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# Giant Left Atrial Thrombus Despite Anticoagulation with Apixaban in a Patient with Mitral Stenosis and Atrial Fibrillation

Authors' Contribution:  
Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
Funds Collection G

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**Conflict of interest:** None declared

**Patient:** Female, 64-year-old  
**Final Diagnosis:** Thrombus  
**Symptoms:** Fatigue • palpitation  
**Medication:** —  
**Clinical Procedure:** —  
**Specialty:** Cardiology

**Objective:** Unusual clinical course  
**Background:** In patients with atrial fibrillation (AF), the presence of a left atrial thrombus correlates with the highest risk of stroke. Mitral stenosis (MS) is an acquired disease that leads to atrial pressure overload and subsequent significant anatomical and electrical remodeling of the left atrium. This promotes the occurrence of AF and atrial thrombus formation. Proper anticoagulation decreases the stroke risk in AF patients. Unfortunately, there is insufficient data on the effectiveness of non-vitamin K antagonist oral anticoagulants (NOAC) in patients with AF and MS.  
**Case Report:** We present a case of 64-year-old woman referred for electrical cardioversion (CV) due to symptomatic AF. She was administered an apixaban for stroke prevention, but she missed the scheduled echocardiography prior to referral. Imaging performed on-site revealed a giant left atrial thrombus and moderate MS. High mobility of the intracardiac mass together with moderate AS and MS were assessed as significant predictors of distal embolization. The patient underwent mitral valve replacement with the thrombus removal. Her further recovery was uneventful.  
**Conclusions:** Mitral stenosis significantly affects the anticoagulant selection in patients with atrial fibrillation. Thus, echocardiography is mandatory if the first diagnosis is atrial fibrillation to exclude contraindications for NOAC therapy.

**Keywords:** Anticoagulants • Apixaban • Atrial Fibrillation • Mitral Valve Stenosis • Thrombosis

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## Background

Atrial fibrillation (AF) increases the risk of stroke [1]. Left atrial thrombus formation occurs in 0.6-7% of AF cases despite proper anticoagulation and places patients at highest stroke risk. In addition, AF patients with mitral stenosis (MS) are at higher risk of left atrial thrombus than those without MS [2-4]. Mitral stenosis is an acquired disease that leads to atrial pressure overload and subsequent significant anatomical and electrical remodeling of the left atrium. This promotes the occurrence of AF and left atrial thrombus formation. Patients with AF who are at risk of stroke should be administered an oral anticoagulant. Non-vitamin K antagonist oral anticoagulants (NOAC) are the recommended treatment for stroke prevention in AF, but their efficacy in AF patients with MS has not been demonstrated. In patients with AF, NOACs have been prescribed as a standard treatment for a few years, but the time from NOAC prescription to initial echocardiographic assessment may be prolonged. Incidentally, NOAC may be inadvertently administered to a patient with a contraindication. Although initially benign, if prolonged, the treatment is inefficient and in some cases can be harmful.

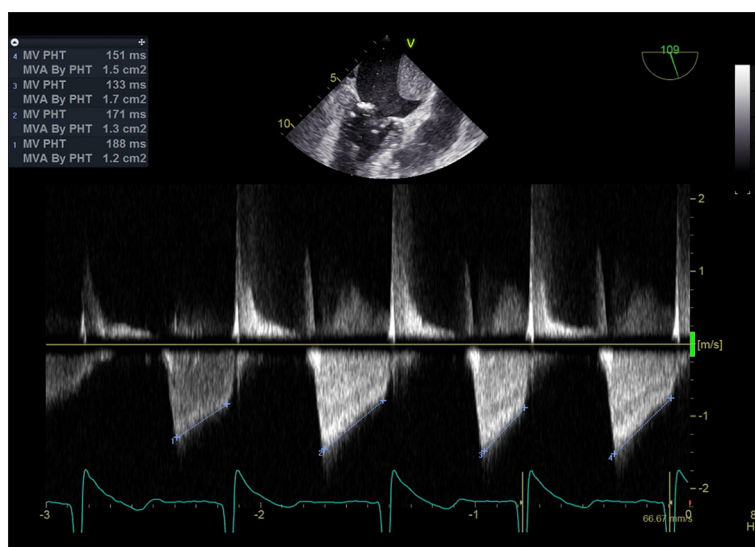
## Case Report

We present a case of a 65-year-old woman with arterial hypertension and dyslipidemia who was referred for electrical cardioversion due to symptomatic AF. Her CHA<sub>2</sub>DS<sub>2</sub>-VASc score was 3. Apixaban 5 mg twice daily had been administered for stroke prevention, but she missed the scheduled echocardiography prior to referral. Echocardiography performed on-site prior to planned cardioversion revealed a moderate MS with moderate calcifications (mitral valve area 1.4 cm<sup>2</sup>, mean transvalvular gradient 7 mmHg) (Figure 1) and an accessory intra-atrial

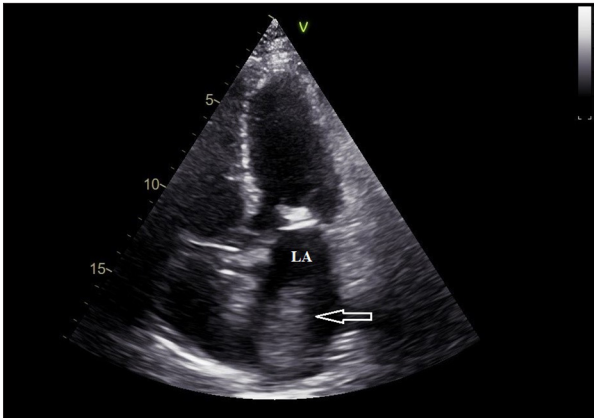
movable mass (Figures 2-4). Cardiac computed tomography demonstrated a well-delineated two-portion structure within the left atrium with calcifications and minimal contrast enhancement (the larger portion was 57×47×39 mm, and the smaller one was 21×9×36 mm) (Figures 5, 6). High mobility of the intracardiac mass together with moderate MS and persistent AF were assessed as significant predictors of distal embolization. The cardioversion was postponed, and the patient qualified for surgery. The patient underwent surgical thrombus removal with the mitral valve replacement without the antecedent vitamin K antagonist (VKA) treatment (Figure 7). The further recovery was uneventful. A low-molecular-weight heparin was initiated and VKA was prescribed for a long-life treatment. The histopathological examination of the excised mass revealed an organized thrombus with a small degree of calcification.

## Discussion

In patients diagnosed with atrial fibrillation, baseline assessment includes transthoracic echocardiography. However, the time from AF diagnosis to initial echocardiographic assessment may be significantly prolonged, and delayed anticoagulation can increase the stroke risk. Therefore, the initiation of anticoagulation frequently occurs before the echocardiographic assessment. Mitral stenosis is rarely, but if accompanied by AF it reduces the hemodynamic performance and markedly increases the thromboembolic events rate [5]. In patients with AF and MS but without anticoagulant, the incidence of left atrial thrombus ranges from 25% to 55% [2,6,7]. The intracardiac thrombotic masses are localized in the left atrium and the left atrial appendage in 57% of cases. Oral anticoagulant is mandatory when AF complicates MS, regardless of its severity and CHA<sub>2</sub>DS<sub>2</sub>-VASc score [8,9]. In patients with moderate

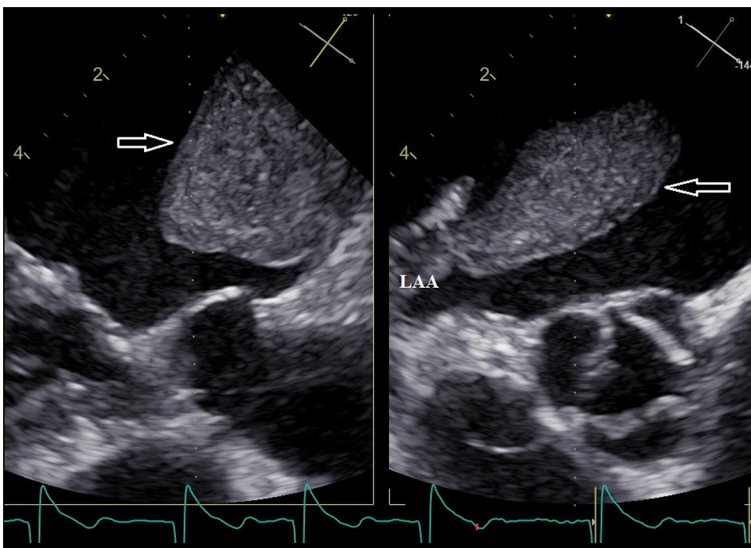


**Figure 1.** Transesophageal echocardiography, mid-esophageal long-axis view of mitral valve showing mitral leaflets and mitral valve area by pressure-half time.

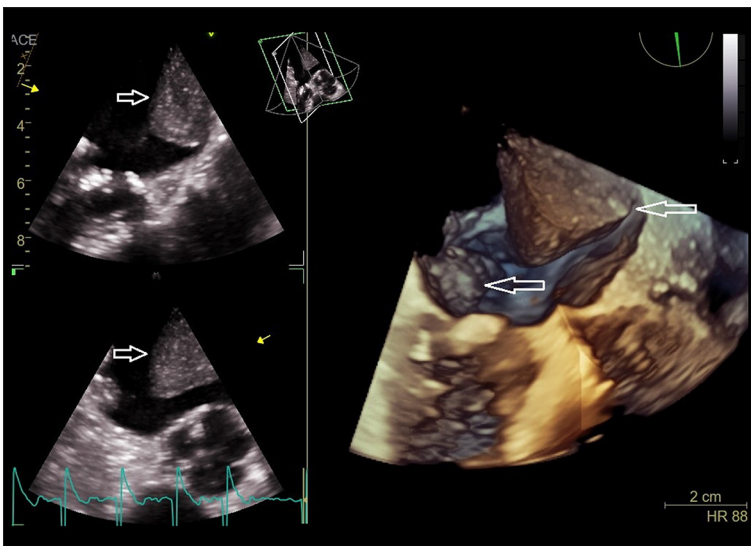


**Figure 2.** Transthoracic echocardiography, apical four-chamber view. Intra-atrial thrombus (arrow) in the left atrium (LA).

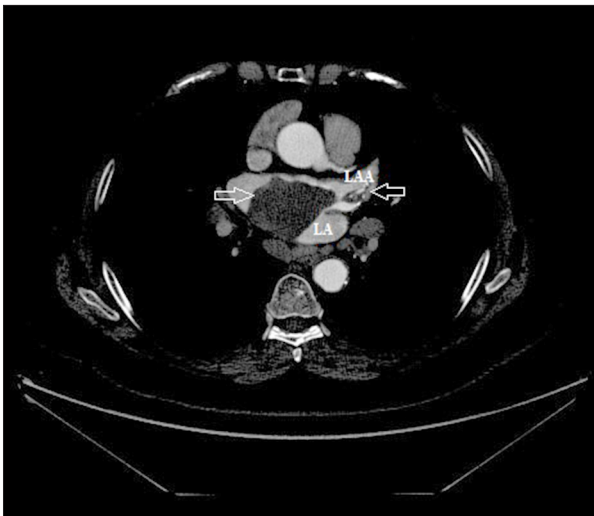
or severe MS, the current guidelines recommend using VKA with regular measurements of international normalized ratio (INR), with typical INR target ranges from 2 to 3. For these patients, NOACs administration for stroke prevention is not recommended [1]. NOACs (apixaban, dabigatran, rivaroxaban, and edoxaban) are favored over VKA for stroke prevention in most cases, excluding severe mitral stenosis and mechanical prosthetic valves. Even if NOAC was administered initially, it should be changed to VKA after the MS diagnosis was confirmed. Our patient did not follow the attending physician's advice and the echocardiography was not available prior hospitalization. In our institution, all cardioversions are transthoracic echocardiography-guided; therefore, the patient avoided an unjustified and potentially harmful procedure. There are gaps in the evidence of efficacy of NOAC in the prevention of thrombotic complications in patients with AF and MS, as



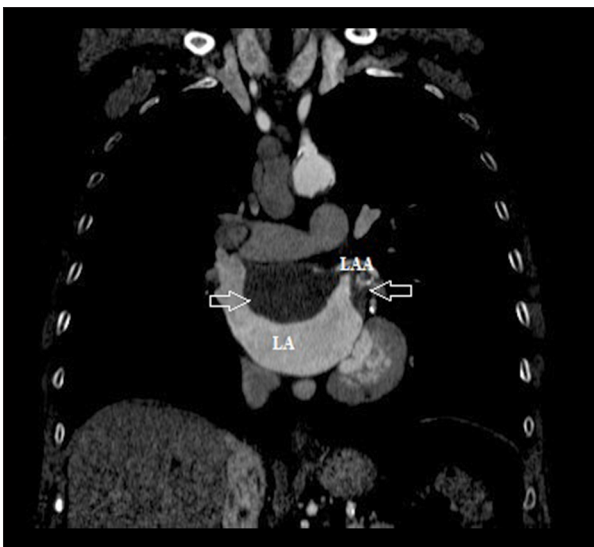
**Figure 3.** Transesophageal echocardiography, mid-esophageal view. Intra-atrial thrombus (arrow).



**Figure 4.** Two- and three-dimensional transesophageal echocardiography, mid-esophageal view. Intra-atrial thrombus (arrow).

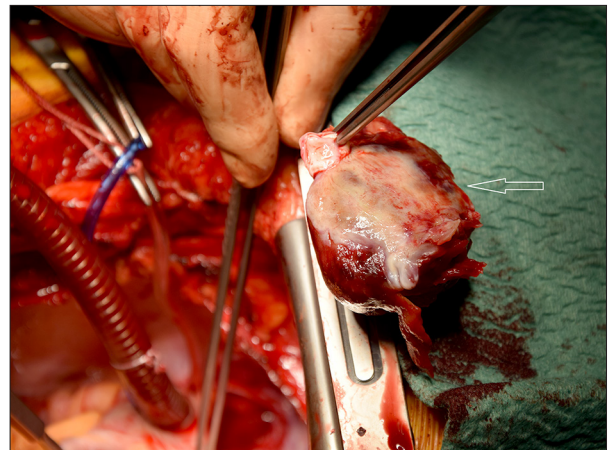


**Figure 5.** Contrast-enhanced computed tomography. Thrombus (arrow).



**Figure 6.** Contrast-enhanced computed tomography. Thrombus (arrow).

these patients were excluded from randomized controlled trials [10-13]. However, there are limited data suggesting a possible beneficial effect. A recent observational study of a Korean population consisting of 2230 patients revealed that NOAC was associated with better results, with lower ischemic stroke incidents and hemorrhagic events compared to warfarin in patients AF and concomitant MS. The study suggests that NOAC therapy may be safe and effective, but there were no data on the severity of mitral stenosis in the study population [14]. Luis et al described a case of a thrombotic event complicating dabigatran management in a patient with AF and concomitant



**Figure 7.** Intraoperative view of the excised abnormal mass (arrow).

significant MS. Dabigatran was ceased and warfarin recommenced. At 11-month follow-up there were no embolic complications, and there was a marked reduction in thrombus size on repeated imaging [15]. The ongoing INVICTUS-VKA trial includes patients with rheumatic heart disease (including MS) and concomitant AF. This is a prospective, randomized, parallel-group, open-label clinical trial of rivaroxaban versus standard VKA therapy to evaluate non-inferiority of rivaroxaban to VKA, with testing for superiority if non-inferiority is satisfied. It is expected to be completed in 2022 [16]. Another randomized controlled clinical trial called Rivoraxaban in Mitral Stenosis (RISE MS) is currently recruiting patients with relevant MS (moderate or severe) and concomitant AF to evaluate safety and effectiveness of rivaroxaban management in comparison to warfarin in these patients. It is estimated to complete in June 2021.

## Conclusions

Although rare, mitral stenosis significantly affects the anticoagulant selection in patients with atrial fibrillation. Thus, to exclude contraindications for NOAC therapy, echocardiography is mandatory if the first diagnosis was atrial fibrillation. In patients receiving NOAC as the first-line treatment, if moderate or severe MS is confirmed, the vitamin K antagonist remains the anticoagulant of choice.

## Declaration of Figures Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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