Dabigatran is an oral direct thrombin inhibitor licensed for use by the Food and Drug Administration.1,2 This novel anticoagulant is effective and approved for prevention of stroke and systemic embolism in nonvalvular atrial fibrillation (AF) and prevention of venous thromboembolism in adults receiving elective total hip or knee replacement surgery.1,2 These images present a cautionary account of failed dabigatran anticoagulation in a patient with valvular AF: an indication for which its use has not been approved.

A 50-year-old female with severe rheumatic mitral stenosis underwent open mitral valvotomy under cardiopulmonary bypass 25 years prior. On subsequent annual surveillance, she remained asymptomatic and her mitral stenosis remained moderate on echocardiography with a mean transmitral gradient of 8 mm Hg. Permanent AF was previously diagnosed 12 months earlier, and she was commenced on warfarin and metoprolol. She had stable anticoagulation monitoring, no bleeding complications, and normal renal function, but was needle-phobic with psychological stress from regular international normalized ratio monitoring. Her family physician considered it worthwhile to switch from warfarin to dabigatran (150 mg BID). A recent transthoracic ECG performed 2 months before the commencement of dabigatran had shown no atrial thrombus (Figure A).

Four months later, routine transthoracic echocardiography demonstrated a large homogenous mobile mass in her dilated left atrium (Figure B and C). Cardiac MRI was performed to differentiate thrombus from tumor and confirmed a large, low signal mass adherent to the left atrial wall without gadolinium enhancement, consistent with thrombus (Figure D and E). She had been compliant with dabigatran. Dabigatran was ceased, and warfarin recommenced under intravenous heparin cover. She was well at 11-month follow-up with no embolic complications and marked reduction in thrombus size on repeated imaging (Figure F).

Discussion
These images demonstrate the first documented case of thrombosis in AF with coexistent valvular heart disease (without valve replacement), despite anticoagulation with a direct thrombin inhibitor.

At present, there is minimal data available on the efficacy of dabigatran in valvular heart disease. Four cases of thrombosis complicating dabigatran use in the setting of bileaflet mechanical valve prostheses have been reported in the literature.1–3 Although the majority of patients presented with dyspnea resulting from mechanical valve thrombosis, stroke complicating valvular thrombus has also been demonstrated.1–3 The propensity for valvular thrombus does not seem to be affected
by valve position with both mechanical aortic and mitral valvular thrombus demonstrated.\textsuperscript{1–3} Further study is hence required before the routine use of dabigatran outside currently approved indications.

The present recruiting Randomized, phase II study to Evaluate the safety and pharmacokinetics of oral dabigatran etexilate in patients after heart valve replacement\textsuperscript{4} will evaluate the therapeutic dosing of dabigatran (150, 220, and 300 mg BID) against warfarin in patients with bileaflet mechanical heart valves. It is hoped that this data will provide definitive results regarding the use of direct thrombin inhibitors in this clinical setting. However, results from this trial are unlikely to be sufficient to address the issue of direct thrombin inhibitors for prevention of embolic events in patients with native valvular disease and AF. Further randomized trials are required to address the efficacy of direct thrombin inhibitor efficacy in patients with native valvular AF.

In the interim off-label usage of dabigatran, particularly in valvular heart disease, both with and without valve replacement should be avoided outside the clinical trial setting until further evidence becomes available. Clinicians need to remain aware that direct thrombin inhibitors have demonstrated efficacy in only limited clinical scenarios (stroke prevention in nonvalvular AF and postsurgical venous thromboprophylaxis), and that usage outside these settings should be strongly avoided. Medication use outside such approved indications warrant careful consideration of the risks associated with administering therapy of unknown clinical efficacy.

**Disclosures**

None.

**References**


**Key Words:** dabigatran • valvular heart disease
Massive Left Atrial Thrombus in a Patient With Rheumatic Mitral Stenosis and Atrial Fibrillation While Anticoagulated With Dabigatran
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