CHA$_2$DS$_2$-VASc 1: to anticoagulate or not?

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The CHA$_2$DS$_2$-VASc score

<table>
<thead>
<tr>
<th>Risk factors for stroke and thromboembolism in non-valvular AF</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous stroke, TIA or systemic embolism</td>
<td>1</td>
</tr>
<tr>
<td>Age ≥ 75 years</td>
<td>1</td>
</tr>
<tr>
<td>Heart failure or moderate to severe LV dysfunction [e.g., LV EF ≤ 40%]</td>
<td>2</td>
</tr>
<tr>
<td>Hypertension - Diabetes mellitus</td>
<td>1</td>
</tr>
<tr>
<td>Female sex - Age 65-74 years</td>
<td>1</td>
</tr>
<tr>
<td>Vascular disease [prior MI, PAD, or aortic plaque]</td>
<td>1</td>
</tr>
<tr>
<td>Aged 65-74 years</td>
<td>1</td>
</tr>
<tr>
<td>Sex category [i.e., female gender]</td>
<td>1</td>
</tr>
</tbody>
</table>

Lip et al. Chest. 2010; 137:263-72
Camm, Kirchhof, Lip et al. Eur Heart J 2010; 31, 2369–2429
The value of the CHA$_2$DS$_2$-VASc score for refining stroke risk stratification in patients with a CHADS$_2$ score 0-1

*Olesen et al Thromb Haemost. 2012 Jun;107(6):1172-9*

In patients with a CHADS$_2$ = 0, c-statistic was 0.573 (0.539–0.608) and increased to 0.641 (0.610–0.671) when CHA$_2$DS$_2$-VASc was included.
### Reliable identification of ‘truly low’ thromboembolic risk in patients initially diagnosed with ‘lone’ AF: Belgrade AF Study

*Potpara ... Lip. Circ Arrhythmia Electrophysiol 2012;5(2):319-26*

Predictive ability and Multivariable Relationships of CHADS$_2$, CHA$_2$DS$_2$-VASc, and van Walraven Scores of 0 With the **Absence of Ischemic Strokes** During Follow-Up

<table>
<thead>
<tr>
<th>Risk score of 0</th>
<th>Predictive ability of score=0</th>
<th>Multivariable analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C-statistic</td>
<td>95%CI</td>
</tr>
<tr>
<td>CHADS$_2$</td>
<td>0.58</td>
<td>0.38-0.79</td>
</tr>
<tr>
<td>CHA$_2$DS$_2$-VASc</td>
<td>0.72</td>
<td>0.61-0.84</td>
</tr>
<tr>
<td>Van Walraven</td>
<td>0.65</td>
<td>0.46-0.85</td>
</tr>
</tbody>
</table>

The CHA$_2$DS$_2$-VASc score reliably identified the ‘lone’ AF patients who were at ‘truly low risk’ for thromboembolism, and was the only tested risk stratification scheme with a significant predictive ability for thromboembolism amongst lone AF patients.
‘This guideline strongly recommends a practice shift towards greater focus on identification of ‘truly low risk’ patients with AF (who do not need any antithrombotic therapy), instead of trying to focus on identifying ‘high risk patients’”

SIMPLICITY IS BEST
2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

January C et al Circulation 2014 DOI: 10.1161/CIR.0000000000000041

Antithrombotic therapy based on shared decision-making, discussion of risks of stroke and bleeding, and patient’s preferences

**CHA\(_2\)DS\(_2\)-VASc** score recommended to assess stroke risk

Warfarin recommended with mechanical heart valves. Target INR intensity should be based on the type and location of prosthesis

Prior stroke, TIA, or **CHA\(_2\)DS\(_2\)-VASc ≥2**

OAC, either VKA or NOAC (dabigatran, rivaroxaban or apixaban) (Class I)

**CHA\(_2\)DS\(_2\)-VASc=1**

No antithrombotic therapy or treatment with OAC or aspirin (Class IIb)

**CHA\(_2\)DS\(_2\)-VASc score of 0**

No antithrombotic therapy (Class IIa)

If end-stage CKD (CrCl <15 mL/min) or on hemodialysis, it is reasonable to prescribe warfarin for OAC [NOACs not recommended]
Benefit of Anticoagulation Unlikely in Patients With AF and a CHA$_2$DS$_2$-VASc Score of 1

*Friberg et al J Am Coll Cardiol 2015;65:225–32*

140,420 patients with a diagnosis of nonvalvular AF in the Swedish National Patient Register between July 1, 2005, and June 31, 2010, who had not been exposed to warfarin at any time during follow-up.

At a CHA$_2$D$_2$-VASc score of 1, the annual event rates varied between 0.5% and 0.9%, depending on whether only ischemic strokes were counted or a more inclusive endpoint was used.

‘The risk of ischemic stroke in patients with AF and a CHA$_2$D$_2$-VASc score of 1 seems to be lower than previously reported’
CHA$_2$DS$_2$-VASc=1: Is it worth taking the risk?
Commentary on Friberg et al

http://www.practiceupdate.com/content/benefit-of-anticoagulation-unlikely-in-atrial-fibrillation-and-a-cha2ds2-vasc-score-of-1/21229/7/2/1

- Focus on headline “ischemic stroke” rates clearly results in absolute rates lower than the more traditional “all stroke and systemic embolism” endpoints in randomized clinical trials of stroke prevention.
  - OAC reduces the risk for ALL stroke/systemic embolism by 64% and all-cause mortality by 26% compared with placebo/control.
- Exclusion of patients who were treated with warfarin 6 months prior to baseline, but also patients who received warfarin treatment during follow-up.
  - The latter approach can introduce a bias away from the null hypothesis (that patients with a CHA$_2$DS$_2$-VASc score of 1 for males and 2 for females will benefit from OAC treatment).
  - All events studied for the excluded patients are omitted by this “conditioning on the future” approach.
Stroke risk in atrial fibrillation: Do we anticoagulate CHADS\textsubscript{2} or CHA\textsubscript{2}DS\textsubscript{2}-VASc \(\geq 1\), or higher?

Jonas Bjerring Olesen\textsuperscript{1}; Christian Torp-Pedersen\textsuperscript{2}
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Thromb Haemost. DOI: http://dx.doi.org/10.1160/TH15-02-0154.

The risks of risk scores for stroke risk assessment in atrial fibrillation

Peter Brønnum Nielsen\textsuperscript{1,3}; Tze-Fan Chao\textsuperscript{3}
\textsuperscript{1}Department of Cardiology, Atrial Fibrillation Study group, Aalborg University Hospital, Aalborg, Denmark; \textsuperscript{2}Aalborg Thrombosis Research Unit, Department of Clinical Medicine, Faculty of Health, Aalborg University, Aalborg, Denmark; \textsuperscript{3}Division of Cardiology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan

Thromb Haemost. DOI: http://dx.doi.org/10.1160/TH15-03-0210.
Event rates from various studies investigating AF patients off oral anticoagulant treatment and stratified according to ESC/NICE guidelines recommendations


<table>
<thead>
<tr>
<th>Authors</th>
<th>Year of publication</th>
<th>Study period</th>
<th>Data source</th>
<th>Number of patients</th>
<th>Outcome of interest</th>
<th>Event rate in CHA2DS2-VASc score of 0</th>
<th>Event rate in CHA2DS2-VASc score 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Friberg et al. (22)</td>
<td>2012</td>
<td>2005 to 2008</td>
<td>Nationwide cohort</td>
<td>90,706</td>
<td>Ischaemic stroke</td>
<td>0.2 %/year (n=15)</td>
<td>0.6 %/year (n=63)</td>
</tr>
<tr>
<td>Olesen et al. (25)</td>
<td>2012</td>
<td>1997–2006</td>
<td>Nationwide cohort</td>
<td>73,538</td>
<td>Ischaemic stroke/SE/PE</td>
<td>0.78 %/year</td>
<td>2.01 %/year</td>
</tr>
<tr>
<td>Singer et al. (26)</td>
<td>2013</td>
<td>1996 to 1997</td>
<td>Ambulatory based cohort</td>
<td>10,927</td>
<td>Ischaemic stroke/thromboembolic events</td>
<td>0.04 %/year</td>
<td>0.55 %/year</td>
</tr>
<tr>
<td>Taillandier et al. (27)</td>
<td>2013</td>
<td>2000 to 2010</td>
<td>Community based cohort</td>
<td>8,962</td>
<td>Ischaemic stroke/thromboembolism</td>
<td>0.69 %/year</td>
<td>NR</td>
</tr>
<tr>
<td>Lip et al. (8)</td>
<td>2014</td>
<td>1999–2012</td>
<td>Nationwide cohort</td>
<td>47,090</td>
<td>Ischaemic stroke/SE/TIA</td>
<td>1.13 %/year</td>
<td>2.94 %/year</td>
</tr>
<tr>
<td>Huang et al. (28)</td>
<td>2014</td>
<td>1997 to 2011</td>
<td>Hospital based cohort</td>
<td>548</td>
<td>Ischaemic stroke</td>
<td>2.4 %/year</td>
<td>6.6 %/year</td>
</tr>
<tr>
<td>Chao et al. (29)</td>
<td>2014</td>
<td>1996–2011</td>
<td>National Health Insurance Research Database</td>
<td>9,416</td>
<td>Ischaemic stroke</td>
<td>1.15 %/year</td>
<td>NR</td>
</tr>
<tr>
<td>Chao et al. (30)</td>
<td>2015</td>
<td>1996 to 2011</td>
<td>National Health Insurance Research Database</td>
<td>12,935</td>
<td>Ischaemic stroke</td>
<td>NR</td>
<td>2.75 %/year</td>
</tr>
<tr>
<td>Lip et al. (9)</td>
<td>2015</td>
<td>1998–2012</td>
<td>Nationwide cohort</td>
<td>39,400</td>
<td>Ischaemic stroke</td>
<td>0.49 %/year</td>
<td>1.50 %/year</td>
</tr>
<tr>
<td>Lip et al. (4)</td>
<td>2015</td>
<td>1999–2012</td>
<td>Nationwide cohort</td>
<td>22,582</td>
<td>Ischaemic stroke/SE/TIA</td>
<td>1.13 %/year</td>
<td>4.32 %/year</td>
</tr>
</tbody>
</table>

Refinement of Ischemic Stroke Risk in Patients with AF & CHA₂DS₂-VASc 1

Huang et al
PACE 2014 doi: 10.1111/pace.12445

Mean follow-up of 38.5 ± 51.0 months (1,758 patient-years),

- 17 strokes occurred in patients with CHA₂DS₂-VASc 0 (annual ischemic stroke risk: 2.4% per year);
- 70 strokes in patients with CHA₂DS₂-VASc 1 (annual ischemic stroke risk: 6.6% per year, HR: 2.58, 95% CI: 1.67–3.97, P = 0.0002).
Is OAC Necessary in AF Patients with a CHA$_2$DS$_2$-VASc Score=1 (males) or 2 (females)? A nationwide cohort study
Chao, Liu ... Lip, Chen. JACC 2014. Presented at ESC 2014

Ischaemic stroke rates in non-anticoagulated male and female patients with 1 additional stroke risk factor

OAC should be considered for AF patients with 1 additional stroke risk factors (ie. CHA$_2$DS$_2$-VASc score of 1 (males) or 2 (females))
Is OAC Necessary in AF Patients with a CHA$_2$DS$_2$-VASc Score=1 (males) or 2 (females)? A nationwide cohort study

Chao, Liu ... Lip, Chen. JACC 2014. Presented at ESC 2014

Ischaemic stroke rates in non-anticoagulated male and female patients with 1 additional stroke risk factor

Oral anticoagulants should be considered for AF patients with 1 additional stroke risk factors (ie. CHA$_2$DS$_2$-VASc score of 1 (males) or 2 (females))
Stroke event rates for untreated low-risk patients (CHADS$_2$-VASc 1/4 0 [male], 1 [female]) were 0.49 per 100 person-years at 1 year and 0.47 per 100 person-years at full FU.

The presence of 1 additional stroke risk factor (CHADS$_2$-VASc= 1 [male], = 2 [female]) among untreated patients increased the stroke rate at 1 year to 1.55 per 100 person-years, representing a significant 3.01-fold increase.
### OAC, Aspirin, or No Therapy in Patients With Nonvalvular AF With 0 or 1 Stroke Risk Factor Based on CHA$_2$DS$_2$-VASc score

Lip et al JACC 2015 [http://dx.doi.org/10.1016/j.jacc.2015.01.044](http://dx.doi.org/10.1016/j.jacc.2015.01.044)

Event Rates Per 100 PYs at 1 Year FU According to Treatment Strategy Initiated at Day 14 After Discharge With Incident AF

<table>
<thead>
<tr>
<th>Treatment Strategy</th>
<th>No Rx</th>
<th>Aspirin</th>
<th>Warfarin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No risk factors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischaemic stroke</td>
<td>0.49</td>
<td>0.78</td>
<td>0.88</td>
</tr>
<tr>
<td>Death</td>
<td>3.87</td>
<td>3.12</td>
<td>2.20</td>
</tr>
<tr>
<td>ICH</td>
<td>0.15</td>
<td>0.10</td>
<td>0.16</td>
</tr>
<tr>
<td><strong>1 risk factor</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischaemic stroke</td>
<td>1.50</td>
<td>1.45</td>
<td>1.02</td>
</tr>
<tr>
<td>Death</td>
<td>11.3</td>
<td>5.66</td>
<td>4.00</td>
</tr>
<tr>
<td>ICH</td>
<td>0.36</td>
<td>0.20</td>
<td>0.44</td>
</tr>
</tbody>
</table>

Low-risk patients have a truly low risk for stroke and bleeding.

With 1 additional stroke risk factor, there was a significant increase in event rates (particularly mortality) if non-anticoagulated.
**CHA$_2$DS$_2$-VASc 1: to anticoagulate or not?**

- Risk scores are designed to be reductionist and simple to facilitate their practical and broad use in various (and busy) clinical settings.
  - This is not indicative of a failure of CHA$_2$DS$_2$-VASc as a stroke risk score, as it is not necessary for risk scores to identify exact risk but to provide useful thresholds at which important dichotomous clinical decisions are made; for example, use of anticoagulation vs no anticoagulation.

> Although the actual stroke risk may vary with respect to any given score in an individual patient, we should be less obsessed with identifying the “exact” stroke risk, which is not possible given the basic fact that a patient’s clinical status does not remain static, and in most patients with at least one risk factor for stroke, we should be considering OAC as they are at an elevated risk.

The ESC and NICE guidelines recommend a two-step approach.

- Step 1: Initially identify the low-risk patients; then ....
- Step 2: Offer OAC to those with one or more stroke risk factors. As the decision is made for OAC, step 2 is irrespective of whether we are dealing with a CHA$_2$DS$_2$-VASc score 2, 3, 4 or more!