Device-Related Thrombus: A Reason for Concern?

Bashar Hannawi, M.D.[a]; *Faheemullah Beg,* M.D.[a]; *Miguel Valderrábano,* M.D.[b]; *Karla Kurrelmeyer,* M.D.[b]

[a]HOUSTON METHODIST HOSPITAL, HOUSTON, TEXAS; [b]HOUSTON METHODIST DEBAKEY HEART & VASCULAR CENTER, HOUSTON METHODIST, HOUSTON, TEXAS

INTRODUCTION

In 2010, atrial fibrillation (AF) affected approximately 5 million individuals in the United States[1,2] and 33.5 million worldwide.[3] It is estimated that nearly 12 million will be affected by year 2030 in the United States alone.[1] Among the many adverse events of AF, stroke is the most devastating and is 4- to 5-fold more common in patients with AF compared to the general population.[4,5] Because this risk varies among patients, the American Heart Association (AHA)/American College of Cardiology (ACC)/Heart Rhythm Society (HRS) guidelines recommend using the CHA2DS2-VASc score as a risk assessment tool.[6] Patients with a score of zero have a risk of only 0.2%, whereas a score of 9 confers a 12.2% risk.[7] Thus, the guidelines recommend using anticoagulation in all patients with scores ≥ 2. However, anticoagulation may lead to major bleeding in up to 5% of patients on warfarin and in 2.1% to 3.6% of those on novel oral anticoagulants (NOACs).[8-10] Risk models such as HAS-BLED (Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile International Normalized Ratio, Elderly, Drugs/Alcohol), ATRIA (Anticoagulation and Risk Factors in Atrial Fibrillation), and HEMORR$_2$HAGES (Hepatic or Renal Disease, Ethanol Abuse, Malignancy, Older Age, Reduced Platelet Count or Function, Re-Bleeding, Hypertension, Anemia, Genetic Factors, Excessive Fall Risk and Stroke) were developed to identify patients at increased risk for bleeding.[11-13] However, many of the clinical factors that contribute to increased stroke risk are associated with bleeding as well.

To mitigate the risk of stroke and bleeding, several left atrial appendage (LAA) occlusion devices have been introduced. These devices isolate the LAA from the left atrium, which is the source of up to 90% of nonvalvular AF-associated emboli.[14] The WATCHMAN Left Atrial Appendage Closure Device (Boston Scientific) is the only device approved by the U.S. Food and Drug Administration for stroke prevention. It is associated with lower rates of hemorrhagic stroke and bleeding and similar rates of all-cause stroke and systemic embolism when compared with warfarin.[15] On the other hand, the device has its own unique set of complications, including but not limited to peridevice leak, device migration, and device-related thrombus. Although a rare entity, device-related thrombus may have a significant impact on patient treatment and outcomes.

In this article, we present a case of device-related thrombus and review the available literature on its incidence, risk stratification, and management.

CASE PRESENTATION

A 76-year-old male with a history of permanent atrial fibrillation underwent a WATCHMAN device implantation due to increased risk of thromboembolism (CHA_2DS_2-VASc score of 3) and recurrent hematuria. The procedure was successful, and the patient was then placed on apixaban. A surveillance transesophageal echocardiogram (TEE) was performed 45 days post implant and showed a well-seated device without evidence of peridevice leak. At this point, the patient was switched to dual antiplatelet therapy (DAPT) with aspirin and clopidogrel.

Four months post implant, the patient presented with loss of peripheral vision in the left eye. On examination, his blood pressure was 148/63 mm Hg and his pulse was 73 bpm. Physical exam was significant for left homonymous hemianopia and irregularly irregular heart rhythm. Magnetic resonance imaging of the brain showed a subacute ischemic stroke with hemorrhagic conversion in the right posterior cerebral artery territory.

Due to the rarity of stroke after WATCHMAN device implantation, a workup was initiated to identify the embolic source. A transthoracic echocardiogram revealed normal left and right ventricular systolic function with no hemodynamically significant valvular disease or identifiable source of embolism. Therefore, a TEE was performed, showing a 1 × 1 cm mass on the WATCHMAN device consistent with a device-related thrombus (Figure 1, arrows). Mild (< 5 mm) peridevice leak was seen anteriorly. After 48 hours, the patient was started on heparin and transitioned to enoxaparin after 48 hours as a bridge to warfarin; however, he developed a headache on day 7. A repeat brain computed tomography showed worsening intracranial hemorrhage with extension into the ventricles, necessitating discontinuation of all anticoagulants. Over the next 3 days, the patient remained clinically stable and the intracranial hemorrhage remained unchanged. The patient was initiated on DAPT with aspirin and clopidogrel. He had

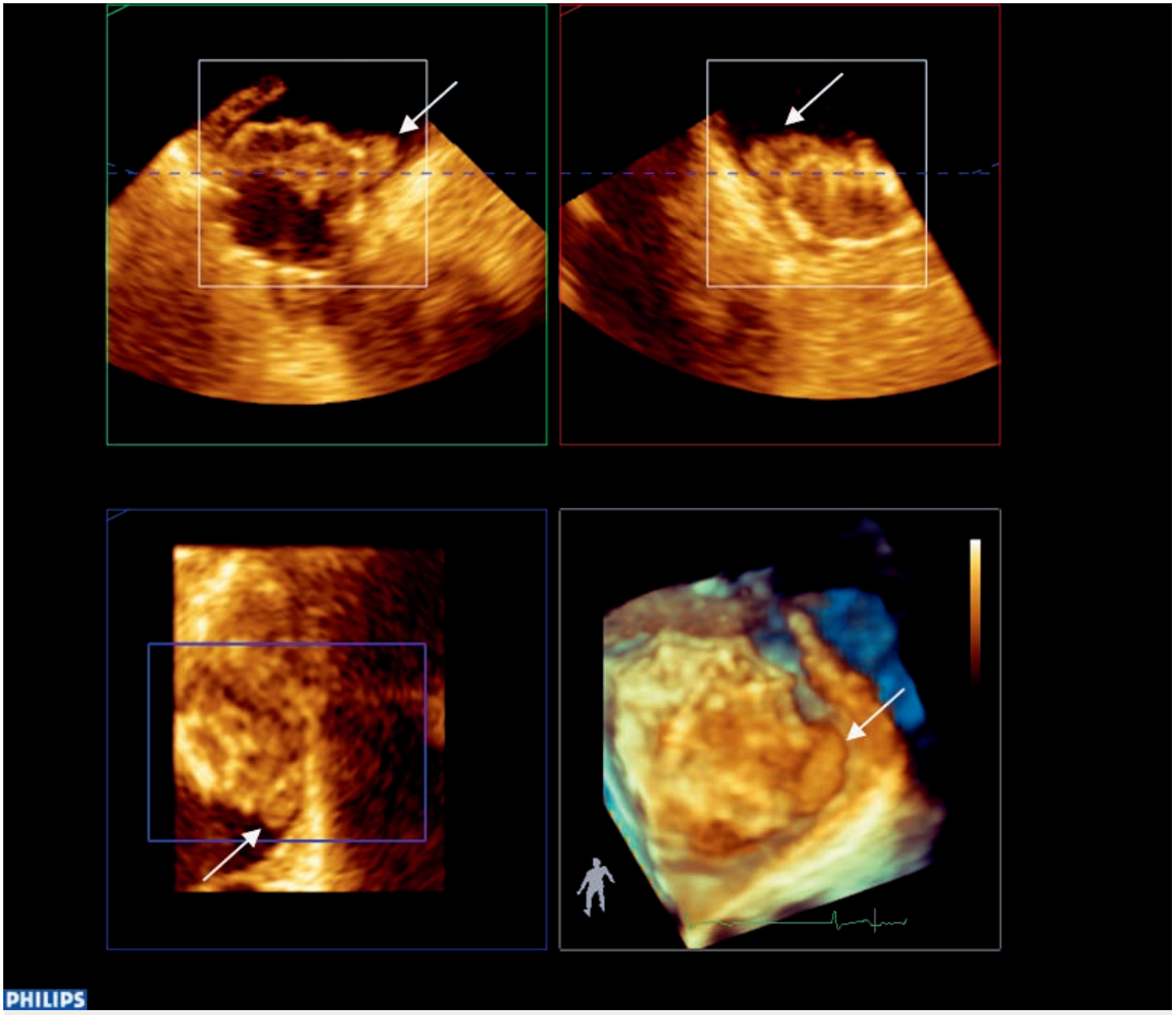

Figure 1.
Transesophageal echocardiogram shows a 1 × 1 cm mass (arrows) on the WATCHMAN device consistent with a device-related thrombus.

no further changes in his clinical status and was subsequently discharged.

DISCUSSION

The incidence of device-related thrombus (DRT) from WATCHMAN implantation ranges from 3.7% to 6.6%. While most cases occur in the first year after implantation, it may occur up to 10 years post implant.[16] DRT is often asymptomatic and diagnosed on surveillance TEE. In fact, the annual stroke rate due to DRT is only 0.3% per 100 patient years according to data from the PROTECT AF (WATCHMAN Left Atrial Appendage System for Embolic PROTECTion in Patients With Atrial Fibrillation) clinical trial and Continued Access Registry.[17] Furthermore, while the annual risk of stroke was 1.1% in the EWOLUTION (Registry on WATCHMAN Outcomes in Real-Life

Utilization) trial, there was only one case of DRT identified in these patients.

Several risk factors were identified as predictors of developing DRT, such as antiplatelet/anticoagulation regimen, device size, and atrial fibrillation burden.[18] Although most cases of DRT in the PROTECT AF trial occurred in patients receiving DAPT, more recent studies failed to demonstrate association with drug regimen post implant.[19,20] However, early discontinuation of anticoagulation or antiplatelet therapy seems to play a role in the development of DRT.[18] It has been reported that lack of endothelialization of the device might occur up to 13 months post implant, but this was not associated with DRT.[21]

DRT is typically managed by restarting or prolonging anticoagulation, and the outcomes are usually favorable. In the EWOLUTION trial, thrombus resolution was noted in all patients who had a follow-up TEE regardless of whether their medications were adjusted based on the TEE findings.[19]

CONCLUSION

The data available thus far indicate that the rate of DRT and DRT-related stroke is small. However, it is important to identify as it may have a significant impact on the duration of anticoagulant or antiplatelet therapy. Although several risk factors have been identified to predict development of DRT, it is unclear which patients are at increased risk for embolization. At this time, it might be reasonable to prolong anticoagulation in high-risk patients for 3 months after their surveillance TEE and ensure that all patients are eventually transitioned to lifelong mono antiplatelet therapy when there is no evidence of DRT or peridevice leak.

Conflict of Interest Disclosure:
The authors have completed and submitted the *Methodist DeBakey Cardiovascular Journal* Conflict of Interest Statement and none were reported.

Keywords:
atrial fibrillation, device-related thrombus, WATCHMAN

REFERENCES

1. Colilla S, Crow A, Petkun W, Singer DE, Simon T, Liu X. Estimates of current and future incidence and prevalence of atrial fibrillation in the U.S. adult population. Am J Cardiol. 2013 Oct 15;112(8):1142-7.

2. Benjamin EJ, Blaha MJ, Chiuve SE, et al.; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics-2017 Update: A Report From the American Heart Association. Circulation. 2017 Mar 7;135(10):e146-e603.

3. Chugh SS, Havmoeller R, Narayanan K, et al. Worldwide epidemiology of atrial fibrillation: a Global Burden of Disease 2010 Study. Circulation. 2014 Feb 25;129(8):837-47.

4. Marijon E, Le Heuzey JY, Connolly S, et al.; RE-LY Investigators. Causes of death and influencing factors in patients with atrial fibrillation: a competing-risk analysis from the randomized evaluation of long-term anticoagulant therapy study. Circulation. 2013 Nov 12;128(20):2192-201.

5. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. Stroke. 1991 Aug;22(8):983-8.

6. January CT, Wann LS, Alpert JS, et al.; ACC/AHA Task Force Members. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society. Circulation. 2014 Dec 2;130(23):2071-104.

7. Friberg L, Rosenqvist M, Lip GY. Evaluation of risk stratification schemes for ischaemic stroke and bleeding in 182 678 patients with atrial fibrillation: the Swedish Atrial Fibrillation cohort study. Eur Heart J. 2012 Jun;33(12):1500-10.

8. Connolly SJ, Ezekowitz MD, Yusuf S, et al.; RE-LY Steering Committee and Investigators. Dabigatran versus warfarin in patients with atrial fibrillation. New Engl J Med. 2009 Sep 17;361(12):1139-51.

9. Granger CB, Alexander JH, McMurray JJ, et al.; ARISTOTLE Committees and Investigators. Apixaban versus warfarin in patients with atrial fibrillation. New Engl J Med. 2011 Sep 15;365(11):981-92.

10. Patel MR, Mahaffrey KW, Garg J, et al.; ROCKET AF Investigators. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. New Engl J Med. 2011 Sep 8;365(10):883-91.

11. Gage BF, Yan Y, Milligan PE, et al. Clinical classification schemes for predicting hemorrhage:results from the National Registry of Atrial Fibrillation (NRAF). Am Heart J. 2006 Mar;151(3):713-9.

12. Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJ, Lip GY. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. Chest. 2010 Nov;138(5):1093-100.

13. Singer DE, Chang Y, Borowsky LH, et al. A new risk scheme to predict ischemic stroke and other thromboembolism in atrial fibrillation: the ATRIA study stroke risk score. J Am Heart Assoc. 2013 Jun 21; 2(3):e000250.

14. Blackshear JL, Odell JA. Appendage obliteration to reduce stroke in cardiac surgical patients with atrial fibrillation. Ann Thorac Surg. 1996 Feb;61(2):755-9.

15. Holmes DR, Doshi SK, Kar S, et al. Left Atrial Appendage Closure as an Alternative to Warfarin for Stroke Prevention in Atrial Fibrillation. J Am Coll Cardiol. 2015 Jun 23;65(24):2614-23

16. Shamim S, Magalski A, Chhatriwalla AK, Allen KB, Huber KC, Main ML. Transesophageal echocardiographic diagnosis of a WATCHMAN left atrial appendage closure device thrombus 10 years following implantation. Echocardiography. 2017 Jan;34(1):128-130.

17. Reddy VY, Holmes D, Doshi SK, Neuzil P, Kar S. Safety of percutaneous left atrial appendage closure: results from the Watchman Left Atrial Appendage System for Embolic Protection in Patients with AF (PROTECT AF) clinical trial and the Continued Access Registry. Circulation. 2011 Feb 1;123(4):417-24.

18. Kubo S, Mizutani Y, Meemook K, Nakajima Y, Hussaini A, Kar S. Incidence, Characteristics, and Clinical Course of Device-Related Thrombus After Watchman Left Atrial Appendage Occlusion Device Implantation in Atrial Fibrillation Patients. JACC Clin Electrophysiol. 2017 Dec 11;3(12):1380-6.

19. Boersma LV, Ince H, Kische S, et al.; EWOLUTION Investigators. Efficacy and safety of left atrial appendage closure with WATCHMAN in patients with or without contraindication to oral anticoagulation: 1-Year follow-up outcome data of the EWOLUTION trial. Heart Rhythm. 2017 Sep;14(9):1302-8.

20. Enomoto Y, Gadiyaram VK, Gianni C, et al. Use of non-warfarin oral anticoagulants instead of warfarin during left atrial appendage closure with the Watchman device. Heart Rhythm. 2017 Jan;14(1):19-24.

21. Massarenti L, Yilmaz A. Incomplete endothelialization of left atrial appendage occlusion device 10 months after implantation. J Cardiovasc Electrophysiol. 2012 Dec;23(12):1384-5.