

PACES Research Meeting May 12, 2015

Boston, MA

Introduction

On Tuesday May 12 before the annual PACES symposium, a research meeting was held. This was sponsored by Johnson and Johnson. This meeting represents the first time that a research meeting of this nature was held for PACES' members. In the previous 3 years, there was an SVT research meeting (ISPRINT), which is now included in this meeting. The studies presented at this meeting were mostly reviewed by the PACES research committee (PRC) in order to be circulated to the membership. Studies which already include members of the PRC are considered to have been reviewed.

Approximately 73 members attended.

Sudden Death in WPW-Dr. Susan Etheridge

In order to better protect those at risk of sudden death in WPW, a prospective database is being built based on a retrospective collection of WPW patients with or without life threatening events (LTE). In addition to patients that were included in the retrospective arm of the study, young patients (from birth to age 21) will be enrolled and detailed information including demographic and clinical characteristics, electrophysiological, info surrounding LTE and interventions will be entered into a WPW database using REDCap. This will allow for comparison of WPW patients with and without LTE, identifying risk factors and the effectiveness of interventions. The investigators are currently seeking international centers to enroll patients. Approximately \$1000 will be available to support study coordinators at the first 15 centers that enroll patients. Please contact Dr. Etheridge at susan.etheridge@hsc.utah.edu for further information.

CPVT Prospective Registry-Dr. Shubhayan Sanatani

Current gaps exist in the risk and management of patients with CPVT. Support has been received from the Heart and Stroke Foundation of Canada to fund a multi-center, prospective registry of all pediatric CPVT patients and their first degree relatives. Patient data including demographics, diagnostic tests, clinical events and family history will be entered into a REDCap database at participating sites. Probands and affected family members will be assessed at baseline and yearly whereas unaffected family members will be assessed once over the study period. This study is seen as a collaboration and ideas for substudies are welcome. The aim is to have 10 sites enrolling patients by the end of the year and a total of 15-20 sites over the next 12 months. Participating sites will receive a nominal fund for site start-up costs and for patient recruitment. For sites wishing to enroll patients into the study, please contact the Coordinating Site Research coordinator at Sonia.Franciosi@cw.bc.ca for assistance with obtaining local IRB approval and study information.

SOLAR SVT- Dr. Carolina Escudero

Knowledge of the management of acute SVT in infants is currently limited. A group of investigators are conducting a prospective, multicenter, observational cohort study in order to

determine the most effective second-line therapies for acute SVT termination in infants when vagal maneuvers and adenosine fail. A secondary objective is to determine the most effective medications for continued control of SVT after discharge from the hospital. Patients that are less than one year with AVRT or AVNRT and receiving a pharmacological agent in addition to adenosine and/or vagal maneuvers will be included in the study. Data including demographics, medical history, acute treatment for SVT, discharge information and one year follow up after SVT presentation will be entered into a REDCap database. The investigators are currently seeking centers to enroll patients. The enrollment goal is at least 120 patients over 2 years from 10 centers (average of 6 patients per site). Please contact Dr. Escudero at carolina.a.escudero@gmail.com, Dr. McCanta, tony.mccanta@gmail.com or Dr. Sanatani, ssanatani@cw.bc.ca for further information.

Riata Lead Failure in Pediatric and Congenital Heart Disease Patients- Dr. Carolina Escudero

Conductor coil externalization (CCE) is a more common lead failure compared to electrical failure of ICDs in adults. Currently, the rate of Riata lead structural or electrical failure in pediatric or CHD patients is unknown. This is a multi-center, retrospective cohort study to determine the rate of CCE failure, electrical failure and the correlation between both failures in pediatric and CHD patients. Data including patient demographics, cardiac structural diagnosis or surgery as well as primary versus secondary prevention from patients with a transvenous Riata or Riata ST lead implantation who are less than 18 years old or patients with congenital structural or congenital heart disease will be entered into REDCap. The investigators are currently seeking participating centers and plan to enroll 56-60 patients by the end of the year. The overall goal of the study is to improve patient outcomes in patients with Riata or Riata ST leads in place. Future studies may include testing Durata leads and similar patient outcomes. Contact Dr. Joseph Atallah, joseph.atallah@albertahealthservices.ca or Dr. Escudero, carolina.a.escudero@gmail.com for further information.

LQTS Novel Gene Discovery Program- Dr. Michael Ackerman

With the use of genetic testing, emerging technologies and a large LQTS patient cohort, over 17 genes have been implicated in LQTS including CAV3, SCN4, AKAP9 and SNTA1 and more recently, CACNA1C, CALM3 and TRDN. Approximately 20% of LQTS patients remain genetically elusive. In order to elucidate further genes that could lead to LQTS, more gene negative individuals with a robust LQTS phenotype are needed. Local IRB approval is not required, rather, patients can be referred directly to the coordinating study site through facilitated enrollment. Currently, this study is well funded and the investigators are seeking more collaborating clinicians with robust LQTS phenotype positive patients. Please contact Carla Haglund at 507-284-8900 or Dr. Ackerman at 507-993-0947; via email to ackerman.michael@mayo.edu for further information.

Exercise in Genetic Cardiovascular Disease (LIVE-LQTS and LIVE-HCM)-Dr. Michael Ackerman

The effect of lifestyle and exercise on LQTS patients and patients with HCM will be investigated in this NIH funded study. Patients with LQTS or HCM aged 8-50 years, with or without an ICD at any level of exercise are included in this study and equipped with a FitBit. Overall aims are to determine the incidence of arrhythmic events over 3 years and quality of life in sedentary vs moderate/vigorous exercisers. Currently, 30 active centers are involved in the study. Patients may be referred directly to the coordinating center and enrolled through facilitated enrollment. All questionnaires and interviews are carried out remotely over the phone so there are no geographic constraints limiting patients from enrolling. The goal is to enroll a total of 4000 patients; approximately 2000 with LQTS and 2000 with HCM. Please call 866-207-9813 or send an email to live.hcm@yale.edu or live.lqts@yale.edu for more information (PI's: Drs. Lampert, Ackerman and Day).

HCM and Risk Stratification for Sudden Death-Dr. Maully Shah

This is a retrospective, multi-center chart review to determine whether risk factors related to clinical history, family history, ECG, echocardiographic, MRI, genetic testing and/or exercise predict sudden cardiac death. This study includes patients less than 20 years of age with HCM, with or without an ICD. Currently, 26 centers are participating in the study and another 20 centers have expressed interest. The goal is to have completed data collection by the end of the year. This study is funded by Medtronic and each participating site is reimbursed \$2000. Please contact the Research coordinator Veronica O'Connor at OConnorV@email.chop.edu for further information.

Timothy Syndrome in the Contemporary Era (Long QT Syndrome Type 8)- Dr. Maully Shah

The primary objective of this study is to determine the mortality rate and average life span of children diagnosed with Timothy Syndrome (TS) in the current era (2000-2013). Other objectives include determining ECG features, mutations and treatments for patients with TS. Data will be entered into REDCap. Currently, 10 US centers have expressed interest. However, the investigators would like to include all patients with TS and therefore, seek participation from local, national and international centers.

PVC-Induced Cardiomyopathy in Children- Dr. Maully Shah

Frequent PVCs results in left ventricular dilatation as well as reversible cardiomyopathy in adults, however, the impact of frequent PVCs in children is unknown. The goal of this retrospective, chart review study is to determine the type and impact of increased PVC burden on left ventricular function in pediatric patients without structural heart disease. An extensive review of medical charts, echocardiograms, Holter, ECG and stress tests will be performed. Currently, IRB approval has been obtained for this multi-center study however, no funding is in place. Ideas for funding include contributions from PACES members or seeking funding from local foundations such as the Children's Heart Foundation.

Congenital Heart Block International Research Network-Dr. Robert Hamilton

The aims of this CHB international network are many and include: establishing a network of CHB collaborators, establish guidelines and protocols for monitoring/treatment of CHB as well as for data sample collection, a registry and biobank, a CIRN website and organizing a CHB international meeting or workshop. To date, funding is in place, IRB approval has been obtained, registry and biobank are established and a CIRN website has been developed. The investigators are seeking participation from additional centers. Future goals are to establish a pediatric ARVC registry and promote gene discovery for ARVC and other arrhythmia syndromes.

Supporting Hemodynamics during Ventricular Tachycardia Ablation using the Impella Transcatheter System: “The SHVITS Trial”- Dr. Steve Fishberger

Ablation of patients with ventricular tachycardia is difficult and leads to poor outcomes. Mapping ventricular tachycardia with ablation leads to better long term outcomes as compared to substrate ablation. The Impella Device, a catheter based miniaturized rotary blood flow pump, which has been used primarily in adults, may also be useful in pediatric patients with structural heart disease and cardiomyopathy where mapping of VT is impeded due to hemodynamic instability. This is a multi-center, prospective study where patients 10 years or older, greater than 50 kgs with documented ventricular tachycardia are included. The investigators are seeking centers to participate in this study in order to determine the value of this device in patients with ventricular tachycardia. The goal is to stabilize patients with ventricular tachycardia and improve patient treatment outcomes.

AVNRT in CHD- Dr. John Papagiannis

The relationship of AVNRT in CHD is unknown. The investigators have started to enroll CHD patients with a diagnosis of AVNRT and are seeking participation from local, national and international centers. The goal is to have 20-25 centers participate, each enrolling 4-5 patients for a total enrollment of 100 patients. Results from this study will address current gaps in our understanding of AVNRT in CHD. For further study information, please contact Dr. Papagiannis at jpapagiannis@cmh.edu.

Molecular Basis of Circadian Variation in Arrhythmias in CPVT- Dr. Christina Miyake (PCG Awardee)

Dr. Miyake was the inaugural recipient of the Paul Gillette Award. As part of the terms of the award, an update on the research progress is required after the first year, at the mid-term mark of the 2 year award. Dr. Miyake's work revolves around circadian variability in CPVT events.

Similar to other arrhythmia syndromes, arrhythmia susceptibility may vary over a 24 hour period in patients with CPVT. Using a RQ176+/- knock in mouse model of CPVT, the circadian variation of arrhythmias after repeated intraperitoneal caffeine and epinephrine challenge was investigated. Highest levels of arrhythmias were observed at 10 am and 6 pm whereas lowest

arrhythmias levels were observed at 10 pm. When the lights were turned off 4 hours in advance to what was performed previously, a reversal in levels of arrhythmias was observed; the highest level of arrhythmias occurred at 10 pm and lowest at 10 am and 6 pm. These results would indicate that arrhythmias are circadian-dependent in CPVT. Isolated cardiac myocytes from RQ176+/- mice demonstrated lower calcium transients at 6 pm consistent with increased calcium leak and lower sarcoplasmic reticulum calcium stores. Studies are currently ongoing and include determining the molecular mechanism responsible for these circadian-dependent changes in arrhythmia levels and whether gender plays a role.

The meeting closed with some comments and open discussion. Dr. Sanatani will be looking to establish a group of research mentors. PACES members who are in need of help in starting a research project will be able to, through the PACES research committee, access an experienced investigator for guidance. A call for such individuals will accompany these minutes.

There will be a research meeting at the next HRS on the Tuesday morning.