CSANZ Clinical Update: Atrial Fibrillation

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Disclosures 2016

- **Advisory Board:** Biosense-Webster, Medtronic, St Jude Medical, Boston Scientific, CathRx

- **Lecture Fees and Research Funding:** Biosense-Webster, Medtronic, Boston Scientific, Biotronik, Sorin and St Jude Medical
Projected prevalence of AF

Projected number of persons with AF (millions)

Year


5.1 5.6 6.1 6.8 7.5 8.4 9.4 10.3 11.1 11.7 12.1

5.1 5.9 6.7 7.7 8.9 10.2 11.7 13.1 14.3 15.2 15.9

Miyasaka Y et al., Circulation 2006
Change in global prevalence of AF

Tse HF et al., Heart Rhythm 2013
AF in the indigenous Australian population

Wong CX et al., BMJ Open 2014
Hospitalizations for AF

Wong CX et al. Archives of Internal Medicine 2012
Health care expenditure related to AF

Almost 1% of the NHS expenditure per year (£460 million)

Stewart S, Heart 2004
AF in Australia

- Estimated prevalence 1.1%
- Contributes to 6,300 extra strokes per year
- > 45,000 hospitalizations
- Estimated cost: AUD 1.25 billion per year
  - Direct medical costs
  - Long term care
  - Lost productive output
  - ‘Conservative’ estimates

*The Economic Costs of AF in Australia – National Stroke Foundation June 2010*
3 Pillars of AF management

- Anticoagulation
- Rate Control
- Rhythm Control
Stroke Prevention
AF presentations over 12 months

- All admitted/non-admitted ICD-10 code I48 over 12 months (n=858; 605 unique)
- Excluded
  - Atrial flutter (elective or acute treatment)
  - Elective procedures for AF (ablation, CV, TOE, PPM)
  - Renal failure requiring dialysis within the capture period
- Final sample (n=356) – pts presenting to the ED for acute treatment of AF

Followed for 1.4±0.3 years

Rangnekar G, CSANZ 2012
Anticoagulation

- 254 had complete drug and risk factor data
- Majority of AF pts are under-OAC, which was marginally improved upon hospital discharge
- ?reasons
  - Guideline non-adherence,
  - Lack of willingness to initiate chronic therapy in acute setting
  - Contra-indications to OAC

Rangnekar G, CSANZ 2012
Readmission for AF within 12 months

- 356 index presentations for AF
- 482 all-cause re-admissions (in 177 pts) within 1.4±0.3 yrs

26% of all-cause re-admissions were for AF

10.2% mortality
Prevention of thromboembolism

CHA$_2$DS$_2$-VASc Risk Score

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure/LV dysfunction</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Age $\geq$75</td>
<td>2</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
</tr>
<tr>
<td>Stroke/TIA/thrombo-embolism</td>
<td>2</td>
</tr>
<tr>
<td>Vascular disease$^a$</td>
<td>1</td>
</tr>
<tr>
<td>Age 65–74</td>
<td>1</td>
</tr>
<tr>
<td>Sex category (i.e. female sex)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Maximum score</strong></td>
<td><strong>9</strong></td>
</tr>
</tbody>
</table>

ESC Guidelines for Management of AF
### CHA$_2$DS$_2$-VASc risk score

<table>
<thead>
<tr>
<th>Risk category</th>
<th>CHA$_2$DS$_2$-VASc score</th>
<th>Recommended antithrombotic therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>One ‘major’ risk factor or $\geq 2$ ‘clinically relevant non-major’ risk factors</td>
<td>$\geq 2$</td>
<td>OAC$^a$</td>
</tr>
<tr>
<td>One ‘clinically relevant non-major’ risk factor</td>
<td>1</td>
<td>Either OAC$^a$ or aspirin 75–325 mg daily. Preferred: OAC rather than aspirin.</td>
</tr>
<tr>
<td>No risk factors</td>
<td>0</td>
<td>Either aspirin 75–325 mg daily or no antithrombotic therapy. Preferred: no antithrombotic therapy rather than aspirin.</td>
</tr>
</tbody>
</table>
Risk of Thromboembolism on the basis of duration of AF

Ganesan AN et al. EHJ (In Press)

<table>
<thead>
<tr>
<th>Study name</th>
<th>Hazard ratio</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTIVE A/AVEROES</td>
<td>1.658</td>
<td>1.316</td>
<td>2.089</td>
<td>0.000</td>
</tr>
<tr>
<td>ROCKET-AF</td>
<td>1.220</td>
<td>1.060</td>
<td>1.403</td>
<td>0.006</td>
</tr>
<tr>
<td>ARISTOTLE</td>
<td>1.429</td>
<td>1.072</td>
<td>1.904</td>
<td>0.015</td>
</tr>
<tr>
<td>GISSI-AF</td>
<td>2.141</td>
<td>0.677</td>
<td>6.774</td>
<td>0.195</td>
</tr>
<tr>
<td>Euro Heart Survey</td>
<td>1.538</td>
<td>0.595</td>
<td>3.980</td>
<td>0.374</td>
</tr>
<tr>
<td>SPORTIF</td>
<td>1.870</td>
<td>1.041</td>
<td>3.359</td>
<td>0.036</td>
</tr>
<tr>
<td>Active W</td>
<td>1.064</td>
<td>0.714</td>
<td>1.586</td>
<td>0.761</td>
</tr>
<tr>
<td><strong>OVERALL</strong></td>
<td><strong>1.384</strong></td>
<td><strong>1.191</strong></td>
<td><strong>1.608</strong></td>
<td><strong>0.000</strong></td>
</tr>
</tbody>
</table>

Statistics for each study:

Hazard ratio, Lower limit, Upper limit, p-Value

Hazard ratio and 95% CI

More risk in PAF | More risk in NPAF
Subclinical AF and stroke


Subclinical Atrial tachyarrhythmia present

Subclinical Atrial tachyarrhythmia absent

RR=2.49
95%CI 1.28-4.85
P=0.007

Follow up (Years)

Cumulative Hazard of stroke/systemic TE

# at Risk Year 0.5 1.0 1.5 2.0 2.5
+ 261 249 238 218 178 122
- 2319 2145 2070 1922 1556 1197
**ASSERT analysis: CHADS2 score stratified stroke risk with subclinical AF**

<table>
<thead>
<tr>
<th>CHADS₂ Score</th>
<th>No. of Patients</th>
<th>Subclinical Atrial Tachyarrhythmias between Enrollment and 3 Months</th>
<th>Hazard Ratio for Ischemic Stroke or Systemic Embolism with Subclinical Atrial Tachyarrhythmias (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of patients</td>
<td>no. of events</td>
<td>%/yr</td>
</tr>
<tr>
<td>1</td>
<td>600</td>
<td>68</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>1129</td>
<td>119</td>
<td>4</td>
</tr>
<tr>
<td>&gt;2</td>
<td>848</td>
<td>72</td>
<td>6</td>
</tr>
</tbody>
</table>

Cryptogenic stroke - detection of AF

Hazard ratio, 8.8 (95% CI, 3.5–22.2)
P<0.001 by log-rank test

Location of thrombus in AF: role of LAA closure

Mahjan R et al. Heart 2012
LAA occlusion: PROTECT-AF

- 700 non-valvular AF patients, 18 months f/up
- Randomized 2:1 design:
- Device group (WATCHMAN + 45 days warfarin) vs. Control group (long term warfarin)

Holmes DR et al. Lancet 2009
PROTECT AF: long-term results of LAA closure

Reddy VY et al. JAMA 2014
Rhythm control: AF Ablation
Exponential use of AF ablation

Kumar S et al. Europace 2013
Clinical success in paroxysmal AF
AAD vs ablation: maintenance of SR

logrank p < .0001

Outcomes of persistent AF ablation

Brooks AG et al. Heart Rhythm 2010
Approaches to Catheter Ablation for Persistent Atrial Fibrillation

Atul Verma, M.D., Chen-yang Jiang, M.D., Timothy R. Betts, M.D., M.B., Ch.B., Jian Chen, M.D., Isabel Deisenhofer, M.D., Roberto Mantovan, M.D., Ph.D., Laurent Macle, M.D., Carlos A. Morillo, M.D., Wilhelm Haverkamp, M.D., Ph.D., Rukshen Weerasooriya, M.D., Jean-Paul Albenque, M.D., Stefano Nardi, M.D., Endri Menardi, M.D., Paul Novak, M.D., and Prashanthan Sanders, M.B., B.S., Ph.D., for the STAR AF II Investigators*

*Corresponding author: Atul Verma, M.D., Section of Arrhythmia, Massachusetts General Hospital, 171 Cambridge Street, Boston, MA 02114 (e-mail: a-verma@partners.org).

**Targile, Joseph W., M.D., and Shlomo Mark, M.D., F.A.C.C.**

Persistent AF: no difference between strategies

Long-term results of antral isolation for paroxysmal AF

Paroxysmal AF with antral isolation

Ouyang et al, Circulation 2010

Medi et al, JCE 2011
Long-term outcomes of AF ablation in mixed cohorts

Single Procedure

Multiple Procedure

8.9% attrition rate

Weerasooriya et al. JACC 2011
### Predictors of recurrence after AF ablation

<table>
<thead>
<tr>
<th>AF Characteristics</th>
<th>Persistent AF</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tzou Circ 10, Cheema JICE 06</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>Shah JCE 08, Sawhney AJC 09</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Wokhlu JCE 09</td>
</tr>
<tr>
<td>OSA</td>
<td>Jongnarangsin JCE 08, Naruse HR 13, Fein JACC 13</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>Shah JCE 08</td>
</tr>
<tr>
<td>Obesity</td>
<td>Mainigi JCE 07</td>
</tr>
<tr>
<td>Metabolic Syndrome</td>
<td>Berkowitsch PACE 12, Mohanty JACC 12</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other Markers</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Left atrial size</td>
<td>Jiang JICE 06, Wokhlu JCE 09</td>
</tr>
<tr>
<td>Aortic stiffness</td>
<td>Lau PLoS 13</td>
</tr>
<tr>
<td>Pericardial Fat</td>
<td>Wong JACC 11</td>
</tr>
</tbody>
</table>
4th Pillar of AF management

Risk Factor management
AF: A Progressive Disease

Schotten et al. - Physiol Rev 2011
Chamberlain et al, ARIC Study, AHJ 2010

**Probability of AF in Metabolic Syndrome**

<table>
<thead>
<tr>
<th>Metabolic Syndrome Component</th>
<th>HR (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated waist circumference</td>
<td>1.40 (1.23-1.59)</td>
</tr>
<tr>
<td>Elevated blood pressure</td>
<td>1.95 (1.72-2.21)</td>
</tr>
<tr>
<td>Elevated triglycerides</td>
<td>0.95 (0.84-1.09)</td>
</tr>
<tr>
<td>Low HDL cholesterol</td>
<td>1.20 (1.06-1.37)</td>
</tr>
<tr>
<td>Impaired fasting glucose</td>
<td>1.16 (1.03-1.31)</td>
</tr>
</tbody>
</table>
Treat the causes of AF

**Risk Factors**
- Aging
- Hypertension
- Diabetes
- Heart Failure
- Alcohol Excess
- Ischemic heart disease
- Valvular heart disease
- Obesity
- Physical Inactivity
- Obstructive Sleep Apnea
- Pre-hypertension
- Aortic Stiffness
- Familial AF

*Nattel et al, JACC 2014*
Weight change and AF risk

<table>
<thead>
<tr>
<th>Weight Change</th>
<th>New Atrial Fibrillation Risk (Hazard Ratio)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable&lt;30</td>
<td>1.2</td>
<td>0.09</td>
</tr>
<tr>
<td>Reduced&lt;30</td>
<td>1.1</td>
<td>0.02</td>
</tr>
<tr>
<td>Increased&gt;30</td>
<td>1.5</td>
<td>0.96</td>
</tr>
<tr>
<td>Stable&gt;30</td>
<td>1.3</td>
<td></td>
</tr>
</tbody>
</table>

WHS JACC 2010
248 highly symptomatic AF patients with BMI >27 & WC >100 (male) or >90 (female)

Exclusions: Serious medical/psychiatric disorder; Recent weight loss program; Malabsorption disorder; Unstable INR; LVEF ≤35%; DM – on insulin; Valvular disease; Endocrinopathy

150 Randomised

75 Control

75 Intervention
**Aggressive Risk Factor Management**

### Weight Management and Exercise

<table>
<thead>
<tr>
<th>Weight Management and Exercise</th>
<th>Hyperlipidaemia</th>
<th>Obstructive Sleep Apnoea</th>
<th>Hypertension</th>
<th>Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Initial target: &gt;10% weight loss</td>
<td>• Initial lifestyle measures</td>
<td>• Overnight sleep study</td>
<td>• Home BP diary: 2-3x daily</td>
<td>• Glucose tolerance test</td>
</tr>
<tr>
<td>• Final target: BMI &lt;27 kg/m²</td>
<td>• At 3 months: Start statins if LDL &gt;2.6 mmol/L</td>
<td>• CPAP if AHI ≥30; or ≥20/h with resistant HT or daytime somnolence</td>
<td>• Reduce salt</td>
<td>• Lifestyle measures</td>
</tr>
<tr>
<td>• Avoid weight fluctuation</td>
<td>• Add fibrates if TG &gt;2.6 mmol/L</td>
<td>• Check adherence: regular CPAP machine data download</td>
<td>• Start ACEI or ARB</td>
<td>• At 3 months: Metformin if HbA1c &gt;6.5%</td>
</tr>
<tr>
<td>• Exercise: 30 minutes for 3-4x per week</td>
<td>• Start fibrates if TG &gt;5.6 mmol/L</td>
<td></td>
<td>• Target: &lt;130/80 mmHg (at rest) &lt;200/100 mmHg (at peak exercise)</td>
<td>• Diabetes clinic or endocrine review</td>
</tr>
<tr>
<td>Increase up to 250 minutes per week</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Smoking Cessation & Alcohol Abstinence** (or reduction to 30g per week)

*Lau DH et al. Eur Heart J - in press*
Changes in anthropometric measurements

Waist Circumference

Body Mass Index

Abed H et al. JAMA 2013
Effect of Short-Term Weight Loss

Symptom Burden Score

Continuous Monitoring

Abed et al. JAMA 2013
Patients with BMI ≥ 27
N=825

Met Exclusion Criteria (N=293)
Terminal Cancer (N=10)
Inflammatory Dx (N=20)
Permanent AF (N=84)
AV Node ablation (N=12)
AF ablation (N=90)
Severe Medical Illness (N=77)

Patients from other States (N=177)

Final Cohort
N=355

10%WL
N=135

3-9%WL
N=103

<3%WL or WG
N=117

A Long-Term Follow-Up Study (LEGACY)

JACC 2015
AF freedom: drug & ablation free

≥10% weight loss was associated with AF free survival: HR 5.7 [95% CI: 3.3-10.1] (P<0.001)

Without ablation or AAD

With ablation and/or AAD

Pathak RK et al. JACC 2015
RFM was associated with AF-free survival: HR 4.8 [95% CI: 2.04-11.4] (P<0.001)

Pathak RK et al. JACC 2014
AF Care Delivery
Integrated Care Management in AF would improve care and patient outcomes in patients with AF
Composite Endpoint: Cardiovascular Hospitalisation or Death

35% RRR
HR 0.65; 95% CI (0.45 – 0.93)
P < 0.05

Hendriks JM et al. Eur Heart J 2012
A new approach to manage AF: Integrated Care

Lau DH et al, Eur Heart J (In Press)
Management of AF

- Stroke prevention is essential
- Evolving role of catheter ablation (outside of symptomatic AF)
- Treating risk factors is an essential component of AF Mx
- Appropriate strategies needed to engage and educate