

when comparing the highest to the lowest quintile, although this was only statistically significant for model B. Pearson's correlations coefficients with dietary intake of the corresponding n-3 PUFA were modest for EPA ($r = 0.36$; $p < 0.001$) and DHA ($r = 0.34$; $p < 0.001$) and weak for DPA ($r = 0.08$; $p = 0.001$).

This study had limitations. The median follow-up was 17.0 years, and dietary measures were not assessed further during the study period. A long follow-up allowed us to accumulate more outcome events, but subjects might change their diet over time. Furthermore, changes in medical care and lifestyle together with public awareness of disease prevention might influence the participants' risk over time. To address this issue we performed supplementary analysis stratifying on the birthdate and tested for interaction from birthdate. No significant interaction was detected.

Several mechanisms have been suggested to explain cardioprotective properties of marine n-3 PUFA, including stabilization of atherosclerotic plaques, which may decrease the risk of plaque rupture and MI (1). The mechanism(s) by which n-3 PUFA interact with the risk of MI in the present study are uncertain, but the results suggest that EPA and DHA play a more important role than DPA. In conclusion, the study supports the view that marine n-3 PUFA may protect against MI.

*Anders Gammelmark, MD
Michael S. Nielsen, MD, PhD
Christian S. Bork, MB
Søren Lundbye-Christensen, MSc, PhD
Anne Tjønneland, MD, PhD, DMSc
Kim Overvad, MD, PhD
Erik B. Schmidt, MD, DMSc

*Department of Cardiology
Aalborg University Hospital
Soendre Skovvej 15
9000-Aalborg
Denmark

E-mail: anders.gammelmark@rn.dk

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The Need for Comprehensive Cardiac Catheterization in Children With Pulmonary Hypertension



We read with interest the paper by O'Byrne et al. (1) on adverse events during cardiac catheterization in children with pulmonary hypertension (PH). However, we are concerned about the effect that this paper may have on patients, family members, and health care providers and on the future clinical care of children with PH. The presented data are based on a chart review of catheterizations performed in both expert and nonexpert centers (the Pediatric Health Information System database) in children with PH of multiple etiologies and settings (acute, perioperative, and chronic). We are concerned about the possible interpretation that children with PH should not undergo cardiac catheterization because of the risks of severe adverse events; such misleading views may counteract the recent efforts of many experts to standardize diagnostic work-up and care in pediatric PH (2,3).

First, exact diagnosis, oxygen saturation, hemodynamics, and laboratory and imaging data were not available to characterize the PHIS population (1) any better. Second, the PH subclassification used was limited and was not in line with the current PH classification (2). Third, O'Byrne et al. (1) included perioperative PH and interventional catheterizations, and thus mixed moderate- with high-risk patients, thereby increasing bias and decreasing validity. Moreover, in cardiomyopathies and structural heart disease, PH hemodynamics and physiology can differ remarkably (e.g., children with a right ventricular decompressing shunt have better outcomes), but were not analyzed separately.

Robust data on the safety of cardiac catheterization in pediatric PH comes from the TOPP (Tracking Outcome and Practice in Pediatric Pulmonary Hypertension) registry: for the total number of cardiac catheterizations ($n = 908$), pulmonary hypertensive crises, need for inotropic support, and/or cardiac arrest were reported in 5.9%, and this included

5 procedure-related deaths (0.6%) (4,5). This adverse event rate was similar to that presented by O'Byrne et al. (1): 61 cases of deaths or extracorporeal membrane oxygenation on the day of catheterization (0.96%; n = 6,339). Hence, the authors' statement that "cardiac catheterization in children with PH carries a risk of cardiac arrest of 4.5 to 5.7 per hundred" (1) is incorrect, and the term "catastrophic" adverse outcome is more on the basis of opinion than on facts.

Clearly, we must be aware that the complication rate for cardiac catheterization with or without anesthesia is higher in children than in adults (4,5). Thus, we must weigh the risks and benefits of invasive procedures and perform the latter in experienced PH centers. Nevertheless, we feel strongly that cardiac catheterization with vasodilator testing remains an essential part of the comprehensive PH work-up at diagnosis.

*Georg Hansmann
Christian Apitz

*Department of Pediatric Cardiology and Critical Care
Hannover Medical School
Carl-Neuberg-Strasse 1
30625 Hannover
Germany

E-mail: georg.hansmann@gmail.com OR capitz@aol.com
<http://dx.doi.org/10.1016/j.jacc.2015.10.102>

Please note: Dr. Hansmann is chair and Dr. Apitz is co-chair of the writing group of the Expert Consensus Statement on the Diagnosis and Treatment of Pediatric Pulmonary Hypertension from The European Pediatric Pulmonary Vascular Disease Network (2015). Dr. Hansmann is the American Heart Association co-chair of the writing group of AHA/ATS Joint Guidelines for Pediatric Pulmonary Hypertension (2015); and is a task force member of the 2015 ESC/ERS Guidelines for the Diagnosis and Treatment of Pulmonary Hypertension.

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To "Cath" or Not in Pediatric Pulmonary Hypertension?



We read with interest the publication of O'Byrne et al. (1) and accompanying editorial by Kreutzer (2) addressing risks associated with heart catheterization (HC) in pediatric pulmonary hypertension (PH). HC is considered crucial in defining diagnosis and prognosis and in guiding treatment strategies. Balancing risks and benefits remains a clinical dilemma. The current study design is flawed by selection of a nonrepresentative, high-risk population of hospitalized children and leaves indications for HC undefined. Diagnoses and complications were on the basis of an administrative registry, a recognized source of error. The observed high risk of the composite endpoint obviously is not representative for the child with PH in general. The risk of catheterization is not consistently adjusted for center volume or experience, and other data from dedicated centers report lower complication rates (3-5). The different complication rates in previous reports could be explained by data from experienced and referral centers for PH, and the current study presentation may now hamper proper discussions on the use of HC. Instead of optimizing an accurate estimate of serious complications of HC, identifying its risk factors and balancing clinical decision making, the current paper will cause a drift away from HC procedures, possibly withholding optimal care. Further, using pulmonary arterial hypertension medications without understanding the pathophysiology may be detrimental, as pulmonary vasodilators can lead to pulmonary edema/worsening ventilation-perfusion matching in certain settings. We support the conclusion of Kreutzer (2) that more accurate outcome assessments are mandatory in large registries within populations of interest, as is the validation of noninvasive tools. Both are aims of the global TOPP (Tracking Outcome and Practice in Pediatric Pulmonary Hypertension)-1 and -2 registries (5).

*Maurice Beghetti, MD
Rolf M.F. Berger, MD, PhD
Dunbar D. Ivy, MD
Damien Bonnet, MD, PhD
Tilman Humpl, MD

*Pediatric Cardiology Unit
Department of Child and Adolescent
Children's University Hospital
University of Geneva