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Catecholaminergic Polymorphic Ventricular Tachycardia Due to Ryanodine Receptor (RYR2) Gene Mutation Presenting as Recurrent Apparent Life-Threatening Event Followed by Sudden Death

By Nathanya Baez Hernandez, MD; Chetan Sharma, MD; Uzoma Okorie, MD; Elizabeth McPherson, MD

Keywords: Catecholaminergic Polymorphic Ventricular Tachycardia, RYR2 gene mutation.

Running Title: Catecholaminergic Polymorphic Ventricular Tachycardia.

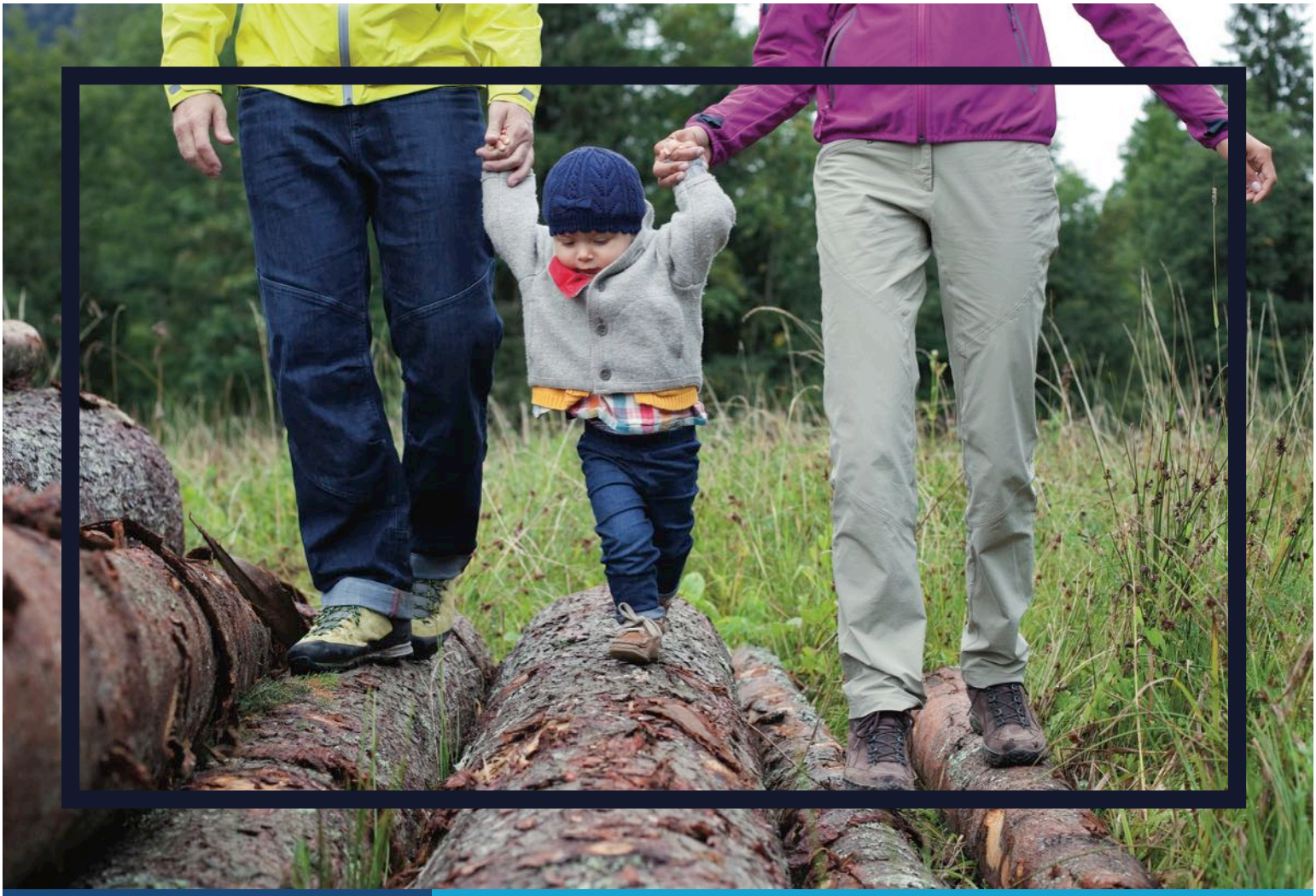
Abstract

While the majority of infants with an apparent life-threatening event (ALTE) recover uneventfully, some may have underlying causes that place them at increased risk for recurrent events and sudden death.[1] Recurrent ALTEs warrant deeper evaluation with high suspicion for cardiac arrhythmias. We present a two month old infant with recurrent ALTE followed by sudden cardiac death that had essentially normal evaluation including electrocardiogram during admission for an ALTE, but postmortem genetic testing showed a rare pathogenic mutation in the *RYR2* gene leading to a retrospective diagnosis of catecholaminergic polymorphic ventricular tachycardia (CPVT). To our knowledge, this is the first case of CPVT presenting as recurrent ALTEs at this young age.

Case Presentation

The patient presented here is a female infant born at 38 weeks to a healthy gravida 3, para 2, mother. Delivery was by Caesarean-section for intrauterine growth retardation. Birth weight was 2470 g (<10%). Apgar scores were 9/9. Family history was notable for sudden death of a sibling at 2 months, which had been attributed to pneumonia despite a normal physical examination just 24 hours prior to his death. Both parents were healthy, but a maternal half aunt had also died suddenly during infancy.

At 7 weeks of age during a minor respiratory infection, our patient presented with an episode of rapid shallow breathing followed by apnea requiring 2 minutes of home cardiopulmonary resuscitation (CPR). On admission, her examination was normal except for mild nasal congestion. Initial work up, including complete blood count, C-reactive protein, comprehensive metabolic panel, chest x-ray, EKG and urinalysis, was unremarkable. Electrocardiogram showed normal sinus rhythm and normal corrected QT interval (QTc) at 449 milliseconds. She was discharged home after 48 hours of observation, but presented again within 10 hours after discharge with a recurrence of apnea and unresponsiveness requiring brief



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CPR. During her second admission, she had a normal video electroencephalogram monitoring, ammonia, amino acids, and organic acids with mildly elevated lactate. Patient was discharged home with a home Apnea-Bradycardia monitor. Three days after hospital discharge, she had a third apneic episode, for which resuscitation was unsuccessful. Post-mortem genetic testing showed a pathogenic mutation Pro466Ala in the *RYR2* gene.

Discussion

An ALTE describes an acute, unexpected change in an infant's breathing, appearance, or behavior that is frightening to the parent or caretaker. It is not a specific diagnosis, but rather a "chief complaint" that brings an infant to medical attention. The incidence is estimated to be 0.05 – 1% in population-based studies.[1-2]

ALTEs should not be considered a precursor to Sudden Infant Death Syndrome (SIDS) because the risk factors differ and only 7.4% of infants dying from SIDS had a previous ALTE.[3] Nevertheless, infants with a history of an ALTE are at increased risk for mortality ranging from 0.2% to 1.1%. [4,5] One study reported sudden unexpected death in 2% of ALTE survivors who had required CPR during their initial episode.[6]

There is no consensus regarding evaluation of infants following an ALTE. While the most frequently observed causes include gastroesophageal reflux, infection, and seizures, many of these diagnoses are apparent clinically and the yield for specific investigations such as esophageal pH probe, brain imaging (except when child abuse is suspected), and video electroencephalogram is low.[7] Cardiovascular disease may be a risk factor for subsequent death, but less than 50% of infants with ALTE undergo cardiac evaluation.[8] In those that do undergo cardiac evaluation, less than 5% have a cardiac disease identified, most commonly small atrial or ventricular septal defects; and only 1% has clinically significant arrhythmias that may explain the ALTE.[9-10]

In our index patient, the ALTE recurrence as well as the family history of sudden infant death in an apparently healthy sibling and maternal half aunt suggested the possibility of an underlying hereditary disorder predisposing to cardiac arrhythmia. At the time of death blood was obtained for the GeneDx Sudden Cardiac Arrest Arrhythmia Panel, which includes the following genes: *KCNQ1, KCNH2, SCN5A, ANK2, KCNE1, KCNJ2, CAV3, RYR2,* and *CASQ2.* No abnormality was found in any of the long QT-associated genes, but a pathogenic mutation, Pro466Ala, was found in *RYR2*. The *RYR*2 gene is associated with CPVT as well as arryhthmogenic right ventricular dysplasia. The specific amino acid change Pro466Ala was previously reported in one individual with aborted cardiac arrest and a family history of multiple people with sudden cardiac death.[11]

Our index patient's mother tested negative for the same mutation, suggesting that the death of her half-sister was not related, but the father and surviving sibling tested positive for the same mutation. This suggests that the patient's deceased brother might also have had a genetic mutation that placed him at risk for cardiac arrhythmia. If his autopsy diagnosis of pneumonia was correct, respiratory infection could have been a trigger for arrhythmia rather than the major cause of his death.

CPVT is a life-threatening cardiac channelopathy that presents predominately in children and young adults. Patients with CPVT have

normal heart structure and an entirely normal-appearing EKG at rest, but exertion may provoke ventricular ectopy. Patients with CPVT most often present in the first or second decade with syncope associated with physical effort or emotion, but cardiac arrest and sudden death can also be the first presentation.[12] CPVT has been reported as cause of sudden death in infants, but has not previously been reported as a cause of recurrent ALTE.[13-14] This is not surprising as the usual evaluation for ALTE would not be expected to identify infants with CPVT unless an EKG was obtained during the ALTE episode. In contrast to Long QT Syndrome in which the QTc is elevated, CPVT is not detectable on resting EKG because the baseline EKG, including QTc, is generally normal. Clinical work-up when CPVT is suspected should include: an evaluation of medical and family history, stress testing, holter monitoring, cardiac imaging, and targeted genetic testing.[15]

In 2007, Tester et al performed a study to assess the spectrum and prevalence of RYR2 mutations in a cohort of 134 SIDS cases. Overall, two distinct and novel RYR2 mutations (R2267H and S4565R) were identified in two cases of SIDS.[14] Subsequently, Larsen et al identified a higher prevalence of variants in the CPVT-associated gene *RYR2* with 7/74 persons aged 0-40 years with sudden unexplained death, including a cohort of infants who died of SIDS, found to be heterozygous for a rare sequence variant in the RYR2 gene.[13] In this study, the prevalence of SIDS-associated RYR2 mutation was 9.4%, much higher than the 1-2% previously reported.[13] No comparable genetic testing has been undertaken in patients with ALTEs.

Conclusion

We suggest that more attention should be given to the possibility of cardiac arrhythmias as a cause of ALTE, especially when ALTEs are recurrent and/or there is a family history of SIDS or sudden cardiac death in children and young adults. A through cardiac evaluation including genetic testing should be considered as part of the ALTE evaluation.

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Highlights of the 1st Bangkok International Adult Congenital Cardiology Symposium

By Alisa Limsuwan, MD

The *1st Bangkok International Adult Congenital Cardiology Symposium,* held January 21st-22nd, 2016, was the inaugural symposium of its kind in Thailand. This symposium was held at the Dusit Thani Hotel in the heart of Bangkok business district. This pioneer international Adult Congenital Heart Disease (ACHD) symposium in Thailand attracted a truly international group (Cambodia, Hong Kong, Malaysia, Maldives, Myanmar, Philippines, U.S.) of attendees, composed predominantly of physicians including pediatric cardiologists, adult cardiologists, cardiac imaging specialists, cardiothoracic surgeons and trainees, but also including: nurse practitioners, sonographers and representatives from industry.

The symposium was directed by Dr. Alisa Limsuwan with organizational support from Drs. Tarinee Tangchareon, Poomiporn Katanyuwong, Mann Chandavimol, and Piya Samankatiwat. One of the highlights of this symposium was the featured international speakers, particularly Dr. Gary Webb - a pioneer in the field of ACHD, Dr. Gruschen Veldtman - Director of Inpatient ACHD Service at Cincinnati Children Hospital, Dr. Mark Sklansky - Chief of Pediatric

"This pioneer international Adult Congenital Heart Disease (ACHD) symposium in Thailand attracted a truly international group (Cambodia, Hong Kong, Malaysia, Maldives, Myanmar, Philippines , U.S.) of attendees, composed predominantly of physicians including pediatric cardiologists, adult cardiologists, cardiac imaging specialists, cardiothoracic surgeons and trainees, but also including nurse practitioners, sonographers and representatives from industry."

Faculty, from left-to-right: Tarinee Tangcharoen, MD; Gruschen Veldtman, MD; Alisa Limsuwan, MD; Lourdes Prieto, MD; Mark Sklansky, MD; Gary Webb, MD; and Boonsong Ongphiphadhanakul, MD, Deputy Dean for Research.

Tarinee Tangcharoen, MD, sharing a lighter moment with some fortunate symposium registrants.

Luncheon presentation by Lourdes Prieto, MD.

Gary Webb, MD, discussing how to build an ACHD center.

Cardiology at UCLA, Dr. Lourdes Prieto - Chief of Pediatric Cardiac Catheterization at Cleveland Clinic, as well as widely respected congenital cardiology experts from Thailand. The symposium provided a comprehensive series of didactic lectures from experts in the field of pediatric cardiology, imaging cardiology, adult congenital cardiology, cardiac intervention, electrophysiology and cardiothoracic surgery. Integrated into the didactic schedule were clinical, enjoyable, yet compelling and challenging, clinical case presentations and debates.

The symposium's didactic line-up began with: the importance of ACHD management to cope with the growing number of ACHD patients, the basics of hemodynamic evaluation in patients with systemic-to-pulmonary shunts, pulmonary hypertension associated with Congenital Heart Disease, long term follow-up of patients

Gruschen Veldtman sharing insights into management of ACHD.

following biventricular repair (particularly Tetralogy of Fallot), the outlook for univentricular heart patients undergoing the Fontan operation, and the locally developed concept of an inferior Glenn operation for selected cases. The afternoon sections included imaging workshops and challenging case discussions, with direct responses from the audiences via electronic voting.

Throughout the conference, registrants enjoyed the Thai hospitality, atmosphere and cuisine from various buffet restaurants at the venue. During additional breaks, registrants also enjoyed interacting with the hosts, invited speakers, and the pharmaceutical and medical instrument representatives.

Given the success of the *1st Bangkok International Adult Congenital Cardiology*, plans are already underway for the *2nd International Adult Congenital Cardiology Advanced Symposium,* planned for January 11th-13th, 2017 at the Shangri-La Hotel Bangkok. Please contact Dr. Alisa Limsuwan for additional information at alimsuwan@yahoo.com or www.adultcongenitalcardiology.com.

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Compiled and Reviewed by Tony Carlson, Senior Editor

Children's Hospital of Michigan DMC Research Team Leads Cardiology Component of Clinical Trial to Protect the Hearts of Children Who Receive Chemotherapy

Newswise — After more than two decades of grueling research for a National Institutes of Health study, Children's Hospital of Michigan Pediatrician-in-Chief and Chair of the Wayne State University School of Medicine Department of Pediatrics Steven E. Lipshultz, MD and a group of pioneering Detroit researchers have co-published a study that breaks new ground in the effort to protect children who survive two major types of blood cancer from the threat of lifelong damage to their hearts caused by chemotherapy.

Published in the *Journal of Clinical Oncology,* the clinical trial found that dexrazoxane is effective in neutralizing the toxic cardiac effects of the often used pediatric cancer-fighting drug doxorubicin. Childhood cancer patients involved in the study were all survivors of newly diagnosed (and often fatal) T-cell acute lymphoblastic leukemia or advanced-stage Lymphoblastic Non-Hodgkin Lymphoma.

"This is the largest dexrazoxane study ever done in children, involving nearly 600 patients who were followed for many years after receiving doxorubicin during their cancer chemotherapy," Dr. Lipshultz said. "The results are very encouraging," he added, "because they show that the kids who received the dexrazoxane after doxorubicin therapy for their cancer had hearts that were normal – and the children who didn't receive dexrazoxane had significantly abnormal hearts. The publication of this study in the J*ournal of Clinical Oncology* says a great deal about the major contributions to clinical research that are being made at the Children's Hospital of Michigan."

The study concluded that, "Dexrazoxane was cardioprotective and did not compromise antitumor efficacy, did not increase the frequencies of toxicities, and was not associated with a significant increase in second malignancies with this doxorubicin-containing chemotherapy regimen. …We recommend dexrazoxane as a cardioprotectant for children and adolescents who have malignancies treated with anthracyclines including doxorubicin."

That finding was underlined by Eric J. Chow, MD, a pediatric oncologist at Seattle (Wash.) Children's Hospital, who said in a podcast appended to the study: "In summary, [this] study adds to the growing evidence that dexrazoxane may have an important role in ameliorating important cardiac late effects in childhood cancer survivors."

Dr. Lipshultz, the senior author of the new study – funded in part by the National Cancer Institute and which included research by members of the national Children's Oncology Group – first began conducting research on dexrazoxane as a potential "cardioprotectant" for children undergoing chemotherapy for leukemia in the late 1980s.

"It was very heartening," he said, "to see that a leading cancer journal not only accepted the study for publication . . . but that they also put it on the fast track to come out immediately [online], because they felt that it could potentially influence the standard of care for pediatric cancer patients who receive chemotherapy."

The study included as co-authors two other Children's Hospital of Michigan and Wayne State University School of Medicine pediatric researchers – Yaddanapudi Ravindranath, MD, MBBS, and Vivian I. Franco, MPH – along with about a dozen researchers at major pediatric health care centers in the National Cancer Institute's Children's Oncology Group Acute Lymphoblastic Leukemia Committee, such as Barbara L. Asselin, MD from the University of Rochester School of Medicine, the Protocol Chair and first author; Upstate Medical Center; the University of Florida; the City of Hope; the University of Mississippi; Johns Hopkins School of Medicine; and the Medical College of Wisconsin.

"This very large study took many years of collaborative effort by a remarkable group of extremely dedicated pediatric oncology and cardiology researchers," Dr. Lipshultz said, "and I think it's a powerful example of how good clinical research at the bedside can help investigators to find 'patient safety signals' and then join together to study and prevent them. When that happens, the result is often improved pediatric patient care – which is our bottom-line goal at the Children's Hospital of Michigan, day in and day out."

Children's Hospital of Michigan Chief Executive Officer Larry M. Gold echoed Dr. Lipshultz's assessment of the study by noting that "pioneering research of the kind Dr. Lipshultz and his team just published in the *Journal of Clinical Oncology* is a crucially important part of the Children's Hospital of Michigan mission. I think we can all take great encouragement from the fact that this breakthrough came about as the result of vigilant patient care by clinicians who were determined to improve outcomes by asking the right questions and then working very hard to come up with the right answers."

Post-Traumatic Stress Disorder Seen in Many Adults Living with Congenital Heart Disease

Adults living with Congenital Heart Disease (CHD) may have a significantly higher risk of Post-Traumatic Stress Disorder (PTSD) than people in the general population.

A single-center study from The Children's Hospital of Philadelphia (CHOP) found that as many as one in five adult patients had PTSD symptoms, with about one in 10 patients having symptoms directly related to their heart condition. The researchers suggest that clinicians and caregivers need to be aware of possible PTSD symptoms, such as anxiety and depression, in their patients.

"Although the life expectancy of adults living with CHD has improved, ongoing care may include multiple surgeries and procedures," said the study's senior author, Yuli Kim, MD, a cardiologist at CHOP. "These patients remain at risk for both

cardiac and non-cardiac effects of their chronic condition, and face unique life stressors that may place them at elevated risk for psychological stress."

Dr. Kim is the Director of the Philadelphia Adult Congenital Heart Center, a joint project of CHOP and the Hospital of the University of Pennsylvania. Her research team's study appeared in the March issue of the *American Journal of Cardiology*. It was the first analysis of PTSD in an adult CHD population.

Due to surgical and medical advances, there are now more American adults living with congenital heart defects than the annual number of children being born with them, even though heart defects are the most common birth defect in the U.S.

The researchers enrolled 134 patients with congenital heart defects, and used two validated mental health scales with questions related to anxiety, depression and PTSD. Of 134 patients who completed one scale, 27 (21%) met criteria for global PTSD symptoms. Of the 127 patients who completed another scale, 14 patients (11%) had PTSD symptoms specifically related to their CHD or treatment.

The high prevalence of PTSD in this patient cohort--11% to 21%--is several times higher than the 3.5% rate observed in the general population. The authors noted that the prevalence is comparable to that found in children with CHD and in adults with acquired heart disease.

The researchers also found two factors most strongly linked to PTSD in their patients: elevated depressive symptoms and the patient's most recent cardiac surgery. Patients who had undergone cardiac surgery at an earlier year were more likely to have PTSD. This finding may reflect recent medical and surgical advances that lessen traumatic impacts, or alternatively, a "residual stress" explanation--that traumatic stress produces chronic, lasting effects.

The study team also noted that non-medical traumatic events may have contributed to PTSD in some patients. In addition, said the authors, the self-report measurements used in the study may not be as accurate as a clinical interview.

Overall, the new study may reveal important unmet needs in a growing population of patients. "The high prevalence of PTSD detected in these adult CHD patients has important clinical implications," said corresponding author Lisa X. Deng, of CHOP's Division of Cardiology. She noted that less than half of the study patients who showed PTSD symptoms were being treated for PTSD, and added that, "We need to conduct more research to identify measures along the lifespan to support our patients and ensure that they have a good quality of life."

A grant from Big Hearts to Little Hearts supported this research.

Lisa X. Deng, et al, "Prevalence and Correlates of Post-Traumatic Stress Disorder in Adults with Congenital Heart Disease," American Journal of Cardiology, March 2016. http://doi.org/10.1016/j.amjcard.2015.11.065

In Pediatric Heart Patients, a Novel Approach Improves Symptoms of Hazardous Lymph Blockage

Newswise — Pediatric researchers have devised an innovative, safe and minimally invasive procedure that helps relieve rare but potentially life-threatening airway blockages occurring in children who had surgery for congenital heart defects.

The physician-researchers developed new imaging tools and used minimally invasive catheterization techniques to treat plastic bronchitis, a condition in which abnormal circulation causes lymphatic fluid to dry into solid casts that clog a child's airways.

The authors reported their retrospective study of 18 children with plastic bronchitis at Children's Hospital of Philadelphia (CHOP) online ahead of print on Feb. 10, 2016 in *Circulation*, the journal of the American Heart Association.

The study, which describes the pathophysiological mechanism of plastic bronchitis and a treatment approach, arose from collaboration between Maxim Itkin, MD, an Associate Professor of Radiology in the Perelman School of Medicine at the University of Pennsylvania, and Yoav Dori, MD, a pediatric cardiologist in the Cardiac Center at The Children's Hospital of Philadelphia. They co-lead a specialized team dedicated to the care of lymphatic disorders as part of the Center for Lymphatics Imaging & Interventions at The Children's Hospital of Philadelphia and the Hospital of the University of Pennsylvania.

"This is a new treatment option for children with plastic bronchitis, and has the potential to offer long-term improvement of this condition," said Dori. "This procedure may even provide cure and avoid the need for a heart transplant."

The current study builds on the team's 2014 article in *Pediatrics*, the first case report of the successful use of their technique in a patient with plastic bronchitis. "We have expanded on that study to report short-term outcomes in a larger group, and to share insights into the development of plastic bronchitis, which has been poorly understood," said Dr. Itkin. In addition to heart patients, children and adults with idiopathic plastic bronchitis, in which the cause is unknown, have also been treated successfully using these techniques.

Itkin and Dori discovered that the primary cause of plastic bronchitis is a lymphatic flow disorder, due to abnormal lymphatic flow into lung tissue. Because physical examinations and conventional imaging may not provide specific findings, lymphatic flow disorders often go undiagnosed.

Over the past several years, Drs. Itkin and Dori developed a customized form of magnetic resonance imaging (MRI), called dynamic contrast-enhanced MR lymphangiogram, to visualize the anatomy and flow pattern of a patient's lymphatic system. This technique allows clinicians to locate the site at which lymph leaks into the airways.

Plastic bronchitis may occur in children as a rare complication of early-childhood heart surgeries used for single-ventricle disease, in which one of the heart's pumping chambers is severely underdeveloped. Approximately 5% of children surviving this surgery experience plastic bronchitis because the surgery alters venous and lymphatic pressure. The authors argue that this altered pressure may interact with pre-existing anatomical differences in the patients' lymphatic vessels.

The abnormal circulation causes lymph to ooze backward into a child's airways, drying into a caulk-like cast formation that takes the shape of the airways. The first sign of plastic bronchitis may be when a child coughs out the cast. However, if unable to cough it up, a child may suffer fatal asphyxiation.

After identifying the leakage site in a lymphatic vessel, the lymphatic team intervenes, using a technique called lymphatic embolization. Through small catheters, the team blocks the abnormal flow with a variety of tools: coils, iodized oil, and covered stents, based on an individual patient's needs.

In the current report, the team was able to perform lymphatic embolization in 17 of their 18 patients, ranging from age two to age 15 (median age 8.6 years). Fifteen of those 17 patients had significant improvements in cast formation, in some cases being cast-free longer than two years. Patients had transient side-effects of abdominal pain and hypotension (low blood pressure), but the authors reported the procedure appeared safe in their patient group.

In addition to his CHOP position, Dr. Dori is on the Penn Medicine faculty.

Dori et al, "Percutaneous Lymphatic Embolization of Abnormal Pulmonary Lymphatic Flow as Treatment of Plastic Bronchitis in Patients with Congenital Heart Disease," *Circulation*, published online ahead of print, Feb. 10, 2016. http://doi.org/10.1161/CIRCULATIONAHA.115.019710

The Children's Hospital of Philadelphia was founded in 1855 as the nation's first pediatric hospital. Through its long-standing commitment to providing exceptional patient care, training new generations of pediatric healthcare professionals and pioneering major research initiatives, Children's Hospital has fostered many discoveries that have benefited children worldwide. Its pediatric research program receives the highest amount of National Institutes of Health funding among all U.S. children's hospitals. In addition, its unique family-centered care and public service programs have brought the 535-bed hospital recognition as a leading advocate for children and adolescents. For more information, visit www.chop.edu.

First Implantable Hemodynamic Monitoring Device in Single-Ventricle Fontan Anatomy

While the Fontan procedure has improved the short- and mid-term outcomes for patients born with single ventricle-anatomy, long-term complications of Fontan circulation include heart failure. These complications are thought to be secondary to elevated central venous pressure, chronic venous congestion and low cardiac output.

In the recent case series published in the journal *Catheterization and Cardiovascular Interventions*, clinicians from The Heart Center at Nationwide Children's Hospital and The Ohio State University Wexner Medical Center describe the first implantable hemodynamic monitor (IHM) placement in single ventricle Fontan anatomy. To date, Nationwide Children's is the first pediatric hospital to perform the procedure, while Ohio State's Wexner Medical Center is the first hospital to perform the procedure in a Fontan patient.

"This pressure gradient between central venous pressure and a combination of ventricular end diastolic pressure and resistance of flow across the pulmonary vascular bed is critical to cardiac output," explains Darren Berman, MD, Co-Director of Cardiac Catheterization and Interventional Therapy in The Heart Center at Nationwide Children's. "Recently, implantable hemodynamic monitors have been used to monitor pressures in patients with left heart disease."

Noninvasive studies are unable to determine these pressures in the Fontan anatomy, thus limiting physicians' understanding of the changes in pressure for a Fontan patient in heart failure, according to Curt Daniels, MD, Director of Adolescent and Adult Congenital Heart Disease in The Heart Center at Nationwide Children's and Professor of Clinical Cardiology at The Ohio State University College of Medicine.

"Our ultimate goal is to improve care for patients with Congenital Heart Disease," says Dr. Daniels. "We are excited to be leading the charge to incorporate the use of this tool to learn more about the hemodynamic changes in real life ambulatory situations in Fontan patients."

Two patients with single ventricle anatomy and Fontan physiology, both with New York Heart Association (NYHA) functional class III heart failure, were implanted with the CardioMEMS® HF System by Drs. Berman and Daniels. Real-time pulmonary artery catheter tracings were shown to correlate with IHM tracings in Fontan anatomy. Additionally, home transmission of IHM readings was successful.

"We have shown early safety and feasibility of placement of the IHM in these two cases, and we will follow these patients to monitor the safety in the medium- and long-term, including assessment for pulmonary arterial thrombus," says Dr. Berman, who is also an Assistant Professor at OSUCM.
Dr. Berman, Dr. Daniels and coauthor Elisa Bradley, MD, cardiologist at Nationwide Children's and Assistant Professor at OSUCM, hope that, as it does in patients with non-congenital heart disease, monitoring hemodynamic information from the transmissions will translate to improved fluid balance and heart failure symptoms, including reduced hospital admissions.

Reference: Bradley EA, Berman D, Daniels CJ. First implantable hemodynamic monitoring device placement in single ventricle fontan anatomy. Catheterization and Cardiovascular Interventions. 2016 Mar 25. [Epub ahead of print].

BePATIENT and Vital Connect Announce Launch of BeVITAL in the U.S. Market

Vital Connect, Inc., a leader in the design and deployment of wearable biosensor technologies, and BePATIENT, an innovative startup that develops patient-centric digital health solutions, announce the first North American deployment of BeVITAL. The remote patient monitoring solution combines Vital Connect's FDA-cleared biosensor, HealthPatch® MD, with BePATIENT's web-based solution and associated app, which allows the implementation of personalized healthcare programs accessible through mobile devices and computers.

This spring, BeVITAL will be used in a post-discharge heart failure patient monitoring study at John Muir Medical Center in Walnut Creek and Concord, California. Dr. Neal White, the Heart Failure Director at John Muir said, "We're looking forward to seeing how sensor technology and connected patients combine to improve heart failure outcomes

for our patients, including reduced readmissions." The BeVITAL Solution will also be used to follow patients returning home after outpatient surgical procedures at Hospital Infantile De Las Californias in Tijuana, Mexico in a study run by Scripps Translational Science Institute in San Diego.

The BeVITAL solution can be used to monitor and transmit eight FDA- and CE- cleared biometric data streams from HealthPatch MD directly to practitioners' smartphones, tablets or computers. In addition, the BeVITAL Solution provides individualized care plans to patients along with meaningful insights to clinicians and researchers.

BeVITAL has already facilitated the post-discharge monitoring of over 80 surgical patients in clinical studies at five hospitals in Europe with two more deployments scheduled for this summer. Dr. Phillipe Topart, a surgeon from the Clinique de l'Anjou in France said, "BeVITAL appears to be a pioneering, innovative solution allowing us to meet the requirements of bariatric surgery follow-up. In general surgery, the vital signs monitoring HealthPatch MD along with the BePATIENT mobile app is a unique tool for remote patient monitoring and detecting post-operative complications. This solution represents a major support tool in complex ambulatory surgery. It seems to me that BeVITAL is a leading connected health solution."

A patient-centric solution, BeVITAL has been positively received by patients. One patient reported, "The BeVITAL solution gave me the confidence I needed to leave the hospital earlier as I knew my medical team was remotely monitoring my health. It was really easy to use and helped me understand what I needed to do after my surgery". Through BeVITAL, BePATIENT and Vital Connect are delivering a true end-to-end solution that helps facilitate the transition toward value-based care.

To learn more about how BeVITAL visit: www.bepatient.com.

Parents Favor Boys Over Girls for Free Heart Treatment in Northern India: Gender Bias Apparent for Children of All Ages of Children and in Both Rural and Urban Communities

Parents in Northern India favour boys over girls when it comes to making sure that their children's heart problems are corrected--even when treatment is provided completely free of charge--reveals research published in the online *journal Heart Asia.*

This gender bias is apparent for all ages of children and for parents living in both rural and urban communities, suggesting deep-rooted attitudes towards the societal value of girls, given that financial imperatives are often cited for gender inequalities in India, say the researchers.

They base their findings on 519 children with an inborn heart defect or Rheumatic Heart Disease who were referred between 2009 and 2014 to a specialist cardiac centre in Northern India that provided treatment completely free of charge under a government funded scheme. Over the entire period, most of the referrals were for boys; on average, only just over a third of the referrals (197, 37.6%) were for girls. A similar pattern was evident for each of the years under study.

Yet the reported prevalence of coronary heart disease in India is 2.25-5.2 per 1000 live births, with an almost equal gender ratio of between 1:1 and 1:1.25.

"Given the almost equal gender prevalence, it is alarming that relatively fewer girls are brought to the tertiary centres and even fewer are having the required corrective procedures done," write the researchers.

This is an observational study, so no firm conclusions can be drawn about the causes of the gender disparity in the referrals made to the centre.

Nevertheless, their findings prompt the authors to describe the current differences in access as a "social evil." And they conclude: "The deep-rooted social issues (beyond just the economic causes) need to be addressed by medical professionals as well as policy makers to ensure equal [access to] healthcare for both genders."

Public Reporting Measures Fail to Describe the True Safety of Hospitals: Study Finds Only One Measure Out of Twenty-One to be Valid

Newswise — Common measures used by government agencies and public rankings to rate the safety of hospitals do not accurately capture the quality of care provided, new research from the Johns

The researchers analyzed 19 studies conducted between 1990 and 2015 that directly addressed the validity of HACs and PSI measures, as well as information from CMS, the AHRQ and the Maryland Health Services Cost Review Commission's websites. Errors listed in medical records were compared to billing codes found in administrative databases. If the medical record and the administrative database matched 80% of the time, the measure was considered a realistic portrayal of hospital performance.

Of the 21 measures developed by the AHRQ and CMS, 16 had insufficient data and could not be evaluated for their validity. Five measures contained enough information to be considered for the analysis. Only one measure—PSI 15, which measures accidental punctures or lacerations obtained during surgery—met the researchers' criteria to be considered valid.

"Patients and payers deserve valid measures of the quality and safety of care," says Pronovost, who is also Johns Hopkins Medicine's Senior Vice President for Patient Safety and Quality. "Despite their broad use in pay for performance and public reporting, these measures no longer represent the gold standard for quality, and their continued use should be reconsidered."

The researchers say they hope their work will lead to reform and encourage public rating systems to use measures that are based in clinical rather than billing data.

Pronovost recently outlined additional fixes that could be implemented by the rating community in a commentary published in the April 2016 issue of *JAMA*. Designating a separate reporting entity to establish standards for data collection and making funds available for systems engineering research were listed as possible starting points by Pronovost and his co-author, Ashish Jha, MD of Harvard University, Boston Massachusetts.

This work was supported by internal funds from the Johns Hopkins Armstrong Institute for Patient Safety and Quality. Established in 2011, the Armstrong Institute works to improve clinical outcomes while reducing waste in health care delivery both at Johns Hopkins and around the world. Led by Pronovost, the institute develops and tests solutions in safety and quality improvement that can then be shared at the regional, national and global levels. Using a scientific approach to improvement, the Armstrong Institute employs robust measures that can be broadly disseminated and sustained.

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CP STENT™

For Coarctation of the Aorta

INDICATIONS FOR USE (COVERED CP STENT): The Covered CP Stent is indicated for use in the treatment of native and/or recurrent coarctation of the aorta involving the aortic isthmus or first segment of the descending aorta where there is adequate size and patency of at least one femoral artery associated with one or more of the following: Acute or chronic wall injury; Nearly atretic descending aorta of 3 mm or less in diameter; A non-compliant stenotic aortic segment found on pre-stent balloon dilation; A genetic or congenital syndrome associated with aortic wall weakening or ascending aortic aneurysm.

WARNINGS/PRECAUTIONS: Coarctation of the aorta involving the aortic isthmus or first segment of the descending aorta should be confirmed by diagnostic imaging. The CP stent has not been evaluated in patients weighing less than 20kg. As with any type of implant, infection secondary to contamination of the stent may lead to aortitis, or abscess. Over-stretching of the artery may result in rupture or aneurysm formation. Crimping the stent on a balloon catheter smaller than 12mm may cause damage to the stent. Excessive handling and manipulation of the covering while crimping the stent may cause the covering to tear off of the stent. This device is intended for single use only. Do not resterilize and/or reuse it, as this can potentially result in compromised device performance and increased risk of cross-contamination.

CONTRAINDICATIONS: Patients too small to allow safe delivery of the stent without compromise to the systemic artery used for delivery. Unfavorable aortic anatomy that does not dilate with high pressure balloon angioplasty. Curved vasculature. Occlusion or obstruction of systemic artery precluding delivery of the stent. Clinical or biological signs of infection. Active endocarditis. Known allergy to aspirin, other antiplatelet agents, or heparin. Pregnancy.

Reference the IFU for a complete listing of indications, contraindications, warnings and precautions. www.bisusa.org

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