed project and determined that it did not represent human subjects research in accordance with the Common Rule [45 CFR 46.102(f)].

STUDY POPULATION. Procedures and diagnoses were identified by International Classification of Disease-9th Revision (ICD-9) codes. We included children and adults, age 0 to 21 years, who had a diagnosis of PH and were undergoing cardiac catheterization at any of the 43 PHIS centers between January 1, 2007, and December 31, 2012. We excluded subjects from centers reporting <25 cardiac catheterization procedures per year or not reporting cardiac catheterization procedures in at least 4 of 6 years during the study period to ensure that only centers with stable reporting practices were included. Subjects for whom the date of catheterization was missing were also excluded. Subjects undergoing electrophysiology studies and those undergoing cardiac catheterization on mechanical circulatory support were excluded because their risk of adverse event was considered to be qualitatively different.

STUDY MEASURES. Data were extracted from the PHIS database by direct query with use of ICD-9 codes and clinical transaction codes for pharmaceutical products as described previously (Online Table 1). The primary outcome was a composite of death or initiation of mechanical circulatory support (extracorporeal membrane oxygenation [ECMO], percutaneous ventricular assist device, or balloon pump) within 1 day of cardiac catheterization. Patient-level data included subject age, sex, race, insurance payer (private, public, other), presence of genetic syndrome (21), presence of noncardiac congenital anomalies, history of prematurity (defined as gestational age <34

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