AF Epidemiology in Hong Kong?

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Division of Cardiology
The University of Hong Kong
The oldest AF description

- An ancient disease
- First described in Chinese Medical text at 2600 BC, *Huang Dee Nai-Ching* <黃帝內經>
AF is the most commonest sustained cardiac arrhythmia

- Caucasian: ~2%
- African Americans: ~1.5%

Asian countries:
- Indian: 0.1%
- Thai: 0.4%
- Korean: 0.7%
- Chinese: 0.7–1.1%
- Japanese: 1.6%

Paradoxically, such ethnic differences cannot be explained by the differences in the risk profiles, as many traditional risk factors such as HT contributing to AF.

Lau CP, Siu CW. JCE 2012

50,000-70,000 AF patients in HK!
AF and Ischemic stroke in HK

- 7,184,000 residents
- ~70,000 AF patients (1% population)
- ~12,000 strokes/year (0.17%/year)
- ~3,000 AF related stroke/year (0.04%/year)
- ~2,000 AF related stroke can be prevented if identified early
Major practice shift towards greater focus on **identification of ‘truly low-risk’ AF patients** instead of trying to focus on identifying **‘high-risk’ patients**.
Beliefs:

1. CHA2D2-VASC and HAS-BLED score have not been validated in Chinese population

2. Chinese might have a lower ischemic stroke risk

2. Chinese might have a higher ICH risk

1. Aspirin might effectively reduce ischemic stroke but of lower ICH risk.
Hong Kong Atrial Fibrillation Registry

Observational Cohort Study
- Study protocol was approved by the local Institutional Review Board
- From July 1997 to December 2011
- Queen Mary Hospital

10,195 Chinese patients with a diagnosis of AF were identified from CMS.

- Exclusion:
  - Significant valvular heart disease
  - Incomplete clinical and/or follow-up data.

- The primary and secondary endpoints were hospital admission with stroke and ICH during the follow-up period, respectively.

Siu CW *Heart Rhythm* 2014
Observational Cohort Study

- **Mean age:** 76.9±12.5 years
- **Male : Female:** 48% vs. 52%
- **Hypertension:** 54.7%
- **Diabetes Mellitus:** 22.0%
- **Heart failure:** 23.1%
- **Coronary artery disease:** 18.2%
- **Prior Stroke:** 23.1%
- **Mean CHA2DS2-VASC:** 2.1±1.4

Siu CW *Heart Rhythm* 2014
How can we stratify ischemic stroke risk of Chinese AF Patients?

CHADS2 or CHA2DS2-VASC?

Siu CW *Heart Rhythm* 2014
Chinese AF patients are at comparable or even higher risk of ischemic stroke compared to Caucasian.
Global Trends in Incidental of CVA

Figure 1. Age-standardized death rates per 100,000 for cerebrovascular disease in 2004.

Kitagawa Y. Cir J 2014
Geographic Distribution of Relative Mortality From Stroke and Ischemic Heart Disease

- Burden of stroke > IHD in Asia
- Stroke mortality and morbidity in Asian > White European patients

Kim A S. Circulation 2011
Using the CHA₂DS₂-VASc Score for Refining Stroke Risk Stratification in ‘Low-Risk’ Asian Patients With Atrial Fibrillation

Tze-Fan Chao, MD, Chia-Jen Liu, MD, Kang-Ling Wang, MD, Yenn-Jiang Lin, MD, Shih-Lin Chang, MD, Li-Wei Lo, MD, Yu-Feng Hu, MD, Ta-Chuan Tuan, MD, Tseng-Ji Chen, MD, Gregory Y.H. Lip, MD, Shih-Ann Chen, MD

NHIRO cohort (1996-2011)
- More than 23 million enrollees
- AF patients older than 20 years (n=354,649)
- AF patients without use of any anti-platelet or anti-coagulant agent (n=186,570)

![Graphs showing CHA₂DS₂-VASc score and ATRA score with comparison between 1-year and 15-year follow-up](image)

P value < 0.0001 between 2 curves

Chao TF JACC 2014
Ischemic Stroke risk in AF: Chinese >> Caucasian?

Possible explanations

• Omission of etiological factors prevalent in Chinese in CHA2DS2-VASC
  • Age 55-64
  • Undiagnosed/undertreated HT
  • Hyperthyroidism

• High prevalence of intracranial atherosclerosis in Chinese
Refinement of Ischemic Stroke Risk in Patients with Atrial Fibrillation and CHA2DS2-VASc Score of 1

DUO HUANG, M.B.B.S.,* † LUO ANGUO, M.B.B.S.,*, † WEN-SHENG YUE, B.Sc., *, † LIXUE YIN, M.D., † HUNG-FAT TSE, M.D., Ph.D.,*, † and CHUNG-WAH SIU, M.D. *

From the *Cardiology Division, Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong, China; †Affiliated Hospital of North Sichuan Medical College & Medical Imaging Key Laboratory, Nanchong, Sichuan Province, China; and #Department of Echocardiography, Sichuan Academy of Medical Sciences & Sichuan Provinical People’s Hospital, Chendu, China

Hypertension
Age=65-74 years
Female
CHA2DS2-VASc =1

0 1 2 3 4 5 6 7 8 9 10 11 12 13
Warfarin and Aspirin reduce ischemic stroke in Chinese AF patients of similar magnitude as in Caucasians.
Warfarin and Aspirin increase the ICH risk of greater magnitude than in Caucasians

Friberg Y. EHJ 2012
Siu CW Heart Rhythm 2014
Net clinical Benefit/Harm of Warfarin in Chinese AF patients
(avoided ischemic strokes with aspirin per year minus excess intracranial hemorrhage with warfarin per year with a weight of 1.5)

<table>
<thead>
<tr>
<th>HAS-BLED</th>
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NNT/year

Siu CW Heart Rhythm 2014
Net Clinical Benefit of Warfarin Therapy in Elderly Chinese Patients With Atrial Fibrillation

Chung-Wah Siu, MD; Hung-Fat Tse, MD, PhD

**CHADS²-VASc: 2-3**
- Warfarin therapy
- No therapy
- HR: 0.60, 95%CI: 0.42-0.85
- Log-rank: 8.05, p=0.005

**CHADS²-VASc: 4**
- Warfarin therapy
- No therapy
- HR: 0.64, 95%CI: 0.45-0.91
- Log-rank: 6.2, p=0.01

**CHADS²-VASc: 5**
- Warfarin therapy
- No therapy
- HR: 0.58, 95%CI: 0.39-0.87
- Log-rank: 6.9, p=0.008

**CHADS²-VASc: 6**
- Warfarin therapy
- No therapy
- HR: 0.57, 95%CI: 0.38-0.86
- Log-rank: 7.25, p=0.0071

Siu CW *Circulation (AEP)* 2014
1/12 to 1/7 80+ year-old Elderly Chinese with AF will develop a stroke every year!

Annual risk of ischemic stroke (%) vs. CHA₂DS₂-VASC score

- No therapy
- Warfarin

Siu CW Circulation (AEP) 2014
Annual ICH risk among 80+ year-old Elderly Chinese with AF

Siu CW Circulation (AEP) 2014
Net clinical Benefit/Harm of Warfarin in Very Elderly (80+ years) Chinese AF patients

(avoided ischemic strokes with aspirin per year minus excess intracranial hemorrhage with warfarin per year with a weight of 1.5)

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Siu CW Circulation (AEP) 2014
Predictive Value of the HAS-BLED Score for the Risk of Recurrent Intracranial Hemorrhage After First Spontaneous Intracranial Hemorrhage

Koon-Ho Chan¹, Gilberto Ka-Kit Leung², Kui-Kai Lau¹, Shasha Liu³, Wai-Man Lui², Chu Pak Lau³, Hung-Fat Tse³, Jenny Kan-Suen Pu², Chung-Wah Siu³

HAS-BLED score

Annual risk of intracranial hemorrhage (%)
SA Me-TT2R2 Score, Time in Therapeutic Range, and Outcomes in Anticoagulated Patients with Atrial Fibrillation

Pilar Gallego, MD, PhD,a,b Vanessa Roldán, MD, PhD,b Francisco Marin, MD, PhD,c José Gálvez, (Student), b Mariano Valdés, MD, PhD, c Vicente Vicente, MD, PhD, b Gregory Y.H. Lip, MDa

| S | Sex (female) | 1 |
| A | Age (<60 years) | 1 |
| M | Medical history (HT, DM, CAD, PAD, CHF, previous stroke, pulmonary disease, hepatic or renal disease.) | 1 |
| T | Treatment (rhythm control strategy) | 1 |
| T | Tobacco use (within 2 years) | 2 |
| R | Race (non-Caucasian) | 2 |

SA Me-TT2R2
TTR subgroup analysis: mean TTR by country

Wallentin L. Lancet 2010
Impact of TTR on ischemic stroke in Chinese AF patients

- N=1,428
- CHA2DS2-VASC≥2
- Mean CHA2DS2-VASC: 2.3
- Median TTR: 38.8%
  - 1st quartile: <17.9%
  - 2nd quartile: 17.9%-38.8%
  - 3rd quartile: 38.8% to 56.2%
  - 4th quartile: >56.2%

Mean FU: 3.0 years

Siu CW. Stroke (2015)
Impact of TTR on ischemic stroke risk in Chinese AF patients

Annual Incidence of ischemic stroke (%)

- No therapy: 10.38%
- Aspirin: 7.95%
- Q1: 7.34%
- Q2: 5.95%
- Q3: 4.39%
- Q4: 3.10%
- Dabigatran: 2.24%
- Overall: 7.74%

Siu CW. Stroke (2015)
Impact of TTR on ischemic stroke risk in Chinese AF patients

No therapy | Aspirin | Q1 | Q2 | Q3 | Q4 | Dabigatran | Overall
---|---|---|---|---|---|---|---
Before 2008 | 19.9 | 9.69 | 9.33 | 7.63 | 7.08 | 8.08 | 8.92
After 2008 | 9.47 | 5.67 | 6.58 | 3.97 | 2.62 | 2.24 | 7.34

Siu CW. *Stroke* (2015)
Impact of TTR on ICH risk in Chinese AF patients

Siu CW. Stroke (2015)
Impact of TTR on ICH risk in Chinese AF patients

Before 2008
After 2008

Annual Incidence of Intracranial hemorrhage (%)

No therapy 0.89 0.51
Aspirin 0.83 0.80
Q1 1.89 1.31
Q2 1.62 0.76
Q3 1.10 0.79
Q4 1.14 0.67
Dabigatran 0.32
Overall 0.87 0.72

Siu CW. Stroke (2015)
Impact of TTR on ischemic stroke and ICH risk in Chinese AF patients

Siu CW. Stroke (2015)
101/467 (21%) Chinese AF patients put on Dabigatran discontinued the Therapy (16 months)

- Dyspepsia: 30.7%
- Minor bleeding: 8.9%
- Major GI bleeding: 7.9%
- Intracranial hemorrhage: 1.0%
- Other side effects: 13.9%
- Drug-drug interaction: 3.0%
- Worsening renal function: 3.0%
- Other medical reasons: 4%
- Patients' concerns: 11.9%
- Financial concerns: 10.9%
- Physicians' choice: 8.9%
- Monitoring concerns: 4.0%
- Dosing frequency: 5.9%
- Unknown: 1.0%

Siu CW. PLOS ONE (2014)
Management of Dyspepsia Symptoms on Dabigatran During RELY-ABLE: Long-term Follow-up Study After RE-LY

R Nieuwlaat, McMaster University, Hamilton Health Sciences
Key conclusions

- Chinese patients with AF are at high risk of ischemic stroke.
- CHADS$_2$ based risk stratification scheme with additional risk factors appears to be the generally agreeable approach.
- Long-term anticoagulation should be considered for AF patients with annual risk >1.3%; and is recommended for those with risk >2.2%.
- For patients whom long-term anticoagulation is indicated, NOAC is always preferable to warfarin.
## Preliminary Program

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*Updated as of 14 August 2014*
Use of antithrombotic therapy in Garfield Registry (n=10,607).

1/4 to 1/3 AF patients were treated with aspirin.

Advantages of Aspirin over Warfarin

- Easy to use (Fixed dose)
- No laboratory monitoring required
  - Less clinic visit
- Less drug-drug / drug-food interaction
- Perceived lower Major bleeding (ICH) risk
Efficacy of Aspirin in Stroke Prevention in AF

- Relative RR vs. Placebo or no Tx: 19% (95% CI: -1 to 35%)
- Absolute risk reduction primary: 0.8% /yr
- Absolute risk reduction secondary: 2.5% /yr
- NNT Primary prevention: 125
- NNT Secondary prevention: 40

Multi-center study: 15 sites

Main inclusion: 1,330 NVAF pts

Aspirin: 325mg daily

Relative Risk Reduction of Stroke:
Group I: 94% ($p<0.001$)
Group II: 8% ($p=0.75$)
Overall Reduction: 42% ($p=0.02$)

The study was prematurely terminated because of superiority of Warfarin over Aspirin

Heterogeneity in Aspirin effects:
- Age <75 years >> Age >75
- HT > No HT

SPAF investigators. *Circulation* 1991

SPAF investigators. *J Stroke and Cerebrovascular Disease* 1993
Evaluation of risk stratification schemes for ischaemic stroke and bleeding in 182,678 patients with atrial fibrillation: the Swedish Atrial Fibrillation cohort study

Leif Friberg¹, Mårten Rosenqvist², and Gregory Y.H. Lip³*

Friberg L, ..Lip GY et al EHJ 2012;
### Net Benefit of Aspirin

**Ischemic stroke prevented + ICH induced**

<table>
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<th>CHA2DS2VASc</th>
<th>Stroke risk %/yr</th>
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<td>8</td>
<td>6.7%</td>
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Aspirin ↓19% Stroke

Aspirin 0.2-0.4% ICH

Annual risk of 2.0%

Annual risk of 1.8%

Annual risk of 2.2%