"I made myself all things to all men" (1 Cor. 9:22)
" 我為一切人成為一切" (格前 9:22)

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聖保祿醫院
St. Paul's Hospital

NEWSLETTER 院訊

Medical Information
醫療資訊

Management of Atrial Fibrillation: New Drugs, New Hopes

Atrial fibrillation (AF) is a relatively common arrhythmia that is more prevalent in men and with increasing age[1]. While assessing for the potential causes for AF, a clinician has to address the following questions before individualizing therapy for a particular patient:

1. Rhythm control versus rate control
2. Prevention of systemic embolization

In the past, many physicians preferred rhythm to rate control. Reversion of AF and maintenance of normal sinus rhythm (NSR) restores normal hemodynamics and had been thought to reduce the frequency of embolism. However, several major clinical trials that compared rhythm and rate control concluded that embolic events occur with equal frequency regardless of which strategy is pursued. More importantly there was a trend towards lower all cause mortality favoring the rate control arm. Taken together these clinical trials support the conclusion that rate control is the preferred initial approach in most patients. However, there are three clinical settings in which a rhythm control strategy using antiarrhythmic drugs to maintain sinus rhythm should be considered:

1. Persistent symptoms despite adequate rate control.
2. An inability to attain adequate rate control
3. Patient's preference

When rhythm control is chosen, the recommended drugs of choice for maintenance of NSR vary with the clinical setting. Optimal antiarrhythmic drug therapy should be both effective and have a low incidence of toxicity and proarrhythmia. Antiarrhythmics can reduce AF recurrences, but their overall value is limited by adverse effects. Virtually all of the antiarrhythmic drugs used to maintain a sinus rhythm are proarrhythmic. Amiodarone is an exception in this regard. It has a low proarrhythmic profile, the best efficacy in maintaining NSR and does not have negative impact on mortality even among patients with severe left ventricular dysfunction. However its many potential adverse effects and toxicities are problematic which has limited its clinical usage.

It has been 10 years since the Food & Drug Administration (FDA) of the United States approved dofetilide, the last antiarrhythmic drug for suppression of atrial fibrillation to reach the U.S. market. Dronedarone is one of several new antiarrhythmic agents that have been under development for the management of AF in recent decades. Its structure closely resembles that of amiodarone (see figure 1). The omission of iodine moieties as found in amiodarone was intended to reduce the likelihood of toxic effects on the thyroid and possibly other organs.

The effect of dronedarone on cardiovascular events in AF was examined in the ATHENA trial. The investigators randomized 4628 patients with AF and at least one other CV risk factor to receive placebo or dronedarone Patients had to be hemodynamically stable and not in NYHA class 4 heart failure. The primary outcome was the first hospitalization due to cardiovascular events or death. Secondary outcomes were death from any cause, death from cardiovascular causes, and hospitalization due to cardiovascular events[2].

Over a mean of 21 months among patients taking the dronedarone, there was a significant 24% drop in death from any cause or CV hospitalization, along with other improved outcomes as compared with placebo. Patients on both treatment arms showed similarly low rates of thyroid, pulmonary, neurologic, and skin-related adverse effects and other toxicities for which amiodarone is well known. About as many patients in one group as the other discontinued the randomized agent prematurely, primarily due to adverse events[2]. The results of the ATHENA forms the bases of its approval by the FDA this Spring for reducing the risk of CV hospitalization in high-risk patients with AF who do not have NYHA Class III/IV decompensated heart failure.

However in many cases patients treated with amiodarone have such side effects (especially

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pulmonary toxic effects) later than two years after initiating therapy; beyond the average follow-up time in the ATHENA trial. The trial also did not look into the drug's efficiency in AF suppression; nor was it tested against with the gold standard drug in this regard: amiodarone. In an indirect meta-analysis together with the data from an unpublished study conducted by the manufacturer, it was shown that dronedarone was less effective than amiodarone in AF suppression in patients with persistent AF. The authors of this indirect meta-analysis estimated that for every 1000 patients treated with dronedarone instead of amiodarone, there would be 228 more recurrences of AF at one year in exchange for 9.6 fewer deaths and 62 fewer adverse events requiring discontinuation of drug.[4]

Should we switch patients who are already doing well on amiodarone to dronedarone? At this time, most authorities in the field say no. They contend that if one is tolerating amiodarone and have not developed any adverse effects, and one has received a good rhythm response, the available evidence suggests that dronedarone is not as good as amiodarone at maintaining sinus rhythm. But that has to be balanced against the fact that dronedarone is associated with fewer adverse events that cause the drug to be discontinued.

For more than three decades, warfarin has been the cornerstone in preventing not only systemic complication in moderate to high risk patients with AF but reducing all cause mortality. Although uncommon, intracranial bleeding or other major organ bleeding remains the most fearsome and catastrophic side-effect of warfarin. Although warfarin has class I recommendations with grade A evidence, it has been underutilized, largely because of the safety issue and the narrow therapeutic index.

Last summer an oral anticoagulant that does not go by the name of warfarin had been shown in a huge randomized trial to prevent strokes and peripheral embolic events in patients with AF significantly better than that much older drug at a higher dose and just as well at a lower dose. It was also just as safe as warfarin or better than it, respectively, with respect to major bleeding events.

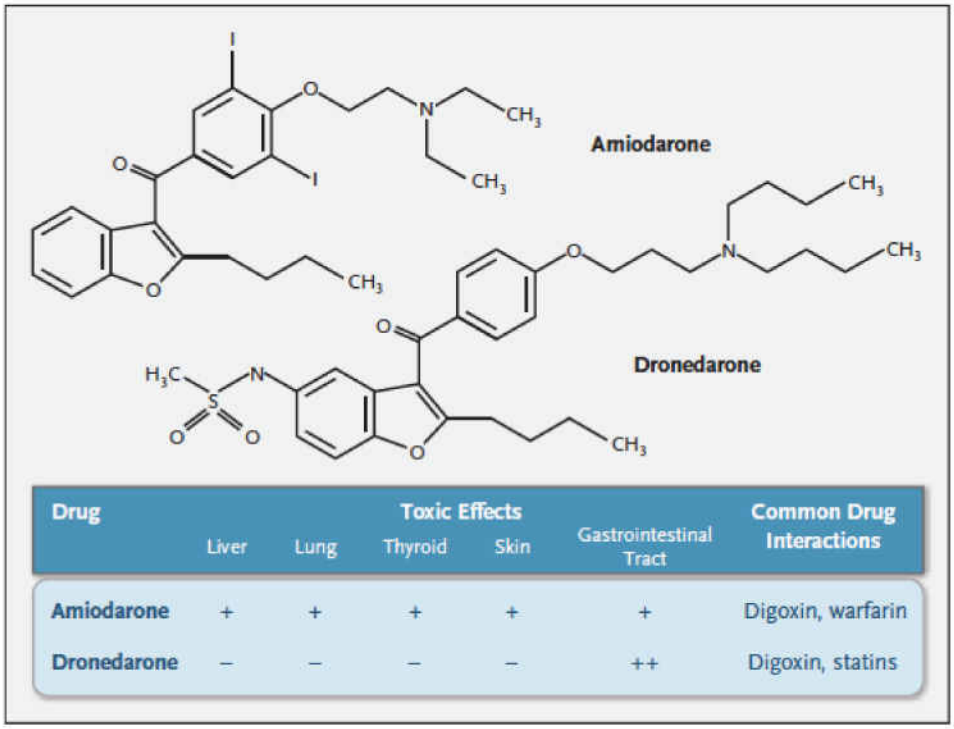
This potential new contender in AF, dabigatran, is one of several oral anticoagulants in clinical trials for the prevention of AF-related thromboembolism, venous thromboembolism (VTE), and other conditions for which warfarin had long been the only choice. A competitive thrombin inhibitor, dabigatran is approved and currently available for VTE prevention during hip- and knee-replacement surgery in the European Union.

Conducted at 951 centers in 44 countries, the RE-LY trial had randomized 18,113 patients with AF and at least one other risk factor for stroke to receive blinded treatment with dabigatran at either 110 mg or 150 mg two times per day or unblinded prophylaxis with warfarin adjusted to an INR of 2.0 to 3.0. The primary endpoint was stroke or systemic embolism[3].

Over a median two-year follow-up, the annualized rates of the primary end point were 1.53% for low-dose dabigatran, 1.11% for the high-dose drug, and 1.69% for those on warfarin. The relative risks vs warfarin were 0.91 for the low-dose ($p<0.001$ for noninferiority) and 0.66 for the high-dose group ($p<0.001$ for superiority). Hemorrhagic stroke rates were 0.12%/year ($p<0.001$) and 0.10%/year ($p<0.001$) for the low- and high-dose groups respectively, and 0.38% for warfarin. The rates for major bleeding were significantly lower than warfarin in the low dose group and similar among high dose group. Significantly more patients taking dabigatran went off the drug, which was attributed largely to the severe dyspepsia, the main side effect that occurred more often with dabigatran than with warfarin.

So it appears that dabigatran represents a newly developed anticoagulant that actually is more effective than warfarin and doesn't have the side effect of increased bleeding. Moreover, a post hoc analysis just announced in the recent American Heart Association Scientific Meeting confirms benefit of dabigatran relative to warfarin at all INR levels. However before we fully embrace the trial's results, one should be aware of the study's limitations and its generalizability. A number of questions remained unanswered: Do the elderlies fare as well with dabigatran as in the trial as a whole? Does it matter that there is no antidote to dabigatran? What should we do when we want to cardiovert a patient—do we change back to warfarin? Will the drug be equally efficacious and safe in preventing thromboembolism among patient's who have metallic prosthetic heart valves?

Without doubt the year 2009 has brought new hopes for patients suffering from AF. Hopefully, the two new drugs as discussed would expand our existing armamentarium to battle against this common 3 illness for our patients.



Drug	Toxic Effects					Common Drug Interactions
	Liver	Lung	Thyroid	Skin	Gastrointestinal Tract	
Amiodarone	+	+	+	+	+	Digoxin, warfarin
Dronedarone	–	–	–	–	++	Digoxin, statins

Figure 1: Amiodarone vs. Dronedarone: Structure and Functional Characteristics[5].

1. *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 May 9;285(18):2370-5*
2. *The ATHENA Trial N Engl J Med 2009;360:668-78.*
3. *The RE-LY Trial N Engl J Med 2009;361.*
4. *Piccini JP, Hasselblad V, Peterson ED, et al. Comparative efficacy of dronedarone and amiodarone for the maintenance of sinus rhythm in patients with atrial fibrillation. J Am Coll Cardiol 2009; 54:1089-1095.*
5. *Zimetbaum PJ. Engl J Med 2009:360;1881-82*

Dr. Raymond Miu
Specialist in Cardiology

Hospital updates 醫院動向

St. Paul's Hospital targets medication safety with First DataBank

FIRSTDATABANK

Hong Kong, China, November 2009 – First DataBank (FDB), the leading global provider of drug databases and clinical decision support, today announced a partnership with St. Paul's Hospital, a private 400-bed hospital located in Hong Kong's Causeway Bay. In the new partnership, First DataBank's clinical decision support and drug database will be linked with the hospital's Siemens i.s.h.med Hospital Information System as part of its patient safety improvement initiative.

FDB's clinical decision support will provide clinicians with tailored warning messages on potential drug-drug interactions, contraindications and precautions, as well as sensitivities and duplicate therapies during prescribing and dispensing.

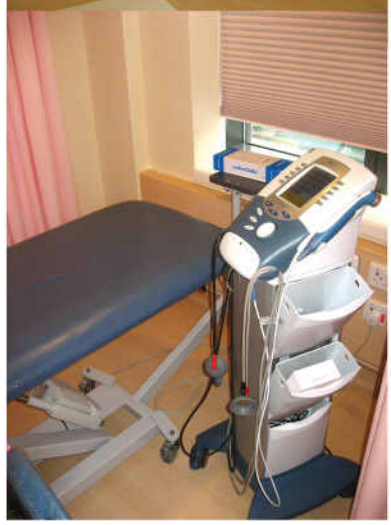
FDB's drug database will further support medical staff by enabling them to access detailed drug information electronically instead of by consulting a reference book. The comprehensive information which includes dosing, side effects, and drug indications, will be available while performing error-prone tasks like prescribing and dispensing.

Mr. Samuel Cheung, General Manager, St. Paul's Hospital, comments on the partnership: "As part of our patient safety initiative at St. Paul's Hospital it is clear that we need to provide better tools to help our clinicians to prescribe and dispense more safely. We choose First DataBank because of its reliability and track record in providing products which support this aim. The extraordinary detail in the database benefits clinicians by providing relevant and useful messages."

Mr. Chung Liauw, Managing Director, First DataBank Australia, adds: "We look forward to a close working relationship with St. Paul's as we support them in the delivery of excellent healthcare to the local community. St. Paul's joins other elite hospitals in the region by providing leadership in the use of clinical decision support."

The Orthopaedic and Rehabilitation Centre

The Orthopaedic and Rehabilitation Centre occupies the whole 7th floor of the newly expanded and modern block A. It hosts a warm and friendly atmosphere in a state-of-the-art 4,630 square feet rehabilitation environment. You will find here comfortable and cozy enough to receive the maximum benefits from your treatment and therapy.



The centre is divided into six zones

1. Reception Lounge and Consultation Rooms:
   Our Orthopaedic specialist will be there seeing patients and performing minor procedures.
   The other consultation room is reserved for visiting doctors and for electrodiagnostic purpose.
2. Physical Reconditioning Zone
   You can find the fitness machine, treadmill, and total body arc trainer here. The main target groups of patients are orthopaedic and cardiovascular patients.
3. Active Rehabilitation Zone
   The facilities here will provide rehabilitations for conditions such as dementia, Parkinsonism, spinal injury and stroke.
4. Passive Rehabilitation Zone
   There are different rehabilitation methods to be carried out in this zone, such as traction, TENS, ultrasound, cryocuff and pulsed shortwave therapy to ease the sufferings of those acute and chronic pain patients.
5. Other Specialty Workshop
   As a further development of the Orthopaedic Centre, we are planning to have our own Orthotic and Prosthetic service.
6. Multi-purpose Room

We have a focused team of experienced surgeons, nurses, physicians and physiotherapist who work together to evaluate and treat. We specialize in a wide spectrum of Orthopaedic cases from total hip and knee replacement surgery, sports injuries, fracture care, post-surgical rehabilitation, to conservative care of neck and low back pain and post stroke patients. The centre offers the most up to date and scientific rehabilitation services.

Dr. Ngai Yiu Hing William
Specialist in Orthopaedics and Traumatology
(Thanks Mr. Wong Chung Lun for information)

Hosptial activities 醫院活動

The Chinese custom of "Lai See" distribution brought us a healthy and lucky year of the Tiger.

St. Paul's Hospital Spring Dinner 2010

The Hospital Spring Dinner was held at Maxim's Palace Chinese Restaurant in Tai Koo Shing on 22nd and 23rd February, 2010. All members of St. Paul's family enjoyed the lively evenings and delicious meal. Let's share the funs with our colleagues in the following photos.

Introduction of new faces
員工動態

Thank you my Lord to let me join St Paul's Hospital as Material Management Manager in October 2009 and I'm very glad to be one of the member in St Paul's Big Family. My name is Connie Lam. I obtained my Master Degree in International Business Management from City University of Hong Kong in 1998 and my 2nd Master in Strategic Purchasing & Supply Management from The Hong Kong Polytechnic University in 2005 and also Chartered Purchasing & Supply qualification. I devoted my career in Purchasing & Supply Chain Management in Innovation & Technology, Semiconductor as well as Computer industries. I hope my working experience enable me to contribute to St Paul's achievement. I like travel, tennis, shopping, reading & bible study. Let's chat & meet!

聖保祿謝主彌撒

為感謝上主於過去一年對我們的恩寵照顧及祈求上主來年繼續降福我們，本院於2010年2月9日(星期二)下午3時30分在基督君王小堂舉行謝主彌撒。部門均安排代表出席參與並於彌撒後在職員餐廳薄備小食款待來賓。

Optical Coherence Tomography (OCT) – The In Vivo Optical Biopsy

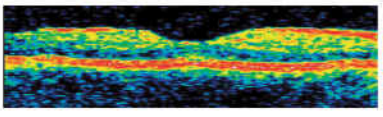
OCT is an imaging method that uses light to scan the retina and optic disc. It can be performed on undilated pupils as small as 3.0mm in diameter. OCT imaging is similar to ultrasound, but instead of sound the OCT uses light. A superluminescent diode projects a near-infrared light beam at 820nm on the retina. The instrument contains an optical interferometer that detects reflection delay and backscattering of light and compares it with a reference reflection from a built-in mirror. Both the reflective delay and the intensity of reflection and backscattering are reconstructed into a cross-section image of the retina anatomy. Images can be obtained with a resolution of 10 um axially from the surface of the retina to the choroid and 20um transversely across the retina.

The OCT is a non-invasive, non-contact optical biopsy of the retina with a resolution so fine that it is sometimes called an in vivo histological section of tissue. This technique is limited to imaging 1 to 2 mm below the surface in tissue, because at greater depths the proportion of light that escapes without scattering is vanishingly small.

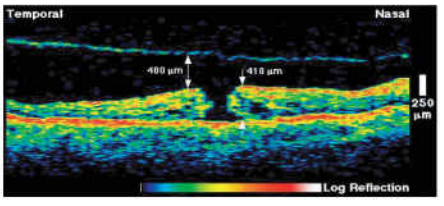
It is effectively "optical ultrasound", imaging reflection from within tissue to provide cross-sectional images, but with much finer resolution than ultrasonagraphy. It also provides much finer resolution than MRI. OCT has also advantage over confocal microscopy in that it provides better penetration. Other advantages of OCT are: 1. in vivo sub-surface image at near-microscopic resolution, 2. instant direct imaging, 3. no penetration of sample (eye) is required and 4. no ionizing radiation.

OCT is now available in our St. Paul's Eye Centre.

Dr. Ho Kai Kit
Specialist in Ophthalmology
Consultant Ophthalmologist
St. Paul's Hospital



OCT image showing a normal macula



OCT image showing a macular hole

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