Risk prediction for stroke in atrial fibrillation

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Disclosures

- Co-author of 2010-2012 ESC Guidelines on Atrial Fibrillation
- Steering Committee member, National Coordinator for Italy, and Co-author of ACTIVE, APPRAISE-2, ARISTOTLE, AVERROES
- Fees, honoraria and research funding from Sanofi-Aventis, Boehringer Ingelheim, Bayer, BMS/Pfizer, Daiichi-Sankyo
A logical sequence to AF management

1. Atrial fibrillation
2. Record 12-lead ECG
3. Presentation EHRA score
4. Associated disease
5. Initial assessment
6. Anticoagulation issues
7. Assess TE Risk
8. Oral anticoagulant
   - Aspirin
   - None
9. Rate and rhythm control
10. AF type
    - Symptoms
11. Rate control
    - ± Rhythm control
    - Antiarrhythmic drugs
    - Ablation
12. Treatment of underlying disease
    - ‘Upstream’ therapy
13. Consider referral
    - ACEIs/ARBs
    - Statins/PUFAs
    - Others

ESC 2010 AF Guidelines
Two intertwined issues: Stratification as a guide to Therapy

- The CHAD$_2$DS$_2$VASc score
- Identifying “truly low risk” patients
- The HAS-BLED score

European Heart Journal 2012 - doi:10.1093/eurheartj/ehs253
### Table 7  CHADS₂ score and stroke rate

<table>
<thead>
<tr>
<th>CHADS₂ score</th>
<th>Patients (n = 1733)</th>
<th>Adjusted stroke rate (%/year)ᵃ (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>120</td>
<td>1.9 (1.2–3.0)</td>
</tr>
<tr>
<td>1</td>
<td>463</td>
<td>2.8 (2.0–3.8)</td>
</tr>
<tr>
<td>2</td>
<td>523</td>
<td>4.0 (3.1–5.1)</td>
</tr>
<tr>
<td>3</td>
<td>337</td>
<td>5.9 (4.6–7.3)</td>
</tr>
<tr>
<td>4</td>
<td>220</td>
<td>8.5 (6.3–11.1)</td>
</tr>
<tr>
<td>5</td>
<td>65</td>
<td>12.5 (8.2–17.5)</td>
</tr>
<tr>
<td>6</td>
<td>5</td>
<td>18.2 (10.5–27.4)</td>
</tr>
</tbody>
</table>

ᵃThe adjusted stroke rate was derived from the multivariable analysis assuming no aspirin usage; these stroke rates are based on data from a cohort of hospitalized AF patients, published in 2001, with low numbers in those with a CHADS2 score of 5 and 6 to allow an accurate judgement of the risk in these patients. Given that stroke rates are declining overall, actual stroke rates in contemporary non-hospitalized cohorts may also vary from these estimates. Adapted from Gage BF et al.⁵⁰

AF = atrial fibrillation; CHADS₂ = Cardiac failure, hypertension, age, diabetes, stroke (doubled).
Problems with the CHADS$_2$ score

- Moderate c-statistics (0.58) in the whole cohort to predict stroke
- Most subjects categorized as “moderate” risk (score=1)
- These subjects overall still appear to derive benefit from oral anticoagulants vs aspirin
Risks and Benefits of Oral Anticoagulation Compared With Clopidogrel Plus Aspirin in Patients With Atrial Fibrillation According to Stroke Risk

The Atrial Fibrillation Clopidogrel Trial With Irbesartan for Prevention of Vascular Events (ACTIVE-W)

Jeff S. Healey, MD, MSc; Robert G. Hart, MD; Janice Pogue, MSc; Marc A. Pfeffer, MD, PhD; Stefan H. Hohnloser, MD; Raffaele De Caterina, MD; Greg Flaker, MD; Salim Yusuf, MD, DPhil; Stuart J. Connolly, MD

### Table 2. CHADS$_2$-Specific Stroke Rates for Patients Treated With Clopidogrel Plus Aspirin vs Oral Anticoagulation (OAC)

<table>
<thead>
<tr>
<th>CHADS Score</th>
<th>Stroke Rate With ASA (/100 pt-yrs)$^*$</th>
<th>No. of Patients in ACTIVE-W</th>
<th>Stroke Rate C+A (/100 pt-yrs)</th>
<th>Stroke Rate OAC (/100 pt-yrs)</th>
<th>Relative Risk (C+A vs OAC)$^†$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.8</td>
<td>178 (3%)</td>
<td>1.90</td>
<td>0.80</td>
<td>3.02</td>
</tr>
<tr>
<td>1</td>
<td>2.2</td>
<td>2436 (36%)</td>
<td>1.21</td>
<td>0.40</td>
<td>3.11</td>
</tr>
<tr>
<td>2</td>
<td>4.5</td>
<td>2286 (34%)</td>
<td>1.93</td>
<td>1.86</td>
<td>1.04</td>
</tr>
<tr>
<td>3</td>
<td>8.6</td>
<td>1107 (17%)</td>
<td>2.79</td>
<td>1.72</td>
<td>1.62</td>
</tr>
<tr>
<td>4</td>
<td>10.9</td>
<td>490 (7%)</td>
<td>6.73</td>
<td>3.25</td>
<td>2.07</td>
</tr>
<tr>
<td>5</td>
<td>12.3</td>
<td>183 (3%)</td>
<td>11.65</td>
<td>2.69</td>
<td>7.01</td>
</tr>
<tr>
<td>6</td>
<td>13.7</td>
<td>26 (0.4%)</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
</tbody>
</table>

$^*$Annual rate of stroke among 2580 aspirin-treated patients with atrial fibrillation.$^4$

$^†$Influence of baseline CHADS$_2$ score on RR ($P$ trend=0.29).

$∥$Patients had to have evidence of peripheral vascular disease or coronary artery disease and be older than 55 years.
Problems with the CHADS$_2$ score (con’t)

- Moderate c-statistics (0.58) in the whole cohort to predict stroke (…but no worse than 11 other risk stratification schemes compared by the Stroke in AF Working Group)
- Most subjects categorized as “moderate” risk (score=1)
- These subjects overall still appear to derive benefit from oral anticoagulants vs aspirin
- Also, the CHADS2 score does not include many stroke risk factors, and other ‘stroke risk modifiers’ needed to be considered in a comprehensive stroke risk assessment
(a) Risk factors for stroke and thrombo-embolism in non-valvular AF

<table>
<thead>
<tr>
<th>‘Major’ risk factors</th>
<th>‘Clinically relevant non-major’ risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous stroke, TIA, or systemic embolism</td>
<td>Heart failure or moderate to severe LV systolic dysfunction (e.g. LV EF ≤40%)</td>
</tr>
<tr>
<td>Age ≥75 years</td>
<td>Hypertension - Diabetes mellitus</td>
</tr>
<tr>
<td></td>
<td>Female sex - Age 65–74 years</td>
</tr>
<tr>
<td></td>
<td>Vascular disease(^a)</td>
</tr>
</tbody>
</table>

\(^a\)Prior myocardial infarction, peripheral artery disease, aortic plaque.
(b) Risk factor-based approach expressed as a point based scoring system, with the acronym CHA<sub>2</sub>DS<sub>2</sub>-VASc
(Note: maximum score is 9 since age may contribute 0, 1, or 2 points)

<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</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&lt;sup&gt;a&lt;/sup&gt;</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>
Since 2010, further validation of the CHA$_2$DS$_2$-VASc score

Abu-Assi E, et al. *Int J Cardiol.* 2011

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>The CHA$_2$DS$_2$-VASc score is recommended as a means of assessing stroke risk in non-valvular AF.</td>
<td>I</td>
<td>A</td>
</tr>
</tbody>
</table>

European Heart Journal 2012 - doi:10.1093/eurheartj/ehs253
<table>
<thead>
<tr>
<th>CHA$_2$DS$_2$-VASc score</th>
<th>Patients (n = 73538)</th>
<th>Stroke and thromboembolism event rate at 1 year follow-up (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>6369</td>
<td>0.78</td>
</tr>
<tr>
<td>1</td>
<td>8203</td>
<td>2.01</td>
</tr>
<tr>
<td>2</td>
<td>12771</td>
<td>3.71</td>
</tr>
<tr>
<td>3</td>
<td>17371</td>
<td>5.92</td>
</tr>
<tr>
<td>4</td>
<td>13887</td>
<td>9.27</td>
</tr>
<tr>
<td>5</td>
<td>8942</td>
<td>15.26</td>
</tr>
<tr>
<td>6</td>
<td>4244</td>
<td>19.74</td>
</tr>
<tr>
<td>7</td>
<td>1420</td>
<td>21.50</td>
</tr>
<tr>
<td>8</td>
<td>285</td>
<td>22.38</td>
</tr>
<tr>
<td>9</td>
<td>46</td>
<td>23.64</td>
</tr>
</tbody>
</table>

Major advantages of the CHA$_2$DS$_2$-VASc scoring system

- A validated scoring system predictor of thromboembolic events **AND EASY TO REMEMBER**, aimed at guiding the medical history and physical examination of a patient with AF by any practicing doctor
- Able to identify, better than the CHADS$_2$ score, the **truly low-risk** patients
The female gender issue

- Female gender independently increases the risk of stroke overall unless the criterion of ‘age <65 and lone AF’ is clearly fulfilled, whereby female gender does not independently increase stroke risk... Thus, female patients with gender alone as a single risk factor (still a CHA$_2$DS$_2$-VASc score of 1) would not need anticoagulation if they clearly fulfil the criteria of ‘age < 65 and lone AF’...


Figure 1 Choice of anticoagulant

- **Atrial fibrillation**
  - **Valvular AF**
    - Yes
      - **No (i.e. non-valvular AF)**
    - No

- **< 65 years and lone AF (including females)**
  - Yes
  - **Assess risk of stroke (CHADS\textsubscript{2}-VASc score)**
    - 0
    - 1**
    - ≥2

- **Oral anticoagulant therapy**
  - **Assess bleeding risk (HAS-BLED score)**
    - Consider patient values and preferences
  - **No antithrombotic therapy**

- **NOAC**
- **VKA**

* Includes rheumatic valvular AF, hypertrophic cardiomyopathy, etc.
** Antiplatelet therapy with aspirin plus clopidogrel, or – less effectively – aspirin only, may be considered in patients who refuse any OAC.

Colour: CHADS\textsubscript{2}-VASc score; green = 1, blue = 2, red = ≤2. Line: Solid: best option; Dashed: alternative option.

If absolute contraindications to any OAC or anti-platelet therapy, left atrial appendage closure device can be considered.

AF = atrial fibrillation; CHADS\textsubscript{2}-VASc = see text; HAS-BLED = see text; NOAC = novel anticoagulants; VKA = vitamin K antagonist.
### Table 9  Approach to thromboprophylaxis in patients with AF

<table>
<thead>
<tr>
<th>Risk category</th>
<th>CHA₂DS₂-VASc score</th>
<th>Recommended antithrombotic therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>One ‘major’ risk factor or ≥2 ‘clinically relevant non-major’ risk factors</td>
<td>≥ 2</td>
<td>OAC&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>One ‘clinically relevant non-major’ risk factor</td>
<td>1</td>
<td>Either OAC&lt;sup&gt;a&lt;/sup&gt; 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>

<sup>a</sup> Male or female!
Emphasis on the low risk (truly low risk)

- Lone atrial fibrillation – defined by the absence of any risk factor for thromboembolism as defined by the CHA$_2$DS$_2$-VASc score system (apart from the female gender)
- Here limited role of antiplatelet agents
Bleeding risk considerations – New evidence

- **HAS-BLED** (Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile INR, Elderly, Drugs/alcohol concomitantly) ¹
- **HEMORR₂HAGES** (Hepatic or renal disease, Ethanol abuse, Malignancy, Older (age > 75 years), Reduced platelet count or function, Rebleeding risk, Hypertension (uncontrolled), Anaemia, Genetic factors, Excessive fall risk, and Stroke ²
- **ATRIA** (AnTicoagulation and Risk factors In Atrial fibrillation) ³

**Valvular AF***

If any antithrombotic therapy is needed, *Valvular AF* can be considered.

- *Valvular AF* includes rheumatic valvular AF, hypertrophic cardiomyopathy, etc.
- Antiplatelet therapy with aspirin plus clopidogrel, or – less effectively – aspirin only, may be considered in patients who refuse any oral anticoagulant.

AF = atrial fibrillation; *CHA₂DS₂-VASc* = see text; HAS-BLED = see text; NOAC = novel anticoagulants; VKA = vitamin K antagonist.

* *CHADS₂-VASc* = see text; green = 1, blue = 2, red = ≤2.

**Line:** Solid: best option; Dashed: alternative option.

If absolute contraindications to any oral anticoagulant or anti-platelet therapy, left atrial appendage closure device can be considered.
Assessing the bleeding risk: the HAS-BLED score

- Better predictive value than that ATRIA
- contains risk factors that can be actively managed to reduce the bleeding risk
- validated in several independent cohorts
- correlates well with intracranial haemorrhage (ICH) risk
- Now also endorsed by the Canadian Cardiovascular Society

Thank you!