APHRS NEWSLETTER

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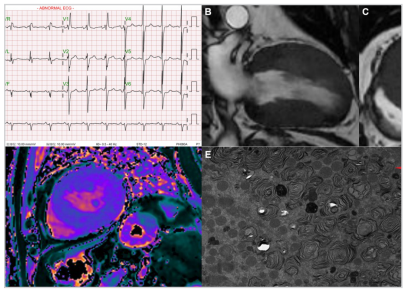

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GETTING TO KNOW APHRS LEADER

Wei Hua, MD, Ph.D. FHRS

Professor of Cardiology

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Cardiovascular Institute, Chinese Academy of Medical Sciences, Peking Union Medical College, China

President of Chinese Society of Pacing and Electrophysiology (CSPE)

Why did you choose to enter medicine and above all, prefer to specialize in Electrophysiology?

I grew up in a medical family. Both my parents are cardiologists and my sister is now a dentist.
My parents worked very hard in the hospital, and they sometimes see patients at home for those who came from remote areas. Although their lives are busy, but they seemed really enjoy and gained deep gratitude from their patients. I was very inspired by them, I chose to study medicine at Shanghai Medical College and then worked at Fu Wai Hospital after I graduate. I was interested in the Cardiac Arrhythmia during my resident training and I have served as Electrophysiologist after I completed the two years fellowship in the Royal Melbourne Hospital.

What do you regard as the most significant development in Electrophysiology in the recent past?

Cardiac Resynchronization Therapy (CRT) for heart failure is the most significant development in the recent past. It now acts as an established treatment of patients with medically refractory, mild-to-severe systolic Heart Failure (HF), impaired left ventricular function, and wide QRS complex. The His-Purkinje System Pacing (HPSP) including His Bundle Pacing (HBP) and Left Bundle Branch Area Pacing (LBBaP) present various advantages including nearly physiological pacing, less complicated procedures, and economic feasibility, indicating a promising alternative to biventricular pacing.

Can you talk about an accomplishment that you are particularly proud of?

The profile of cardiovascular disease of China is very different from Western populations. There were no available data on the incidence rate of Sudden Cardiac Death (SCD) in China, until I first explored and reported the epidemiologic features of SCD in Journal of the American College of Cardiology. The results show that the incidence of SCD in China was 41.8/100,000. For effective prevention of SCD across China, such variations need to be considered when developing programs to reduce this risk.

If you could have an alternative career, what would it be and why?

I would like to be a teacher. It is a profession that requires expertise, charity and patience no less than a doctor. Accordingly, I will receive more respect and gratefulness from my students, which will be a further motivation for me. Helping every student discover their possibilities and live own their lives would really be a pleasure.

Who has inspired you the most in your life and why?

My parents. Both of them are cardiologists. Their dedications to their careers and kind attitudes toward each patient inspired me a lot since I was young. Although working in remote and underdeveloped area, they never complain but take the full advantage of limited medical resource. As a result, tons of patients and local people show their respect for them. I have determined to be a doctor as great as my parents since then.

What are your hobbies and interests outside of medicine?

Sports and music.
I really love listening to music. I practiced violin for three years in middle school and guitar in university. Even though now I don't play any instruments, my daughter is a huge music fan as well so we often listen to music together. Sometimes I also wonder if I could pick up the guitar again from her!
Apart from music, I really enjoy swimming. It really helps me to relax from the intense work.

What is the funniest thing that has happened to you recently?

I once received a scam message, it saying that she is my daughter and her iPhone was dropped, need buy a new piece. But I replied that never mind, so your eyes won't be glued to your phone all day, it's good for you.

What is your best life advice, motto or favorite quote?

I would like to quote a Chinese philosopher - Wang Yangming: "Knowledge as action". I believe first of all we should know what's the right things we should do, and then put them into practice.

What advice would you give to your yourself self?

I would say never give up. I have been a cardiologist for nearly 30 years, and I am going to be completely honest with you—it's not easy, not at all. Along the way, I encountered various difficulties but I somehow managed to overcome them and gained some achievement from there. I am really grateful for my patience and persistence.

What are your thoughts about some of the emerging technologies, and the way they will shape the future care of arrhythmia patients?

Remote and ambulatory monitoring devices for cardiac disorders are showing great promise for the early detection of life-threatening conditions and critical events through long-term continuous monitoring. Moreover, great new paradigms are enabled through these technologies, such as personalized medicine, which can help the diagnosis and develop treatments for previously less well understood diseases and conditions. In the future, App-based remote monitoring provides patients with rapid access to their cardiac data, which may improve compliance with remote monitoring. Furthermore, with the popularization of 5G technology, robotic surgery would allow doctors to operate remotely, thus facilitating doctor-patient interactions.

A MEMO FROM THAILAND EP FELLOW: MY POSTER PRESENTATION AT HEART RHYTHM 2022 CONFERENCE

Dr. Sanatcha Apakuppakul
Faculty of Medicine, Ramathibodi Hospital, Bangkok, Thailand

Hello everyone.

My name is Dr Sanatcha Apakuppakul, I am a Senior EP Fellow from Ramathibodi Hospital, Bangkok, Thailand. I would like to share my first ever trip to the Heart Rhythm Society (HRS) Annual Meeting 2022 – Heart Rhythm 2022 (HRS 2022), held in **San Francisco, CA from 29th April to 1st May, 2022.**

Back in 2021, my Junior Attending Staff - Dr Nilubon Methachittiphan, he gave me advice to send an interesting case to HRS. After that, I realized that I have an extremely interesting case of Coronary Sinus (CS) Pacing in a patient with Right Ventricular (RV) Endomyocardial fibrosis (EMF). Then I wrote the case, titled as **"How can we pace the dead myocardium?"** and submitted it to HRS. And bravo, the case was accepted for poster presentation.

Figure 1: Dr Sanatcha Apakuppakul with his poster during the poster presentation session.

I went to San Francisco with one of the Junior EP Staff in Thailand - Dr Sonthichai Jirachaisakul. We arrived on Thursday, 28th April 2022, the weather is nice over there. To me, San Francisco was one of the most beautiful cities in the world.

During the meeting, I met many famous electrophysiologists around the world, from senior to junior generations. I met Drs. Eric Prystowsky, Kenneth Ellenbogen, Roderick Tung, and etc; to name just a few, and Dr Eric Prystowsky was kind enough to take a selfie with me.

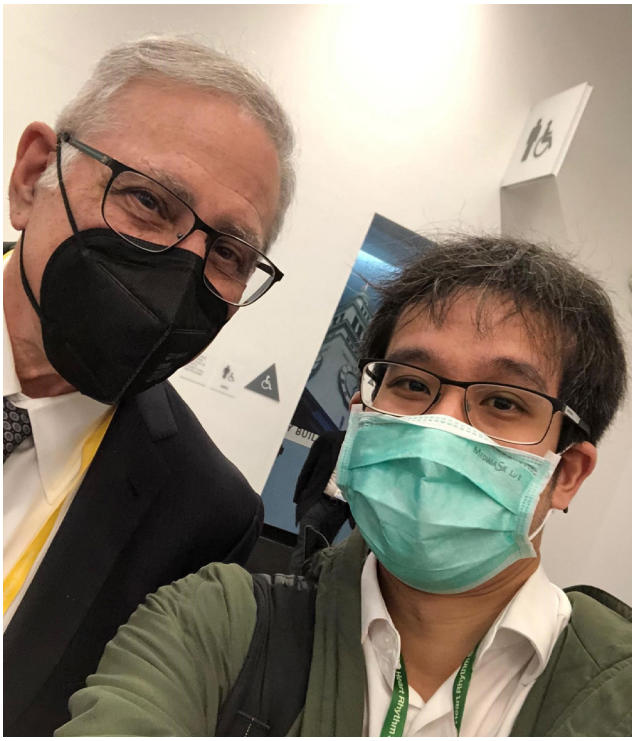

Figure 2: Dr Sanatcha Apakuppakul selfie with Dr. Eric Prystowsky.

The HRS 2022 was a very fascinating conference, especially the workshop sessions. The Anatomy Workshop was the one I loved the most, there were real pig hearts for hands-on dissection.

At the conference sessions, I learned a lot of new knowledge, new concepts, as well as interesting EGMs and ECGs.

More importantly, I made a lot of new friends. During the poster session, I met Dr. Weeranun Bode, an EP fellow at University of Pennsylvania.

We had a fruitful discussion about the complex EP cases and procedures, and I learned a lot and got inspired from her.

At the end of the day after the conference, I travelled to several landmarks of San Francisco, such as the Golden Gate Bridge, Pier 39, Ghiradelli Square and the first Swensen shop.

I ran into Dr Pattarapong Makarawate and his friends, we shared experiences and hung out together that evening.

Figure 3: Dr Sanatcha Apakuppakul hangs out with the gang in San Francisco. Funny enough, some of us still wore the HRS name badge.

I learned a lot from HRS, not only new knowledge and concepts but also new friendships and connections.

I had special thanks to Dr Chutimon Nan Junkrasien, Dr Nilubon Methachittiphan, Dr Sirin Apiyasawat, Dr Tachapong Ngarmukos and Dr Pakorn Chandanamattha and Ms Natcha Soontornmanokati for this great opportunity and experience.

Hope to see you all in HRS 2023 at New Orleans, LA!!!

FABRY DISEASE AND CARDIAC ARRHYTHMIAS

Chiao-Chin Lee, Yuan Hung, Wen-Yu Lin, Wei-Shiang Lin
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Fabry Disease (FD) is a rare X-linked lysosomal storage disorder caused by pathogenic variants in the α-galactosidase A (GLA) gene, leading to failure of glycosphingolipids degradation. This consequent accumulation of Globotriaosylceramide (Gb3) and related glycosphingolipids in various organ systems results in progressive organ damage *(Figure 1)*.[1] There are more than 1,000 gene variants been identified currently, and the onset of disease, clinical pictures and organs involvement are related to the mutation.[2,3,4] Cardiac involvement is associated with a significant impact on life expectancy and cause of death.[5] Progressive accumulation of Gb3 affects the myocytes, intramyocardial vessels, endocardium, valvular fibroblasts, and conduction tissue.[6] Development of advanced heart failure and arrhythmia is the major cause of cardiac death in FD. In this review, we focus on the cardiac arrhythmias in FD, which is the crucial prognostic determinant.

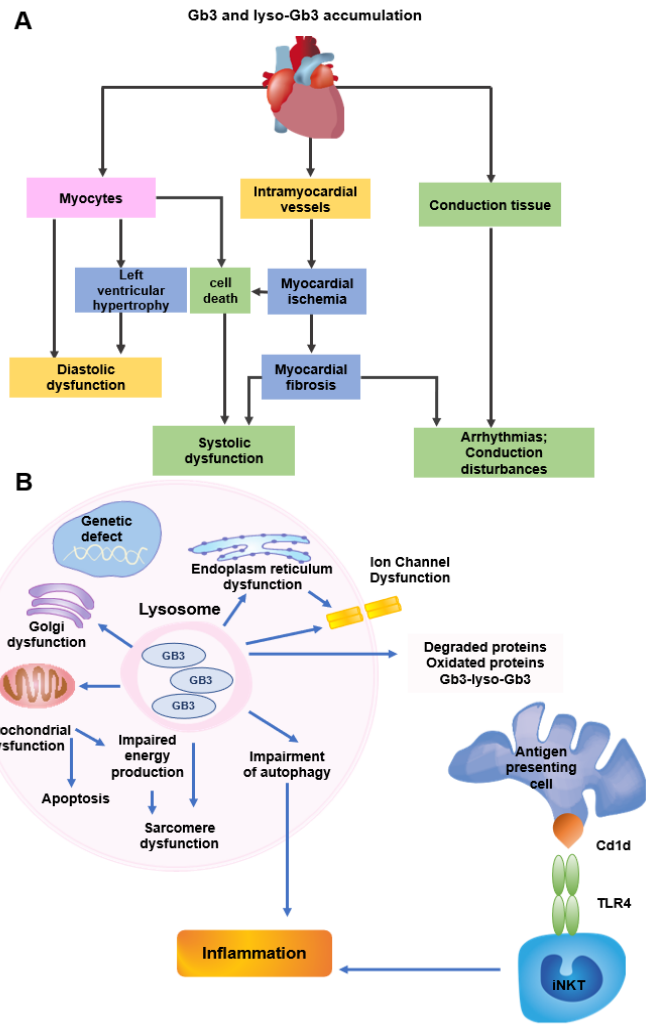

Figure 1: (A) The classic pathophysiology of Fabry disease (FD) as a myocardial storage disorder. (B) The secondary pathways operating in FD. Gb3 = globotriaosylceramide; iNKT = invariant natural killer T; lyso-Gb3 = globotriaosylsphingosine; TLR4 = toll-like receptor-4. (The figure is revised from J Am Coll Cardiol. 2021;77(7):922–36.)

Clinical Symptoms

Palpitation and syncope are the most frequent symptoms in FD patients with arrhythmias and conduction system disorders. The prevalence of symptoms has been reported as around 26-27% with palpitation and 2-4% with syncope.[7] Palpitation is more associated with atrial arrhythmias, while syncope is more related to atrioventricular block or ventricular arrhythmias. An implantable loop recorder might be considered in such patients if a 24-hour Holter electrocardiogram can't detect clinically significant arrhythmias.[8]

Atrial Arrhythmias

The prevalence of atrial fibrillation (AF) is around 1% in the normal population, and the prevalence is < 1% in the population < 55 years old.[9] However, the incidence of AF in FD patients is 4 times higher than in the general population. The prevalence of persistent AF and paroxysmal AF among patients with FD is estimated at 3.9% and 13.3%, respectively. The prevalence is higher in a late-onset phenotype with predominant cardiac involvement.[3,10] The mechanism of AF in FD is probably multifactorial, and the direct presence of Gb3 deposits in atrial cardiomyocytes plays an important role in the early-stage development of AF.[7,11]

Cardiac Conduction System Disorders

The accumulation of Gb3 and related glycosphingolipids in the conduction tissue is constant in men and variable in women owing to X-chromosome skewed inactivation. In the early stages of the disease, the process causes accelerated conduction resulting in a shortened PR interval without an accessory pathway.[12,13]

As the disease progresses, sinus node dysfunction, prolongation of the PR interval, atrioventricular node block, and bundle branch block are not uncommon manifestations *(Figure 2)*.[14,15] Aleš Linhart et al. has reported that the prevalence of conduction abnormality is 12.1% in male and 6.7% in female, and the pacemaker implantation rate is 4.8% in male and 1.6% in female.[7] An observational, longitudinal, retrospective cohort also reports that the rate of anti-bradycardia pacemaker implantation in FD patients is >25 times higher than that observed in the general population.[16]

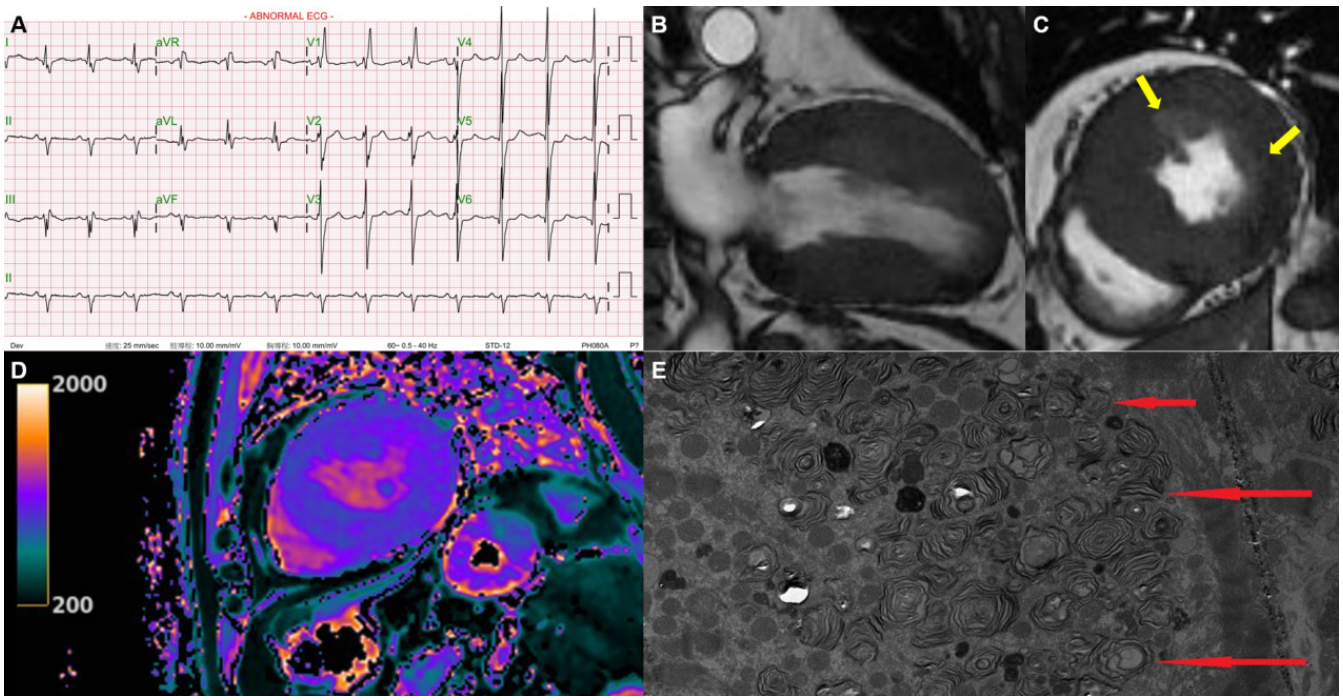

Figure 2: A Representative Case of c.640-801G>A Cardiac Variant with Concentric LVH. A 55-year-old man presented with progressive chest pain and shortness of breath in recent two years. (A) Electrocardiography showed sinus rhythm with right bundle branch block, giant R-waves in the precordial leads. (B and C) Cardiac magnetic resonance revealed concentric HCM with late gadolinium enhancement (yellow arrows) and (D) low myocardial T1 values suggesting FD. (E) Pathological findings based on electron microscopy of endomyocardial biopsy show central vacuolations and lamella bodies in cardiomyocytes (red arrows). The genetic analysis detected c.640-801G>A mutation causing the FD cardiac variant.

Ventricular Arrhythmias

The leading cause of death in FD is cardiovascular disease (75%), with the majority of sudden cardiac death (SCD) events (62%), and ventricular arrhythmia (VA) is thought to be the primary cause.[17] The development of VA in FD is thought to be the progressive process associated with Gb3 accumulation, which may cause left ventricular hypertrophy, inflammation, and myocardial fibrosis.[18,19]

To identify the risks factors, including male gender, older age (>40 years in males), increasing left ventricular mass index, the presence of late gadolinium enhancement in cardiac magnetic resonance image and non-sustained ventricular tachycardia of VA is the primary issue to prevent catastrophic outcome.[17,20]

FD-specific Therapy

Supportive care in FD patients, especially for renal failure and hypertension, has improved significantly in recent years. It has been proved that the enzyme replacement therapy (ERT) can clear microvascular endothelial deposits of Gb3 from the targeted organs and relieve symptoms in FD patients.[21,22] The ERT may also contribute to changes in morbidity and mortality related to FD. Therefore, the importance of renal failure as a cause of death is decreasing, whereas the importance of cardiac disease is increasing.[23] However, in one long-term following study demonstrated that the ERT did not influence the clinical important outcome, including sudden cardiac death in advanced FD.[24] Novel treatment, pharmacological chaperone Migalastat, is promising and associated with a statistically significant decrease in left ventricular mass index. However, the favorable outcome can only be demonstrated in patients carrying amenable pathogenic variants, and whether reduction of death or not still needs further investigation.[25,26,27] Otherwise, there are several therapies in development, including second generation ERT, substrate reduction therapies, and gene-, stem cell- and mRNA therapies.[18,20,28]

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