

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

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**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

Baseline characteristic	OR (95% CI)	p-value	Chi-square
Age (yrs), OR for 10 units increase	1.82 (1.62–2.04)	<0.0001	101.3
Region		<0.0001	47.2
Western Europe vs North America	1.42 (1.00–2.02)		
Western Europe vs Central Europe	2.27 (1.49–3.44)		
Western Europe vs Latin America	2.81 (1.36–5.81)		
Western Europe vs Asia	2.48 (1.75–3.52)		
Western Europe vs Other	2.64 (1.32–5.27)		
Pulse rate (beats/min), OR for 10 units decrease	1.41 (1.27–1.56)	<0.0001	40.5
Body mass index (kg/m <sup>2</sup> ), OR for 5 units increase	1.18 (1.05–1.32)	0.0054	7.7
Hypertension, yes vs no	1.35 (1.02–1.79)	0.0356	4.4
History of heart failure, yes vs no	1.71 (1.03–2.83)	0.0383	4.3

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.