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The APHRS Summit 2019 was held in Jakarta on 23rd -24th February 2019, hosted by the Asia Pacific Heart Rhythm Society and organized by the Indonesia Heart Rhythm Society.

The summit was an important activity of APHRS where the key board members came together to meet and discuss on the future activities of APHRS. The subcommittee chairpersons of the various subcommittees of APHRS were also discussing on their plans for their current and future activities. At the same time during the summit, the device and pharmaceutical companies were also having private meetings with the key members of the APHRS board to discuss how together we get to improve electrophysiology development in the Asia Pacific region.

During the board meeting, there was also a full day arrhythmia symposium delivered by the APHRS Board Members and Indonesian EP specialists which consists of review of the latest key topics in EP and device therapy. Topics such as Atrial Fibrillation, SVT, VT, Bradycardia, and Device Therapy were covered. The summit was well-received with more than 760 participants (2 from Australia, 1 from Vietnam, 2 from Malaysia and 755 from all over Indonesia).
**The Scientific Symposium**

Dr. Dicky A. Hanafy

Left to Right: Prof. Yoga Yuniadi, Dr. Myung-Jin Cha and Prof. Chen-Chuan Cheng

**Opening Ceremony**

Opening speech from Prof. Chu-Pak Lau, President of the APHRS (2019)

A “Gong” beaten by Prof. Chu-Pak Lau as a sign of symposium opening

The Angklung (Indonesian traditional bamboo tube musical instrument) played by all attendees during the opening ceremony

Attendees at the symposium

**Participants’ Evaluation**

- **Participants’ impression on venue of symposium**
  - Good: 45%
  - Very Good: 55%

- **Participants’ impression on symposium in general**
  - Good: 60%
  - Very Good: 40%

- **Participants’ willingness to recommend the meeting in the future**
  - Yes: 100%
  - Maybe: 0%

**Professionals Present**

- Prof. Shih-Ann Chen
- Prof. Young-Hoon Kim
- Dr. Tachapong Ngarmukos
The use of warfarin in Asians with non-valvular atrial fibrillation (NVAF)

Atrial fibrillation (AF) is the most common cardiac arrhythmia with a global prevalence of 2% to 3%, which significantly increases the risk of embolic stroke and death. Oral anticoagulants, like vitamin K antagonists (e.g., warfarin), is a commonly used anticoagulant to prevent possible thromboembolic events in AF patients. Previous studies indicated that warfarin significantly reduces the risk of embolic stroke and mortality, while it also doubles the risk of intracranial hemorrhage at the same time. Furthermore, Asian patients with non-valvular AF (NVAF) are at an unacceptably higher risk of intracranial hemorrhage (ICH) while taking warfarin, even when the international normalized ratio (INR) is ideally maintained in the target range of 2 to 3. The reasons why Asian patients are more prone to warfarin related major bleeding compared to non-Asians was partially explained by the variations of genetic polymorphisms for VKA metabolism, multiple drug-food interaction, and use of herbal medicine among Asians.

The use of direct oral anticoagulants (DOACs) in Asians with NVAF

Unlike warfarin, direct oral anticoagulants (DOACs)—namely dabigatran, rivaroxaban, apixaban, and edoxaban—do not require routine monitoring and have fewer potential drug–drug or drug–food interactions. Furthermore, several large trials have indicated that DOACs have non-inferior or improved efficacy compared with warfarin and are safer alternatives to warfarin. The safety profiles showed that most DOACs caused a lower risk of ICH and major bleeding, but an increased risk of gastrointestinal bleeding compared with warfarin. Of particular note, Asians may receive greater benefit from DOACs compared with non-Asians as they carry a higher risk of ICH and have a greater difficulty maintaining the therapeutic range of INR when taking warfarin. The post-hoc analyses from four pivotal NOACs trials indicated that DOACs may be more effective and safer in Asians than in non-Asians.

The use of direct oral anticoagulants (DOACs) among NVAF Patients in Taiwan’s real-world practice

The National Health Insurance (NHI) system in Taiwan is a mandatory universal health insurance program which provides comprehensive medical care coverage to all Taiwanese. As of 2016, there were > 23 million enrollees and a > 99% coverage rate of the entire population. DOAC is covered by NHI for NVAF patients with CHA2DS2-VASc ≥ 2 and it is estimated that at least 50,000 patients have the experience of DOACs in Taiwan from June 01, 2012 to December 31, 2016 (Figure 1). The result indicated that three DOACs (apixaban, rivaroxaba, and dabigatran) were all associated with lower risks of thromboembolism and major bleeding compared with warfarin, and the phase III results of DOACs trials in Asian subgroup all translated well into Taiwan’s real world practice (Figure 2-4). Recent study also demonstrated that after the introduction of DOACs in Taiwan, the...
It is the largest Asian-specific cohort taking DOACs around the world.

The phase III result of ARISTOTLE (East Asia) ‘translates’ well into Taiwan’s real-world practice.

The Taiwan Cohort
- **Apixaban** N = 5,843
- **Warfarin** N = 19,375

Mean CHA$_2$DS$_2$-VASc = 3.3

**Incidence rate (per 100 PYs)**
- IS/SE: 2.52 (Apixaban) vs. 3.55 (Warfarin), *P < 0.05*
- AMI: 0.45 (Apixaban) vs. 0.61 (Warfarin), *P < 0.05*
- ICH: 0.52 (Apixaban) vs. 0.61 (Warfarin), *P < 0.05*
- ALL MAJOR BLEEDING: 1.77 (Apixaban) vs. 2.12 (Warfarin), *P < 0.05*

The phase III result of ROCKET-AF (East Asia) ‘translates’ well into Taiwan’s real-world practice.

The Taiwan Cohort
- **Rivaroxaban** N = 27,777
- **Warfarin** N = 19,375

Mean CHA$_2$DS$_2$-VASc = 3.9

**Incidence rate (per 100 PYs)**
- IS/SE: 2.63 (Rivaroxaban) vs. 3.38 (Warfarin), *P < 0.05*
- AMI: 0.99 (Rivaroxaban) vs. 1.00 (Warfarin), *P < 0.05*
- ICH: 0.59 (Rivaroxaban) vs. 1.14 (Warfarin), *P < 0.05*
- ALL MAJOR BLEEDING: 2.46 (Rivaroxaban) vs. 5.14 (Warfarin), *P < 0.05*

The phase III result of RE-LY (Asia) ‘translates’ well into Taiwan’s real-world practice.

The Taiwan Cohort
- **Dabigatran** N = 20,079
- **Warfarin** N = 19,375

Mean CHA$_2$DS$_2$-VASc = 3.7

**Incidence rate (per 100 PYs)**
- IS/SE: 2.26 (Dabigatran) vs. 3.55 (Warfarin), *P < 0.05*
- AMI: 0.52 (Dabigatran) vs. 0.61 (Warfarin), *P < 0.05*
- ICH: 0.76 (Dabigatran) vs. 1.41 (Warfarin), *P < 0.05*
- ALL MAJOR BLEEDING: 1.52 (Dabigatran) vs. 3.25 (Warfarin), *P < 0.05*

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**Figure 1**
The population of Taiwanese with non-valvular atrial fibrillation (NVAF) taking direct oral anticoagulants (DOACs) from June 01, 2012 to December 31, 2016.

**Figure 2**
The phase III results of DOACs trial (apixaban) in Asian subgroup translated well into Taiwan’s real-world practice.

**Figure 3**
The phase III results of DOACs trial (rivaroxaban) in Asian subgroup translated well into Taiwan’s real-world practice.

**Figure 4**
The phase III results of DOACs trial (dabigatran) in Asian subgroup translated well into Taiwan’s real-world practice.

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Yi-Hsin Chan, Lai-Chu See and Chi-Tai Kuo. JAHA. 2018;7:e008150


Wong et al., Stroke. 2014;45:1739-1747


Goto et al., Am Heart J 2014;168:303-9


Yi-Hsin Chan, Lai-Chu See and Chi-Tai Kuo. JAHA. 2018;7:e008150
The use of direct oral anticoagulants (DOAC) in newly diagnosed patients with NVAF significantly increased from 13.6% to 35.6%. A lower risk of ischemic stroke and mortality was temporally associated with the increasing prescription rates of OACs.\textsuperscript{15}

There are some interesting phenomenons for the DOAC prescription in Taiwan. We had observed a high prevalence of low-dose DOACs prescription among the large Asian cohort, with an approximately 62%, 88%, and 94% of patients taking low-dose apixaban (2.5 mg twice daily), rivaroxaban (15/10 mg once daily), and dabigatran (110 mg twice daily), respectively. The smaller body size of Asians as compared with non-Asians, fear of the iatrogenic bleeding events caused by DOACs, and multiple underlying comorbidities including chronic kidney diseases (CKD) in Asian patients render physicians reluctant to prescribe standard-dose DOACs for their patients. Another case is for the rivaroxaban in Taiwan's real-world practice. Taiwan and Japan are the only two countries where low-dose rivaroxaban (15/10 mg once daily according to the J-ROCKET AF trial) has been approved for stroke prevention in NVAF patients. The 94% prescription of rivaroxaban 15/10 mg indicated that most physicians chose to follow the regimen of J-ROCKET AF (15/10 mg) rather than the ROCKET AF (20/15 mg) in Taiwan's real-world practice. Interesting, our results indicated that the J-ROCKET AF (15/10 mg) regimen was associated with lower risks of thromboembolism and major bleeding compared with warfarin (INR target of 2 to 3) in Taiwan's real-world practice (Figure 5).\textsuperscript{16}

\textbf{The concern of renal safety among NVAF Patients taking oral anticoagulants}

Another issue is the renal safety among patient with NVAF taking OAC. It is estimated that as high as 20.5% of all patients taking warfarin have experienced at least one episode of warfarin-related nephropathy (WRN) during their treatment course, with most cases occurring within 1 year after the initiation of treatment. The mechanisms underlying WRN are complicated and multifactorial but supra-therapeutic doses of warfarin with an INR of > 3.0 may result in glomerular hemorrhage and consequent tubular injury caused by obstructive tubular RBC casts and heme-induced free radical injury. Warfarin also facilitates renal vascular calcification and the consequent decline in renal function via inhibition of the activation of matrix G1a protein and growth arrest specific gene 6 (GAS-6).\textsuperscript{17} Whether the DOACs with its anticoagulant mechanism independent from the Vitamin K related cascade, is associated with a lower risk of acute kidney injury (AKI) in patients with NVAF remains unknown. Our previous study indicated that use of warfarin carried a significantly higher annual risk of AKI than that of dabigatran especially for those with high CHA2DS2-VASc score (Figure 6).\textsuperscript{18} We also evaluated the risk of AKI in NVAF Asians taking other DOACs including apixaban, dabigatran, rivaroxaban as compared with warfarin. The results also confirmed that three DOACs were all associated with a significantly lower risk of AKI compared with warfarin for both CKD-free and CKD cohorts. The annual incidence of AKI for all NOACs and warfarin increased gradually as the increment of CHA2DS2-VASc for both CKD-free and CKD cohorts after propensity score weighting.\textsuperscript{19} Our results were supported by previous study showing that DAOCs were associated with lower risks of several renal outcomes including more than 30% decline of eGFR, doubling of serum creatinine, and the risk of AKI.\textsuperscript{20}

\textbf{Several concurrent medications may increase the risk of major bleeding among NVAF Patients taking DOACs}

Polypharmacy among patients taking DOAC may increase plasma levels and the risk of bleeding. Particular attention has been paid to medications such as CYP3A4 inhibitors or P-glycoprotein competitors that share common metabolic pathways with NOACs. However, current knowledge of drug-drug interactions associated with NOACs mainly comes from limited pharmacokinetic measurement, whereas the evidence of large clinical data was lacking. This nationwide population-based cohort study in Taiwan tested the concurrent use of 12 commonly prescribed medications that share
The effectiveness/safety of Japan-dose rivaroxaban 15/10 mg in Taiwan’s real world practice (after baseline co-morbidities adjustment)

Figure 5
The J-ROCKET AF (15/10 mg once daily) regimen was associated with lower risks of thromboembolism and major bleeding compared with warfarin (INR target of 2 to 3) in Taiwan’s real-world practice

Dabigatran showed a lower risk of acute kidney injury than warfarin for high CHA2DS2-VASc score in CKD(-) and CKD(+) cohorts

Figure 6
Dabigatran showed a lower risk of acute kidney injury than warfarin for high CHA2DS2-VASc score in chronic kidney disease free (CKD(-)) and CKD(+) cohorts in Taiwan’s real-world practice
metabolic pathways with DOACs, which demonstrated that concurrent use of amiodarone, fluconazole, rifampin, and phenytoin was associated with increased risk of major bleeding in patients taking DOAC, whereas some combinations not recommended by the ESC guidelines were not associated with major bleeding.\textsuperscript{21}

**Conclusion**

In conclusion, consistent with the RCT evidence of the four DOACs in the post-hoc analysis of Asian subgroups, DOACs appear to preserve the superior efficacy and safety profile over warfarin in Taiwan’s real-world practice. DOACs may be a safer alternative to warfarin in Asians with NVAF in terms of the risk of anticoagulant-related AKI. Several concurrent medications may be associated with increased risk of major bleeding in Asians with NVAF taking DOAC. Further prospective and randomized controlled validation of our results in a future study is warranted.

**Concurrent use of amiodarone, fluconazole, rifampin, and phenytoin was associated with increased risk of major bleeding in patients taking DOACs**

![Graph showing risk of major bleeding with concurrent use of medications](image)

*Figure 7* Concurrent use of amiodarone, fluconazole, rifampin, and phenytoin was associated with increased risk of major bleeding in patients taking DOACs in Taiwan’s real-world practice

**References**


5. Gaikwad T, Ghosh K, Shetty S. Vkorc1 and cyp2c9 genotype distribution in Asian countries. Thrombosis research. 2014;134:537-544

22. Quoc Khanh Pham (Vietnam), APHRS Country Representative (2018)
I am a senior cardiac physiologist at Nelson Hospital in the South Island of New Zealand, in charge of the pacemaker/ICD service in the Nelson/Marlborough district. Our relatively small ICD population (160) comes from the city of Nelson, neighbouring town of Blenheim and surrounding rural areas. We see them annually in hospital clinics as well as most having home monitoring.

It was one of our more unstable patients, with a history of working in health initiatives in the UK, who helped organise our inaugural ICD Support Group meeting and coined the name “Shock Absorbers”. It was invaluable to have an “ICD Wearer” (as he calls himself) on the team so that the meeting could involve the wishes and needs from a patient perspective. It was a well attended meeting but half of the ICD population had to drive several hundred kilometres to attend as the two main centres are separated by hills and a 2-hour drive.

The biggest city in the South Island, Christchurch, has a long established and well-run support group that includes some great speakers and input from their team of EP docs and physiologists. Some people in our region with ICDs regularly travel to Christchurch from Blenheim and Nelson to attend their meetings but it is a 4-5hr drive for our patients to attend.

After our inaugural meeting, the wife of an ex-ICD patient, who has since had cardiac transplant, suggested we set up a Facebook group for those with ICDs and their spouses, whanau (family), parents of young people with ICDS and other loved ones. I then set up the Shock Absorbers Facebook group.

Social media is not for young people anymore and the younger ones are often horrified that their parents and grandparents want to “friend” them on Facebook. Older people are much more savvy on computers now and most of our ICD people, even the older ones, are already on Facebook.

The “Shock Absorbers” Facebook group is a closed group, meaning that the group admin has to approve any new members and only group members can read or post on the page, thereby giving a secure environment to share health issues that you may not want to share with your regular Facebook friends and family.

I co-administrate the group with Adele Clayton who is both an ICD patient and Arrhythmia Nurse Specialist at North Shore Hospital (Auckland NZ).

“Shock Absorbers” was started as a support group for Nelson/ Marlborough people but has extended to other parts of New Zealand, and even Australia, the USA and UK. The group now has 250 members. The members also include health professionals working with ICDs.

What does it achieve?
Many will read but not post, but we have a few who are regular posters and activity has increased as new members join and tell their story and ask questions. If anyone has a specific problem, they will ask on the Facebook page and will get answers and comment from other ICD wearers, family, or one of the techs/ nurses/ cardiologists on the site.

As an ICD tech, I try to answer the questions in a general and non-specific way so as to educate others with a similar problem, or suggest they talk to their ICD clinic for more individualised advice.

I also try to keep the site alive with educational and topical posts that are relevant to our ICD group.

The other advantage of a social media group is that it allows people with ICDs to get around the hospital confidentiality and communicate with each other. If they don’t want to share on the group page, they can private message each other or arrange to meet in real life.

It is a real advantage that it brings people together who are geographically separated, even within our own large catchment of Nelson/ Marlborough.

We have the Facebook link if you would like pass it on to your ICD patients.

https://www.facebook.com/groups/ShockAbsorbers/
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APHRS 2019
Highlights
Keynote Speakers

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24-27 October 2019
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Centara Grand & Bangkok Convention Centre
at CentralWorld, Bangkok, Thailand

Keynote speech by
Dr. Koonlawee Nademanee

Stroke Prevention: State of the Art by
Dr. Gregory YH Lip

Morning with
Dr. Sonny Jackman
AVNRT

Afternoon with
Dr. David Hayes
Device Troubleshooting

How to have fun implanting an LV lead by
Dr. Seth Worley

Registration Opens in March 2019
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