

Original Article

A dilemma of hemorrhage vs thrombosis: a case of watchman device thrombus in a patient with intracranial hemorrhage history

Tamer Amer, Caitlin Merrin, Zaw Win Tun, Mena Yacoub, Ali Ebrahimi, George Degheim

Department of Cardiology, HCA Graduate Medical Education, West Florida Division, Northside Hospital, St. Petersburg, Florida, USA

Received November 2, 2020; Accepted June 17, 2021; Epub August 15, 2021; Published August 30, 2021

Abstract: Recently updated guidelines for Atrial Fibrillation (AF) outline that percutaneous left atrial appendage (LAA) occlusion with the Watchman device may be a reasonable alternative for those who have contraindications to long-term oral anticoagulation. However, optimal periprocedural antithrombotic therapy remains disputable, particularly in patients who are ineligible for oral anticoagulation or those with history of intracranial hemorrhage (ICH). We present the case of a 67-year-old male with a history of ischemic stroke with hemorrhagic conversion and permanent AF, who was treated with the Watchman device and subsequently developed device related thrombus and recurrent ischemic stroke. We discuss the dilemma and review the literature regarding anticoagulation for device related thrombus in this patient with increased bleeding risk, given his history of ICH. His course and antithrombotic strategy are described and despite the use of anticoagulation with warfarin in the setting of recurrent ischemic stroke, he did not develop hemorrhagic transformation. He also did, ultimately, achieve device related thrombus resolution on repeat Transesophageal Echocardiogram (TEE). This case supported the use of warfarin for device related thrombus in the setting of ischemic stroke and history of ICH. However, evidence-based guidelines for periprocedural antithrombotic regimens in patients with high bleeding risk have yet to be released and further research is needed.

Keywords: Watchman, intracranial hemorrhage, warfarin, device thrombus

Introduction

Oral anticoagulation therapy remains the preferred method for most patients with atrial fibrillation (AF) and elevated stroke risk. Anticoagulation, however, carries an increased risk of bleeding, including Intracranial Hemorrhage (ICH). Updated guidelines for AF outline that Percutaneous Left Atrial Appendage (LAA) Occlusion with the Watchman device may be a reasonable alternative for those who have contraindications to long-term oral anticoagulation [1]. However, usual practice following Watchman device implantation still requires short-term anticoagulation for periprocedural antithrombotic therapy with Warfarin and Aspirin for 45 days. At present, there are no guidelines for periprocedural antithrombotic therapy for patients with a history of ICH who have undergone Watchman implantation, as those patients were excluded from the initial random-

ized Watchman trials [2, 3]. Furthermore, there is little data regarding treatment of device related thrombus in this population. We present the case of a 67-year old male with a history of ischemic stroke with hemorrhagic conversion and permanent AF, treated with a watchman device, subsequently requiring a higher INR goal due to device thrombosis causing a sub-acute infarct.

Case report

The patient is a 67-year-old male who presented with ischemic stroke that was treated with tPA and was subsequently complicated by hemorrhagic conversion. He was found to be in Atrial Fibrillation during this hospitalization and was initiated on anticoagulation 6 weeks following discharge. Following rehabilitation, he continued to struggle with disequilibrium and partial vision loss. During this time, he suffered

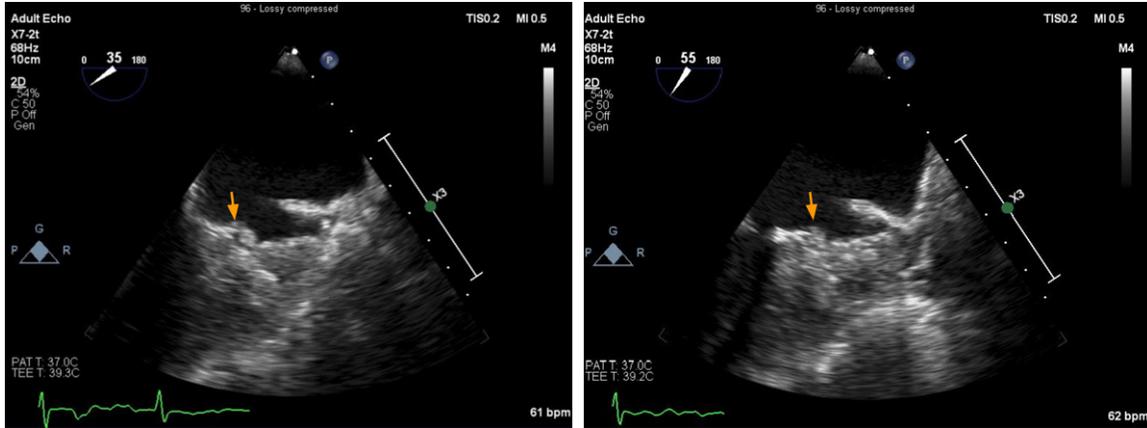


Figure 1. Transesophageal echocardiogram performed 6 weeks post-implantation demonstrated a thrombus associated with the device (arrow).

multiple mechanical falls while on anticoagulation, 2 of which required hospitalization, and was thus recommended for Left Atrial Appendage Occlusion with a Watchman device. He underwent successful implantation of a 27 mm Watchman device and was discharged on Warfarin and Aspirin for antithrombotic therapy. He then presented 3 weeks post implant with altered mental status and was found to have a right temporal occipital lobe subacute infarct (**Figure 3**).

Decision-making

The patient's presentation with new ischemic stroke and history of intracerebral hemorrhage put him at increased risk for hemorrhagic transformation. However, given the recent implantation of his Watchman device, 24 days prior, he was well within the endothelialization period and continued to require anticoagulation with Warfarin. This presented a clinical dilemma-whether to risk hemorrhagic conversion and continue Warfarin or discontinue Warfarin and risk device thrombosis. It was felt that due to; how recently the patient had the device implanted, his history of permanent AF and his elevated CHADS₂ VASC score, that he was at increased risk for device thrombosis. In addition, following discussion with Neurology and review of CT films, his infarct was felt to be at less risk for hemorrhagic conversion, due to its small size and characteristics. Given this, the patient's Warfarin was continued with narrower INR goal of 2.0-2.5. He was monitored closely and did not develop hemorrhagic conversion or complication and was subsequently discharged. However, trans-

esophageal echocardiogram 6 weeks post implantation was obtained and despite uninterrupted anticoagulation, revealed device associated thrombus (**Figure 1**). His anticoagulation was subsequently adjusted with a higher INR goal of 2.5-3.0. A repeat transesophageal echocardiogram performed 6 months post-implantation showed complete resolution of the device-associated thrombus (**Figure 2**).

Discussion

At present, there are no guidelines pertaining to anticoagulation in patients who have undergone Watchman implantation with a history of intracranial hemorrhage and concomitant increased risk of ischemic stroke or device related thrombus. In the initial randomized Watchman trials, those patients with prior history of ICH were excluded [2, 3]. In general, the annual rate of ICH in patients taking Warfarin was 0.3% to 0.6% [4]. Although rates of hemorrhagic stroke are low in patients who undergo LAA occlusion, it is still a devastating and fatal complication for patients who are taking oral anticoagulation. Following an ICH, there are reviews conducted recommending cessation of anticoagulation for 2 weeks, or alternatively resumption of anticoagulation 24 hours after stable imaging [5]. There are also studies in patients with AF and ICH which resumed warfarin that showed the relative risk for recurrent ICH associated with resumption of warfarin treatment was higher in patients with hemorrhagic stroke than those with traumatic ICH [6].

Device related thrombosis is a known complication of LAA closure with Watchman, with

Treatment of device related thrombus in a patient with high bleeding risk

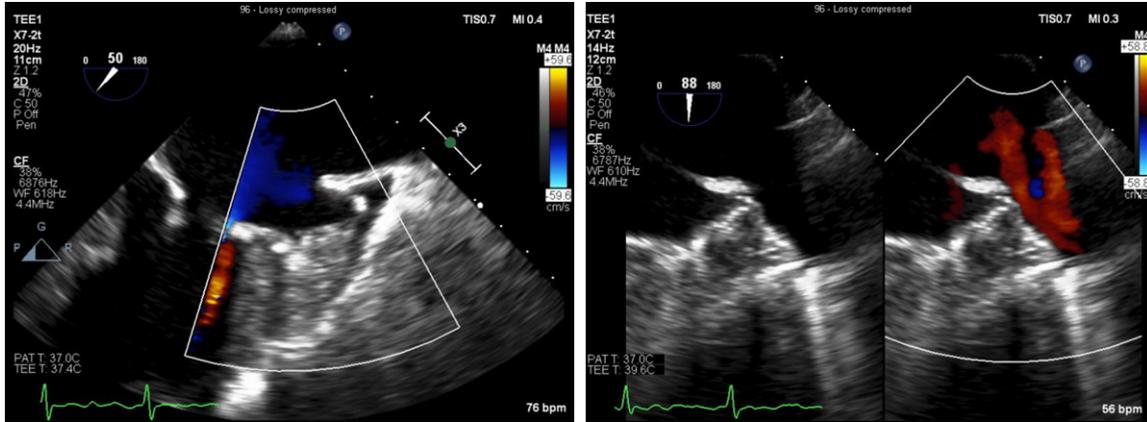


Figure 2. Follow-up transesophageal echocardiogram performed 6 months post-implantation showed complete resolution of the device-associated thrombus.

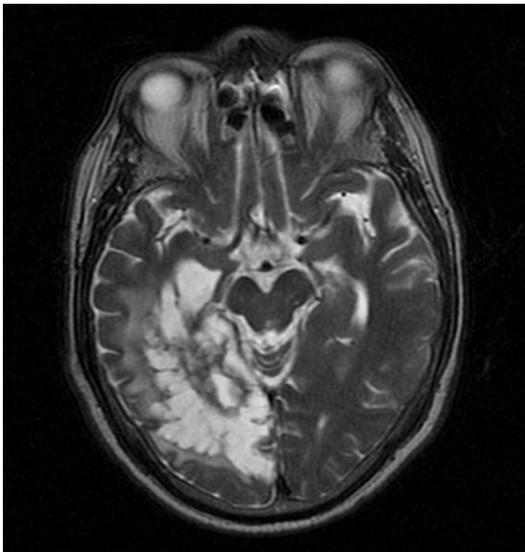


Figure 3. MRI of the brain demonstrated right temporal occipital subacute infarct diagnosed 3 weeks after Watchman implantation.

rates of thrombosis of 3.4% in patients who received anticoagulation with warfarin for at least 45 days [7]. This current antithrombotic regimen of warfarin for 45 days was derived from animal models where nearly complete endothelialization was shown at 1 month and was complete by 3 months [8]. However, reducing the risk for device related thrombosis with anticoagulation until endothelialization comes at the cost of increased bleeding risk.

This has led to interest in alternatives to anticoagulation for periprocedural antithrombotic therapy. One study performed evaluated the safety and efficacy of LAA occlusion in non-

valvular atrial fibrillation patients with a contraindication to warfarin. Patients received a thienopyridine antiplatelet agent for 6 months in addition to aspirin indefinitely with annual all-cause stroke and ischemic stroke of 2.3% and 1.7%. This was comparable to patients who received the usual antithrombotic treatment with warfarin where annualized rates of all cause-stroke and ischemic stroke were 2.3% and 2.2%, respectively. Of note, device-related thrombosis resulting in ischemic stroke was 0.7% [9].

An additional study comparing antithrombotic therapy acquired data on patients who underwent device implantation and were assigned to one of four post-procedure anticoagulation groups: warfarin, novel oral anticoagulation, dual antiplatelet therapy, single antiplatelet therapy, and no anticoagulation, which found no difference in ischemic or hemorrhagic stroke between groups. Device thrombus developed in 3.7% patients with only one patient suffering an ischemic stroke, but this was not correlated with antithrombotic regimen [10].

At present, there is a large, randomized control trial being conducted in patients who are deemed unsuitable for oral anticoagulation and will be treated only with single or dual antiplatelet therapy after watchman device implantation [11]. We anticipate that subgroup analysis of this study in both patients with history of ICH as well as in those with increased thrombotic risk will help to further guide clinical decision making in selection of an appropriate anti-thrombotic regimen in this challenging cohort of patients.

Conclusion

This case exemplifies the importance of individualizing patient care and the utility in interdisciplinary collaboration. Although there are subgroups and ongoing trials studying variations in periprocedural antithrombotic therapy with the Watchman device, no clear guidelines yet exist for patients with high bleeding risk. In this unique case we revealed the ability to continue anticoagulation with Warfarin in a patient presenting with ischemic stroke and history of intracerebral hemorrhage without resulting in hemorrhagic transformation or bleeding complication.

Acknowledgements

This research was supported (in whole or in part) by HCA and/or an HCA affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA or any of its affiliated entities.

Patient consent was obtained, as displayed in the attached guideline.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. George Degheim, Department of Cardiology, HCA Graduate Medical Education, West Florida Division, Northside Hospital, 6006 49th Street North, #200, St. Petersburg, Florida 33709, USA. Tel: 727-490-2100; Fax: 866-222-3965; E-mail: degheim_84@hotmail.com

References

- [1] January CT, Wann LS, Calkins H, Chen LY, Cigarroa JE, Cleveland JC Jr, Ellinor PT, Ezekowitz MD, Field ME, Furie KL, Heidenreich PA, Murray KT, Shea JB, Tracy CM and Yancy CW. 2019 AHA/ACC/HRS focused update of the 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 clinical practice guidelines and the Heart Rhythm Society in collaboration with the Society of Thoracic Surgeons. *Circulation* 2019; 140: e125-e151.
- [2] Holmes DR, Reddy VY, Turi ZG, Doshi SK, Sievert H, Buchbinder M, Mullin CM and Sick P; PROTECT AF Investigators. Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomized non-inferiority trial. *Lancet* 2009; 374: 534-42.
- [3] Holmes DR Jr, Kar S, Price MJ, Whisenant B, Sievert H, Doshi SK, Huber K and Reddy VY. Prospective randomized evaluation of the watchman left atrial appendage closure device in patients with atrial fibrillation versus long-term warfarin therapy. *J Am Coll Cardiol* 2014; 64: 1-12.
- [4] Hart RG, Diener HC, Yang S, Connolly SJ, Walentin L, Reilly PA, Ezekowitz MD and Yusuf S. Intracranial hemorrhage in atrial fibrillation patients during anticoagulation with warfarin or dabigatran: the RE-LY trial. *Stroke* 2012; 43: 1511-1517.
- [5] Divito A, Kerr K, Wilkerson C, Shepard S, Choi A and Kitagawa RS. Use of anticoagulation agents after traumatic intracranial hemorrhage. *World Neurosurg* 2019; 123: e25-e30.
- [6] Nielsen PB, Larsen TB, Skjøth F and Lip GY. Outcomes associated with resuming warfarin treatment after hemorrhagic stroke or traumatic intracranial hemorrhage in patients with atrial fibrillation. *JAMA Intern Med* 2017; 177: 563-570.
- [7] Lempereur M, Aminian A, Freixa X, Gafoor S, Kefer J, Tzikas A, Legrand V and Saw J. Device-associated thrombus formation after left atrial appendage occlusion: a systematic review of events reported with the watchman, the Amplatzer cardiac plug and the amulet. *Catheter Cardiovasc Interv* 2017; 90: E111-E121.
- [8] Nakai T, Lesh MD, Gerstenfeld EP, Virmani R, Jones R and Lee RJ. Percutaneous left atrial appendage occlusion (PLAATO) for preventing cardioembolism. *Circulation* 2002; 105: 2217-2222.
- [9] Reddy VY, Möbius-Winkler S, Miller MA, Neuzil P, Schuler G, Wiebe J, Sick P and Sievert H. Left atrial appendage closure with the watchman device in patients with a contraindication for oral anticoagulation. *J Am Coll Cardiol* 2013; 61: 2551-2556.
- [10] Boersma LV, Ince H, Kische S, Pokushalov E, Schmitz T, Schmidt B, Gori T, Meincke F, Prottopov AV, Betts T, Foley D, Sievert H, Mazzone P, De Potter T, Vireca E, Stein K and Bergmann MW; 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; 14: 1302-1308.
- [11] Holmes DR, Reddy VY, Buchbinder M, Stein K, Elletson M, Bergmann MW, Schmidt B and Saw J. The assessment of the watchman device in patients unsuitable for oral anticoagulation (ASAP-TOO) trial. *Am Heart J* 2017; 189: 68-74.