CONGENITAL CARDIOLOGY TODAY

Timely News and Information for BC/BE Congenital/Structural Cardiologists and Surgeons

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North American Edition

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Contacts: Umberto Squarcia, MD, FACC - squarciaumberto@gmail.com or Donald J Hagler, MD - hagler.donald@mayo.edu

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Pericardial Effusion with a Properly Placed Umbilical Venous Catheter

By Ahmad A. Aboaziza, MD; Darshan Shah, MD; Jennifer Gibson, MD; Otto H. Teixeira, MD

Introduction

Pericardial effusion caused by Umbilical Venous Catheter (UVC) is described with intracardiac location of the tip of the UVC. Mechanisms of injury range from direct myocardial perforation to thrombus formation and myocardial necrosis.

Case Presentation

A preterm, 27-week, appropriate-for-gestational age female was immediately transferred to the Neonatal Intensive Care Unit (NICU) after delivery due to prematurity and Respiratory Distress Syndrome (RDS). Her Apgar scores were 6 and 8 at 1 and 5 minutes, respectively.

"Pericardial effusion caused by Umbilical Venous Catheter (UVC) is described with intracardiac location of the tip of the UVC. Mechanisms of injury range from direct myocardial perforation to thrombus formation and myocardial necrosis."

A physical exam revealed an active preterm female in moderate respiratory distress with subcostal retractions. Vital signs included: a temperature of 100.9° F, a pulse 189bpm, respiratory rate 61bpm, blood pressure 57/27mmhg, and weight 1335g. On lung auscultation there were diffuse rhonchi over both lung fields. Mild hypotonia was present. The remainder of the exam was unremarkable.

Umbilical artery and venous lines were placed upon arrival to the NICU. As demonstrated in Figure 1, the umbilical arterial catheter tip was located at the level of the T6, and the umbilical venous catheter tip projected at the cavoatrial junction.

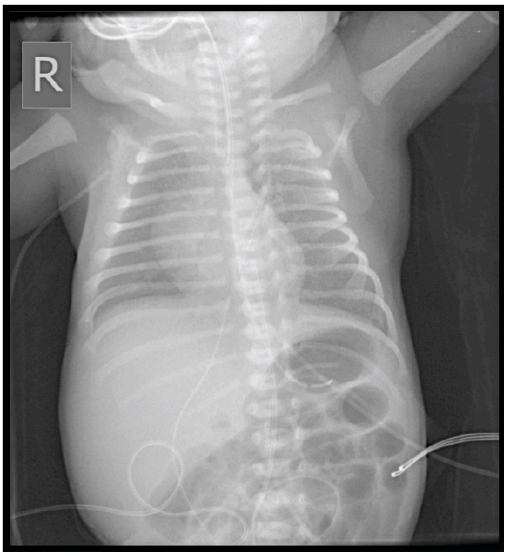
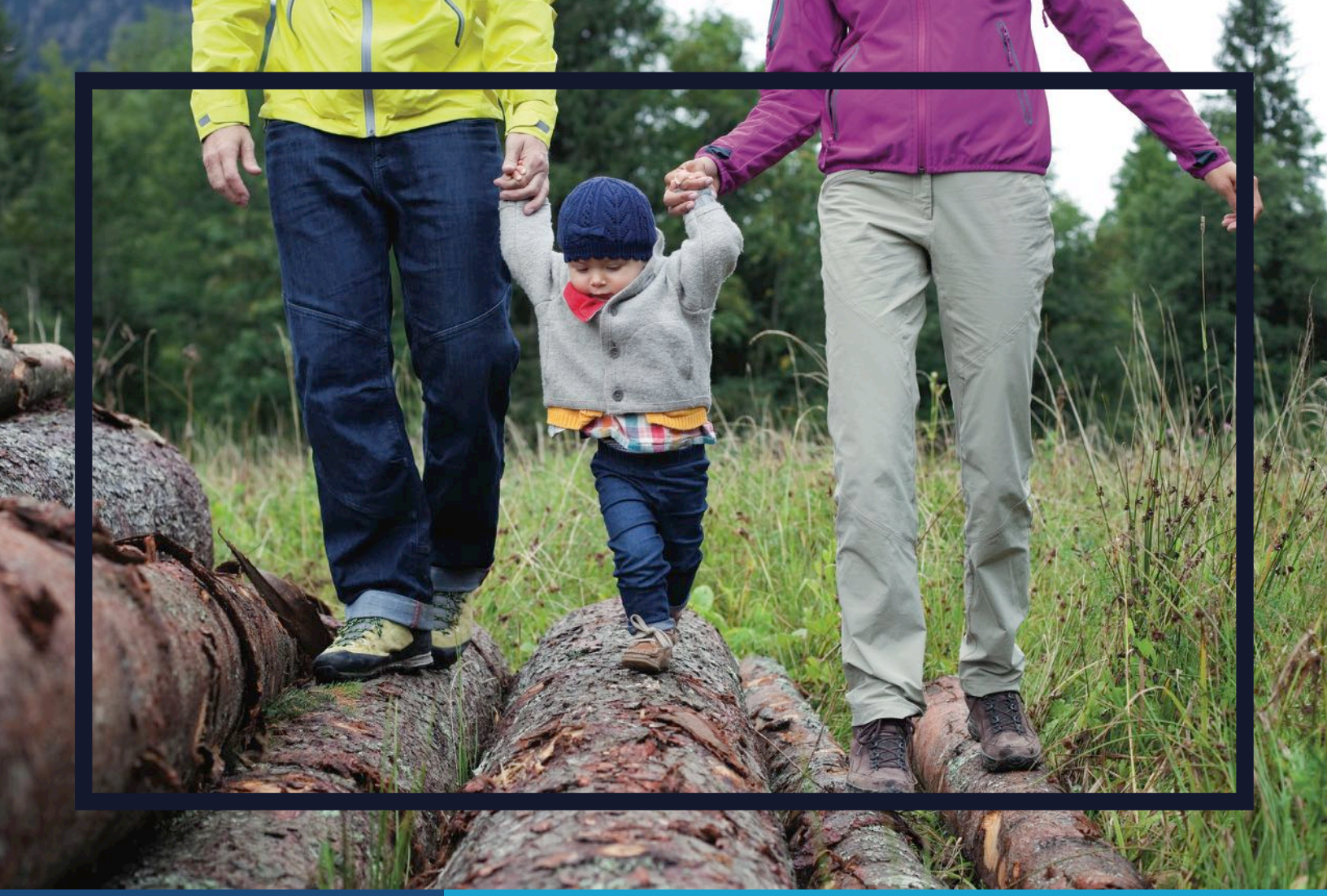


Figure1. Chest- X-ray (PA view) showing UVC and UAC line placements.



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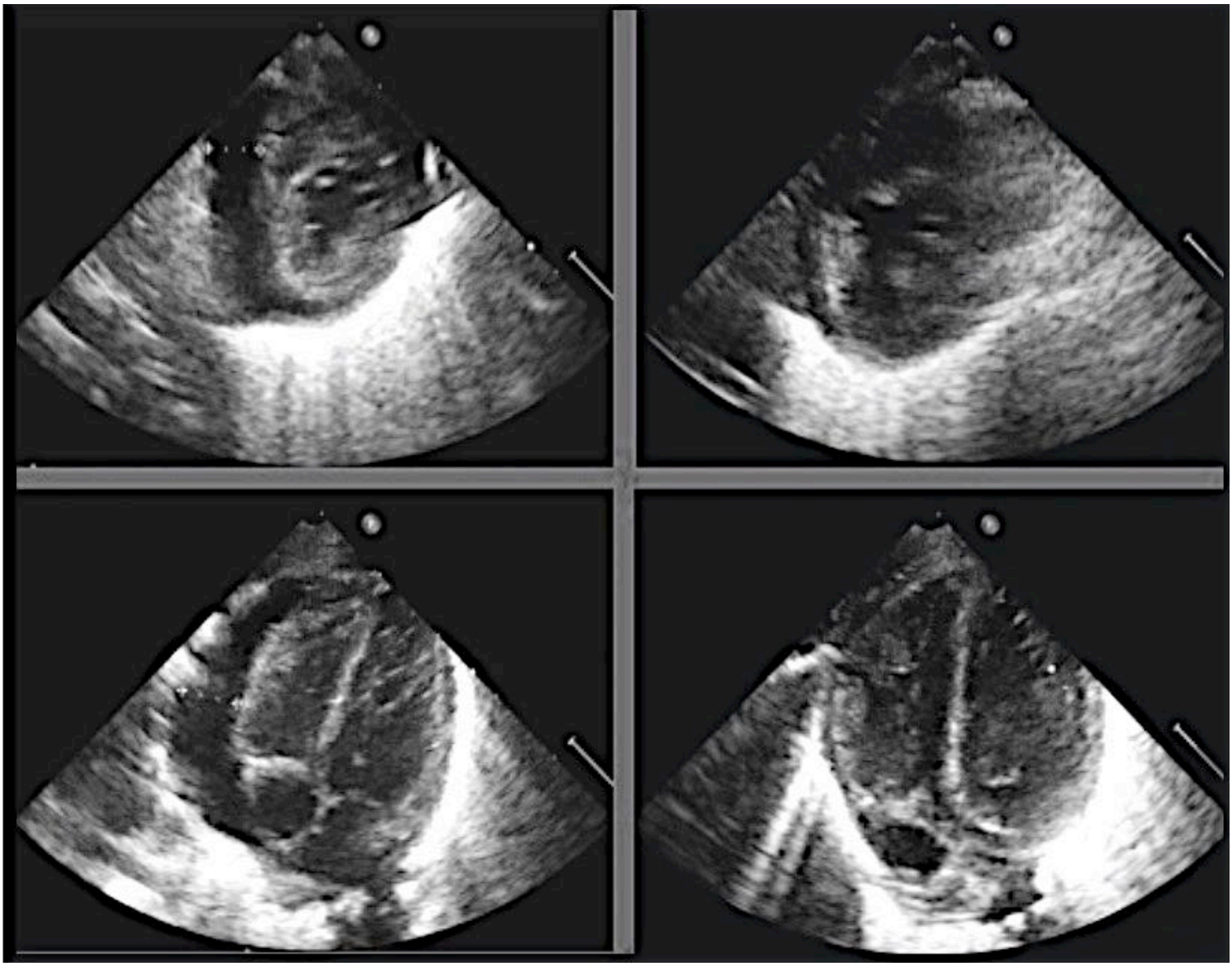

Figure 2. Echocardiograms (apical 4-chamber and short axis view) before and after UVC removal.

On Day of Life (DOL) 1, an echocardiogram did not show any pericardial effusion.

Repeat imaging showed the arterial line with its tip at the T7 level and the venous line with its tip at the T6 level.

On DOL 3, an echo showed a small circumferential pericardial effusion. The X-ray showed 'optimal position' of the UVC. Echocardiograms failed to show the catheter tip in the heart on Day 1 or on Day 3. Ejection fraction was 91.7%. Clinically, the infant deteriorated and required intubation for worsening blood gas.

On DOL 4, a repeat echo showed a moderate circumferential pericardial effusion with no evidence of cardiac tamponade. The effusion was mainly located posteriorly, and was slightly larger compared to the previous day. Ejection fraction remained unchanged. In view of these findings, the umbilical lines were then removed, and a PICC line was placed.

On DOL 5, the pericardial effusion had decreased as the infant remained stable on vent support.

By DOL 7, there was no pericardial effusion seen on echocardiogram.

Discussion

It is possible for a properly placed UVC to cause pericardial effusion as happened with our patient. Even if the UVC is not in the heart, it is always important to take it out ASAP in the event of pericardial

"It is possible for a properly placed UVC to cause pericardial effusion as happened with our patient. Even if the UVC is not in the heart, it is always important to take it out ASAP in the event of pericardial effusion. Pericardial effusion associated with UVC may be treated conservatively if signs of cardiac tamponade are absent."

effusion. Pericardial effusion associated with UVC may be treated conservatively if signs of cardiac tamponade are absent.

Possible causes of pericardial effusion in this setting include direct trauma to the endothelial wall during UVC placement or irritation to the endothelial lining caused by hyperosmolar infusates.

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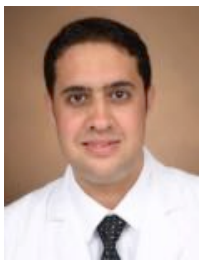

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Non-Compaction Cardiomyopathy in a Patient with Holt-Oram Syndrome: A Case Report

By Kritika Patel, BS; Khalisa Syeda, DO, Andrew J. Griffin, MD;Maria Serratto, MD

Abstract

Holt-Oram Syndrome is a genetic disease characterized by cardiac and upper extremity abnormalities. The presentation is variable, with those affected displaying multiple bone abnormalities in their upper extremities, most commonly carpal bone fusion or malformations, and cardiac issues, classically a septal defect. In the case of this Holt-Oram Syndrome patient, on follow-up for Atrial Septal Defect (ASD), it was noted that she had an atypical form of non-compaction involving the lower one-third of the myocardium.

Case Report

A 22-month-old female with Holt-Oram Syndrome and bilateral polydactyly presented to Pediatric Cardiology clinic for evaluation of a heart murmur and failure to thrive. The patient was a foster child with no birth or family history available. On physical exam, a III/VI systolic ejection murmur heard best at the left sternal border was appreciated. Initial echo showed secundum-type ASD that was 11 mm at its maximum diameter, and significant right ventricular dilation. The ASD was percutaneously repaired with a 20 mm ASO Amplatzer device. The patient was lost to follow-up for several years. At age 11-years-old, she returned for follow-up; she continued to be asymptomatic with no complications since the ASD repair. Her most recent echo, done at age 14-years-old, revealed non-compaction in the left ventricular chamber, largely in the apical region.

Echo

The results of her initial echo (Figure 1) at age 14-years-old were essentially normal, with the exception of the finding of non-compaction in the apical region of the left ventricle; however, the contractility of the left ventricle was not quantitatively affected due to the non-compaction being largely confined to the apical region. A repeat echo showed a systolic non-compacted to compacted endomyocardial layer ratio (NC:C) of about 2, and a diastolic X/Y ratio of 0.3, both of which confirm the diagnosis of non-compaction in this patient.

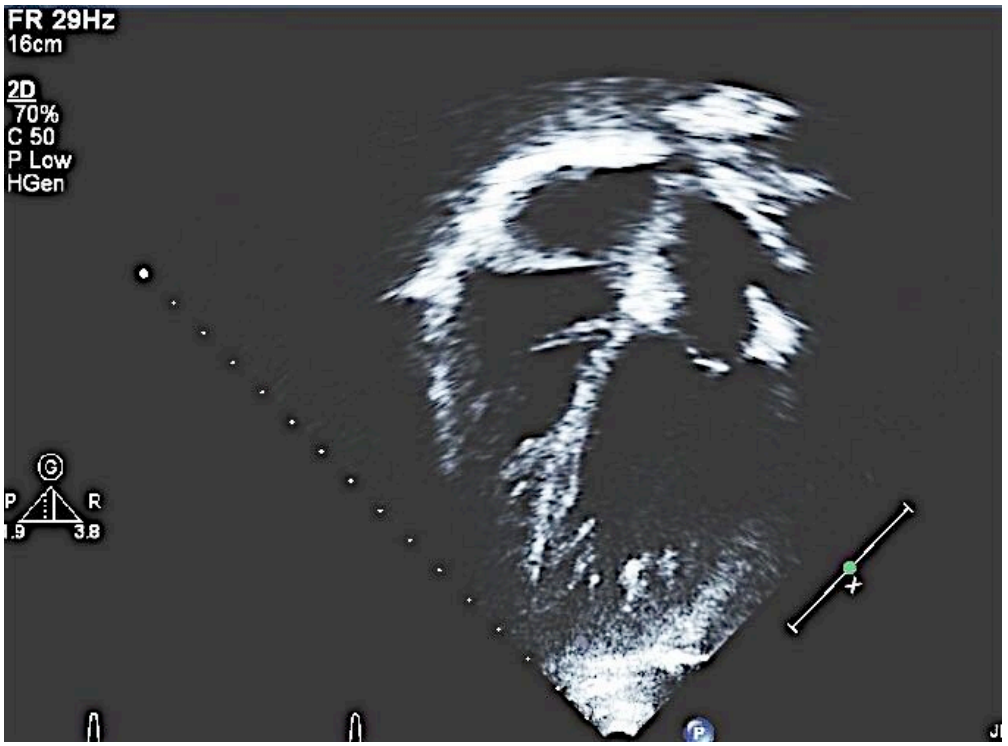

Figure 1. Echo demonstrating non-compaction in the apical region of the left ventricle.

Genetics

Holt-Oram Syndrome is caused by mutations in the TBX5 gene located on chromosome 12q24. The TBX5 gene codes for the transcription factor T-box 5, which is involved in the development of the radial ray, the cardiac septum, and the cardiac conduction system. Normally, the TBX-5 protein interacts with the NKX2-5 and GATA4 proteins to promote normal cardiac septation and normal development of the AV canal. In addition, cells designated for the cardiac conduction system highly express TBX-5; its role is to promote the development of the cardiac conduction system and upregulate CX40 expression, which is involved in the development of normal AV node conduction, and activate TBX-3, which

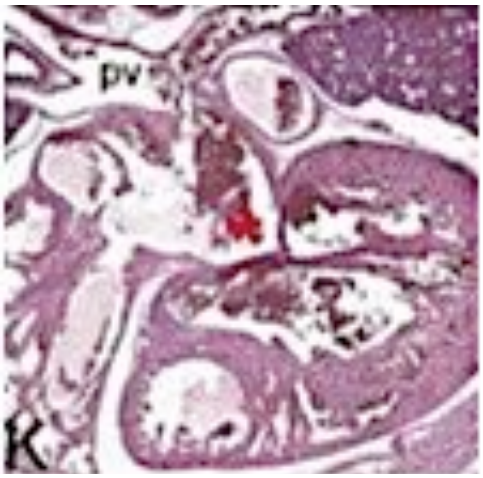

Figure 2. Left ventricle of mouse fetus with TBX5 haploinsufficiency.

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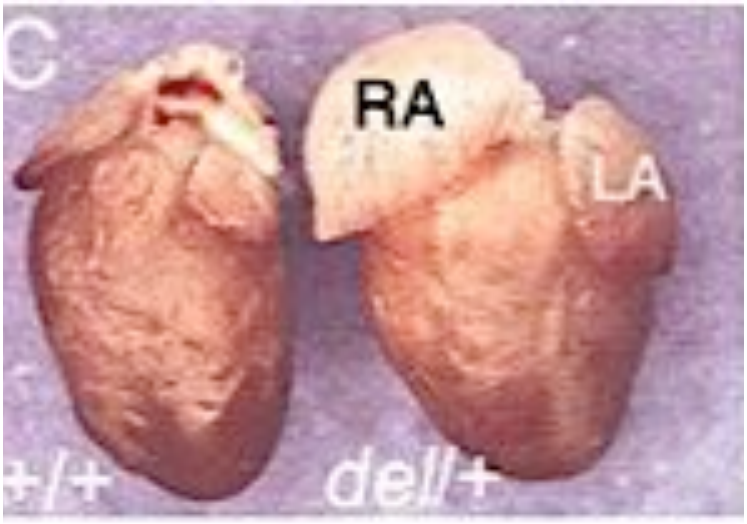

Figure 3. Hearts from 8-week-old mice with TBX5 haploinsufficiency.

promotes the differentiation of precursor cells into conduction system cells instead of myocardial cells. As mentioned previously, the most common cardiac manifestation in Holt-Oram Syndrome is a septal defect, commonly a secundum type Atrial Septal Defect. In addition, there have been multiple other cardiac anomalies observed in this syndrome, including cardiac conduction abnormalities, leading to manifestations such as: heart block, fibrillation, or bradycardia.

Cardiomyopathy has not previously been described in Holt-Oram Syndrome; more specifically, non-compaction has never been described in this entity. A study done by Brunea et al. looked at the cardiac and forelimb abnormalities in an animal model of Holt-Oram Syndrome. It was noted that in mice with TBX5 haploinsufficiency, one mouse fetus was noted to have a deformed left ventricle (Figure 2). The ventricles of 8-week-old

"Our case is the first to describe an association between non-compaction and Holt-Oram Syndrome. While this may be an incidental relationship, it may be useful to carefully evaluate the echo of patients with Holt-Oram Syndrome for not only the classical cardiac abnormalities associated with it, such as ASD, but also more subtle cardiac anatomical abnormalities, especially given the implications of non-compaction long-term."

mice with TBX5 haploinsufficiency were also noted to have a bulbous appearance (Figure 3).

Conclusion

Non-compaction is felt to be a developmental abnormality present at birth, but not found until later in life because of the variable manifestations it can cause related to ventricular function. The etiology of non-compaction has yet to be completely elucidated. While it does not appear to have a single mutation associated with it, it has been associated with mutations in cytoskeleton, sarcomere, and mitochondrial encoding genes. Our case is the first to describe an association between non-compaction and Holt-Oram Syndrome. While this may be an incidental relationship, it may be useful to carefully evaluate the echo of patients with Holt-Oram Syndrome for not only the classical cardiac abnormalities associated with it, such as ASD, but also more subtle cardiac anatomical abnormalities, especially given the implications of non-compaction long-term.

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Early Detection - China California Heart Watch Mission in Yunnan Province

Meredith Yang

As I stared at her pulsing, swollen belly, I couldn't tell if she was pregnant or not. I tried not to look, but I could only stare. My eyes traced the veins on her stomach along the surface of her belly. Her ankles were swollen like balloons.

"Edema…patient presents abdominal swelling as a result of congestive heart failure," Dr. Robert Detrano said as he pressed the ultrasound head against her chest. I watched in awe. Edema had only been a textbook concept to me a few months ago, an indicator in a long list of a series of variables that would qualify a child as "deprived" or not.

Dr. Detrano finished the examination, and prescribed her a few medications to relieve her pulmonary hypertension and help her feel better. She'll need to go to the hospital to renew her prescription after 3 months. "They're 10,000 RMB per box," he said. Her mother looked distraught. Dr. Detrano asked me, "How much do they make?" I looked down nervously. I had just previously asked for their average family income a year and written it down on the intake sheet: "2,000 RMB a year," I read. The equivalent of about $300 USD.

After the pair had left, Dr. Detrano told us that the 17-year old girl probably had one more year left of her life, at most two. Having been diagnosed as a child, her parents had rushed her to surgery. The surgery drained both her parents' finances. I listened as Dr. Detrano explained, "But the doctor should have never performed the surgery. They shouldn't have closed the VSD." A VSD (Ventricular Septal Defect) is a hole in the ventricular wall of the heart. Literally, it is a hole in the heart.

"They shouldn't have done it," he repeated. "At the time, she had progressed too far with Eisenmenger's Syndrome. Once you reach that stage, your pulmonary arteries become too resistant, and your right heart isn't strong enough to push blood through to them. With a VSD, the right heart can at least push the rest of the deoxygenated blood into the left heart so that it empties properly… But then, if you close the VSD, the right heart isn't strong enough to empty itself, so the system backs-up. The blood in the veins that would be draining into the right heart instead pools into the lower body."

As I listened, I tried to ascertain whose fault it was that she slipped through the cracks. Was it the system? Was it a faulty assessment by her doctor? Was it her parents' need to just get her to surgery, in hopes that it would solve everything? Or was it more her lack of circumstance? Had she been born in Shanghai or Beijing, there is no doubt that her condition would have been detected early and immediately treated. She could have lived well into old age.

China California Heart Watch (www.chinacal.org), founded by cardiologist Dr. Robert Detrano, believes that the simple act of proper screening of newborns could have prevented her case. In the West and in many developed countries, virtually all newborns are screened for congenital heart defects within the first 24 hours and during their first year of life. Undiagnosed congenital cardiac shunt lesions with pulmonary hypertension and Critical Congenital Heart Disease (CCHD) kill 3 to 4 of every thousand children in developing countries. If detected early, these cases are completely curable.

The sheer number of complex cases that Dr. Detrano has seen in children and adolescents in Yunnan alone grossly outnumbers those that he sees in the United States. After traveling and providing general clinical care in rural villages for nearly a decade—through his experience and through the recognition of a societal need—Dr. Detrano embarked on a training programme of village doctors in rural Yunnan.

To date, China Cal has visited 52 hospitals within half a year, and plans to visit all hospitals in Yunnan, totaling 125 hospitals. He and his team train doctors in how to listen for heart murmurs using a stethoscope, in combination with pulse oximetr,y to conduct a proper neonatal cardiac examination.

Pulse oximetry is a noninvasive method to monitor a person's oxygen saturation levels using a sensor device placed on the patient's finger, or in an infant's case, across the foot. Masimo Corporation, headquartered in San Diego, California, has additionally gifted 125 pulse oximeters to be used in each of the rural Yunnan county hospitals for screening newborns. Pulse oximeters are valued at around $180 to $200 USD each.

This combined strategy has been proven as an effective screening method to detect

ChinaCal staff using a dummy baby to train doctors how to listen for heart murmurs.

Traveling across rural Yuxi county, Yunnan, in ambulances.

Doctor Zhao from Kunming First Affiliate Medical University training doctors in pulse oximetry on a neonate. China Cal sources doctors from locally renowned universities to act as trainers in the training programme.

CCHD in its early stages by many studies, including a landmark study by Dr. Qu-ming Zhao et al and the Children's Hospital of Fudan University in Shanghai. The addition of pulse oximetry to clinical assessment alone improved detection from 77.4% to 93.2% (www.ncbi.nlm.nih.gov/pubmed/24768155). The study concluded that this simple and accurate method is feasible and reliable for the detection of major Congenital Heart Disease (CHD) and should be used widely in maternity hospitals.

Doctor Zhao, from Kunming First Affiliate Medical University, has been training doctors in pulse oximetry on neonates. China Cal sources doctors from locally renowned universities to act as trainers in the training programme.

Together, Dr. Detrano and his wife Shan Shan have saved over 400 children, providing free screening services, diagnosis, referral, and follow-up. There are another 100 children are on their list, for who they monitor, helping rural families in terms of prescriptions, medical bills, navigating hospitals, making appointments for surgery, and giving advice on how to use the rural insurance system. As one China Cal staff worker recounted, "the hardest part of my job is communicating with rural families and letting them know what documents are required and how to get to the hospitals...I have to repeat over and over, until my mouth is dry (口水都说干掉了)."

What struck me most is China Cal's practice and success in utilizing and implementing both an individual and societal approach, combining the strengths of both clinical practice and the efficiency of public health solutions. In Yunnan alone, it is estimated that approximately 400 infants

Dr. Detrano screens a patient in the basement of his home.

China Cal is headquartered in Dali, Yunnan, China

die from heart defects every year. It is hard to imagine that their training programme will not have a hand in preventing the deaths of hundreds of future infants in Yunnan. As I quote from China Cal's site, "If nothing is done, by 2050, twelve million Chinese people (equal to the population of New York City), will die every year from heart disease and stroke."

Dr. Detrano became inspired to help Yunnan province after cycling through the region and meeting kind and very impoverished villagers who offered him a bed for the night. For the next 15 years, he learned Chinese, allowing him to communicate with patients, and diagnose their conditions. He established strong connections with regional hospital in Chengdu and Kunming in order to refer patients to not only local, but also trusted expertise. His hard work is testament to the person that he is. Dr. Detrano first trained as a physicist. After earning his PhD and realizing that he wanted to pursue medicine, he went on to study for a medical degree in Rome, Italy, eventually becoming a renowned cardiologist in the United States. He moved to China when he was 60-years old.

As I think back to China Cal's message, work, and purpose, I am heartened to realize that sometimes the best solutions are the simplest. Watching a 72-year old American doctor devote his life to rural China gives me hope.

As we travelled with Dr. Detrano through Yuxi county in Yunnan, we set up clinics essentially wherever was possible—in a free room in the hospital, in his motel room, and even in the basement of his home. I was enamored by the simplicity of the work: from diagnosing patients to diagnosing the root of the problem. I felt a very real connection from my work to the people for whom it was intended - no bells and whistles.

I'd like to think that early detection is a broadly applicable concept, beyond CCHD. I leave the experience with a profound belief in the value of time-sensitive, early childhood interventions. From education and health, to proper parental care, often an individual's outcomes are shaped most profoundly in the first two years of life. World-renowned Heckman (2008) and his team have successfully translated this into the language of economics, highlighting that the early childhood period is the most "cost effective for delivering returns." Beyond economics, beyond ROIs, beyond cost effectiveness, I am reminded that intervening early, as in the case of the 17-year old girl with edema, can very simply—save a life.

China Cal is headquartered in Dali, Yunnan, and welcomes the donation of money and equipment, and volunteers who would like to help (www.chinacal.org).

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Ms. Meredith Yang currently works as a researcher in social policy for children. She is particularly interested in health-based interventions. She is based in Shanghai, China.

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Digisonics Introduces New enhancements for Cardiovascular Information System Solutions at ACC.16

Digisonics (Booth #11103) will exhibit its latest functionality for Cardiovascular Information System (CVIS) Solutions at the A*merican College of Cardiology's 65th Annual Scientific Session & Expo* in Chicago, Ill. Digisonics will showcase significant enhancements to streamline cardiovascular workflows, particularly for Adult and Pediatric cath labs. Integration with hemodynamics systems creates workflow efficiency by autopopulating demographics, hemodynamic measurements, medications and other data directly into clinical report. An interactive display tablet with drawing pen provides an easy way to label and reference coronary anatomy. A complete library of Mullins congenital heart and peripheral vascular procedure-based diagrams can be edited to display in the cardiovascular reports.

Utilizing a consistent, structured format for cardiovascular reporting creates a solid database for data mining with the Digisonics Search and Business Analytics Package. Clinicians use the Digisonics tool to gain insight into patient populations, measure performance, determine areas for improvement and plan for future growth.

Digisonics solutions are standards-based and vendor-neutral, combining image review, structured reporting, an integrated clinical database and powerful PACS image archive into one complete solution for all cardiovascular modalities. Coupled with seamless integration to incumbent 3rd party systems, the Digisonics system creates a streamlined workflow to facilitate improved efficiency, greater reporting accuracy and faster report turnaround times.

Digisonics structured reporting solutions combine high performance image review workstations, a powerful PACS image archive, an integrated clinical database, comprehensive analysis capabilities and highly configurable reporting for multiple modalities. Key applications are complemented with interfaces to information systems and 3rd party vendors, providing facilities with a seamless, efficient clinical workflow. For more information, www.digisonics.com.

Penumbra Introduces POD® Packing Coil for the Embolization of Peripheral Vessels and Aneurysms

Penumbra, Inc., a global interventional therapies company, announced the U.S. launch of its new POD® Packing Coil, designed to be used as a complementary device with Penumbra's Ruby® and POD (Penumbra Occlusion Device) embolization products. This latest launch adds to the company's rapidly expanding peripheral vascular product portfolio. Nearly 900,000 Americans each year suffer from peripheral vascular conditions involving acute clots or aneurysms that occur outside the brain or heart, and this represents a large and growing patient population.

Penumbra has developed a suite of thrombectomy and embolization products for use in a range of peripheral vascular conditions, and these products are driving significant growth:

- Penumbra's embolization platform includes Ruby and POD and the new POD Packing Coil, which is uniquely designed to pack very densely behind Ruby and POD to occlude arteries and veins throughout the peripheral vasculature, including aneurysms.
- Penumbra's next-generation Indigo® System is a continuous aspiration thrombectomy device designed to remove fresh, soft emboli and thrombi from the peripheral arteries and veins. The Indigo System includes four catheter sizes (CAT 3, 5, 6 and 8). The aspiration lumen is paired with a proprietary continuous vacuum aspiration pump to evacuate clots effectively and efficiently.

"With the Indigo System and POD, Penumbra has recently introduced products that have had significant impact on the treatment of vascular disease. Indigo represents a significant advancement in the treatment of thrombotic and embolic disease, which until now has had limited treatment options," said Corey Teigen, MD, at Sanford Health in Fargo, ND, who uses Penumbra's peripheral vascular products. "With the Indigo System, physicians now have the ability to remove limb- and life-threatening clots quickly and efficiently. Likewise the POD, Ruby

and now, the POD Packing Coil optimize embolization procedures by decreasing procedure time while providing increased control."

"Our embolization platform and the Indigo System are examples of our commitment to innovating new technologies for challenging vascular conditions for which there are significant unmet clinical needs," said Adam Elsesser, Chairman and CEO of Penumbra. "We are intent on changing treatment paradigms to improve clinical outcomes across two large and growing markets: neuro and peripheral vascular."

Peripheral vascular disease includes blood clots or aneurysms that affect the vessels of the upper and lower extremities and all other parts of the body, except the brain and heart. There are nearly 900,000 people in the U.S. annually who suffer from acute clots or aneurysms in the body that may be treated by thrombectomy or embolization procedures.

Penumbra's peripheral vascular product portfolio currently focuses on thrombectomy and embolization therapies:

- Peripheral thrombectomy involves the removal of blood clots. There are an estimated 850,000 people in the U.S who develop such conditions, and approximately 150,000 are treated per year with existing procedures including catheter-directed thrombolysis (clot-busting drugs).
- Peripheral embolization involves obstructing blood flow to target vessels, aneurysms and vascular anomalies, and assisting with the treatment of oncological disease. There are approximately 50,000 patients treated each year in the U.S for such conditions.

For more information, www.penumbrainc.com.

The Children's Cardiomyopathy Foundation (CCF) Announces the Availability of One-Year Research Grants for Studies Focused on All Forms of Pediatric Cardiomyopathy

CCF's research grant program aims to advance medical knowledge on the causes and mechanism of pediatric cardiomyopathy and to develop diagnostic guidelines and targeted therapies.

- Eligibility: Principal investigators must hold an MD, PhD or equivalent degree, reside in the United States or Canada, and have a faculty appointment at an accredited U.S. or Canadian institution.
- Funding: US $25,000 to US $50,000 for one year of total direct costs.
- Application Process: CCF requires a letter of intent in advance of the grant application. The 2016 deadline for letters of intent is Wednesday, June 15th by 5:00 pm EST. Only investigators who have submitted a letter of intent and have been invited to submit a formal grant application will be considered for CCF funding.

Visit CCF's website www.childrenscardiomyopathy.org (click on Research/Grants & Awards) for application guidelines and to view past grant awards.

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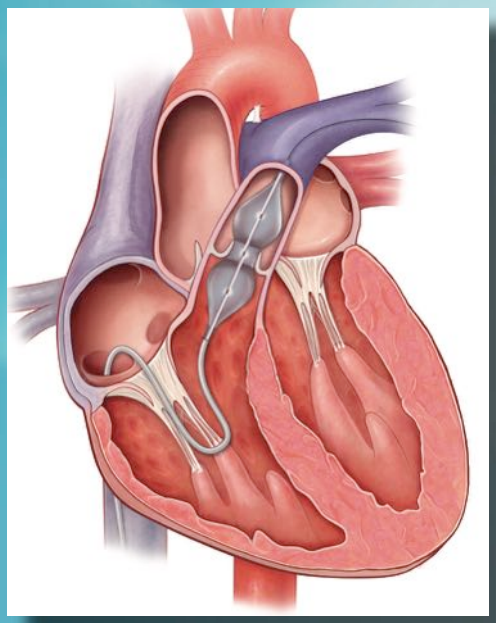
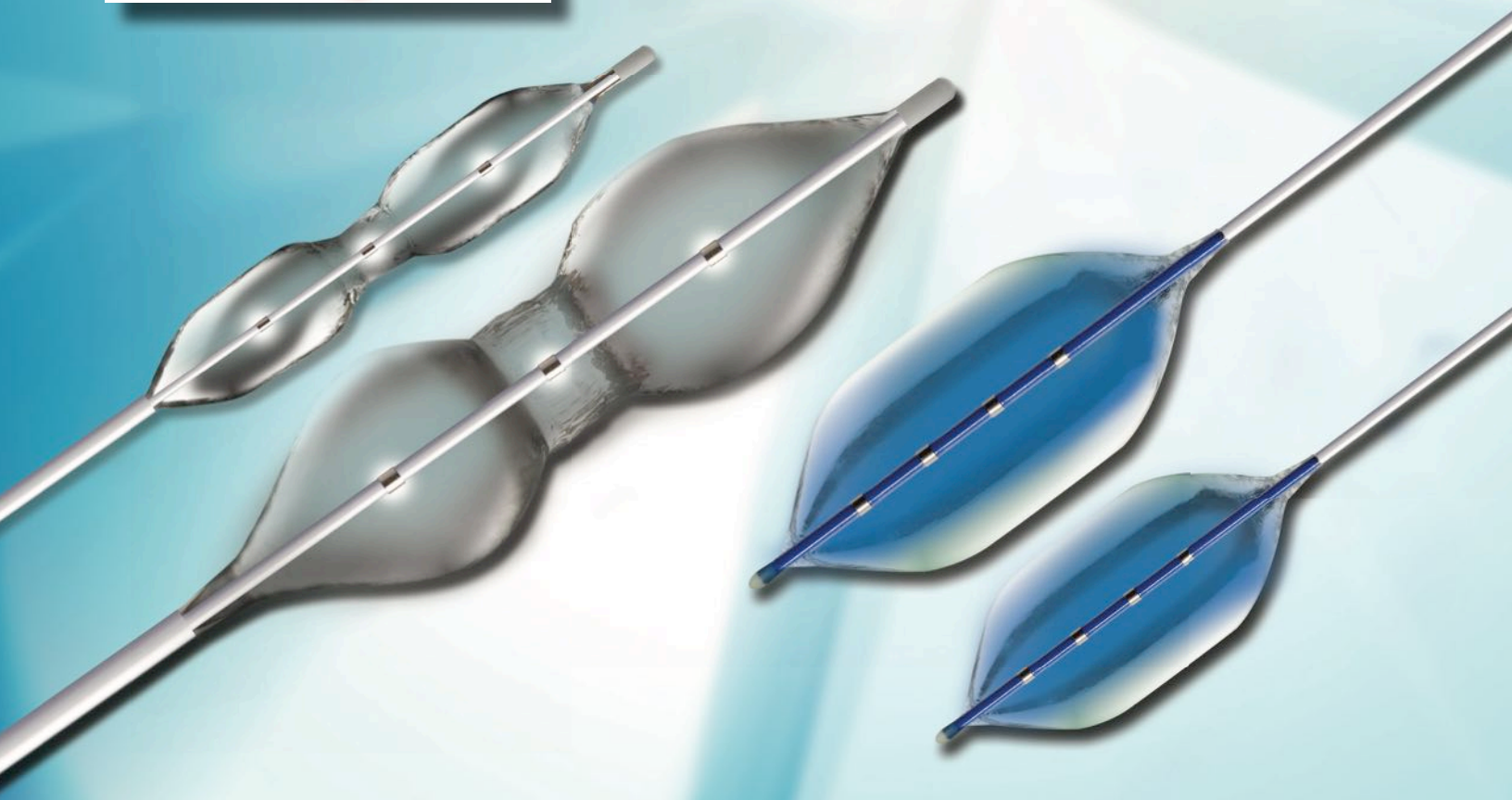


When Precise Sizing is the Heart of the Matter

Tyshak NuCLEUS™ PTV Catheters

PTS-X™ Sizing Balloon Catheters



Rx only
CV9018 - 6/15

The Tyshak NuCLEUS™ PTV Balloon Dilatation Catheters are recommended for Percutaneous Transluminal Valvuloplasty (PTV) of the pulmonary valve in the following: A patient with isolated pulmonary stenosis. A patient with valvular pulmonary stenosis with other minor congenital heart disease that does not require surgical intervention. The PTS-X™ Sizing Balloon Catheters are recommended for use in those patients with cardiovascular defects wherein accurate measurement of the defect is important to select the appropriately sized occluder device. Refer to the Instructions for Use for relevant warnings, precautions, complications, and contraindications.

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