Abstract: 286

Predictors of atrial fibrillation in patients with embolic stroke of undetermined source: an analysis of the RE-SPECT ESUS trial

Authors:
C.B. Granger¹, R.L. Sacco², J.D. Easton³, J. Meyerhoff⁴, L. Cronin⁵, E. Kleine⁶, C. Grauer⁶, M.C. Bahit⁷, M. Brueckmann⁴, H.-C. Diener⁸, ¹Duke University Medical Center - Durham - United States of America, ²University of Miami - Miami - United States of America, ³University of California-San Francisco - San Francisco - United States of America, ⁴Boehringer Ingelheim International GmbH - Ingelheim am Rhein - Germany, ⁵Boehringer Ingelheim (Canada) Ltd/Lte - Burlington - Canada, ⁶Boehringer Ingelheim Pharma GmbH & Co. KG - Ingelheim am Rhein - Germany, ⁷INECO Neurociencias Oroño - Rosario - Argentina, ⁸University of Duisburg-Essen - Duisberg - Germany

On behalf: The RE-SPECT ESUS Steering Committee and Investigators

Topic(s):
Stroke: Cardiogenic Embolism

Citation:
European Heart Journal (2019) 40 (Supplement), 92

Background: A proportion of patients with embolic stroke of undetermined source (ESUS) may have silent atrial fibrillation (AF) or develop AF after the initial evaluation. Better understanding of risk for identification is critical to implement optimal monitoring strategies with the goal of preventing recurrent stroke. The RE-SPECT ESUS trial provides an opportunity to assess predictors for developing AF and associated recurrent stroke.

Methods: RE-SPECT ESUS was a randomized, controlled trial (564 sites, 42 countries) assessing dabigatran versus aspirin for the prevention of recurrent stroke in patients with ESUS. Of 5390 patients enrolled and followed for a median of 19 months, 403 (7.5%) were found to develop AF reported as an adverse event or using cardiac monitoring per standard clinical care. Univariable and multivariable regression analyses for predictors of AF were conducted.

Results: In a multivariable analysis, clinical predictors for developing AF were: older age, history of heart failure, lower heart rate, hypertension, higher body mass index, and being from Western Europe (Table). Using several published predictive models, including HAVOC, C2HEST, ASSF, ARIC, and CHA2DS2-VASc, high scores were associated with increased rates of AF. In patients who developed AF, recurrent stroke occurred in 7.0% per year, versus 4.2% per year in patients who did not develop AF (hazard ratio 1.75; 95% CI 1.30–2.35, p=0.0002).

Conclusion: Besides age as the most important variable, several other factors, including lower heart rate, higher body mass index, and hypertension, are independent predictors of AF after ESUS. Understanding who is at higher risk of developing AF may help identify patients requiring more intense, long-term cardiac monitoring.
Abstract:

Predictors of atrial fibrillation in patients with embolic stroke of undetermined source: an analysis of the RE-SPECT ESUS trial

Authors:
C.B. Granger 1, R.L. Sacco 2, J.D. Easton 3, J. Meyerhoff 4, L. Cronin 5, E. Kleine 6, C. Grauer 6, M.C. Bahit 7, M. Brueckmann 4, H.-C. Diener 8,

1 Duke University Medical Center - Durham - United States of America,
2 University of Miami - Miami - United States of America,
3 University of California-San Francisco - San Francisco - United States of America,
4 Boehringer Ingelheim International GmbH - Ingelheim am Rhein - Germany,
5 Boehringer Ingelheim (Canada) Ltd/Lte - Burlington - Canada,
6 Boehringer Ingelheim Pharma GmbH & Co. KG - Ingelheim am Rhein - Germany,
7 INECO Neurociencias Orono - Rosario - Argentina,
8 University of Duisburg-Essen - Duisberg - Germany

On behalf: The RE-SPECT ESUS Steering Committee and Investigators

Topic(s):
Stroke: Cardiogenic Embolism

Citation:
European Heart Journal (2019) 40 (Supplement), 92

Background:
A proportion of patients with embolic stroke of undetermined source (ESUS) may have silent atrial fibrillation (AF) or develop AF after the initial evaluation. Better understanding of risk for identification is critical to implement optimal monitoring strategies with the goal of preventing recurrent stroke. The RE-SPECT ESUS trial provides an opportunity to assess predictors for developing AF and associated recurrent stroke.

Methods:
RE-SPECT ESUS was a randomized, controlled trial (564 sites, 42 countries) assessing dabigatran versus aspirin for the prevention of recurrent stroke in patients with ESUS. Of 5390 patients enrolled and followed for a median of 19 months, 403 (7.5%) were found to develop AF reported as an adverse event or using cardiac monitoring per standard clinical care. Univariable and multivariable regression analyses for predictors of AF were conducted.

Results:
In a multivariable analysis, clinical predictors for developing AF were: older age, history of heart failure, lower heart rate, hypertension, higher body mass index, and being from Western Europe (Table). Using several published predictive models, including HAVOC, C2HEST, AS5F, ARIC, and CHA2DS2-VASc, high scores were associated with increased rates of AF. In patients who developed AF, recurrent stroke occurred in 7.0% per year, versus 4.2% per year in patients who did not develop AF (hazard ratio 1.75; 95% CI 1.30–2.35, p=0.0002).

Conclusion:
Besides age as the most important variable, several other factors, including lower heart rate, higher body mass index, and hypertension, are independent predictors of AF after ESUS. Understanding who is at higher risk of developing AF may help identify patients requiring more intense, long-term cardiac monitoring.

Table: Clinical predictors for AF during the RE-SPECT ESUS trial: multivariable regression model

<table>
<thead>
<tr>
<th>Baseline characteristic</th>
<th>OR (95% CI)</th>
<th>p-value</th>
<th>Chi-square</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs), OR for 10 units increase</td>
<td>1.82 (1.62–2.04)</td>
<td>&lt;0.0001</td>
<td>101.3</td>
</tr>
<tr>
<td>Region</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Western Europe vs North America</td>
<td>1.42 (1.00–2.02)</td>
<td>&lt;0.0001</td>
<td>47.2</td>
</tr>
<tr>
<td>Western Europe vs Central Europe</td>
<td>2.27 (1.49–3.44)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Western Europe vs Latin America</td>
<td>2.81 (1.36–5.81)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Western Europe vs Asia</td>
<td>2.48 (1.75–3.52)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Western Europe vs Other</td>
<td>2.64 (1.32–5.27)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulse rate (beats/min), OR for 10 units decrease</td>
<td>1.41 (1.27–1.56)</td>
<td>&lt;0.0001</td>
<td>40.5</td>
</tr>
<tr>
<td>Body mass index (kg/m²), OR for 5 units increase</td>
<td>1.18 (1.05–1.32)</td>
<td>0.0054</td>
<td>7.7</td>
</tr>
<tr>
<td>Hypertension, yes vs no</td>
<td>1.35 (1.02–1.79)</td>
<td>0.0356</td>
<td>4.4</td>
</tr>
<tr>
<td>History of heart failure, yes vs no</td>
<td>1.71 (1.03–2.83)</td>
<td>0.0383</td>
<td>4.3</td>
</tr>
</tbody>
</table>

Variables selected by backward selection (using SLSTAY=0.1), re-calculated on the maximal patient set.

AF, atrial fibrillation; CI, confidence interval; OR, odds ratio.