Improving Stroke Risk Stratification Using the CHADS₂ and CHA₂DS₂-VASc Risk Scores in Patients With Paroxysmal Atrial Fibrillation by Continuous Arrhythmia Burden Monitoring

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Background and Purpose—In patients with atrial fibrillation (AF), stroke risk stratification schema do not consider AF parameters. The aim of the study is to assess the impact of combining risk factors with continuous AF burden monitoring.

Methods—In this retrospective study 568 patients implanted with a DDDR-P pacemaker (AT-500; Medtronic) and a history of AF were continuously monitored for 1 year.

Results—During follow-up, 14 patients (2.5%) had a thromboembolic event. Patients were divided into 3 groups: AF burden ≤5 minutes per day (AF-free; n=223 [39%]), AF burden >5 minutes but <24 hours per day (AF-5 minutes; n=179 [32%]), and AF burden ≥24 hours (AF-24 hours; n=166 [29%]). Patients were also classified according to CHADS₂ and CHA₂DS₂-VASc risk scores. The discrimination ability of each risk score was evaluated performing a logistic regression analysis and calculating the corresponding C-statistic. The addition of AF burden improved C-statistics: for CHADS₂ from 0.653 (P=0.051) to 0.713 (P=0.007); for CHA₂DS₂-VASc, from 0.898 (P<0.0001) to 0.910 (P<0.0001).

Conclusions—The CHA₂DS₂-VASc score had a high sensitivity to predict thromboembolism. Implementation of device data on AF presence/duration/burden has the potential to contribute to improved clinical risk stratification and should be tested prospectively. (Stroke. 2011;42:1768-1770.)

Key Words: anticoagulation ■ antithrombotics ■ atrial fibrillation ■ embolic stroke ■ heart–brain relationships ■ platelet inhibitors ■ prevention ■ prognosis

The burden of atrial fibrillation (AF) and the duration of arrhythmia episodes have never been included in risk stratification schemes because reliance on clinical symptoms and intermittent electrocardiographic assessments can underestimate AF burden.1,2 Diagnostic features in implantable devices are sophisticated enough to provide reliable information on atrial arrhythmias, allowing data to generate hypotheses on stroke risk stratification.1–4 The aim of the study is to test the hypothesis that continuous AF burden monitoring would enhance the sensitivity/specificity of stroke risk stratification schema based on clinical risk factors.

Methods

Patients with a dual-chamber pacemaker (Medtronic AT-500) and a history of paroxysmal atrial tachyarrhythmias were included in this study. A day-by-day trend of AF burden (=time spent in AF during each day) was available for each patient during 1-year follow-up with data on minutes/hour spent at high atrial rates.2 Patients were divided into 3 groups: (1) maximum AF burden ≤5 minutes per day (AF-free); (2) maximum AF burden >5 minutes but <24 hours per day (AF-5 minutes); and (3) AF burden of ≥24 hours, the latter considering also the following days (AF-24 hours). Patients were also classified according to the CHADS₂ and the CHA₂DS₂-VASc risk scores. A committee of 2 physicians, blinded to AF burden, evaluated the thromboembolic

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events (TEs): stroke, transient ischemic attack, and peripheral arterial embolism.

Sensitivity and specificity of each score in predicting TE events, either alone or in combination with AF, were assessed. The number of patients who would require long-term oral anticoagulation therapy (OAC) was calculated according to each combination. Uni- and multivariable logistic regressions were performed considering the CHADS2 and the CHA2DS2-VASc scores as continuous variables, whereas AF burden was analyzed by class. For each regression model, the predicted probabilities were used to assess the discriminating ability of each score by means of the C-statistic and its 95% CI. Statistical analysis was made by SPSS (SPSS Inc, Chicago, IL) software, Version 11.5.

Results

Data from 568 patients (70 ± 10 years) were analyzed. Patients were categorized into 3 AF groups: AF-free (n = 223 [39%]), AF-5 minutes (n = 179 [32%]), and AF-24 hours (n = 166 [29%]). In groups AF-free, AF-5 minutes, and AF-24 hours, respectively, aspirin was prescribed in 30%, 23%, and 18%; OAC in 19%, 22%, and 42%; and aspirin and OAC in 6%, 1.7%, and 4%. OAC use was higher in the AF-24 hours group versus AF-free or AF-5 minutes (P < 0.0001).

Fourteen patients (2.5%) had a TE (cerebral embolism: 12; peripheral embolism: 2). Table 1 shows the baseline characteristics of the patient population. Sensitivity, specificity, and C-statistic for CHADS2 score, CHA2DS2-VASc score, and their combination with AF data are summarized in Table 2.

Compared with CHADS2 score alone, its combination with AF parameters gave the best compromise between sensitivity (79%) and specificity (63%). The CHA2DS2-VASc score alone had 100% sensitivity. However, its specificity was low: 7% and 24%, respectively. When combined with AF data, it increased specificity up to 42% without relevant changes in sensitivity. The Figure shows the percentage of candidates for OAC according to each schema.

Discussion

The major finding of this study is that risk stratification for stroke can be improved by combining either CHADS2 or CHA2DS2-VASc score with AF parameters. CHA2DS2-VASc scheme has the highest sensitivity to predict TE; its integration with continuous AF burden improves specificity and the discriminating ability for TE. Thus, data on AF burden may refine risk stratification for stroke and this is evident even when OAC is more commonly prescribed, as expected, in patients with the highest AF burden.

The CHADS2 score is a simple and widely used scheme; OAC is recommended in patients with a score ≥2. Greater uncertainty arises for those with a score of 0 to 1.5 The CHA2DS2-VASc score is very helpful in this category of patients, but its specificity is limited, thus identifying a high number of candidates for long-term OAC. Any method for additional improvement of risk stratification is of clinical interest, especially in low-risk patients in whom the risk of bleeding linked to OAC may be a clinical concern.  

Table 1. Study Population Baseline Characteristics

<table>
<thead>
<tr>
<th>Overall Population</th>
<th>AF-free</th>
<th>AF-5 min</th>
<th>AF-24 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>568</td>
<td>166 (29%)</td>
<td>179 (31%)</td>
</tr>
<tr>
<td>Female gender</td>
<td>288 (51)</td>
<td>68 (41)</td>
<td>115 (64)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>8 (1.4)</td>
<td>2 (1.2)</td>
<td>3 (1.7)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>274 (48)</td>
<td>73 (44)</td>
<td>88 (49)</td>
</tr>
<tr>
<td>Age ≥75 y</td>
<td>202 (36)</td>
<td>51 (31)</td>
<td>68 (38)</td>
</tr>
<tr>
<td>Age 65–74 y</td>
<td>237 (42)</td>
<td>79 (48)</td>
<td>83 (46)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>45 (8)</td>
<td>13 (7.8)</td>
<td>13 (7.3)</td>
</tr>
<tr>
<td>Prior thromboembolism</td>
<td>8 (1.4)</td>
<td>2 (1.2)</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Vascular disease</td>
<td>108 (19)</td>
<td>23 (14)</td>
<td>45 (25)</td>
</tr>
<tr>
<td>Thromboembolic events at follow-up</td>
<td>14 (2.5)</td>
<td>2 (1.2)</td>
<td>3 (1.7)</td>
</tr>
</tbody>
</table>

Vascular disease indicates prior myocardial infarction, peripheral artery disease, or aortic plaque; AF, atrial fibrillation; h, hours; min, minutes.

*Data are shown as no. (%).

Table 2. Sensitivity, Specificity, and Predictive Ability (C-Statistics and Their 95% CIs) for the CHADS2 and CHA2DS2-VASc Stroke Risk Stratification Schema in Relation to Atrial Fibrillation Burden

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>C-Statistic</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHADS2</td>
<td>0.653</td>
<td>0.50–0.81</td>
<td>0.051</td>
<td></td>
</tr>
<tr>
<td>CHADS2 ≥1</td>
<td>86</td>
<td>30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHADS2 ≥2</td>
<td>43</td>
<td>78</td>
<td></td>
<td></td>
</tr>
<tr>
<td>[CHADS2 ≥3]+[CHADS2 = 2 except AF-free]+[CHADS2 = 1 with AF ≥24 h]</td>
<td>79</td>
<td>63</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHADS2+AF burden</td>
<td>0.713</td>
<td>0.56–0.86</td>
<td>0.007</td>
<td></td>
</tr>
<tr>
<td>CHA2DS2-VASc</td>
<td>0.898</td>
<td>0.84–0.96</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>CHA2DS2-VASc ≥1</td>
<td>100</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHA2DS2-VASc ≥2</td>
<td>100</td>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>[CHA2DS2-VASc ≥3]+[CHA2DS2-VASc = 2 except AF-free]</td>
<td>100</td>
<td>34</td>
<td></td>
<td></td>
</tr>
<tr>
<td>[CHA2DS2-VASc ≥3]+[CHA2DS2-VASc = 2 with AF =24 h]</td>
<td>93</td>
<td>42</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHA2DS2-VASc+AF burden</td>
<td>0.910</td>
<td>0.86–0.93</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation.
The study was performed in a relatively modest sample size and in a specific population with previous AF and sick sinus syndrome. The follow-up period was limited to 1 year. According to the hypothesis-generating nature of our findings, there is the need for further studies on larger cohorts.

**Conclusions**
The CHA2DS2-VASc score has a high sensitivity, indicating good predictive value for truly low-risk subjects for TE. Integration of AF presence/duration/burden has the potential to contribute to improved clinical risk stratification and its aid to clinical decision-making should be tested prospectively.

**Acknowledgments**
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**Disclosures**
G.C. and T.D.S. are employees of Medtronic. G.Y.H.L. served as a consultant for Bayer, Astellas, Merck, AstraZeneca, Sanofi, BMS/ Pfizer, and Boehringer and has been on the speakers bureau for Bayer, BMS/Pfizer, Boehringer, and Sanofi.

**References**
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SUPPLEMENTAL MATERIAL
Supplemental Methods

APPENDIX

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Supplemental Figure

Example of Cardiac Compass by AT 500 pacemaker

Full Summary Report

Cardiac Compass

Program/Template
Drop Change
CVA/Stroke/Other
AT/AF Patient/Check

AT/AF total/day
AT/AF episode/day
AT/AF Change
Treated AT/AF episode/day

% ATP Success
Antibiotic Change

% Pace/day
- A. Total
- A. AntiARRP

% V Pace/day

Trend of the Daily AF Burden (h/day)
**Figure Legend**

Example of Cardiac Compass diagnostics available in the pacemakers used in the study (Medtronic AT 500).

AF: atrial fibrillation; APP: atrial preference pacing; ARS: atrial rate stabilization; AT: atrial tachycardia; ATP: anti-tachycardia pacing.