6 rue Willy-Donze
CH-1211 Geneva 14
Switzerland
E-mail: Maurice.Beghetti@hcuge.ch

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REFERENCES

1. O'Byrne ML, Glatz AC, Hanna BD, et al. Predictors of catastrophic adverse outcomes in children with pulmonary hypertension undergoing cardiac catheterization: a multi-institutional analysis from the Pediatric Health Information Systems database. J Am Coll Cardiol 2015;66:1261–9.

2. Kreutzer J. Catastrophic adverse events during cardiac catheterization in pediatric pulmonary hypertension may not be so rare. J Am Coll Cardiol 2015;66:1270–2.

3. Bobhate P, Guo L, Jain S, et al. Cardiac catheterization in children with pulmonary hypertensive vascular disease. Pediatr Cardiol 2015;36:873–9.

4. Zuckerman WA, Turner ME, Kerstein J, et al. Safety of cardiac catheterization at a center specializing in the care of patients with pulmonary arterial hypertension. Pulm Circ 2013;4:831–9.

5. Beghetti M, Schulze-Neick I, Berger RM, et al., for the TOPP Investigators. Haemodynamic characterisation and heart catheterisation complications in children with pulmonary hypertension: insights from the global TOPP Registry (Tracking Outcomes and Practice in Paediatric Pulmonary Hypertension). Int J Cardiol 2016;203:325–30.

REPLY: The Need for Comprehensive Cardiac Catheterization in Children With Pulmonary Hypertension

To "Cath" or Not in Pediatric Pulmonary Hypertension?

We welcome the comments and interest of Drs. Hansmann and Apitz and Dr. Beghetti and colleagues regarding our study. We agree that cardiac catheterization is an essential component of the evaluation of pulmonary hypertension (PH). Our study utilized administrative data from 38 primary children's hospitals in the United States to measure the risk of a catastrophic outcome using a standard definition (1) in children undergoing cardiac catheterization during inpatient and observation admissions. The use of administrative data overcomes the challenge of studying low event rates in a rare condition, and we included more than 6,000 procedures in 4,401 unique patients with a range of risk factors in our analysis. The data from the TOPP (Tracking Outcome and Practice in Pediatric Pulmonary Hypertension) registry were drawn from 31 expert centers in which 908 procedures were performed in 456 patients whose families provided informed consent. As acknowledged by the authors, patients who died may not have been included in the TOPP registry due to the absence of informed consent (2). Our analysis may be more generalizable, because it includes expert and nonexpert centers, many more procedures, and a patient population with a broader range of severity of illness.

The TOPP study and other single-center studies cited in the letter by Drs. Hansmann and Apitz and Dr. Beghetti and colleagues are valuable because they include detailed data from highly experienced pediatric centers with a narrower range of conditions and illness severity. Interestingly, the mortality estimates from these studies are consistent with that from ours. In the series from Beghetti et al. (2), Zuckerman et al. (3), and Bobhate et al. (4), the 95% confidence intervals (CIs) for the observed risks of mortality were 0% to 3.7%, 0.2% to 1.0%, and 0.2% to 1.3%, respectively. The observed risk of mortality within 1 day of catheterization in our study (0.3%; 95% CI: 0.2% to 0.4%) falls within these CIs, suggesting that the study populations and their outcomes are more comparable than implied.

We acknowledge the limitations of administrative data (i.e., reliance on billing codes and missing clinical data); however, our analysis also has several strengths. First, we accounted for the relatedness of procedures within the same individual. A patient who did "well" with the first procedure will be more likely to undergo a second or third procedure, leading to a biased "healthier" population if this relatedness is not considered when analyzing multiple procedures. In TOPP and other studies, every procedure (even if performed on the same patient) was considered independently, which does not fulfill necessary assumptions underlying the analysis (independence of outcomes) and may lead to "over-representation" of lower-risk individuals. Second, our significantly larger study population allowed us to use multivariable analysis to adjust for confounders and provide standardized estimates, which were not calculated in the referenced studies. The estimated risk of a catastrophic adverse outcome for a "standard risk profile" patient (a school-age patient with idiopathic pulmonary hypertension who is not receiving a pulmonary vasodilator and without other risk factors) may be a more useful statistic for comparison than unadjusted observed risk.

We agree that there are benefits of cardiac catheterization in pulmonary hypertension and that there may be an advantage to performing these procedures in experienced centers. Large studies that include both expert and nonexpert centers and inclusive cohorts of patients (such as ours) provide the best chance to support this anecdotal impression (5). Indeed, our study showed for the first time that higher-volume centers had significantly lower risks of adverse outcomes in pediatric patients with pulmonary hypertension compared with lower-volume centers.

As we state in our paper, "Despite advances in noninvasive imaging technology, cardiac catheterization remains the gold standard for initial diagnosis, choice of initial pharmacotherapy, and longitudinal assessment of patients with PH." We do not agree with Drs. Hansmann and Apitz about the "possible interpretation that children with PH should not undergo cardiac catheterization because of the risks of severe adverse events" or with Dr. Beghetti and colleagues that our paper will "cause a drift away from HC [heart catheterization] procedures." Instead, we are hopeful that our study and others focused on accurately measuring risk of cardiac catheterization in children with PH will lead to improvements in the safety of the procedure in this population.

*Michael L. O'Byrne, MD, MSCE
Jonathan J. Rome, MD
Steven J. Kawut, MD, MS

*Children's National Health System
George Washington University School of Medicine and Health Sciences
111 Michigan Avenue NW
Washington, DC 20010
E-mail: mlobyrne@childrensnational.org

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REFERENCES

1. Bergersen L, Gauvreau K, Jenkins KJ, Lock JE. Adverse event rates in congenital cardiac catheterization: a new understanding of risks. Cong Heart Dis 2008;3:90–105.

2. Beghetti M, Berger RMF, Schulze-Neick I, et al. Diagnostic evaluation of paediatric pulmonary hypertension in current clinical practice. Eur Resp J 2013;42:689–700.

3. Zuckerman WA, Turner ME, Kerstein J, et al. Safety of cardiac catheterization at a center specializing in the care of patients with pulmonary arterial hypertension. Pulm Circ 2013;3:831–9.

4. Bobhate P, Guo L, Jain S, et al. Cardiac catheterization in children with pulmonary hypertensive vascular disease. Pediatr Cardiol 2015;36:873–9.

5. O'Byrne ML, Glatz AC, Shinohara RT, et al. Effect of center catheterization volume on risk of catastrophic adverse event after cardiac catheterization in children. Am Heart J 2015;169:823–32.e5.