How Should I Manage All Of Those Patients With Atrial Fibrillation?

Cardiology Update
RCP, London
10th October 2016

Dr Simon Fynn
Consultant Cardiologist
Clinical Director for Cardiology
Papworth Hospital
Prevalence of atrial fibrillation by age group

Cowan C et al. Heart 2013;99:1166-1172
Mechanisms of Persistent AF

- Mechanism of persistent AF remains controversial
- Interaction between initiating triggers and remodelled substrate

- Pulmonary Vein Foci
- Multiple Wavelets
- Sustained Focal Sources
- Rotor Activity
## Cardiovascular morbidity and mortality associated with atrial fibrillation

<table>
<thead>
<tr>
<th>Event</th>
<th>Association with AF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>Increased mortality, especially cardiovascular mortality due to sudden death, heart failure or stroke.</td>
</tr>
<tr>
<td>Stroke</td>
<td>20–30% of all strokes are due to AF. A growing number of patients with stroke are diagnosed with ‘silent’, paroxysmal AF.</td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>10–40% of AF patients are hospitalized every year.</td>
</tr>
<tr>
<td>Quality of life</td>
<td>Quality of life is impaired in AF patients independent of other cardiovascular conditions.</td>
</tr>
<tr>
<td>Left ventricular dysfunction and heart failure</td>
<td>Left ventricular dysfunction is found in 20–30% of all AF patients. AF causes or aggravates LV dysfunction in many AF patients, while others have completely preserved LV function despite long-standing AF.</td>
</tr>
<tr>
<td>Cognitive decline and vascular dementia</td>
<td>Cognitive decline and vascular dementia can develop even in anticoagulated AF patients. Brain white matter lesions are more common in AF patients than in patients without AF.</td>
</tr>
</tbody>
</table>
Atrial Fibrillation
- very costly public health problem -

"Cost of AF to NHS in 2000 was £459 million – equiv to 0.97% of total NHS expenditure"
Natural time course of AF

- ‘Upstream’ therapy of concomitant conditions
  - Anticoagulation
  - Rate control
    - Antiarrhythmic drugs
    - Ablation
    - Cardioversion

Time course:
- Silent
- Paroxysmal
- Persistent
- Long-standing persistent
- Permanent

AF: Atrial Fibrillation
Management of AF
- My approach -

Take a history
Management of AF
- My approach -

Discussion with the patient
Atrial fibrillation: management

Clinical guideline
Published: 18 June 2014
nice.org.uk/guidance/cg180

Personalised package of care and information

- Offer people with atrial fibrillation a personalised package of care. Ensure that the package of care is documented and delivered, and that it covers:
  - stroke awareness and measures to prevent stroke
  - rate control
  - assessment of symptoms for rhythm control
  - who to contact for advice if needed
  - psychological support if needed
  - up-to-date and comprehensive education and information on:
2016 ESC Guidelines for the management of atrial fibrillation
Types of Atrial Fibrillation

First diagnosed episode of atrial fibrillation

- **Paroxysmal** (usually ≤ 48 h)
- **Persistent** (requires CV)
- **Long-standing Persistent** (> 1 year)
- **Permanent** (accepted)
Atrial Fibrillation

Paroxysmal or Persistent

Rate vs Rhythm

Stroke Risk
Atrial Fibrillation - persistent -

symptoms?
Rate control
Long-term heart rate control in patients with atrial fibrillation

Long-term heart rate control of AF

Perform echocardiogram (IC)
Choose initial rate control therapy (IB) and combination therapy if required (IIaC)
Target initial resting heart rate <110 bpm (IIaB), avoiding bradycardia

LVEF <40%

- Beta-blocker
- Digoxin

Consider early low-dose combination therapy
- Add digoxin
- Add beta-blocker

LVEF ≥40%

- Diltiazem/verapamil
- Beta-blocker
- Digoxin

Add therapy to achieve target heart rate or if ongoing symptoms
- Add digoxin
- Add digoxin
- Add diltiazem, verapamil or beta-blocker
What is the left ventricular function?
Ablation of AV node
Cardiac Resynchronisation Therapy
Stroke risk
## CHA$_2$DS$_2$-VASc

<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 ≥ 75 ans</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*</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>

*Refer to the notes for clarification on the term 'vascular disease'.
### CHA$_2$DS$_2$-VASc

<table>
<thead>
<tr>
<th>CHA$_2$DS$_2$-VASc score</th>
<th>Patients (n = 7329)</th>
<th>Adjusted stroke rate (%/y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>0%</td>
</tr>
<tr>
<td>1</td>
<td>422</td>
<td>1.3%</td>
</tr>
<tr>
<td>2</td>
<td>1230</td>
<td>2.2%</td>
</tr>
<tr>
<td>3</td>
<td>1730</td>
<td>3.2%</td>
</tr>
<tr>
<td>4</td>
<td>1718</td>
<td>4.0%</td>
</tr>
<tr>
<td>5</td>
<td>1159</td>
<td>6.7%</td>
</tr>
<tr>
<td>6</td>
<td>679</td>
<td>9.8%</td>
</tr>
<tr>
<td>7</td>
<td>294</td>
<td>9.6%</td>
</tr>
<tr>
<td>8</td>
<td>82</td>
<td>6.7%</td>
</tr>
<tr>
<td>9</td>
<td>14</td>
<td>15.2%</td>
</tr>
</tbody>
</table>
**HAS-BLED bleeding risk score**

<table>
<thead>
<tr>
<th>Letter</th>
<th>Clinical characteristic*</th>
<th>Points awarded</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>A</td>
<td>Abnormal renal and liver function (1 point each)</td>
<td>1 or 2</td>
</tr>
<tr>
<td>S</td>
<td>Stroke</td>
<td>1</td>
</tr>
<tr>
<td>B</td>
<td>Bleeding</td>
<td>1</td>
</tr>
<tr>
<td>L</td>
<td>Labile INRs</td>
<td>1</td>
</tr>
<tr>
<td>E</td>
<td>Elderly (e.g. age &gt; 65 years)</td>
<td>1</td>
</tr>
<tr>
<td>D</td>
<td>Drugs or alcohol (1 point each)</td>
<td>1 or 2</td>
</tr>
</tbody>
</table>

Maximum 9 points
Stroke prevention in atrial fibrillation

Mechanical heart valves or moderate or severe mitral stenosis

Yes

No

Estimate stroke risk based on number of CHA$_2$DS$_2$-VASc risk factors

0$^a$

No antiplatelet or anticoagulant treatment (IIIB)

1

OAC should be considered (IIaB)

≥ 2

Oral anticoagulation indicated
Assess for contra-indications
Correct reversible bleeding risk factors

LAA occluding devices may be considered in patients with clear contra-indications for OAC (IIbC)

NOAC (IA)$^b$

VKA (IA)$^c$

$^a$ Includes women without other stroke risk factors

$^b$ IIaB for women with only one additional stroke risk factor

$^c$ IB for patients with mechanical heart valves or mitral stenosis
Left Atrial Appendage Occlusion

PROTECT AF JAMA 2014
Targets for anticoagulants

Inactive Factor → Active Factor → Transformation → Catalysis

**Direct Factor Xa inhibition**
- Rivaroxaban
- Apixaban
- Edoxaban
- Betrixaban

**Direct Factor IIa inhibition**
- Dabigatran

### Relevant clinical characteristics and dose adjustment in the four phase III NOAC trials in patients with atrial fibrillation

<table>
<thead>
<tr>
<th></th>
<th>Dabigatran (RE-LY)</th>
<th>Rivaroxaban (ROCKET-AF)</th>
<th>Apixaban (ARISTOTLE)</th>
<th>Edoxaban (ENGAGE AF-TIMI 48)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal clearance</td>
<td>80%</td>
<td>35%</td>
<td>25%</td>
<td>50%</td>
</tr>
<tr>
<td>Number of patients</td>
<td>18 113</td>
<td>14 264</td>
<td>18 201</td>
<td>21 105</td>
</tr>
<tr>
<td>Dose</td>
<td>150 mg or 110 mg</td>
<td>20 mg</td>
<td>5 mg</td>
<td>60 mg (or 30 mg)</td>
</tr>
<tr>
<td></td>
<td>twice daily</td>
<td>once daily</td>
<td>twice daily</td>
<td>once daily</td>
</tr>
<tr>
<td>Exclusion criteria</td>
<td>CrCl &lt;30 ml/min</td>
<td>CrCl &lt;30 mL/min</td>
<td>Serum creatinine</td>
<td>CrCl &lt;30 mL/min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt;2.5 mg/dL or</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CrCl &lt;25 mL/min</td>
<td></td>
</tr>
<tr>
<td>Dose adjustment with</td>
<td>None</td>
<td>Rivaroxaban 15 mg</td>
<td>Apixaban 2.5 mg</td>
<td>Edoxaban 30 mg</td>
</tr>
<tr>
<td>CKD</td>
<td></td>
<td>once daily if CrCl</td>
<td>twice daily if at</td>
<td>(or 15 mg)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30–49 mL/min</td>
<td>least two of age</td>
<td>once daily if</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>≥80 years, weight ≤60</td>
<td>CrCl &lt;50 mL/min</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>kg, or serum</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>creatinine ≥1.5 mg/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(133 μmol/L)</td>
<td></td>
</tr>
<tr>
<td>Percentage of patients with CKD</td>
<td>20% with CrCl 30-49 mL/min</td>
<td>21% with CrCl 30-49 mL/min</td>
<td>15% with CrCl 30-50 mL/dl</td>
<td>19% with CrCl &lt;50 mL/min</td>
</tr>
<tr>
<td>Reduction of stroke and systemic embolism</td>
<td>No interaction with CKD status</td>
<td>No interaction with CKD status</td>
<td>No interaction with CKD status</td>
<td>NA</td>
</tr>
<tr>
<td>Reduction in major haemorrhages compared to warfarin</td>
<td>Reduction in major haemorrhage with dabigatran was greater in patients with eGFR ≥80 mL/min with either dose</td>
<td>Major haemorrhage similar</td>
<td>Reduction in major haemorrhage with apixaban</td>
<td>NA</td>
</tr>
</tbody>
</table>
Rhythm Control

Cardioversion

vs

Catheter Ablation
Recurrence of Atrial Fibrillation after DC Cardioversion

246 pts. with AF / AFLutter
Amiodarone to Prevent Atrial Fibrillation

Amiodarone (n=201) 69% SR at 1 yr
P<0.001

Propafenone (n=101) 39% SR at 1 yr
Sotalol (n=101)

Roy et al, NEJM 2000
Long-term follow up after ablation of persistent AF

Wynn GJ et al Open Heart 2016
Long-term follow up after ablation of persistent AF
Acutus Medical
ECGi
Catheter ablation for patients with AF and left ventricular impairment

Improvement in instrumental (echocardiographic and laboratory) parameters after atrial fibrillation catheter ablation.

Matteo Anselmino et al. Circ Arrhythm Electrophysiol. 2014;7:1011-1018

Copyright © American Heart Association, Inc. All rights reserved.
Atrial Fibrillation - paroxysmal -

P on T
Rhythm at time of symptoms might not be AF
Rhythm at time of symptoms might not be AF
Rhythm control

“The treatment for AF is weight loss”

John Mandrola
Medscape 2015
Outcomes of Atrial Fibrillation Freedom According to Weight Trend and Weight Fluctuation

(A) Kaplan-Meier curve for total AF-free survival (multiple ablation procedures with and without drugs) according to weight trend. (B) Kaplan-Meier curve for total AF-free survival (multiple ablation procedures with and without drugs) according to weight fluctuation. Abbreviations as in Figure 1.
Weight Management and Atrial Fibrillation

(Left) Obesity is associated with a variety of associated comorbidities. These are all associated with progression of the atrial substrate and the development of atrial fibrillation (AF). (Top) A dedicated weight management program with weight loss (WL) is associated with reverse remodeling of the atrial substrate and a dose-dependent reduction in the AF burden, which is sustained in the long term. (Bottom) The consequence of weight fluctuation, which somewhat curtails the beneficial effects of WL.
Rhythm control

Antiarrhythmic Drugs

vs

Catheter Ablation
### Recommendations

- **Catheter ablation of symptomatic paroxysmal AF** is recommended to improve AF symptoms in patients who have symptomatic recurrences of AF on antiarrhythmic drug therapy (amiodarone, dronedarone, flecainide, propafenone, sotalol) and who prefer further rhythm control therapy, when performed by an electrophysiologist who has received appropriate training and is performing the procedure in an experienced centre.  
  - **Class**: I  
  - **Level**: A

- **Ablation of common atrial flutter** should be considered to prevent recurrent flutter as part of an AF ablation procedure if flutter has been documented or occurs during the AF ablation.  
  - **Class**: IIa  
  - **Level**: B

- **Catheter ablation of AF** should be considered as first-line therapy to prevent recurrent AF and to improve symptoms in selected patients with symptomatic paroxysmal AF as an alternative to antiarrhythmic drug therapy, considering patient choice, benefit, and risk.  
  - **Class**: IIa  
  - **Level**: B

- All patients should receive oral anticoagulation for at least 8 weeks after catheter (IIaB) or surgical (IIaC) ablation.  
  - **Class**: IIa  
  - **Level**: B C

- **Anticoagulation for stroke prevention** should be continued indefinitely after apparently successful catheter or surgical ablation of AF in patients at high-risk of stroke.  
  - **Class**: IIa  
  - **Level**: C

- When catheter ablation of AF is planned, continuation of oral anticoagulation with a VKA (IIaB) or NOAC (IIaC) should be considered during the procedure, maintaining effective anticoagulation.  
  - **Class**: IIb  
  - **Level**: B C

- Catheter ablation should target isolation of the pulmonary veins using radiofrequency ablation or cryotherapy balloon catheters.  
  - **Class**: IIa  
  - **Level**: B
Cryoballoon or Radiofrequency Ablation for Paroxysmal Atrial Fibrillation

Karl-Heinz Kuck, M.D., Josep Brugada, M.D., Alexander Fürnkranz, M.D., Andreas Metzner, M.D., Feifan Ouyang, M.D., K.R. Julian Chun, M.D., Arif Elvan, M.D., Ph.D., Thomas Arentz, M.D., Kurt Bestehorn, M.D., Stuart J. Pocock, Ph.D., Jean-Paul Albenque, M.D., Ph.D., and Claudio Tondo, M.D., Ph.D., for the FIRE AND ICE Investigators*
Cryoablation
Catheter Ablation at Papworth Hospital - GA vs sedation -

- During the follow up period of up to 12 months, 72.41% of patients in the GA group compared to 49.09% in the deep sedation group were free of AF (P 0.008).

- The recurrence of AF did not correlate with age, gender, duration of AF, atrial size, ablation strategy or duration of RF application.

- Recurrence of AF correlated with the mode of sedation (r 0.236, P 0.005).

- In a linear regression, conscious sedation was an independent predictor of AF recurrence (Beta 0.236, P 0.005).
Conclusion

• Be aware of:
  – NICE guidance
  – Clinical Guidelines

• Risk stratification for stroke

• Paroxysmal AF vs Persistent AF
  - if paroxysmal – PLEASE REFER EARLY!!
  - if Persistent - symptoms?
Thank you