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Hybrid Cardiovascular Procedures Without Cardiopulmonary Bypass in Pediatric Patients - Experience in a Single Center

By Javier Ozores Suárez, MD, MS; Juan Ramiro Novoa, MD; Francisco Díaz Ramírez, MD; Yisel Gallardo Medina, MD; Marcelo Puga Bravo, MD

Introduction

Pediatric interventional catheterization application is affected by the low body weight of the patient, making vascular access difficult due to high profiles of the devices and systems currently available. Therefore, surgeons and interventionalists have worked together to optimize the results in this population. This mixture of procedures is known as hybrid procedures.[1] This manuscript will discuss the different hybrid procedures performed in a single pediatric center.

Methods

Between 2007 and 2017, we enrolled 13 consecutive patients with Congenital Heart Disease (CHD) who underwent hybrid procedures (average age was 11 months, minimum age 3 days and maximum 3 years). The study was approved by the ethical committee of the Pediatric Cardiac Center "William Soler," Havana, Cuba.

SPSS statistical package was used for data analysis. The results of continuous variables were represented as: mean ± standard deviation (mean ± SD) and those categorical variables as numbers and percentages (n, %).

Results

Table 1 summarizes the characteristics of the 13 consecutive patients in which a hybrid procedure was performed. Fifty-seven percent weighed less than 5 kg. Three patients were less than 30 days-old during the procedure.

Ten patients (from four months to three years-old and weighing between 4.3 and 13 kg; 7 ± 3 kg), had muscular Ventricular Septal Defects (VSD); one-fourth of them showed this entity associated with other Congenital Heart Diseases. Therefore, the perventricular approach for closure of muscular VSD by implanting an occlusive device (Amplatzer from 8 to14 mm) was the most frequently performed procedure in this series, and resulted in a 90% success rate. Also associated lesions in four of these cases were treated as shown in Table 1. A failed perventricular closure attempt was presented in an 8-month-old female patient and weighing 4.5 kg, with Trisomy 21, who during the procedure went into cardiac arrest; however, after the emergency was resolved, and a surgical banding of the branch pulmonary arteries was performed.

Hypoplastic Left Heart Syndrome (HLHS) was found in two patients. The first one, a 7-day-old female weighing 3.7 kg, underwent a hybrid palliative approach with

Table 1. Hybrid Cardiovascular Procedures without Cardiopulmonary Bypass in Pediatric Patients					
Sex	**Age / Weight**	**Diagnosis**	**Intervention**	**Immediate Complications**	**Follow-up (months)**
F	2 years / 6.7kg	Muscular VSD	Perventricular approach for closure of muscular VSD by Amplatzer # 10mm + release pulmonary artery banding	Any	38¥
M	8 months / 5.9kg	Muscular VSD	Perventricular approach for closure of muscular VSD by Amplatzer # 12mm	Any	43¥
F	6 months / 5.3kg	Muscular VSD	Perventricular approach for closure of muscular VSD by Amplatzer # 8mm	Any	58¥
M	1 year / 10kg	Muscular VSD	Perventricular approach for closure of muscular VSD by Amplatzer # 12mm	Any	105¥
M	8 months / 4.7kg	Muscular VSD	Perventricular approach for closure of muscular VSD by Amplatzer # 14mm	Any	105¥
F	3 years / 13Kg	Muscular VSD	Perventricular approach for closure of muscular VSD by Amplatzer # 8mm	Any	101¥
F	1 year / 7.5Kg	Muscular VSD + Secundum ASD	Perventricular approach for closure of muscular VSD by Amplatzer # 8mm + perventricular approach for closure of secundum ASD by Amplatzer # 10mm	Any	65¥
F	8 months / 4.5 Kg	Muscular VSD + Secundum ASD	Perventricular approach for closure of muscular VSD (failed) + surgical banding of the branch pulmonary arteries	Cardiac arrest	80¥
M	4 months / 4.3kg	Muscular VSD + aortic coarctation	Perventricular approach for closure of muscular VSD by Amplatzer # 12mm + aortic coarctation surgical correction	Any	69¥
F	7 months / 4.9kg	Muscular VSD + PDA	Perventricular approach for closure of muscular VSD by Amplatzer # 12 mm + surgical PDA closure	Any	73¥
F	27 days / 2.9kg	Pulmonary stenosis	Pulmonary valve balloon dilatation # 12mm by thoracotomy	Any	60¥
F	7 days / 3.7Kg	HLHS	Surgical banding of the branch pulmonary arteries + percutaneous stenting (4.5 mm stent diameter) of the arterial duct	Any	6Δ
F	27 days / 2.2Kg	HLHS	Surgical banding of the branch pulmonary arteries + percutaneous stenting of the arterial duct (failed)	Death	-

Legend: ASD: Atrial Septal Defect; F: female; HLHS: Hypoplastic Left Heart Syndrome; M: Male; PDA: Patent Ductus Arteriosus; VSD: Ventricular Septal Defect; ¥: Control; Δ: Death

surgical banding of the branch pulmonary arteries and percutaneous stenting (4.5 mm stent diameter) of the arterial duct. This patient died 6 months after the intervention (Figure 1).

The second one, a 27-day-old female and weighing 2.2 kg, died during surgery immediately after surgical banding of the branch pulmonary arteries.

The last case of the series was a 27-day-old female, weighing 2.9 kg, with the diagnosis of pulmonary stenosis, underwent perventricular pulmonary artery dilation.

In the 11 patients (excluding two HLHS patients), the follow-up period was 72 ± 23 months. No deaths were found.

Discussion

The perventricular approach for closure of muscular VSD, without the need for cardiopulmonary bypass or ionizing radiation, reduces mechanical and chemical myocardium damage. The effectiveness of this hybrid procedure ranges between 77%-100%.[2,3] Similar data was found in this series (90%). For these reasons it is common to find a high percentage of this procedure in many published series, like Bacha et al[1] where of the total hybrid interventions, 68% corresponded to perventriculares closures of VSD, which coincides with our data (71%).

HLHS is a Congenital Heart Disease with a high mortality.[4] Hybrid palliative Stage I approach to HLHS may be indicated instead of the Norwood procedure, in those patients with a high surgical risk as a bridge to heart transplantation.[5-8] In our study, we performed just two hybrid palliative procedures in ten years, with one hundred percent mortality.

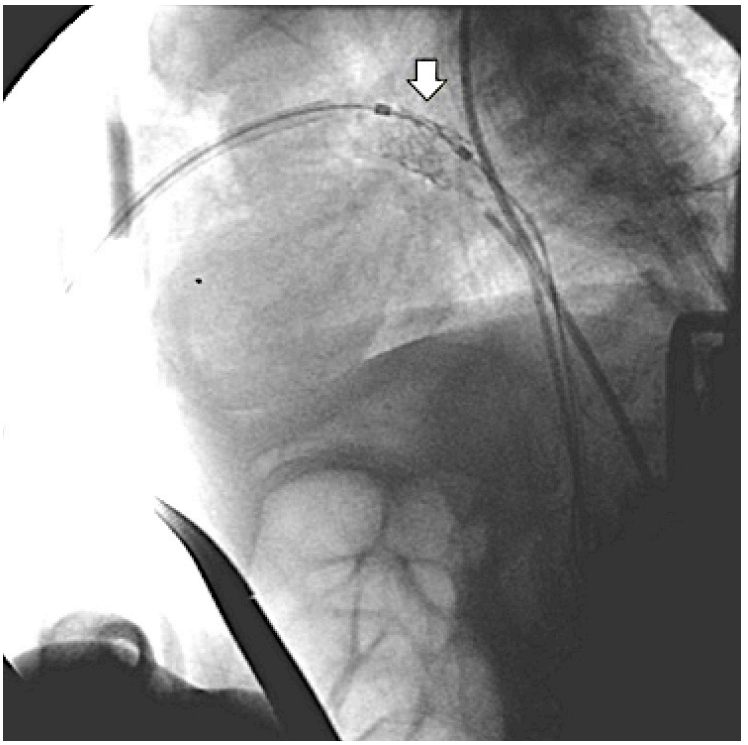
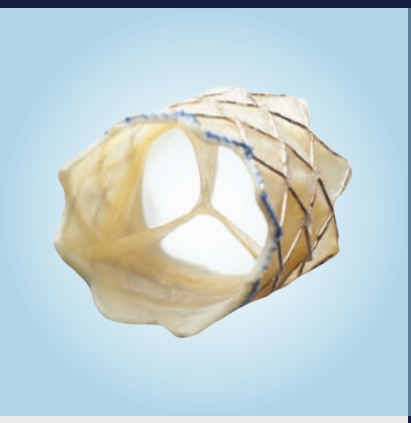


Figure 1. Percutaneous stenting (4.5 mm stent diameter) of the arterial duct, as part of hybrid palliative Stage I, in a patient with Hypoplastic Left Heart Syndrome.

Legend: Left anterior oblique view, note the 4.5mm stent placed at the level of arterial duct (arrow).

RIGHT DATA.



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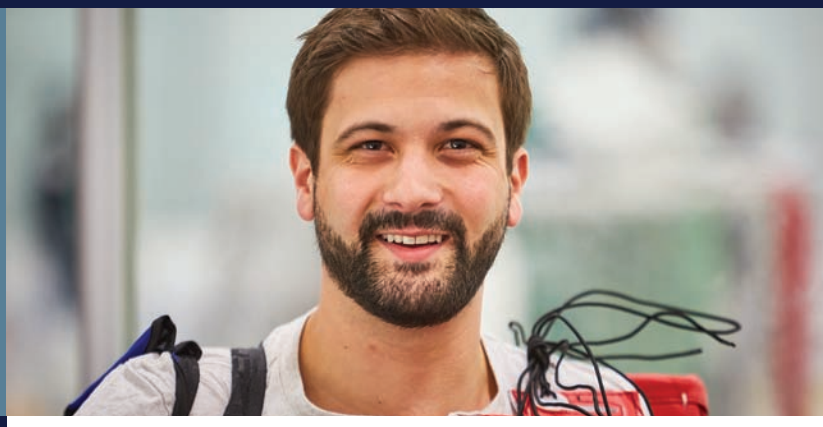

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- The potential for stent fracture should be considered in all patients who undergo TPV placement. Radiographic assessment of the stent with chest radiography or fluoroscopy should be included in the routine postoperative evaluation of patients who receive a TPV.
- If a stent fracture is detected, continued monitoring of the stent should be performed in conjunction with clinically appropriate hemodynamic assessment. In patients with stent fracture and significant associated RVOT obstruction or regurgitation, reintervention should be considered in accordance with usual clinical practice.

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*The term "stent fracture" refers to the fracturing of the Melody TPV. However, in subjects with multiple stents in the RVOT it is difficult to definitively attribute stent fractures to the Melody frame versus another stent.

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Right ventricular outflow tract obstruction is usually treated with surgery or percutaneous intervention. However, in patients where the application of percutaneous procedure is limited by low body weight or limited vascular access, the hybrid procedure has become an acceptable option.[9]

Conclusions

Hybrid procedures are a viable option in the approach to different CHD. Always prior assessment of a multidisciplinary group that includes medical interventional cardiologists and cardiovascular surgeons.

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Myopericarditis Associated with Giardia Intestinalis in a Teenage Patient - A Case Report

By Lamya Mubayed, MD; Daniel Blatt, MD; Brieann Muller, MD

Abstract

Myocarditis and pericarditis share very similar clinical manifestations, as well as etiological agents.[1,2] Many cases in developed countries are deemed idiopathic and presumed to be secondary to viral or autoimmune agents, given that these are the most common causes in developed countries.[2,3] Here we present a case of myopericarditis associated with an acute Giardia infection in a teenage patient. To our knowledge, this is only the second case of such an association to be reported in the literature, and the first to be reported in the pediatric population.[4] Such reports may serve as important leads to identification of new etiological factors not previously known to be common causes of Myocardial and Pericardial Inflammatory Syndromes.

Introduction

Myopericarditis or perimyocarditis are terms used to define a spectrum of pericardial disease with concurrent myocardial involvement. The former term reflects predominantly pericardial involvement/manifestation, and the latter reflects predominantly myocardial involvement.[1] In clinical practice, the two terms tend to be used interchangeably without distinction of predominance.

In contrast to isolated pericarditis, myocarditis is diagnosed when there is evidence of pericarditis in addition to evidence of myocardial inflammation, ie. troponin elevation, echogenic enhancement on echocardiography, or contrast enhancement as seen on cardiac MRI. If there is evidence of advanced myocardial involvement, such as regional wall motion abnormality or reduced function, the syndrome becomes predominantly myocardial and hence the term perimyocarditis is used.[1,2] Myopericarditis or perimyocarditis share similar etiological factors (Table 1), which most commonly include infection, auto-immune, and idiopathic.[5–7] Here we present a case of a teenage patient who presented to our institution with non-specific symptoms and was ultimately diagnosed with myopericarditis with a concurrent Giardia intestinalis infection.

Table 1: Causes of Pericarditis and Myocarditis[5–7]

Idiopathic and Infectious	Non-Infectious
Idiopathic cases are presumed to be secondary to a viral or autoimmune process	Autoimmune, eg: Lupus, Vasculitis, Connective Tissue Disease
Viral, eg. coxsackievirus, echovirus, adenovirus, EBV, CMV, influenza, varicella, rubella, HIV, hepatitis B, parvovirus B19	Cardiac, eg: post-surgical, post-myocardial infarction (Dressler's Syndrome)
Bacterial, eg. Mycobacterium Tuberculosis, Staphylococcus, Streptococcus, Haemophilus, Neisseria, Chlamydia psittaci, Borrelia burgdorferi	Neoplasms: metastatic or primary
Fungal, eg. Histoplasma, Aspergillus, Blastomyces, Coccidioides, Candida	Trauma; blunt or penetrating
Parasitic eg. Echinococcus granulosis, Entamoeba histolytica, Toxoplasma gondii	Metabolic, eg. Uremia, hypothyroidism
Infective Endocarditis	Radiation and Drugs, such as procainamide, isoniazid and hydralazine

Case Report

A 16-year-old male without a significant past medical history presented to an ER with a two-day history of chest pain and subsequent shortness of breath. The chest pain was non-radiating and pleuritic in nature. It was not aggravated or alleviated by leaning forward. The patient also complained of non-bloody non-bilious vomiting and diarrhea, as well as a subjective fever with chills and sweats. He had just returned from an 18-hour flight back from the Philippines, five days prior to presentation. Gastrointestinal symptoms were noted immediately upon arrival to the U.S.

On initial examination in the outside hospital ER, the patient was afebrile and hemodynamically stable. Cardiovascular, lung and abdominal exams were noted to be benign. The patient only complained of a mild headache at the time.

Lab work at the outside hospital was significant for mild leukocytosis with WBC 11.5 x 109/L. Electrolytes, BUN/Cr were normal. CRP and ESR were elevated at 49.8mg/L and 39mm/hr respectively. Initial troponin was 0.28. Rapid streptococcal antigen test was negative. D-dimer was <0.22. Lorazepam 0.5 mg PO, aspirin 324 mg, and IV normal saline 1L bolus were administered after which the patient had complete resolution of symptoms.

On arrival to our institution, the patient was in no acute distress, breathing comfortably on room air without complaint of chest pain or shortness of breath, but reported pressure-like headache localized to the sides of his head. An initial EKG showed normal sinus rhythm and diffuse ST segment elevation (Figure 1). A transthoracic echocardiogram performed during chest discomfort and ST elevation showed normal left ventricular size and systolic function with normal contractility in all segments. There was no significant pericardial effusion. A chest X-ray was normal. Troponin level upon arrival to our institution was elevated at 9.09ng/mL.

Given the combination of chest pain, ST segment elevation and troponin bump, a provisional diagnosis of myopericarditis was made. The initial ST elevation resolved on Day 3 of admission and new T wave inversion was seen in anterior and lateral leads (Figure 2). Troponin T levels trended down after a peak of 12.32 on Day 2 of hospitalization. No arrhythmias recorded on inpatient telemetry. The EKG was normalized by day of discharge (Day 3) (Figure 3). Symptoms were completely resolved at the time.

A cardiac MRI was performed on Day 4 of admission, which revealed no definite myocardial edema, early or late gadolinium enhancement. No pericardial effusion, thickening, or enhancement. Left and right ventricular function was normal. Patient was subsequently discharged with outpatient follow-up.

With the complaint of diarrhea, stools studies were ordered, including: stool culture, ova and parasites, feces hemoccult, stool viral culture for enterovirus/adenovirus, and cryptosporidium and Giardia antigens. Feces hemoccult was negative. Stool culture, and stool cryptosporidium were negative. The complete metabolic panel showed mild transaminitis, which resolved prior to discharge. A rapid viral panel, cytomegalovirus (CMV) polymerase chain reaction (PCR), Epstein-Barr virus (EBV) PCR, adenovirus PCR human herpesvirus 6 (HHV-6), human immunodeficiency virus (HIV) antibody/antigen, hepatitis C virus antibody, Mycoplasma pneumoniae IgM, Toxoplasma gondii IgM/IgG, Entamoeba histolytica IgM/IgG, interferon gamma release assay, and blood culture were negative. EBV IgG/IgM and parvovirus IgG/IgM were consistent with previous exposure. Viral serology was negative for enterovirus, influenza A/B, HHV6, EBV, CMV. Anti-nuclear antibody (ANA) was negative.

Giardia intestinalis cysts were identified by stool microscopy, and Giardia antigens were detected on stool ELISA immunoassay. PCR testing of stool was negative for common viral and bacterial pathogens, including enterovirus and Campylobacter spp. The patient was diagnosed with giardiasis, which was a likely consequence of travel to an endemic area. He was started on

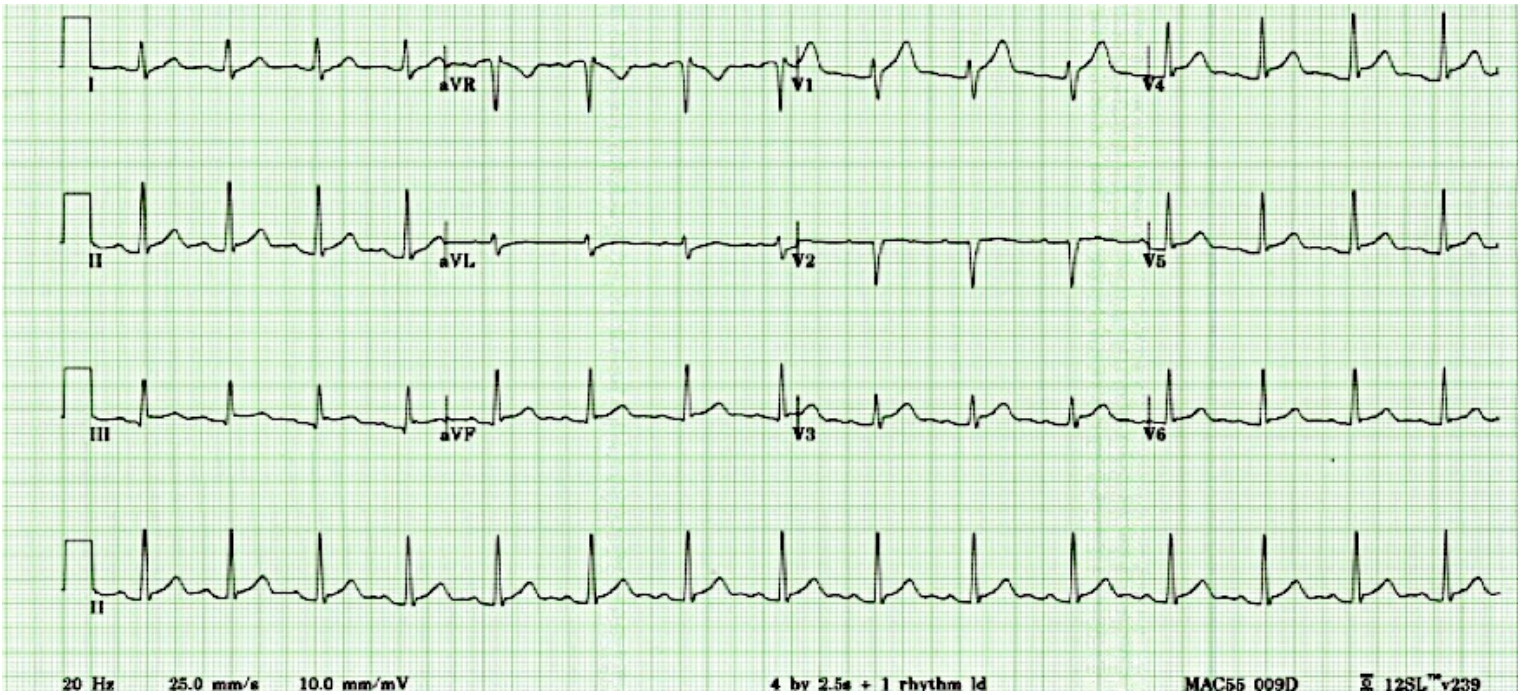

Figure 1. Initial EKG upon arrival. Note diffuse ST segment elevation and PR interval depression.

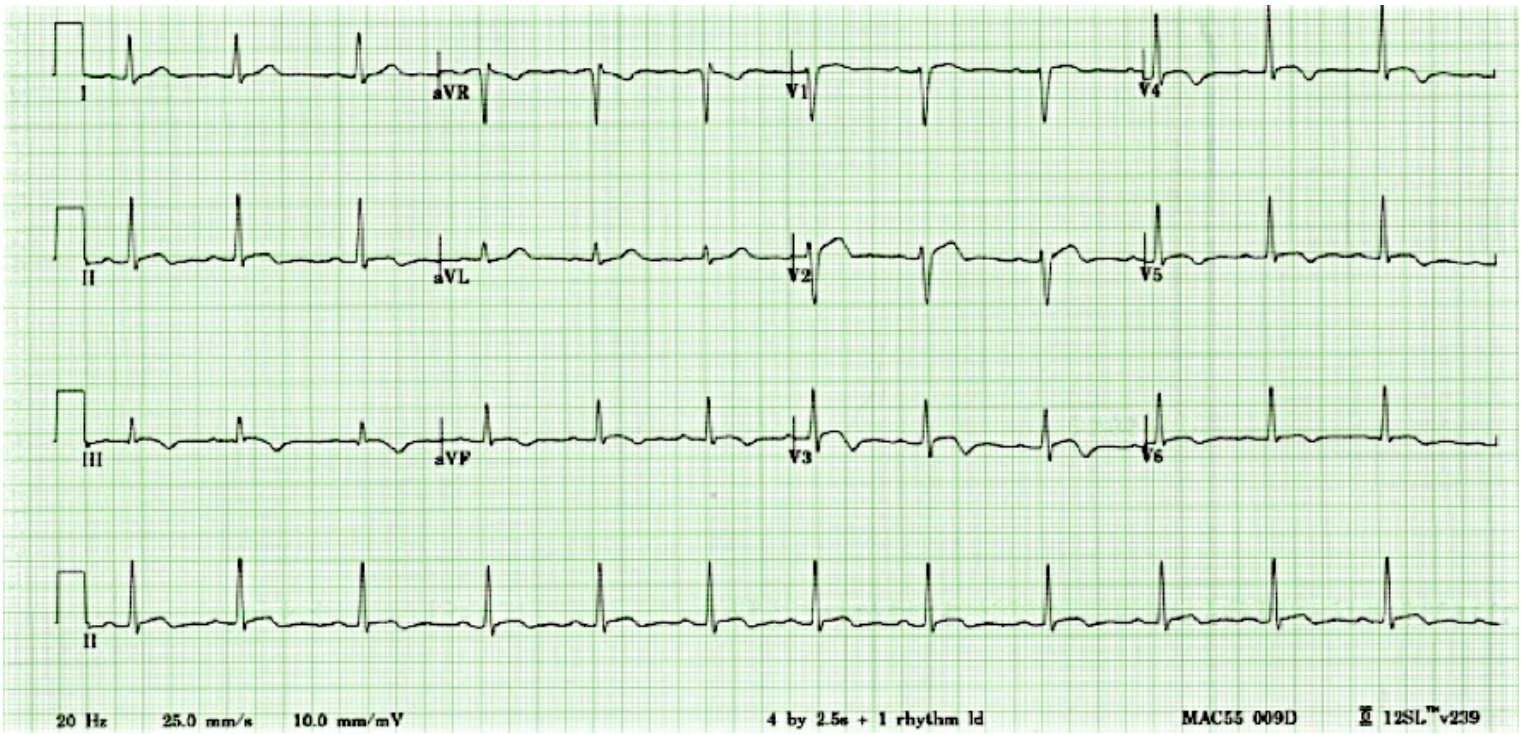

Figure 2. EKG on Day 2 of admission. Note T wave inversion in anterior and lateral leads.

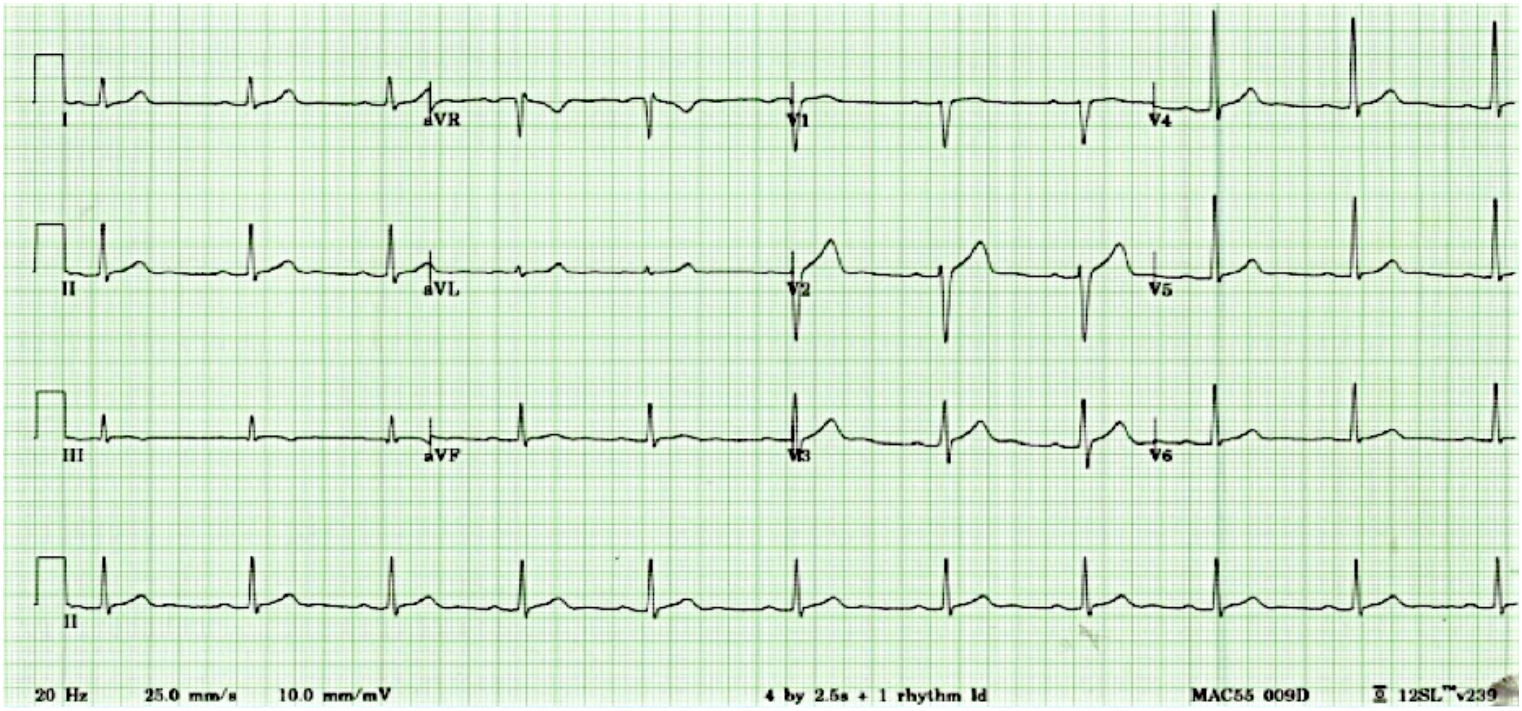

Figure 3. EKG on day of discharge. T wave inversion less evident in Inferior leads. T wave inversion no longer evident in anterior leads.

metronidazole 250 mg TID for 10 days. He also underwent abdominal ultrasound of the liver to assess for cysts/abscesses associated with Entamoeba histolytica. The ultrasound was unremarkable apart from mild right hydronephrosis.

Discussion

The etiology behind many cases of myocarditis remain elusive despite extensive testing, with the gold standard 'biopsy' being not only invasive, but also deemed unwarranted in the majority of cases where symptoms are limited. Many idiopathic cases are thought to be secondary to unidentified infectious agents, either ones that are not detected on standard myocarditis panels or ones which standard testing has insufficient sensitivity to detect. Here we presented a case of myopericarditis associated with acute Giardia infection. While causation cannot be confirmed unless a biopsy is obtained, the chronological order of events and the constellation of presenting symptoms, strongly suggests at least an association, if not causation. There is only one similar case report of the association of Giardia infection with myocarditis in an adult.[4]

Giardia intestinalis (formerly Giardia lamblia and Giardia duodenalis) is a widespread protozoan parasitic pathogen known to be a common cause of environmentally acquired diarrheal infection.[8] People who are immunocompromised, infants and travelers are at particularly high risk of acquiring the infection. It tends to be a common pathogen responsible for non-dysenteric diarrhea amongst children in the United States.[9] Giardia species are flagellated, motile parasites whose life cycle includes cysts and trophozoite morphologies. Cysts, the infectious form, are typically excreted in feces and subsequently exist in contaminated water. Once ingested, excystation results in the release of trophozoites which then undergo binary fission. The trophozoites mobilize to the proximal small bowel where they proceed to adhere to the duodenum and jejunum.

This adhesion likely causes direct mucosal damage without invasion. The exact pathophysiology of this is unclear, as giardiasis may or may not cause villous atrophy. There is thought that secretion of virulence factors induces direct intestinal damage.[10] Also unclear is the exact immune response associated with G.intestinalis infection. The host response incorporates innate and adaptive systems. The primary mechanism of host immune response towards this parasitic infection is the production of IgA.[12]

There is little known in the way of association between G.intestinalis and myocarditis. There is no evidence that the parasite directly attacks the myocardium. However, antigenic expression of the parasite could theoretically produce an antibody response which can damage the myocardium due to antigenic mimicry. Molecular and antigenic mimicry by many different organisms are implicated in the development of myocarditis. Infecting microbes prompt the generation of a secondary autoimmune response. Cross-reactivity between foreign and host antigens is one mechanism in which this pathogenesis can occur. The adaptive immune system (antibodies and T-cells) then recognize the host cell antigenicity as foreign. Antibody cross-reactivity occurs towards amino acid sequences identical to the self-antigens. T-cell cross-reactivity relies on degeneracy, allowing for many different types of peptides to stimulate a T-cell via MHC Class II molecules, anchor residues, peptide sequences, T-cell receptor residues and the T-cell.[11]

It is unclear which mechanism Giardia may use to induce an autoimmune response. Given that Giardia has a large antigenic variance, T-cell stimulation and antigen-antibody reactions are both theoretically possible mechanisms.[12] There is another case report suggesting the correlation of Giardia induced myocarditis which also suggests antigenic mimicry. However, no definitive link has been described.[4]

Conclusion

Here we presented a case of a teenage patient who was ultimately diagnosed with myopericarditis with concurrent Giardia intestinalis infection. To our knowledge, there is only one other case reporting this association, and it involved an elderly male. Identification and reporting of such cases will add to the repertoire of knowledge of etiological agents behind many cases of idiopathic myocarditis, many of which remain elusive to diagnostic testing.

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Highlights from the Third Fetal Cardiac Symposium at Rush University in Chicago- July 12th-13th, 2018

By Karim Diab, MD

The Third Fetal Cardiac Symposium took place at Rush University Medical Center in Chicago on July 12th-13th, 2018. With its vibrant atmosphere and its rich culture, the Windy City provided an excellent venue for this meeting. This year's symposium continued to focus on improving the technical scanning skills of the fetal heart in order to help increase the rate of prenatal detection of Congenital Heart Disease (CHD) A few years ago, the revised guidelines from the American Institute of Ultrasound in Medicine (AIUM) and the American College of Obstetricians and Gynecologists (ACOG) clearly emphasized the need to include the outflow tracts view in addition to the 4-chamber view, as an integral part of the ultrasonographic assessment of the fetal heart. This meeting continued to focus on disseminating the practical application of such guidelines in addition to discussing various Congenital Heart Disease malformations encountered in the fetus.

As was the case in previous years, the symposium continued to be a tremendous success and was sold-out with an audience of 150 registrants who came from various regions. About 62% of the attendees came from the Midwest, while 38% came from other states and countries. Although more than 30% of the attendees were physicians, most attendees were sonographers, likely reflecting the attractiveness of hands-on workshops included in the meeting, which provided the attendees with practical scanning opportunities rather than only didactic lectures. The attendees came from various specialties including: Pediatric Cardiology, OB and MFM, as well as other specialties such as Neonatology and Radiology.

This year, the conference featured a two-day meeting that offered thorough and updated presentations on scanning the fetal heart, and diagnosing and managing various common fetal Congenital Heart Disease malformations. The activity was designated for a maximum of 16.25 AMA PRA Category 1 continuing medical education credits, and 16.25 CME credits in medical sonography (SDMS). Lectures, given by an internationally acclaimed faculty in Pediatric Cardiology and Maternal-Fetal Medicine specialists, emphasized the basics of fetal cardiac scanning coupled with live case demonstrations and tips for diagnosing various anomalies.

The first day of the meeting started with an overview on the basics of fetal cardiovascular physiology and the current guidelines and indications for performing fetal echocardiography by Drs. Abdulla and Pombar. Dr. M. Sklansky then emphasized the importance of optimizing the image for adequate cardiac diagnosis with practical tips on how to improve imaging the fetal heart. This was followed by a live scanning demonstration of a complete fetal echocardiographic study which sequentially focused on the essential screening views of the fetal heart, including the four chamber and the outflow tract views, as well as the three-vessel view. This demonstrated the normal findings, as well as typical cardiac lesions diagnosed with the particular view, which helped give the audience practical tips for scanning and diagnosing various cardiac

malformations. A live scan of a fetus with truncus arteriosus was presented afterwards with highlights of the major imaging findings. The second session then focused on the normal and abnormal four-chamber view with lectures focusing on specific lesions. Dr. N. Ayres went over ASD, VSD and AVC lesions, Dr. E. Jaeggi discussed TV abnormalities including: Ebstein's Anomaly (EA), Tricuspid atresia and dysplasia, and Dr. K. Friedman lectured on HLHS and mitral atresia. The third session of the day focused on the outflow tract views. Lectures went over the value of the three-vessel view, aortic stenosis and coarctation, D-TGA and ccTGA. Dr. L. Hornberger discussed conotruncal anomalies including DORV and TOF, and Dr. Awad presented some interesting cases with unusual pathologies. The first day ended with the first hands-on session of the symposium with SIX stations for hands-on scanning on fetuses with normal hearts as well as cardiac pathologies.

The symposium featured a unique two- hour workshop on both days of the meeting which gave the attendees an opportunity to scan pregnant volunteers with both normal hearts and cardiac pathology. This provided an excellent opportunity for becoming more familiar with the required cardiac views including the 4-chamber, the outflow tracts, and the three-vessel views. It also allowed participants to experience scanning using various technological instruments and machines that are currently on the market. All this was done under the supervision of expert faculty in the field of Fetal Cardiology and Maternal Fetal Medicine.

The second day of the symposium started with a session focusing on the techniques to evaluate the fetal rhythm by echo, as well as diagnosing and managing fetal tachy and brady-arrhythmias and heart block. The second session of the day focused on fetal interventions including fetal cardiac interventions as well as laser surgery for Twin-Twin Transfusion Syndrome and total tracheal occlusion for

congenital diaphragmatic hernia. There was another hands-on session with an additional six stations for scanning and practice on the afternoon of the second day as well.

Another highlight of the symposium was the audience participation sessions on the second day that provided the opportunity for discussion and learning from each other. This included, "The Most Interesting Case I've Seen" session that allowed participants to present their interesting cases to the audience and faculty, as well as a Jeopardy session with a contest between four teams. There were eight presenters for the "Most Interesting Case I've Seen" session. Z. Roytman, RDCS and Dr. S. Patel from Lurie Children's Hospital won the contests for both sessions.

In addition to an extensive series of didactic presentations and live-scanning sessions, the symposium offered a variety of exhibitors that showcased the latest in ultrasound technology. The symposium also offered an exceptional opportunity for fellows and attendees to network and meet with pioneers in the field, as well as an opportunity to catch up with colleagues and meet new friends.

With the current rates of prenatal detection of CHD, it is evident that the need for such fetal symposia is a must in order to improve the skills of various practitioners in the field and ultimately help improve the detection of CHD and outcome in these babies.

"With the current rates of prenatal detection of CHD, it is evident that the need for such fetal symposia is a must in order to improve the skills of various practitioners in the field and ultimately help improve the detection of CHD and outcome in these babies."

Keep an eye out for our next meeting in 2019 as the registration sold out this year!! Dates for the next symposium will be announced in the future; for more information, you can reach Dr. Diab at Karim_Diab@rush.edu or visit : www.FetalCardiacSymposium.com.

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Pediatric Heart Failure / Heart Transplant Cardiologist
Rank Dependent on Qualifications / Clinical or Tenure Track
Division of Pediatric Cardiology

The Division of Pediatric Cardiology at the University of Utah School of Medicine has an immediate opening for a Pediatric Cardiologist with expertise in heart failure/heart transplant. This is an outstanding opportunity to join a vibrant and collegial academic environment and work in a children's hospital ranked as one of the best in the US. Responsibilities will include focused care to inpatients and outpatients with cardiomyopathy, heart failure due to either cardiomyopathy or congenital heart disease, those supported on a ventricular assist device and patients pre- and post-heart transplantation. In addition to clinical service, there is an expectation for academic work, including teaching, research, administration, as well as advocacy. There will be protected time for clinical research with mentoring available within the Division. Depending on experience, there may be opportunities for leadership responsibilities.

The Heart Transplant Program performs an average of 8-12 heart transplants per year and provides care for over 100 post-transplant patients. Activity in the Mechanical Circulatory Support Program will include patient selection for ventricular assist device support and follow up care in conjunction with cardiothoracic surgeons. Clinical activities will be carried out at Primary Children Hospital and the Division of Pediatric Cardiology affiliated outreach sites.

Qualified candidates must have an M.D. or D.O. degree, be Board Qualified/Board Certified in Pediatric Cardiology, and must have advanced training or expertise in heart failure/heart transplant and mechanical circulatory support. The selected candidate will receive a faculty appointment in the Department of Pediatrics on the Clinical or Tenure track at the academic level commensurate with experience and qualifications.

The University offers a competitive salary and an unmatched benefits program, including non-contributory retirement contributions of 20.2% of annual salary that vest immediately. The Department offers an education loan repayment program, in addition to a faculty development and mentoring program designed to help faculty succeed in translational or basic research.

Salt Lake City offers an incredible quality of life with a growing economy, rich cultural scene with ballet, theatre, symphony, opera and museums, outstanding restaurants, and a moderate cost of living. The city is a ski destination and a gateway to the state's renowned landscapes. In addition to its 14 ski resorts, Utah boasts five national parks (with five more within a day's drive), a variety of golf courses allowing for year-round play, hundreds of miles of hiking and biking trails, and numerous other outdoor activities.

Interested individuals can apply for the position at:
http://utah.peopleadmin.com/postings/82504.
Cover letter and curriculum vitae will be required.

For additional information about the position, please contact:
Lloyd Y. Tani, M.D., Division Chief,
at Lloyd.tani@hsc.utah.edu.

The University of Utah Health Sciences Center is a patient focused center distinguished by collaboration, excellence, leadership, and Respect. The University of Utah HSC values candidates who are committed to fostering and furthering the culture of compassion, collaboration, innovation, accountability, diversity, integrity, quality, and trust that is integral to the mission of the University of Utah Health Sciences Center.

The University of Utah is an Affirmative Action/Equal Opportunity employer and does not discriminate based upon race, national origin, color, religion, sex, age, sexual orientation, gender identity/expression, status as a person with a disability, genetic information, or Protected Veteran status. Individuals from historically underrepresented groups, such as minorities, women, qualified persons with disabilities and protected veterans are encouraged to apply. Veterans' preference is extended to qualified applicants, upon request and consistent with University policy and Utah state law. Upon request, reasonable accommodations in the application process will be provided to individuals with disabilities. To inquire about the University's nondiscrimination or affirmative action policies or to request disability accommodation, please contact: Director, Office of Equal Opportunity and Affirmative Action, 201 S. Presidents Circle, Rm 135, (801) 581-8365.

The Challenging Path of Understanding Coronary Artery Anomalies in Children

By Silvana Molossi, MD, PhD; Tam Doan, MD, MS

Congenital and acquired coronary artery anomalies leading to myocardial ischemia, though not frequent, may have catastrophic consequences in the pediatric population. Detection, risk stratification, surveillance, and timely recognition of coronary problems in children who are at risk of ischemic events are imperative and noninvasive imaging has increasingly been utilized for these purposes.

Congenital coronary artery anomalies may occur alone or in association with structural heart disease. In the absence of structural heart disease, certain coronary anomalies can be associated with sudden cardiac events in older children. Anomalous aortic origin of a coronary artery (AAOCA) is a congenital abnormality of the origin or course of a coronary artery that arises from the aorta. AAOCA from the opposite aortic sinus of Valsalva constitutes the second most common cause of sudden cardiac death related to ischemia in healthy children or young athletes during or shortly after exertion. The pathophysiology of these events has not been fully understood. It was observed that the course of the coronary arteries in between the great vessels (inter-arterial course) may result in possible compression. The acute angle of the take-off of the anomalous coronary artery, the slit-like orifice, and the presence and length of an intramural segment of the anomalous coronary artery may have contributed to the impairment of coronary perfusion during exertion. A slit-like orifice and a narrow intramural segment of the anomalous artery seemed to be important players in increasing the risk for events. Anomalous origin of the right coronary artery (ARCA) from the opposite (left) aortic sinus is more common but the number of cases with SCD associated with this entity is much less commonly seen than anomalous origin of the left coronary artery (ALCA) from the opposite (right) aortic sinus. Computerized tomography angiography (CTA) with virtual angioscopy is the preferred mode of imaging in many centers which shows detailed course of the anomalous vessel and precise description of the location, shape and spatial relationship of the coronary ostia (Figure 1).

There has been a trend that patients who were diagnosed with AAOCA would be referred for surgery. It is generally agreeable that patients who present with myocardial ischemia and associated arrhythmia is a surgical candidate, most commonly ALCA from the right aortic sinus. Following surgery, post-operative studies including exercise stress test and pharmacologic perfusion stress magnetic resonance imaging (CMR), typically determine return to exercise activities and/or sports participation.

Very short segments of superficial myocardial bridge are commonly seen and not functionally important. There are, however, documented examples of myocardial ischemia or infarction associated with these bridges, including relief of ischemia after myotomy. During coronary angiography, a portion of the coronary artery appears to be narrowed in systole, but widely patent in diastole, distinguishing it from a partially occlusive lesion of the artery. Because myocardial bridges are so common, and do not necessarily indicate present or future coronary arterial disease, the decision about myotomy to relieve anginal symptoms must be made carefully. Not only should there be a well-defined muscle bridge, but there should be ischemia, based on additional functional studies, including nuclear scans, stress echocardiography, stress CMR, cardiac catheterization with FFR measurement, in the region supplied by the artery with the bridge.

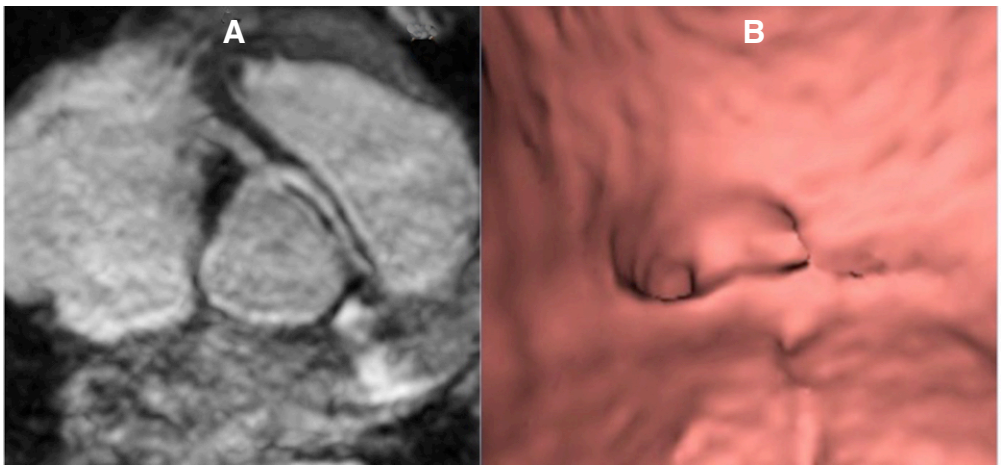

Figure 1. CT angiography demonstrating anomalous aortic origin of the left coronary artery from the opposite (right anterior) sinus of Valsalva (A) with correlated virtual angioscopy (B) demonstrating ostial morphology.

Kawasaki Disease (KD) is an acute febrile arteritis of childhood that affects medium size arteries, typically the coronary arteries, and can result in coronary artery aneurysms if untreated in the first 7 days of illness. Clinical manifestations of KD include the presence of five or more days of fever, together with clinical criteria of extremity changes, rash, conjunctivitis, oral changes, and unilateral cervical lymphadenopathy. Echocardiography is the cornerstone imaging modality to identify coronary involvement and should be performed at the time of diagnosis, then 1-2 weeks and 4-6 weeks later, with more frequent studies in certain patients with more pronounced involvement of these vessels. Long-term sequelae of KD can lead to myocardial ischemia and the optimal treatment for those presenting with coronary artery thromboses and/or stenosis is yet to be determined with certainty given the inherent difficulties of coronary revascularization in children. KD has been more frequently associated with acute MI in young adults presenting with acute coronary syndrome and presenting for emergent coronary revascularization.

Managing patients with coronary anomalies continues to be a challenge. With pre-participation screening programs and other screening program, more healthy children and young adults have been incidentally found to have such anomalies. There are many variations in coronary artery origins and courses, each may have different clinical implication. The pathophysiologic mechanisms responsible for sudden death, and the benefits conferred by different management strategies are unclear. Risk stratification for myocardial ischemia of these individuals with incidental findings is critically important. Retrospective studies carry inherent limitations of not having a consistent pre-operative and post-operative evaluation. The scientific community has been urged to form a multi-institutional collaboration to follow a large group of patients to better understand the natural and surgical history of this anomaly and to develop evidence to guide management such

as seen in the work of The Congenital Heart Surgeons' Society Registry of AAOCA. At Texas Children's Hospital, these challenges were recognized and led to the establishment of a multidisciplinary team and the inception of the Coronary Anomalies Program, which has been active since December 2012. Patients referred to the program have been risk stratified, and managed following a standardized algorithm that has been revised annually according to prospective data gathered, and all cases are discussed at monthly multidisciplinary meeting. It is believed that close long-term follow-up and prospective data collection with interval analyses of the data are instrumental to evaluate the adequacy of the algorithm and modify it based on new evidence. These efforts are promising to fill in the existing knowledge gaps and improve management in order to alter the risk profile of this interesting population. In addition, we have established the first dedicated forum to discuss challenges in diagnosing, risk stratifying, and managing these patients - the *Coronary Artery Anomalies Symposium.* Since 2016, Texas Children's Hospital has partnered with the Children's Hospital of Philadelphia to continue to develop excellence in this scientific quorum. This coming December 7th to 8th, 2018, we will have the 4th Symposium at Texas Children's Hospital, in Houston. This year's event has once again a comprehensive agenda with outstanding faculty, which will undoubtedly shed additional light in this interesting and challenging topic.

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"Congenital and acquired coronary artery anomalies leading to myocardial ischemia, though not frequent, may have catastrophic consequences in the pediatric population."

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4th Symposium on Coronary Artery Anomalies 2018
December 7-8, 2018
Texas Children's Hospital
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This symposium provides a dedicated forum to discuss the diagnosis and management of patients with coronary artery anomalies (CAA). Topics include: anomalous aortic origin of a coronary artery (AAOCA), Kawasaki Disease, and myocardial bridges.

https://www.texaschildrens.org/health-professionals/conferences/symposium-coronary-artery-anomalies-2018

Medical News, Products & Information

Compiled and Reviewed by Kate Baldwin, Special Projects Editor

Siemens Healthineers FDA Approves New Test for Diagnosing Heart Attacks Faster

- The Siemens Healthineers High-Sensitivity Troponin I assays can detect lower levels of troponin compared to conventional assays.
- Troponin indicates damage to the heart muscle, and greater precision measures slight, yet critical, changes so physicians can properly triage patients sooner.
- The TnIH assays that enable fast results and earlier diagnosis for heart attack patients are now available in the U.S.

Siemens Healthineers announced in late July it is helping to shorten the time doctors can diagnose a life-threatening heart attack with the introduction of two assays that offer unparalleled precision. U.S. Food and Drug Administration (FDA) cleared High-Sensitivity Troponin I assays (TnIH)[1] for the Atellica IM and ADVIA Centaur XP/XPT in vitro diagnostic analyzers from Siemens Healthineers to aid in the early diagnosis of myocardial infarctions—commonly known as heart attacks. When a patient experiencing chest pain enters the emergency department, a physician orders a blood test to determine whether troponin is present. As blood flow to the heart is blocked, the heart muscle begins to die in as few as 30 to 60 minutes and releases troponin into the bloodstream.

The high-sensitivity performance of the two new Siemens Healthineers TnIH assays offers the ability to detect lower levels of troponin at significantly improved precision at the 99th percentile, and detect smaller changes in a patient's troponin level as repeat testing occurs. This design affords clinicians greater confidence in the results with precision that provides the ability to measure slight, yet critical, changes to begin treatment.[2,3] As science progresses, guidelines for determining high-sensitivity also evolves. These TnIH assays meet the latest industry guidelines.

Chest pain is the cause of more than eight million visits annually nationwide to emergency departments, but only 5.5% of those visits lead to serious diagnoses such as heart attacks.[4] Armed with data to properly triage patients sooner or to exclude myocardial infarctions, the Siemens Healthineers TnIH assays can help support testing initiatives tied to improving patient experience.

"Our emergency department is overcrowded with patients. If we can do a more efficient job at triaging patients to receive the proper level of care and to discharge the patients who do not need to stay in the emergency department, this will have a tremendous economic advantage for our healthcare system," said Dr. Alan Wu, Chief of Clinical Chemistry and Toxicology at Zuckerberg San Francisco General Hospital and Trauma Center.

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Siemens Healthineers enables healthcare providers worldwide to increase value by empowering them on their journey towards expanding precision medicine, transforming care delivery, improving patient experience and digitalizing healthcare. A leader in medical technology, Siemens Healthineers is constantly innovating its portfolio of products and services in its core areas of diagnostic and therapeutic imaging and in laboratory diagnostics and molecular medicine. Siemens Healthineers is also actively developing its digital health services and enterprise services. Further information visit www.siemens-healthineers.com.

Getting to the Heart of Congenital Cardiac Defects
UNC Researchers Shed Light on How Gene Defects Lead to Congenital Heart Malformations

Newswise — Heart defects are the most common type of birth defect, and can be caused by mutations in the gene CHD4. Researchers at the UNC School of Medicine have now revealed key molecular details of how CHD4 mutations lead to heart defects.

The team, in their study published in *Proceedings of the National Academy of Sciences*, found that the CHD4 protein normally works in developing heart muscle cells to repress the production of muscle-filament proteins that are meant to operate in non-heart types of muscle cell. The failure of this repression leads to the development of abnormal, "hybrid" muscle cells that can't pump blood as efficiently as normal heart cells.

"For patients with congenital heart defects linked to CHD4 mutations, this research helps explain why their hearts don't work as well as normal, and suggests strategies for therapeutic intervention," said study senior author Frank Conlon, PhD, a Professor in the departments of Biology and Genetics at UNC and a member of the UNC McAllister Heart Institute.

The research was a collaborative effort involving the Conlon Laboratory, the laboratory of Ian Davis, MD, PhD, Associate Professor in UNC's Division of Pediatric Hematology-Oncology, and the laboratory of Paul Wade, PhD at the National Institute of Environmental Health Sciences.

The team, including first author Caralynn M. Wilczewski, a graduate student in the Conlon Laboratory, began by engineering mice whose developing embryos lack CHD4 just in their heart cells. The embryonic mice developed severe cardiac defects midway through gestation, and none were born alive. These results confirmed the necessity for CHD4 in heart development.

CHD4, the protein encoded by the CHD4 gene, normally works as part of a multi-protein "machine" that helps regulate gene activity within the nuclei of cells. The researchers therefore conducted a set of experiments to measure and analyze the changes in developing heart-muscle cell gene activity when CHD4 is absent. They found that the CHD4 protein normally binds directly to DNA in a way that represses the activity of genes that encode non-heart muscle proteins. These proteins help make up the springy fibers (myofibrils) that contract and relax when muscles work.

The team determined that when the CHD4 protein is absent, these other, non-cardiac muscle proteins are inappropriately produced in developing heart muscle cells. They become incorporated into the myofibrils in these cells, forming abnormal, hybrid myofibrils that lack the functional properties of the normal heart.

Wilczewski developed an advanced ultrasound technique and used it to record the activity of the tiny hearts developing in mice—organs which in mid-gestation are only about as large as the period at the end of this sentence.

"We observed that the hearts lacking CHD4 and having these abnormal cardiac myofibrils had severely reduced ventricular contractions, indicating a loss of the ability to pump blood normally," Wilczewski said.

"These findings indicate that normal cardiac development in mice depends on the repression of non-cardiac myofiber proteins in heart muscle cells, to allow the formation of normal cardiac myofibers capable of sustaining normal heart contractions," Conlon said.

The findings provide the first clear insight into the mechanism of CHD4-related cardiac defects. They also suggest the possibility that restoring the normal repression of non-cardiac myofiber proteins could prevent heart defects in cases where CHD4 is mutated.

The researchers now plan to investigate the ways in which specific human CHD4 mutations lead to cardiac defects.

In addition, they plan to use the new ultrasound technology developed by Wilczewski in further research. "This technology has broad applications for testing models of Congenital Heart Disease," Conlon said.

Funding for the study was provided by the National Institutes of Health (R01 HL112618, R01 HL127640, 5T32 HL069768, 1F31 HL136100, ES101965).

See orignal artcile: http://www.pnas.org/content/early/2018/06/05/1722219115.

New Target for Treating Heart Failure Identified by Penn Medicine Researchers, Reversing Stiffness of Diseased Heart Muscle Cell Strut is Key

Changes in cellular struts called microtubules (MT) can affect the stiffness of diseased human heart muscle cells, and reversing these modifications can lessen the stiffness and improve the beating strength of these cells isolated from transplant patients with heart failure, found researchers from the Perelman School of Medicine at the University of Pennsylvania. This *Nature Medicine* new study is a continuation of research conducted two years ago on how MTs are involved in regulating the heartbeat.

"These findings provide compelling evidence from human samples for a new therapeutic target for heart disease," said senior author Ben Prosser, PhD, an Assistant Professor of Physiology. The Penn investigators aim to develop therapies that seek out the damaged MTs to reverse their harmful influence.

By suppressing impaired MTs, the team improved heart muscle cell function in damaged human cells. Normally, MTs of the cell's inner support system have diverse structural and signaling roles. Alterations in this network have been suggested to contribute to heart disease. Recent studies suggest that chemical changes to the MTs, called detyrosination (the removal of a tyrosine chemical group), control the mechanics of heart beats. Detyrosinated MTs provide resistance that can impede the motion of contracting heart muscle cells.

The Penn team used mass spectrometry and mechanical tests of single heart muscle cells to characterize changes to the MT network and its consequences for normal heart function. Analysis of tissue from the left ventricle of heart transplant patients revealed a consistent upregulation of proteins that leads to the stiffening of MTs. Using super-resolution imaging, the team also saw a dense, heavily detyrosinated MT network in the diseased heart muscle cells, which is consistent with increased cell stiffness and decreased ability to contract. Proper cell elasticity and contraction is crucial for normal circulation throughout the body.

Using a drug, the team suppressed the detyrosinated MTs, which restored about half of lost contractile function in the diseased cells. Genetically reducing the MT detyrosination also softened the diseased cells and improved their ability to contract.

Past clinical data from Penn showed a direct correlation between excess MT detyrosination and a decline in heart function among patients with hypertrophic cardiomyopathy, a condition in which thickened heart muscle can cause problems in maintaining proper blood pressure levels and flow of blood through the heart.

The team found that detyrosination was greater in diseased hearts by comparing human heart tissue donated from heart transplant patients to normal heart tissue from other donors, obtained from work with transplant cardiologist and coauthor Ken Margulies, MD, a Professor of Cardiovascular Medicine. Cells from diseased hearts have more MTs, and these MTs have more detyrosination. This process correlated with impaired function within this patient population in that their whole hearts, before the transplant, had a lower ejection fraction that correlated with greater detyrosination. Ejection fraction, an indicator of heart health, measures the amount of blood pumped out of ventricles with each contraction.

The team is now working on ways to target only heart muscle cell MTs. They are refining gene therapy approaches with the Penn Gene Vector Core to deliver an enzyme to the heart that reverses detyrosination in heart muscle cells.

This study was funded by the National Institute of Health (R01-HL133080, T32 R05346-09), the American Heart Association (17POST33440043) and the Center for Engineering MechanoBiology through a grant from the National Science Foundation's Science and Technology Center (15-48571). The procurement of human heart tissue was enabled by grants from the NIH (HL089847, HL105993).

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Digital, Mobile Advances Will Define Future of Cardiology
Trio of Review Papers Examine How Technology Will Change Prevention and Treatment of Heart Disease

American College of Cardiology: The future of cardiovascular care will be transformed by advances in artificial intelligence, digital health technology, and mobile as a means to prevent and treat heart disease, according to several review articles published in early June in a *Journal of the American College of Cardiology* Focus Seminar on the "Future Technology of Cardiovascular Care."

"Artificial Intelligence in Cardiology"

As the type and breadth of data available to cardiologists and the cardiovascular care team continues to grow more sophisticated, physicians are increasingly being asked to provide more rapid and personalized interpretations of data to their patients. One solution to providing this level of personalized medicine efficiently is artificial intelligence, also known as machine learning.

In this review, researchers analyze select applications of artificial intelligence in cardiology and identify how the specialty could incorporate more artificial intelligence in the future to enhance the capabilities and experiences of clinicians and patients.

"[Artificial intelligence] has clear potential to enhance every stage of patient care--from research and discovery, to diagnosis, to selection of therapy," said Joel Dudley, PhD, senior author of the review, and Director of the Next Generation Healthcare Institute at Mount Sinai. "A key next step to incorporating artificial intelligence into cardiology is to align available data and technologies with clinical and business use. This way, we can prioritize short-term opportunities and understand gaps in available data or algorithms that are holding back applications of artificial intelligence in areas of high clinical need."

According to the review, artificial intelligence is currently only performed by those with specialized training, but in the future, these methods will be increasingly easy and widely available. It may eventually be incorporated into day-to-day practice by interacting with electronic health records and billing.

"Using Digital Health Technology to Better Generate Evidence and Deliver Evidence-based Care"

Digital health is the use of digital information, data and communication technologies to collect, share and analyze health information to improve patient health and health care delivery. It can broadly include electronic medical records and artificial intelligence applied to large datasets. These technologies have the potential to accelerate, streamline and optimize clinical research operations and reduce costs, but their use comes with concerns about data quality, patient safety and privacy, which contributes to the delay in their use.

In this review paper, participants from a 2016 think tank on digital health discuss the purpose and findings of the meeting. The participants, which included academic, industry and regulatory representatives, convened to understand the current landscape of digital health technology use in health care delivery and clinical trials, identify issues and barriers to the development and adoption of these technologies, and identify potential solutions.

"These technologies could facilitate and advance more conventional randomized clinical trials (RCTs), which is particularly necessary since RCTs are becoming increasingly expensive and complex, are slow to complete and take an extensive amount of time to implement into practice," said Abhinav Sharma, MD, lead author of the review and Stanford University Advanced Heart Failure Fellow (previously a Duke Clinical Research Institute Research Fellow).

Think tank participants reported that there are several solutions that can accelerate the use of these technologies, including: developing innovation networks to rapidly test new innovations, validate findings and provide value cost-effectiveness data; collaborating with regulatory agencies to streamline development; working with professional societies to identify critical knowledge gaps that could be filled by digital health technologies; and expanding the role of public-private partnerships.

"Mobile Health Advances in Physical Activity, Fitness and Atrial Fibrillation: Moving Hearts"

Cardiovascular disease management and prevention involves a commitment to heart healthy physical activity, diet, medication adherence and self-monitoring. These daily activities are largely unmeasured, but the emergence and rapid growth of mobile devices and wearables has made continuous health monitoring a possibility and, for many patients, a reality.

Mobile health, or mHealth, is the subset of digital health that focuses on the use of mobile and wearable devices and software applications. Authors in this article provide an update on cardiovascular mHealth, with a focus on research and clinical advances in measuring and promoting physical activity and fitness plus using these same mobile devices for heart rate and rhythm monitoring, especially for atrial fibrillation.

"Only recently has the medical community started to embrace the reality that most 'health' takes place outside the hospital and clinic, namely the daily activities and clinical events that occur 'the other 362 days' per year when people are not seen by a clinician," said Michael McConnell, MD, MSEE, lead author of the review, and Clinical Professor of Cardiovascular Medicine at Stanford University and Head of Cardiovascular Health Innovations at Verily Life Sciences. "Enabling patients and clinicians to leverage these technologies for proactive health care can transform cardiovascular prevention and disease management."

The authors specifically looked at atrial fibrillation because it can go undetected and be difficult to manage. Office visits and short-term monitoring provide limited information on disease presence and burden, which can result in serious complications. However, ongoing monitoring with mHealth devices is an opportunity to prevent strokes, manage symptoms and reduce hospitalizations from atrial fibrillation. Machine learning has emerged as a powerful technology to enhance atrial fibrillation detection from wearable devices. Importantly, physical activity and fitness are also linked with primary prevention of atrial fibrillation and reduced atrial fibrillation burden and recurrence. The authors note the importance of broad collaboration to further integrate mHealth technology into clinical care, with the potential for substantial individual and societal benefits.

The American College of Cardiology is the professional home for the entire cardiovascular care team. The ACC leads in the formation of health policy, standards and guidelines. The College operates national registries to measure and improve care, offers cardiovascular accreditation to hospitals and institutions, provides professional medical education, disseminates cardiovascular research and bestows credentials upon cardiovascular specialists who meet stringent qualifications. For more, visit acc.org.

The Journal of the American College of Cardiology ranks among the top cardiovascular journals in the world for its scientific impact. JACC is the flagship for a family of journals--*JACC*: *Cardiovascular Interventions, JACC: Cardiovascular Imaging, JACC: Heart Failure, JACC: Clinical Electrophysiology* and *JACC: Basic to Translational Science*--that prides themselves in publishing the top peer-reviewed research on all aspects of cardiovascular disease. Learn more at JACC.org.

CORRECTION:

On page 7 of the lead article in the September 2018 issue, "Case Study of Severe Hemolysis Following Atrial Septal Defect Closure," the corresponding author was listed as Pooja Nawathe, MD, FAAO, CHSE. FAAO was a typo, and it should read FAAP.

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