### **EDITORIAL COMMENT**

# Can We Predict Thromboembolic Events in Low-Risk Patients Undergoing Catheter Ablation of Atrial Fibrillation?

## The Hanging CHAD\*

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Atrial fibrillation (AF) is the most common arrhythmia. It is associated with a decreased quality of life, increased hospitalizations, and a 2-fold increased risk of death. Perhaps most importantly, the risk of a thromboembolic (TE) event in patients with AF is increased 5-fold (1–3).

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Multiple schema have been proposed to risk stratify patients with AF for TE events. A simple risk assessment scheme is the  $CHADS_2$  score (4), which evolved from the Stroke Prevention in AF (SPAF) investigators criteria, and is the primary basis for guiding antithrombotic therapy in the 2006 American College of Cardiology/American Heart Association (ACC/AHA) AF guidelines (2). More recently, the CHA<sub>2</sub>DS<sub>2</sub>-VASc score was described (5). This scoring system provides an increased emphasis on age >75years and includes the additional risk factors of vascular disease and female gender. The CHA2DS2-VASc score improves the predictive value for TE events in patients with AF (5,6). Both the CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc scores were validated as predictors of TE events in patients with AF who were treated pharmacologically for rate and/or rhythm control. Importantly, and perhaps under-recognized, these studies demonstrate that the CHA2DS2-VASc score

can identify the patients with a CHADS<sub>2</sub> score of 0 or 1 who have an increased risk of a TE event. That is,  $CHA_2DS_2$ -VASc can identify the low-risk CHADS<sub>2</sub> patient who is actually high risk for a TE event (5,6).

Catheter ablation is a standard treatment for patients with drug-refractory, symptomatic AF (2). Although the modalities and approaches to catheter ablation of AF differ between centers, left atrial (LA) ablation with pulmonary vein isolation is generally a cornerstone to this therapy. The success rate of catheter ablation varies according to the pattern and duration of AF, the LA size, and LA substrate, and is approximately 70% (7). The major complication rate associated with catheter ablation of AF is 3% to 5%, and is generally related to vascular access, although there is a small risk of a TE event and death (7,8). TE events immediately after catheter ablation of AF are thought to be related to thrombus formation on the trans-septal sheaths and catheters, or to char and thrombus formation at the ablation sites. TE events remote from the ablation procedure may be due to decreases in LA transport after catheter ablation of AF or to the intrinsic risk of TE events in patients with AF (9).

There have been several attempts to quantify and predict TE events and death rates in patients undergoing catheter ablation of AF. Oral et al. (10) studied 755 consecutive patients undergoing catheter ablation of AF. All patients were placed on oral anticoagulation for 3 months after the procedure. A TE event occurred in 1.1% of patients, with the majority of events occurring within the first two weeks. A worldwide survey of 20,825 catheter ablation procedures for AF reported a TE event rate of 1.0% and a death rate of 0.15% (7). In a recent study, 232 consecutive patients underwent brain magnetic resonance imaging after catheter ablation of AF. The symptomatic TE rate was 0.4%, and the rate of silent TE events was 14% (11). These studies were unable to demonstrate clinical predictors of TE events or death in patients undergoing catheter ablation of AF. In addition, the findings of a transesophageal echocardiogram (TEE), with the exception of a LA thrombus, do not predict the patient at risk for a TE event after catheter ablation of AF (12).

In this issue of the *Journal*, Chao et al. (13) provide some data that help predict who is at risk for a TE event after catheter ablation of AF. The authors evaluate the usefulness of the CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc scores to predict the risk of TE events and death in patients undergoing catheter ablation of AF. A total of 565 patients, of whom 440 had paroxysmal AF, were enrolled in the study and followed for a mean of 39.2 months. Before catheter ablation of AF, oral anticoagulation therapy was based on the patient's CHADS<sub>2</sub> score. A TEE was performed on all patients prior to catheter ablation of AF in order to exclude the presence of a LA thrombus. Catheter ablation of AF was performed in a standard fashion with 2 circumferential sets of lesions around the right and left pulmonary vein (PV) ostia with confirmation of PV isolation, using either a conventional

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4-mm-tip or irrigated-tip catheter. Additional linear ablation sets in the LA and coronary sinus were performed based on the persistence or inducibility of AF after PV isolation. After catheter ablation of AF, warfarin was administered for at least 3 months to those patients who were receiving it before ablation. The decision to discontinue warfarin after ablation was individualized and based on physician preference. Clinical follow-up occurred every 1 to 3 months after catheter ablation of AF, with adverse events and deaths evaluated by chart review, telephone consultations, and review of the National Death Registry of Taiwan.

The combined endpoint of adverse events included ischemic stroke, transient ischemic attack (TIA), peripheral embolism, pulmonary embolism, and death. Overall, 27 (4.8%) adverse events occurred, including 9 deaths, 9 ischemic strokes, 6 TIAs, 1 peripheral embolus, and 2 pulmonary emboli. Baseline CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc scores were calculated. The predictive accuracy of each score, as well as the optimal cutoff values to predict adverse events was identified using receiver-operator characteristic curves. Univariate analysis demonstrated that older age, hypertension, congestive heart failure, coronary artery disease, previous TE event, larger LA diameter, and persistent AF were associated with adverse events. Multivariate analysis demonstrated that the only independent predictors of adverse events were the CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc scores.

Therefore, the authors conclude that the CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc scores may be useful for predicting adverse events after catheter ablation of AF. A linear relationship between the CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc scores, and the rate of adverse events was observed. Using a cutoff value of 2 for both the CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc scores, there was a significant difference in event rates in patients undergoing catheter ablation of AF with CHADS<sub>2</sub> scores  $\geq 2$  or < 2 (15.2% vs. 2.4%), as well as in patients with  $CHA_2DS_2$ -VASc scores  $\geq 2$  or  $\leq 2$  (11.1% vs. 1.1%). However, the most striking finding in this study was seen among the 460 patients with a CHADS<sub>2</sub> score of 0 or 1. There were 11 (2.4%) adverse events in this group. Among these 460 patients, 98 (21%) had a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of  $\geq$ 2. The adverse event rate of the 362 patients with a CHADS<sub>2</sub> score of 0 or 1 and a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of <2 was 1.1%, whereas the adverse event rate among of the 98 patients with a CHADS<sub>2</sub> score of 0 or 1 and a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of  $\geq 2$ was 7.1%. These data demonstrate the improved sensitivity of the CHA<sub>2</sub>DS<sub>2</sub>-VASc scoring system.

The authors point out at least 2 important limitations of this study. First, the use of anticoagulation therapy was not standardized, and low-risk patients may not have received oral anticoagulation therapy for the first 3 months after catheter ablation of AF. Generally, oral anticoagulation therapy is recommended for at least the first 3 months after catheter ablation of AF, regardless of the baseline risk of a TE event. This may explain the relatively high rate of TE events in this study. Second, this was an observational study with nonuniform follow-up.

Overall, the authors should be congratulated for their successful effort in identifying a method to predict which patients undergoing catheter ablation of AF may be at increased risk for TE events and death. The CHA2DS2-VASc score has been incorporated into the European Society of Cardiology 2010 AF guidelines, but is not mentioned in the AHA/ACC 2011 update to the 2006 AF guidelines (1,2,14). Perhaps this is why healthcare providers in the United States mainly utilize the CHADS<sub>2</sub> risk stratification scoring system to help guide antithrombotic therapy in patients with AF. For patients with AF and  $CHADS_2$  scores >2, oral anticoagulation therapy is clearly superior to aspirin in prevention of TE events (1,2). However, for patients with AF and a CHADS<sub>2</sub> score of 0 or 1, the CHA2DS2-VASc score may help to identify the "low risk" patient at "high risk" for a TE event. The data from Chao et al. (13) may allow us to identify the patient who is at high risk for a TE event, but has a hanging CHAD.

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