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Report: APHRS Summit Scientific Symposium

Wee Siong Teo, MD

National Heart Centre Singapore

The Asia Pacific Heart Rhythm Society (APHRS) held the first summit of its committee members in Singapore on 29 March 2014. All in 22 of the board members and subcommittee chairs were able to come for this initial meeting. There was intense discussion about strategic plans for the society for the next 10 years by all the members present.

The official journal of APHRS which is now under the leadership of Prof. Shih Ann Chen was also discussed in detail. The various subcommittee chairpersons for membership; basic and clinical research; practice guidelines; document writing; education; scientific program; web and arrhythmia news; fellowship and global relations presented to the board and discussed about how to move forward and improve on the achievements so far.

The scientific chairperson for APHRS 2014 in New Delhi, India and APHRS 2015 in Melbourne, Australia also reported on the progress of the preparations for the 2 upcoming meetings. The discussions lasted till the night with a dinner where the various members could continue their discussions. On the next day, various members of the APHRS board also met with representatives from the industries to discuss on how we can work together to improve on the education and training in the Asia Pacific region.

In conjunction with the meeting a scientific session was held on 30 March 2014. All the lectures were given by the committee members of APHRS. The session reviewed all the current advances in electrophysiology, ablation and device



President of the APHRS Young-Hoon Kim, MD



Masayasu Hiraoka, MD (in the middle), Richard NG, MD (left side), Bernard Kwok, MD (right side)



therapy. The meeting was co-organized with the Singapore Cardiac Society. More than 100 doctors and allied professionals from Singapore; Malaysia; Indonesia; Thailand; Vietnam; Myanmar; Sri Lanka and Bangladesh attended the meeting. The feedback from the attendees was that the meeting was very useful as it was a summary of all the important new

advances in understanding and treatment of cardiac arrhythmias.

The President, Prof. Young Hoon Kim, thanked all participants and the various companies for the support of the meeting. With the success of this first summit, it is likely that future summits will be planned in future.



Muhammad Munawar, MD (the standing one)
APHRS summit scientific session



Shih Ann Chen, MD APHRS summit scientific session



APHRS summit scientific session



APHRS summit scientific session



A group photo of board members and subcommittee chairs taken after the 1st APHRS summit meeting.

First line from left to right: Drs. Congxin Huang, Muhammad Munawar, Jonathan Kalman, Wee Siong Teo, Masayasu Hiraoka, Young Hoon Kim, Shih Ann Chen, Mohan Nair, Satoshi Ogawa, Chu Pak Lau

Second line from left to right: Drs. Chi Keong Ching, Tachapong Ngarmukos, Prashanthan Sanders, Martin Stiles, Kazuo Matsumoto, Juin Chueh Wang, Yoshinori Kobayashi, Hung Fat Tse, Yong Seon Oh



Current Treatments for Atrial Fibrillation in Asia: The Entry of Cryoballoon

Kazuo Matsumoto, MD

Professor of Cardiology, International Medical Center, Saitama Medical University, Hidaka, Saitama, Japan

Incidence of AF World Wide

Atrial Fibrillation (AF) has a far reaching impact because of the well described prevalence of this disease in older populations and the associated risks in morbidity and mortality due to the natural disease progression. Specifically AF is a fairly rare disorder for groups of people less than 60 years old with a prevalence of less than 1%. Yet, amongst individuals who are 80 years old or older the prevalence of AF grows to greater than 7% of the population. Additionally, AF in many epidemiological surveys is the most common type of cardiac arrhythmia. 1,2 Analysis of the Framingham Heart study cohort determined that the lifetime risk of developing AF was one-in-four for those individuals at 40 years of age while it was one-in-six if the individual did not have a preceding myocardial infarction or heart failure.2

In the field of cardiology, the Framingham Heart study remains the premier longitudinal study to examine disease epidemiology including AF prevalence; however, more recently the incidence of AF has been further analyzed to investigate the similarities and differences between geographic populations. By examining populations with different environmental and genetic backgrounds, the investigator(s) may be able to derive more relevant information and more effective treatment(s) for AF. For instance, when examining large community based population studies, the occurrence of AF in Japan ranges from 0.7% to 1.6% (n=253,818 and n=41,436; respectively) with the largest Japanese population study reporting an overall prevalence of 1.09% (n=630,138).3 By comparison, China' s rate of AF prevalence is between 0.8% to 2.8% when examining large community based cohorts (n=29,079 and n=30,000; respectively).4 Other smaller community based population studies in Asia have been completed in Thailand, South Korea, and Taiwan which have reported AF prevalence rates of 0.4%, 0.7%, and 1.1% (n=8,791; n=14,540; and n=3,560; respectively).

Examination of these AF epidemiological studies conducted in Asia leads the physician

investigator to conclude that AF in the broader Asian community is heterogeneous (at least by country-tocountry investigation) but with prevalence towards higher incidence rates similar to those of Caucasian populations. In fact, the AF rates for Japan, China, Taiwan, and South Korea are remarkably similar to a survey of patients ≥20 years old in the US which observed that 1.12% had non-transient AF and/or atrial flutter and to a European evaluation of patient which demonstrated that 0.7% of people had AF. With regard to AF amongst racial and ethnic categories in the elderly, older people of Caucasian and Asian heritage have the highest overall prevalence of AF (8.0% compared to 3.9%, respectively). Also, a systematic review of Asia based community studies found that the AF incidence was generally higher in men when compared to women which was in agreement with the historic North American and European studies evaluating AF within populations.

Cause of AF, Risk of Stroke, and Hospitalization

Unfortunately the rate and incidence of AF in most Asian populations are remarkably similar to those previously established in the historic demographic studies which where predominately Caucasian patients (Framingham Heart cohort). Consequently AF is also a major Asian healthcare problem. However, the root cause of AF may be different based on geography and patient group selection. When examining the Japanese and Chinese incidence of AF, it is demonstrated that AF is secondary to valvular heart disease in up to 22% of the patients, but the valvular heart disease associated AF rate may be even higher in other parts of Asia where rheumatic fever and rheumatic heart disease are still problematic, such as some parts of India. Additionally, when examining the cause of AF, it is important to consider the clinical patient population that is represented in the data set. For instance, when examining community based studies, the most common etiologic factor for AF is long-standing hypertension. By contrast, when a similar study is conducted in a hospital survey the



most commonly reported etiologic factors for AF are ischemic heart disease and heart failure.

Stroke remains a primary complication of AF regardless of geography. With regard to AF in healthcare epidemiology, AF is associated with a four- to five-fold increased risk of stroke, and a two-fold increase in risk of death even when the traditional cardiovascular risk factors have been previously adjusted. Regarding stroke frequency, a retrospective examination of Chinese AF patients demonstrated that the prevalence of stroke was 17.5%. In a Japanese multicenter registry (J-TRACE study), the incidence of stroke was 14.3% in patients with non valvular atrial fibrillation.²⁵ This incidence of stroke in Chinese and Japanese AF patients is extremely similar to the approximately 15% rate of stroke that was reported from the Framingham study which categorized AF as a major contributor to stroke in the elderly.²⁶ Although the Chinese and Japanese rate of AF associated stroke are similar, the pharmaceutical intervention is different. For instance, consider the differential usage of warfarin in China and Japan. The usage of warfarin in Japan is relatively high at 70.1%,6 while considerably lower in China at 2.7%.4 This differential usage of warfarin (a primary tool for pharmaceutical anticoagulation therapy) highlights the broad differences in AF treatment that reside even within Asia.

Lastly, in recent mainland China studies which investigated rates of hospitalization, AF accounted to for 7-8% of all cardiovascular disease hospital admissions from 1999 to 2001, and AF amounted to 35% of all hospital admissions for cardiac arrhythmia in 2007⁷. Also,an epidemiological study in mainland China found that 64% of AF was categorized between first diagnosis and paroxysmal AF (Figure 1).⁷ Mercifully, these two early disease categories of AF

remain highly responsive to therapeutic intervention.

AF Therapy

Currently in China and most of Southeast Asia, antiarrhythmic drug (AAD) therapy remains the primary treatment for AF. Further investigation of a mainland China retrospective hospitalization study demonstrated that rhythm control was the predominate treatment for paroxysmal AF (56.4%), while rate control was the prevalent strategy for patients with chronic AF (82.8%). Although drug therapy is the predominate therapy for AF in China, the usage of catheter ablation of AF has dramatically increased since the first Chinese radiofrequency (RF) ablation case was performed in 1998. This higher utilization of catheter ablation was demonstrated during a Chinese registry study in patients with AF. From 1998 until 2005, the Chinese registry study found a total of 3196 catheter ablations had been performed in 40 hospitals (2193 male and 1003 female patients).8

By contrast, catheter ablation of AF is currently more prevalent in Japan and South Korea. In the most recent Japanese Circulation Society, catheter ablation of AF has been recommended as a class I therapy (JCS 2011; Guidelines for Non-Pharmacological Therapy of Cardiac Arrhythmias). This class I recommendation will apply to only symptomatic AAD-resistant paroxysmal AF patients with normal left atrial size, normal left ventricular function, and no pulmonary disease. The method of ablation will include pulmonary vein isolation (PVI) which has become a central pillar to AF ablation strategy since the introduction of spontaneous initiation of AF by ectopic in the pulmonary vein (PV) was first described by Haïssaguerre.

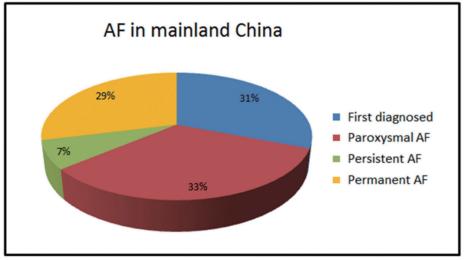


Figure 1. Demographics of AF disease prevalence in mainland China.

In the US and EU, catheter ablation has become an important therapeutic option in the long-term treatment and care of AF patients. Simply, there is still a substantial amount of highly symptomatic, drug refractory AF patients in the US and EU. In these patients, cardiac ablation of the focal asynchronous AF electrical source is often the only treatment available to alleviate or terminate the arrhythmia and the associated symptoms. Currently the US and EU consensus statements suggest that when AF ablation is warranted, PVI is a primary method for most AF ablation procedure strategies. As much as 94% of the foci that are attributed to AF appear to originate from the pulmonary veins (PVs). Finally, PVI ablation strategies have been shown to be important in AF with regards to the long-term outcome and the improved Quality of Life for an AF patient. Typically these improvements on life quality cannot be fully achieved with pharmaceutical therapy alone.

The Cryoballoon System

When a PVI ablation is warranted, newly designed catheters recently termed "anatomic" ablation catheters have been developed and used to apply ablation energy simultaneously around a PV during isolation. This uniform application of energy may have an advantage over traditional focal RF catheters at creating homogenous and circumferential lesions. Various power sources have been evaluated for anatomic procedures, including RF, phased RF, laser, ultrasound, and cryothermal energy; however, the deployment systems have been somewhat more uniform to include mainly balloons, wire-mesh baskets, or circular conforming wires. All anatomic approaches have attempted to address the significant challenges of PVI by focal RF catheters - which require significant time, user experience, dexterity, and proficiency with 3D mapping interpretation - by facilitating an easier and more predictable lesion at the antral portion of the PV.

Most recently, the cryoballoon (Medtronic, Inc.) has led the anatomic market with regard to approved market release and clinical use. In fact, within Asia, cryoballoon procedures have already been performed in Australia, Hong Kong, and New Zealand, with regulatory approval processes ongoing in China, India, Japan, and Taiwan. The cryoballoon is the only FDA approved and marketed anatomic ablation catheter, and the clinical adoption of the cryoballoon system has been significant globally: approximately 65,000 patients in 33 countries across more than 500 medical centers have been treated with the cryoballoon for the isolation of asynchronous AF triggers that originate from focal PV

locations (Medtronic, Inc. user database).

In this system, the Arctic Front Cardiac Cryo Ablation Catheter uses cryothermal energy via cryoballoon deployment and application. In brief, the cryoballoon is placed and guided to the left atrium (LA) with the FlexCath sheath. This deflectable sheath will guide the cryoballoon into position near the entrance of a PV. Then the cryoballoon is deployed over-a-wire and positioned at the antral entrance of a PV (Figure 2). Most often, a transluminal circular diagnostic catheter - the Achieve mapping catheter (Medtronic, Inc.) - is used in this regard. The advantages of using the Achieve mapping catheter are several, including: 1) a single transseptal entry can be utilized, 2) LA mapping can be done while the Achieve mapping catheter resides within the central lumen of the cryoballoon, and 3) procedure duration and radiation exposure can be reduced. When full occlusion is attained between cryoballoon and PV, nitrous oxide is released via internal ports within the cryoballoon. The LA cardiac tissue that is in contact with the cryoballoon will act as a heat source during the phase shift of the liquid nitrous oxide into a gaseous form. This liquid-to-gas phase shift withdraws heat energy and forms a freeze zone in the cardiac tissue that is in contact with the cryoballoon.

The cryoballoon establishes a well demarcated, broad, and dense scar which will act as a zone of electrical isolation, preventing ectopic conduction arising from PV triggers. Additionally, there is a well described lowered incidence of thrombus formation with cryothermal energy compared to RF heated power, probably secondary to the resultant intact extracellular matrix. Most PVI procedures will be accomplished with the single usage of one cryoballoon; however, when focal ablation targets are also present, a cryothermal focal catheter (FreezorMAX) can also be used with the same

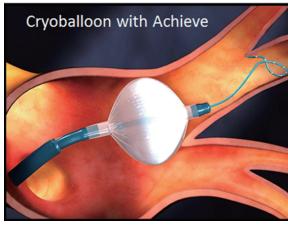


Figure 2. Cryoballoon deployment in FlexCath with Achieve mapping catheter used as guide-wire into LSPV.



cryoconsole. The entire package of cryoballoon, delivery sheath, circular mapping catheter, and focal cryocatheter were designed to be used together and operated easily from one main cryoconsole (CryoConsole Cardiac CryoAblation System).

Safety and Efficacy Data

STOP AF (Sustained Treatment of Paroxysmal Atrial Fibrillation) was the US FDA pivotal trial designed to evaluate the safety and effectiveness of the Arctic Front Cardiac Cryoablation System, in which cryoballoon therapy was compared to AADs in symptomatic drug refractory paroxysmal AFpatients. The STOP AF trial was a 2:1 randomized, multicenter trial with 163 patients in the cryoablation group and 82 patients in the AF AADs group. In this study, 98.2% of patients receiving cryoablation therapy demonstrated acute procedural success, defined as electrical isolation in three or more PVs immediately after the procedure. In fact, 97.6% of patients had all four PVs successfully isolated, and PVI by cryoballoon alone was achieved in 83% of the time. Treatment success at 12 months was recorded as 69.9% of cryoablation patients which was in comparison to 7.3% of patients who achieved treatment success on AADs. Also the STOP AF study met all safety endpoints; however, phrenic nerved palsy and PV stenosis were present in the cryoballoon group (11.2% and 3.1%, respectively).

Since the completion of STOP AF, a better awareness of the general cryoballoon positioning within the PV has led to better control of PV stenosis. Physicians are asked to examine each PV ablation under fluoroscopy to ensure that the cryoballoon does not appear to be cone-shaped at the distal balloon end. This is an indicator that the cryoballoon is inserted too far into the PV and that a more antral position is necessary. With this better understanding of cryoballoon spatial awareness, PV stenosis rates have declined to levels consistent with focal RF catheters. In a large 346 patient prospective threecenter study of cryoballoon ablation, the Neumann study consecutively enrolled all patients and found no PV narrowing in this multicenter examination as determined by computed tomography (CT) scan or magnetic resonance imaging (MRI) within three to twelve months after the ablation procedure. Similarly, the largest published Australian experience with cryoballoon demonstrated no PV stenosis in 200 consecutive patients while still demonstrating 70% freedom from AF at one year in paroxysmal AF patients. Lastly the Traullé study demonstrated that a "cryoballoon-alone" strategy is best with regards to PV stenosis.44 In the Traullé examination 49

patients were examined during cryoballoon ablation which encompassed 189 ablated PVs of which 117 PVs were isolated with cryotherapy alone and 72 PVs were isolated with the addition of RF ablation (hybrid ablation). At the three-month post-ablation CT scan evaluation for PV stenosis, all the hybrid ablations (cryoballoon plus RF ablation) detected a decrease in PV diameters (19.2 \pm 3.0 mm to 17.8 \pm 4.9 mm) while the cryoballoon-alone ablated PVs had no PV stenosis(P = 0.0140). The Traullé study postulated that the cryoballoon was able to keep an antral position during ablation.

With regard to phrenic nerve palsy, the general recommendation with cryoballoon procedures has been to pace the phrenic nerve during rightsided PV ablations and to feel (with the physician' s hand) the diaphragmatic contractions actively duringcryoablation. Immediate termination of ablation is recommended when any decrease in diaphragmatic contraction is detected. Two recent studies have attempted to use imaging and temperature protocols to try and predict those patients who may be more prone to phrenic nerve interruption during a cryoballoon procedure. In the Kühne study of 65 paroxysmal AF patients, no phrenic nerve palsy was reported, but transient phrenic nerve interruption (tPNI) was detected in 6% of patients which all resolved in 24 hours (four patients). Those four patients with tPNI had a significantly shorter distance between the right superior PV (RSPV) and the superior vena cava as assessed by CT scans(14.0± 2.3mmtPNI group versus 17.1±2.8 mm rest of group; P = 0.0300). Additionally the same four patients with tPNI, also experienced the lowest cryoballoon temperatures during the early freeze period (-44°C ± 2°C at 30 sec tPNI group versus -28°C ± 8°C at 30 sec rest of group; P = 0.0003). In a similar study design, the Canpolat study examined 162 patients with CT scans before a cryoballoon procedure. 46 The Canpolat study also detected no phrenic nerve palsy, but the study did report a 3% incidence of tPNI. In the Canpolat examination, the distance between the RSPV and right pericardiophrenic artery was a significant predictor of tPNI, and tPNI was present when this distance was short (7.2±2.0 mm) while it was absent when this distance was long (12.6±4.9 mm; P = 0.0330). Both the Kühne and Canpolat study demonstrated that the incidence of phrenic nerve injury can be minimized with imaging and monitoring usage during the procedure.

Procedural Ease and Economics

The STOP AF study demonstrated a short learning curve for physician proficiency with the

cryoballoon which was shown to occur within twenty procedures. In fact, physicians in STOP AF who performed over twelve cases in the study observed a 90% effectiveness rate in those patients at twelve months. The combination of STOP AF¹² and longerterm European studies have demonstrated the safe and effective nature of cryoballoon ablation procedures.

Also, the procedural ease of the cryoballoon has demonstrated reduced staff time, reduced procedural time, and better hospital resource management across several studies. During the usage of the cryoballoon, the Klein study demonstrated that the cryoballoon reduced lab occupancy by 33%, reduced primary physician time by 33%, and reduced fluoroscopy time by 24% when compared to focal RF ablation catheters (Figure 3).13 Since the original Klein study, two separate evaluations of the cryoballoon have demonstratedsimilar reductions in procedure time and fluoroscopy time. 14 The more global introduction of the cryoballoon catheter has demonstrated that these hospital efficiencies have been observed across a wide range of healthcare systems. Exact ablation economics will be dictated by local costs; however, the cryoballoon efficiencies compared to focal RF catheters have been real and measurable.

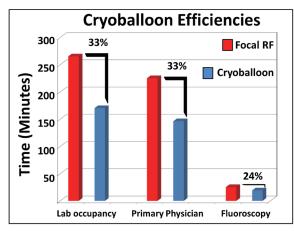


Figure 3. Results from FAST PVI study: Cryoballoon efficiencies detected when comparing to focal RF ablation catheters.*

The Future

As the aging population is expected to grow in Asia, the occurrence of AF may rise with this

demographic change. Only by improving today's treatments can we expect to keep pace with this demographic shift in aging populations. Catheter ablation of AF is a modern approach to an old problem, and the new cryoballoon usage in Asia is an exciting opportunity.

References

- Go AS, Hylek EM, Phillips KA, et al. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. JAMA 2001; 285: 2370-2375.
- Lloyd-Jones DM, Wang TJ, Leip EP, et al. Lifetime risk for development of atrial fibrillation: the Framingham Heart Study. Circulation 2004; 110: 1042-1046.
- Inoue H, Fujiki A, Origasa H, et al. Prevalence of atrial fibrillation in the general population of Japan: an analysis based on periodic health examination. Int J Cardiol 2009; 137: 102-107.
- Zhou Z, Hu D. An epidemiological study on the prevalence of atrial fibrillation in the Chinese population of mainland China. J Epidemiol 2008; 18: 209-216.
- Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. Stroke 1991; 22: 983-988.
- Uchiyama S, Shibata Y, Hirabayashi T, et al. J-TRACE Investigators. Risk factor profiles of stroke, myocardial infarction, and atrial fibrillation: a Japanese Multicenter Cooperative Registry. J Stroke Cerebrovasc Dis 2010; 19: 190-197.
- 7. Zhang S. Atrial fibrillation in mainland China: epidemiology and current management. Heart 2009; 95: 1052-1055.
- 8. Huang CX, Zhang S, Ma CS, et al. The registration study of catheter ablation in patients with atrial fibrillation in China. Chin J Card Arrhythm 2006; 10: 468-474.
- Okumura K. Catheter ablation as a class I recommendation therapy for symptomatic, drug-resistant, paroxysmal atrial fibrillation. J Arrhythm 2012; 28: 81.
- Haïssaguerre M, Jaïs P, Shah DC, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med 1998; 339: 659-666.
- 11. Khairy P, Chauvet P, Lehmann J, et al. Lower incidence of thrombus formation with cryoenergy versus radiofrequency catheter ablation. Circulation 2003; 107: 2045-2050.
- Packer DL, Kowal RC, Wheelan KR, et al. STOP AF Cryoablation Investigators. Cryoballoon ablation of pulmonary veins for paroxysmal atrial fibrillation: first results of the North American Arctic Front (STOP AF) pivotal trial. J Am CollCardiol 2013; 61: 1713-1723.
- Klein G, Deneke T, Schreieck J, et al. AF ablation procedure time with anatomically-designed catheters. 2010 CardioStim conference.
- Fürnkranz A, Bordignon S, Schmidt B, et al. Improved procedural efficacy of pulmonary vein isolation using the novel second-generation cryoballoon. J CardiovascElectrophysiol 2013; 24: 492-497.

^{*} Klein G, Deneke T, Schreieck J, et al. AF ablation procedure time with anatomically-designed catheters. 2010 CardioStim conference.



ECG Quiz

The model commentary will be provided in the next issue No. 14

Yoshinori Kobayashi, MD

Professor, Division of Cardiology, Department of Internal Medicine, Tokai University Hachioji-hospital, Tokyo, JAPAN

A 30 year-old female experienced frequent episodes of palpitation, which has been diagnosed as supraventricular tachycardia associated with Wolff-Parkinson-White (WPW) syndrome, admitted to our hospital for catheter ablation. The 12 leads ECG before ablation (left panel) and after successful ablation (right panel) are shown below (Figure 1).

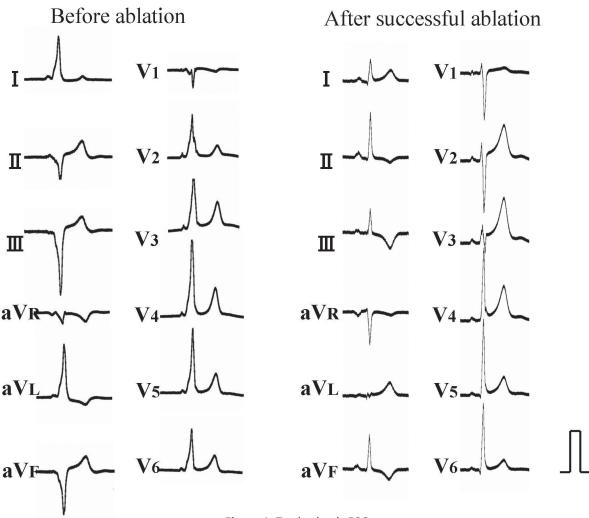
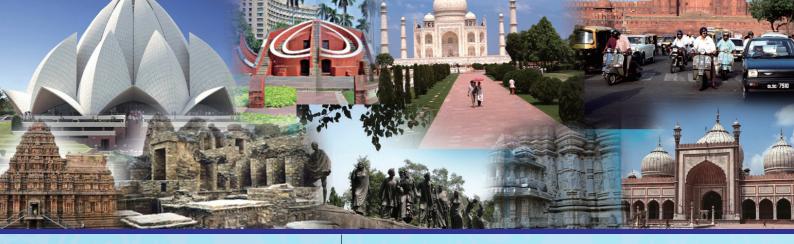


Figure 1. Twelve leads ECG

Question:

- 1) Where is the most likely location of the accessory pathway (Kent bundle)?
- 2) What is the structural abnormality which is sometimes associated with Kent bundle of this location?





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In conjunction with the "10th Asia-Pacific Atrial Fibrillation Symposium"





EP World: Queen Mary Hospital/University of Hong Kong

Prof. Hung-Fat Tse, MD, PhD

Queen Mary Hospital, the affiliated Hospital of the University of Hong Kong, began as a 546-bed public hospital at the South Western side of the Hong Kong Island in 1937. Now, more than 70 years later, Queen Mary Hospital is now an acute teaching hospital with about 1,400 beds and more than 20 clinical departments.

The development of cardiology in the University dates back to 1954, when the first cardiorespiratory laboratory was established at the Queen Mary Hospital. In 1970s, like in many other Asian countries, the Cardiology Division at Queen Mary Hospital moved ahead at an unprecedented pace, and marked important milestones. In late 1970s, more than 300 cardiac catheterizations, and around 40 permanent cardiac pacemaker implantations were performed each year at the Lewis Laboratory, Queen Mary Hospital. In 1990, cardiac electrophysiology and catheter ablation was started. In the subsequent decades, the volume of cardiac procedure as well as the complexity of the procedure progressively grew.

Clinical Research

In addition to clinical service, the Division is also renowned as a leader in cardiovascular research. In 1990s, the Division involved extensively in the research in various implantable sensors such as evoked ventricular response, intra-thoracic impedance and body acceleration forces; many of them were subsequently incorporated into the modern cardiac pacemakers in order to provide more physiological cardiac pacing. Furthermore, in early 2000s, the Division extended its wings to the research and development of novel device technologies for patients with cardiac arrhythmias and heart failure. Our research findings paved the way to development of stand-alone atrial defibrillator, cryoablation for cardiac arrhythmias, alternative atrial and ventricular sites pacing, cardiac resynchronization therapy, transcutaneous ultrasound energy mediated leadless pacing and spinal cord stimulation for heart failure. More recently, the Queen Mary Hospital has successfully performed the first implant of total subcutaneous implantable cardiac defibrillator in Asia.

Basic and Translational Research

The new millennium has been considered as the era of biological therapy. Since 2000, the Division has been focused on the development of novel biological therapies for treatment of cardiovascular disease. Stem-cell therapy and regenerative medicine



were conceptualized more than a decade ago in the treatment of cardiovascular disease.

The Division is amongst the first few laboratories in the world to report the application of a bioengineered pacemaker gene via somatic gene transfer in large animal models to initiate cardiac rhythm, and thus act as bio-artificial pacemaker. This therapeutic approach may potentially obviate or act as a hybrid therapy to reduce the dependence of patients with cardiac arrhythmias on electronic pacemaker.

Recently, the generation of human induced pluripotent stem cells, via reprogramming of somatic cells has circumvented some of the potential technological and ethical issues related to the use of embryonic stem cells for tailor-made patient specific cell-based therapies for the treatment of various human diseases, as well as for development of human cell-based platform for disease modeling and drugs screening.

In 2010, the Division was the first laboratory to report the successful generation of human induced pluripotent stem cells in Hong Kong. In collaboration with the Researcher from Mainland China, the Division derived new protocol to generate human induced pluripotent stem cells using human urine, eliminating the need for invasive skin biopsy procedure. Currently, the Division has successfully established multiple disease-specific human induced pluripotent stem cell platforms for the disease modeling and drug development for inherited cardiac arrhythmias and cardiomyopathy. To-date, the Division has generated more than 30 human induced pluripotent stem cell lines from patients with inherited diseases such as long QT syndrome, Brugada syndrome, Friedreich's ataxia, Danon disease, Lamin A/C related cardiomyopathy and so on. These provide unique opportunities for researchers to study various pathogenic mechanisms as well as the development disease specific treatment to these deadly cardiac conditions.



ECG Commentary Related to the Quiz in the No.12 Issue

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Answer:

The correct answer is option 2.

The rhythm occurring in groups of three is comprising of gradually widening QRS complexes.

The PR interval preceding the second QRS is longer. The lengthening of the PR interval could either be physiological (Long – Short sequence) or manifestation of underlying A-V conduction pathology. The wider QRS in addition could also be due to 'fusion' by a ventricular ectopy.

Hence, the differential diagnoses of the rhythm are:

- 1. Sinus Rhythm with A-V conduction disease and ventricular ectopy.
- 2. Sinus Rhythm with ventricular couplets.

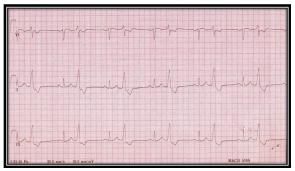


Figure 1.0A. This is the rhythm strip taken during ventricular bigeminy. Note the RS pattern in lead V1 indicating the likely origin of the PVC from the LVOT.

A casual look at the wide QRS complexes may give an impression that the PVCs are originating from RVOT. A closer look at the third complex in the precordial leads however reveals the likely origin is LVOT. LVOT being the site of origin of ventricular ectopy becomes clear during the ventricular bigeminy rhythm (Figure 1.0A and 1.0B).

The underlying A-V conduction defect which was suspected due to the longer PR during fusion complex becomes evident following ablation of the ectopy in the LVOT. The underlying LBBB was unmasked after successful ablation of the ventricular ectopy (Figure 2.0).

The masking of LBBB could be reproduced post ablation by delivering a PVC (Figure 3.0)



Figure 1.0B. Intracardiac trace during ventricular bigeminy.



Figure 2.0. The fluoroscopic image shows ablation catheter placed in the left coronary cusp (A) at the site of earliest activation map (B) resulted in loss of ventricular ectopics within 4 seconds of radiofrequency delivery and unmasking the LBBB (C).



Figure 3.0. Post RFA, single ventricular ectopy delivered (5^{th} QRS complex) masks the underlying LBBB in the 6^{th} QRS complex. The last QRS complex reveals again the underlying conduction disease.



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Brief Statement