As the treatment of symptoms related to atrial fibrillation has advanced, the management of associated thromboembolic risks has progressed as well through the newly developed oral anticoagulants. The 2014 American Heart Association/American College of Cardiology/Heart Rhythm Society and the 2012 European Society of Cardiology guidelines on thromboprophylaxis for atrial fibrillation grant a class IIa and class Ib recommendation, respectively, for using 1 of the new anticoagulants instead of warfarin for at least 3 weeks before cardioversion (1,2). This recommendation is based on subgroup analyses from RE-LY (Randomized Evaluation of Long-Term Anticoagulation Therapy) (dabigatran), ROCKET-AF (Rivaroxaban Once-Daily Oral Direct Factor Xa Inhibition Compared With Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation) (rivaroxaban), and ARISTOTLE (Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation) (apixaban), suggesting that electrical cardioversion in patients treated with these agents has a low thromboembolic risk that is comparable to warfarin (3–6). None of these trials had detection of left atrial appendage thrombus on transesophageal echocardiography (TEE) as an endpoint. These strategies have been adapted to patients undergoing ablation for atrial fibrillation. The management of anticoagulation therapy before and at the time of the ablation procedure has progressed from withholding to continuing these oral agents as the experience in centers performing ablation has resulted in improved safety profiles (7).

In this issue of JACC: Clinical Electrophysiology, Frenkel et al. (8) present data that further shed light on the adequacy of this strategy. Atrial thrombus was detected in 2.9% of 183 patients receiving a “non-vitamin K antagonist oral anticoagulant” (new oral anticoagulant [NOAC]) and in 4.4% of 205 patients receiving warfarin after at least 4 weeks of continuous use. There was no statistical difference between the 2 therapies. Not surprisingly, the incidence of reported thrombus was higher in patients with a high CHA2DS2-VASc (Congestive Heart Failure, Hypertension, Age ($\geq$75 years), Diabetes, Stroke/Transient Ischemic Attack, Vascular Disease, Age (65–74 years), Sex (Female) score) score. Heart failure and persistent atrial fibrillation were predictors of thrombus detection. The other finding of intrigue was a nonsignificant trend in the absence of any thrombus with the use of apixaban, but the study was underpowered to evaluate potential differences among NOACs.

This study uncovers several relevant questions. Is it possible that by not performing routine TEE before cardioversion in patients treated with either warfarin or a NOAC, we are missing some of these thrombi in the presence of adequate anticoagulation in the periconversion period? Is 3 to 4 weeks of recommended anticoagulation long enough for all patients with atrial fibrillation regardless of their CHA2DS2-VASc? Subclinical events not readily detectable by routine examinations should not be overlooked, as learned from magnetic resonance imaging and cognitive
testing findings in patients post-atrial fibrillation ablation (9,10).

Conversely, this current study reported higher incidences of detected thrombus and dense spontaneous echocardiographic contrast in patients who are systemically anticoagulated than in other previous studies (11-13). Puwanant et al. (12) reported a larger cohort of 1,058 patients who underwent TEE in preparation for atrial fibrillation ablation. All patients were maintained on warfarin with a relatively stringent schedule of international normalized ratio monitoring before the planned procedure. Compared to the data by Frenkel et al. (8), Puwanant et al. (12) found significantly lower incidences of detected intracardiac thrombus (0.6%) and dense echocardiographic contrast, “sludge” (2.1%). Although it may be opportune to attribute the differences in the incidences between the 2 studies to the differences in the study population, with the patients in the Frenkel et al. (8) study reporting higher composite and averaged thromboembolic risk scores. Side-by-side comparison, however, shows that the Frenkel et al. (8) study reported substantially higher rates of detected thrombus across all patients with lower risk scores of 0 to 2, which is notable, especially because the lower CHA2DS2-VASc used in the study by Frenkel et al. (8) is more sensitive for detecting lower-risk patients than is the CHADS2 (Congestive Heart Failure, Hypertension, Age, Diabetes, Stroke/Transient Ischemic Attack) score used in the study by Puwanant et al. (12).

Despite the availability of other imaging modalities, TEE has remained widely accepted as the “gold standard” test to rule out the presence of intracardiac thrombus in patients with atrial fibrillation (14). However, the techniques used in testing and interpretation of results may vary. Although the finding of spontaneous echocardiographic contrast is relatively uniform, identifying thrombus in the left atrium can be more subjective. Although the test is well documented in its sensitivity, the specificity of the test is, to a degree, subject to operator interpretation because of the differences in the techniques used, such as imaging duration, use of echocardiographic contrast, imaging frequency, multiple orthogonal biplane views, and criteria such as thrombus size. This study was a retrospective compilation of patients undergoing TEE before ablation for atrial fibrillation, and the primary intent likely was the safety of the planned procedure. It is unclear if the transesophageal echocardiographic findings in this report were assessed by more than 1 observer per case. From the perspective of investigation, it would be helpful if the transesophageal echocardiographic results were confirmed, particularly by an observer who was not immediately confronted with the consequences of potential thromboembolic risks from the ablation procedure.

Findings in this report may potentially shift the risk/benefit ratio in pre-procedural TEE in patients undergoing atrial fibrillation ablation. At present, routine TEE should still be considered in most patients undergoing conversion treatment for atrial fibrillation, even with uninterrupted anticoagulation using warfarin or a NOAC. Distilled from these retrospective studies, patients with a CHA2DS2-VASc of zero with a normal left atrium size, left ventricular function, and no congestive heart failure appear to be at low risk for thromboembolic findings. There is now a need for well-designed and properly powered prospective trials to assess the presence and clinical impact of intracardiac thrombi before ablation, and perhaps cardioversion, in at-risk patients with assured anticoagulation. Furthermore, the best approach to patients with demonstrated atrial thrombus despite anticoagulation therapy remains elusive. Switching to a different anticoagulant or extending the duration of the same agent by several weeks continue to be the 2 main strategies. Individual patient circumstances certainly play an important role in selecting either strategy or combining the 2 strategies. RE-LATED_AF (Resolution of Left Atrial-Appendage Thrombus—Effects of Dabigatran in Patients with Atrial Fibrillation) (with dabigatran) and X-TRA (Efficacy of Once Daily Oral Rivaroxaban for Treatment of Thrombus in Left Atrial/Left Atrial Appendage in Subjects With Nonvalvular Atrial Fibrillation or Atrial Flutter) (with rivaroxaban) are 2 upcoming trials that will address this issue.

REFERENCES


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