Device-Associated Thrombus with Watchman FLX Left Atrial Appendage Closure Device: A Report of Two Cases

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INTRODUCTION

Medical therapy with warfarin, and more recently with direct oral anticoagulant (DOAC) agents, has historically been the mainstay of therapy for stroke prevention in patients with atrial fibrillation (AF). However, in patients with nonvalvular AF who cannot tolerate long-term oral anticoagulation, left atrial appendage (LAA) closure plays an essential role in preventing thromboembolism.[1] Although the Watchman device (Boston Scientific), a percutaneously implanted LAA occluder (LAAO), offers a minimally invasive means to achieve LAA closure, it has been shown to have a risk for device-associated thrombus (DAT).[2] The latest generation of the device, named the Watchman FLX, was redesigned to minimize rates of DAT. Individual cases of DAT with this new device outside of a clinical trial have not yet been reported in literature.

We report two cases of percutaneous LAA closure using this new device leading to DAT in the setting of nonadherence with oral anticoagulation. Our aim is to demonstrate that although this new device has proved to have lower rates of DAT than earlier generations of LAAO devices, thrombus formation may still occur in certain cases.

CASE PRESENTATIONS

Case 1

An 86-year-old patient with nonvalvular AF and extensive comorbidities was referred for percutaneous LAA closure using a Watchman FLX device. His CHA_2DS_2-VASc score was 5 (age, systolic heart failure with left ventricular ejection fraction of 45%, hypertension, and vascular disease). He was intolerant to long-term anticoagulation and antiplatelet therapy because of a history of gastrointestinal bleeding and severe thrombocytopenia. His HAS-BLED score was 4 (hypertension, prior major bleeding, age, and medication).

The patient's medical history included coronary artery disease (status post coronary artery bypass grafting), stomach cancer (status post gastrectomy), early-onset Alzheimer's dementia, chronic obstructive pulmonary disease, and complete heart block requiring permanent pacemaker implantation.

Intraprocedural transesophageal echocardiogram (TEE) revealed a broccoli-shaped LAA free of thrombus and with a maximum landing zone LAA diameter of 22 mm and sufficient LAA depth (Figure 1, Video 1). No spontaneous echocardiographic contrast ("smoke") was noted in the LAA. There was no significant valvular disease and only moderate flat plaque in the thoracic aorta. The patient then underwent successful implantation of a 27-mm Watchman FLX device, with a device compression rate ranging from 26% to 34% and no paradevice leak (Figure 2, "Implant" column, Video 2).

The patient was started on short-term anticoagulation therapy with apixaban 5 mg twice a day with a plan to continue the medication until follow-up TEE at 45 days after device implantation. At day 30, the patient's serum creatinine rose to 1.6 mg/dL (normal range, <1.4 mg/dL), and the apixaban dose was lowered to 2.5 mg twice a day.

Follow-up TEE on day 45 revealed a sessile DAT on the left atrial surface of this device, mostly around the threaded insert. The thrombus measured 10 × 7 mm and had an approximate thickness of 5 mm (Figure 2, "Post 6 Weeks" column, Video 3). Along the posterior aspect of the LAAO device, there was a small 2-mm gutter. There was no evidence of a paradevice leak. Moreover, the echoes behind the device were dense (white), consistent with appropriate intradevice thrombus formation. Of note, the patient reported nonadherence with apixaban for ≥3 days before follow-up TEE.

The patient was then educated on the importance of compliance with apixaban. Repeat TEE 6 weeks later revealed complete resolution of the DAT (Figure 2, "Post 12 Weeks" column, Video 4). Apixaban was then replaced with aspirin with a plan to repeat TEE 6 months later.

Case 2

A 91-year-old patient with anemia, hypertension, coronary artery disease, surgical aortic bioprosthesis, surgical mitral valve repair with an annuloplasty band, and persistent AF was referred for LAA closure with the Watchman FLX. The patient's CHA_2DS_2-VASc score was 5 (age, female, hypertension, coronary artery disease), and her HAS-BLED score was 2 (age, prior bleeding). She was intolerant of long-term anticoagulation and antiplatelet therapy because of previous episodes of bleeding into the glenohumoral joint.

Intraprocedural TEE revealed at baseline a windsock-shaped LAA free of thrombus and with a maximum landing zone LAA diameter of 22 mm and sufficient LAA depth (Figure 3, Video 5). LAA emptying velocity was low (16 cm/sec; normal range, >40 cm/sec). There was spontaneous echocardiographic contrast ("smoke") in the LAA. The bioprosthetic valves appeared normal in function and position. There was right heart dilation, and the left heart showed no evidence of a thrombus. The closure was

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Keywords: Left atrial appendage, Atrial fibrillation, Percutaneous closure, Watchman device

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2468-6441
https://doi.org/10.1016/j.case.2023.01.010

VIDEO HIGHLIGHTS

Video 1: Case 1: Pre–Watchman FLX LAA sizing. This video is a composite of clips obtained on TEE at four key imaging angles: 0° (display #1), 45° (display #2), 90° (display #3), and 135° (display #4), which also includes a biplane view of 45°. It demonstrates measurements of the LAA landing zone diameter and LAA depth. *AV*, Aortic valve; *LA*, left atrium; *LV*, left ventricle; *LUPV*, left upper pulmonary vein. This video corresponds to Figure 1.

Video 2: Case 1: Watchman FLX at the time of implantation. This video is a composite of clips obtained on TEE at four key imaging angles: 0° (display #1), 45° (display #2), 90° (display #3), and 135° (display #4). It demonstrates the absence of DAT at the time of Watchman FLX implantation. *FLX*, Watchman FLX device; *LA*, left atrium; *LUPV*, left upper pulmonary vein; *PA*, pulmonary artery. This video corresponds to the "Implant" column in Figure 2.

Video 3: Case 1: Watchman FLX at 6 weeks after implantation. This video is a composite of clips obtained on TEE at four key imaging angles: 0° (display #1), 45° (display #2), 90° (display #3), and 135° (displays #4 and #5). It demonstrates the presence of DAT at the time of Watchman FLX implantation (*yellow arrow*). At 135°, there was also a small paradevice leak along the posterior aspect of the device (*white arrow*). *FLX*, Watchman FLX device; *LA*, left atrium; *LUPV*, left upper pulmonary vein; *PA*, pulmonary artery. This video corresponds to the "Post 6 Weeks" column in Figure 2.

Video 4: Case 1: Watchman FLX at 12 weeks after implantation. This video is a composite of clips obtained on TEE at four key imaging angles: 0° (display #1), 45° (display #2), 90° (display #3), and 135° (displays #4 and #5). It demonstrates the resolution of DAT. *FLX*, Watchman FLX device; *LA*, left atrium; *LUPV*, left upper pulmonary vein; *PA*, pulmonary artery. This video corresponds to the "Post 12 Weeks" column in Figure 2.

Video 5: Case 2: Pre–Watchman FLX LAA sizing. This video is a composite of clips obtained on TEE at four key imaging angles: 0° (display #1), 45° (display #2), 90° (display #3), and 135° (display #4). It demonstrates measurements of the LAA landing zone diameter and LAA depth. *AV*, aortic valve; *LA*, left atrium; *LAA*, left atrial appendage; *LV*, left ventricle; *LUPV*, left upper pulmonary vein. This video corresponds to Figure 3.

Video 6: Case 2: Watchman FLX imaging at the time of implantation. This video is a composite of clips obtained on TEE at four key imaging angles: 0° (display #1), 45° (display #2), 90° (display #3), and 135° (display #4). It demonstrates the absence of DAT at the time of Watchman FLX implantation. *FLX*, Watchman FLX device; *LA*, left atrium; *PA*, pulmonary artery. This video corresponds to the "Implant" column in Figure 4.

Video 7: Case 2: Watchman FLX imaging at 6 weeks. This video is a composite of clips obtained on TEE at four key imaging angles: 0° (display #1), 45° (display #2), 90° (display #3), and 135° (display #4). It demonstrates the presence of DAT at the time of Watchman FLX implantation (*yellow arrow*). *FLX*, Watchman FLX device; *LA*, left atrium; *PA*, pulmonary artery. This video corresponds to the "Post 6 Weeks" column in Figure 4.

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successfully achieved with a 31-mm device (Figure 4, "Implant" column, Video 6). The device compression rate ranged from 11% to 22%, and no paradevice leak was noted.

The patient was discharged on apixaban 5 mg twice daily and aspirin 81 mg/d. She stopped taking apixaban early because of a misunderstanding of her treatment plan, but she continued aspirin. Follow-up TEE 45 days later showed a sessile DAT on the left atrial aspect of the device (Figure 4, "Post 6 Weeks" column, Video 7). The thrombus was 12 × 4 mm in size. On color Doppler imaging at 90° using a Nyquist limit of 38.5 cm/sec, a small, 2-mm paravalvular leak was seen near the mitral aspect of the Watchman FLX device. The patient was restarted on apixaban, and repeat TTE was scheduled for 45 days later. Unfortunately, she declined further follow-up.

DISCUSSION

LAA closure plays an important role in the prevention of thromboembolism in patients with nonvalvular AF. LAA closure with the Watchman device offers an alternative to warfarin therapy for patients who cannot be put on long-term anticoagulation and have CHA_2DS_2-VASc scores of ≥2.[2-4] Postimplantation anticoagulation is recommended until full endothelialization occurs.[5] The anticoagulation regimen typically consists of either warfarin or a full-dose DOAC plus aspirin for 45 days. Recently, some data have been published using a half-dose DOAC, suggesting that some antithrombotic therapy is necessary, but not necessarily full-dose therapy.

Anticoagulation therapy is replaced with clopidogrel after TEE rules out any device-related thrombus formation or significant peridevice

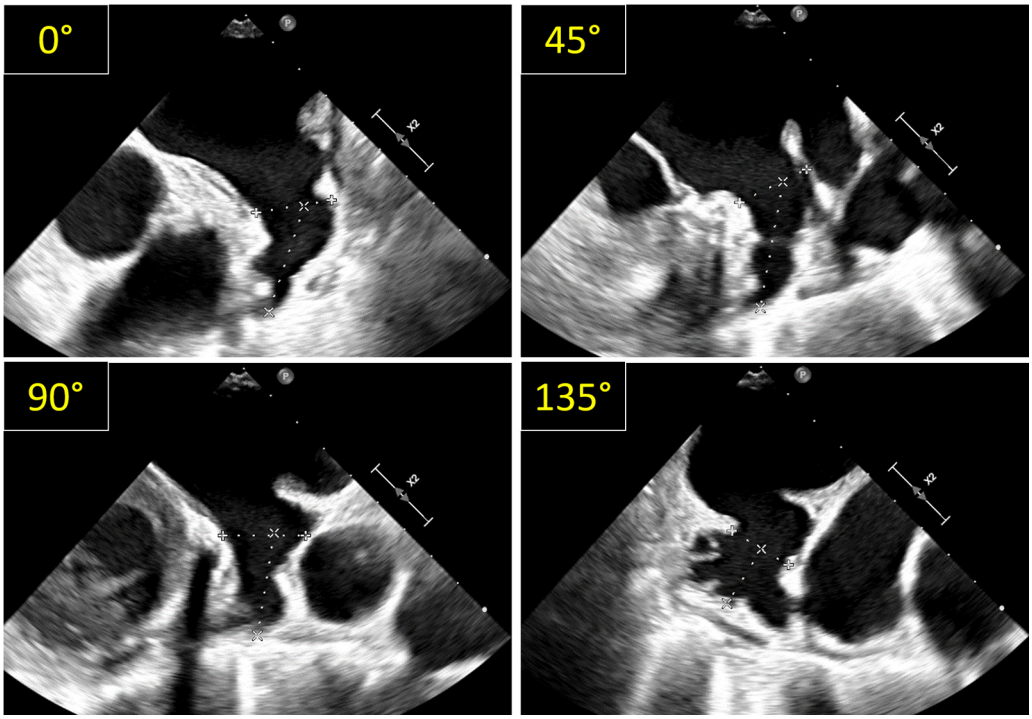

Figure 1 Case 1: Pre–Watchman FLX LAA sizing. Two-dimensional TEE at four key imaging angles (0°, 45°, 90°, and 135°) demonstrates measurements of the LAA landing zone diameter and LAA depth. Video 1 corresponds to this figure.

leak (>5 mm). After 6 months, clopidogrel is discontinued, with lifelong continuation of aspirin.[6,7]

Despite adherence to this regimen, thrombus formation on the earlier generation Watchman device is not uncommon and ranges from 3.4% to 6.6% of cases.[2,8,9] The most comprehensive data on the rate of DAT have been evaluated within the four US Food and Drug Administration trials for the Watchman device: the randomized control trials PROTECT-AF (Watchman Left Atrial Appendage System for Embolic Protection in Patients With Atrial Fibrillation) and PREVAIL (Evaluation of the Watchman LAA Closure Device in Patients With Atrial Fibrillation Versus Long Term Warfarin Therapy) and the prospective registries CAP (Continued Access to PROTECT-AF) and CAP2 (Continued Access to PREVAIL). The overall rate of DAT was 3.74% within the four trials, particularly in patients with histories of transient ischemic attack or stroke, vascular disease, and large LAA diameters. Among patients with DAT, 26.2% experienced either ischemic stroke, hemorrhagic stroke, or systemic emboli.[2] Another single-center study showed complete resolution of DAT with prompt, short-term warfarin therapy.[9]

Similarly, the European EWOLUTION (Registry on Watchman Outcomes in Real-Life Utilization) trial also saw Watchman device thrombi in 3.7% at 1 year regardless of medication status or drug regimen, as did the ASAP (ASA Plavix Feasibility) study, which recorded a DAT rate of 4%.[1,10] The current-generation Watchman device (referred to as Watchman FLX) was developed in part to mitigate this incidence of DAT. It offers a flatter left atrial surface and reduced area of threaded insert to promote endothelization and deter clot formation.[11]

Recent studies have shown that the Watchman FLX with a 6-week postprocedural course of a DOAC and aspirin has reduced rates of DAT and procedural complications and improved effectiveness of LAA closure.[12-14] In PINNACLE FLX (Protection against Embolism for Nonvalvular AF Patients: Investigational Device Evaluation of the Watchman FLX LAA Closure Technology), the Food and Drug Administration approval clinical trial, only 1.75% of patients developed DAT formation, and no device embolization with the second-generation Watchman FLX.[12]

Similarly, another prospective, multicenter study had only seven cases of DAT, with one case of ischemic stroke, further supporting

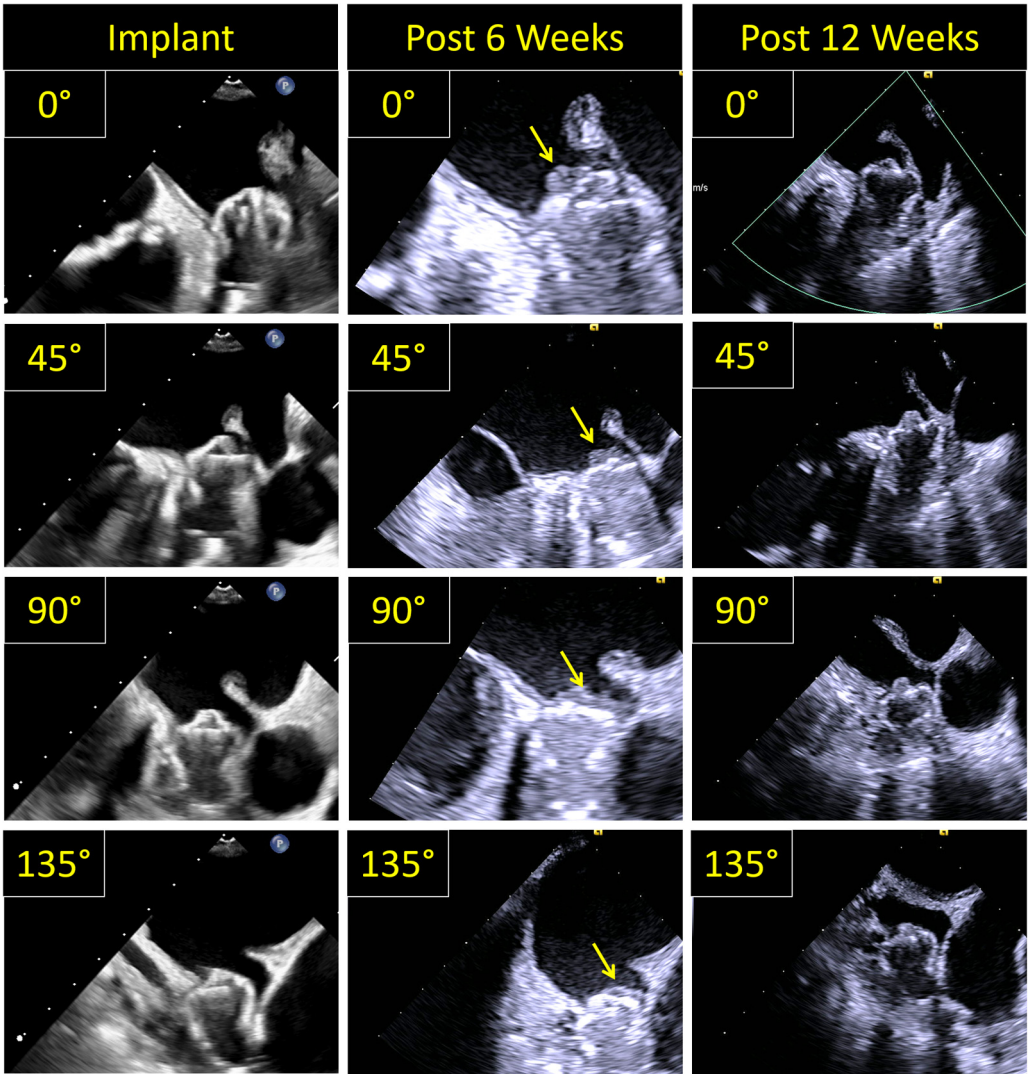

Figure 2 Case 1: Watchman FLX imaging at the time of implantation, after 6 weeks, and after 12 weeks. Two-dimensional TEE at four key imaging angles (0°, 45°, 90°, and 135°) at three time points (implant, after 6 weeks, and after 12 weeks) demonstrates DAT formation on the left atrial surface of the device (*arrow*) at 6 weeks only. The thrombus was not present at the time of implantation and had resolved by week 12. Videos 2, 3, and 4 correspond to this figure.

the superior efficacy of the Watchman FLX device.[13] Last, one European study of 91 patients had no DAT with the Watchman FLX and a higher follow-up closure rate than previously found with other devices.[15]

DAT with the novel Watchman FLX has not been previously reported outside clinical trials. Both events occurred in the setting of medication nonadherence. These patients did not complete their course of apixaban and were found to have DAT on follow-up. However, in the first patient, the thrombus did resolve after he was compliant with the medication for 6 weeks, as seen on repeat TEE. Of the 266 patients who underwent implantation with this specific LAAO device at our institution, these were the only two cases of DAT formation, yielding a rate of 0.75%.

CONCLUSION

We report two cases of percutaneous LAA closure using the Watchman FLX device leading to DAT in the setting of nonadherence

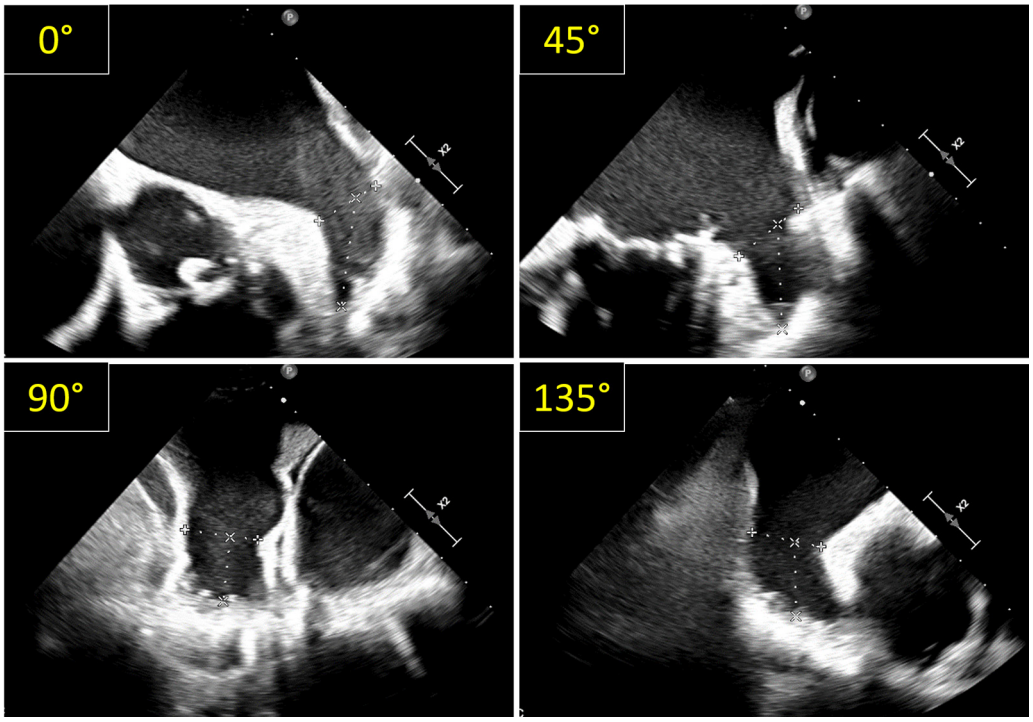

Figure 3 Case 2: Pre–Watchman FLX LAA sizing. Two-dimensional TEE at four key imaging angles (0°, 45°, 90°, and 135°) demonstrates measurements of the LAA landing zone diameter and LAA depth. Video 5 corresponds to this figure.

to oral anticoagulation. It appears that such cases were not previously reported outside of a clinical trial. These cases highlight that although this newer LAAO device has been shown to have lower rates of DAT than its predecessor, thrombus formation is still possible in rare instances.

ETHICS STATEMENT

The authors declare that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

CONSENT STATEMENT

The authors declare that since this was a non-interventional, retrospective, observational study utilizing de-identified data, informed consent was not required from the patient under an IRB exemption status.

FUNDING STATEMENT

The authors declare that this report did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

DISCLOSURE STATEMENT

The authors report no conflict of interest.

SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.case.2023.01.010.

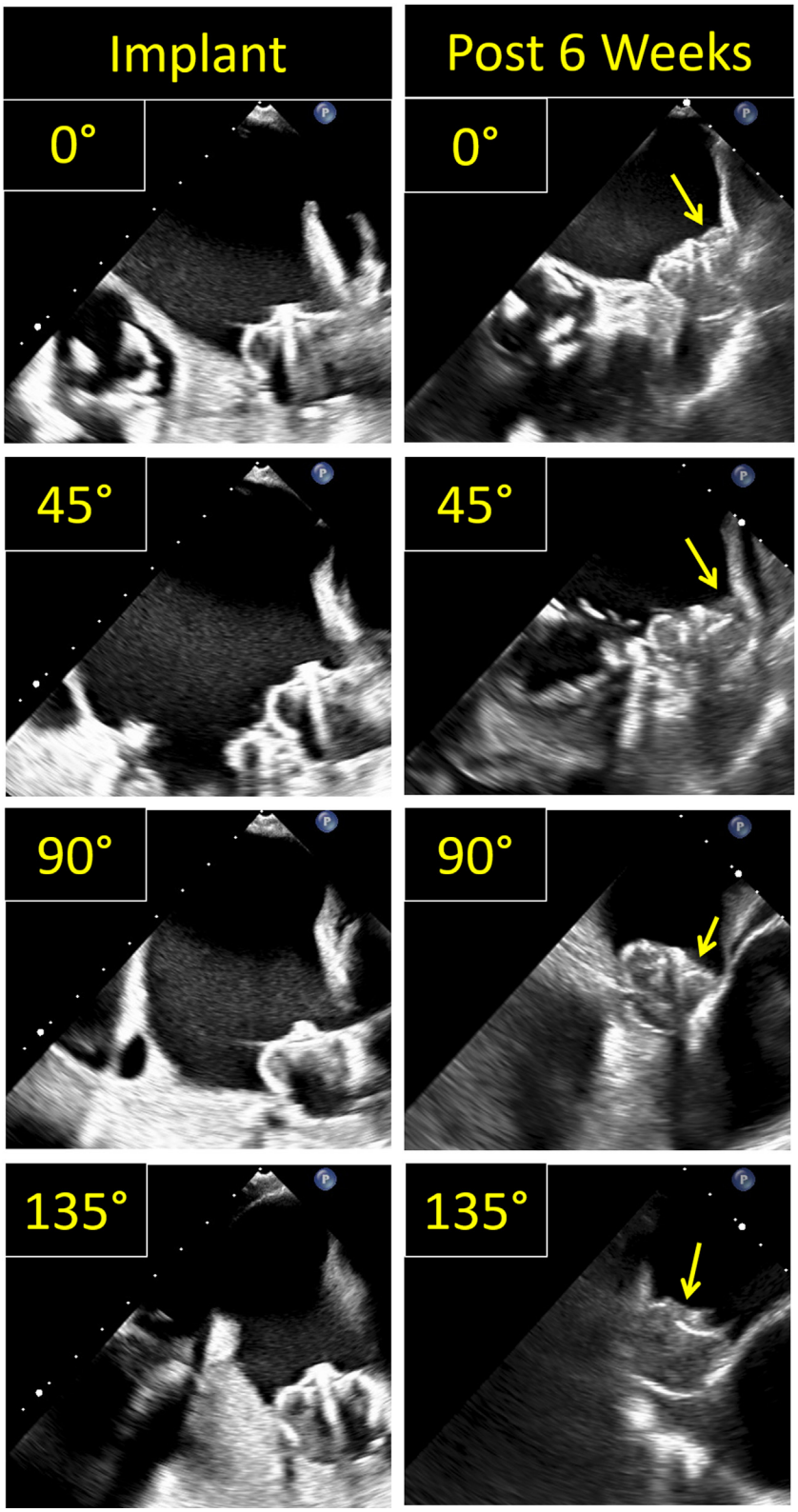

Figure 4 Case 2: Watchman FLX imaging at the time of implantation and after 6 weeks. Two-dimensional TEE at four key imaging angles (0°, 45°, 90°, and 135°) at two time points (implantation and after 6 weeks) demonstrates DAT formation on the left atrial surface of the device (*arrow*) at 6 weeks only. The thrombus was not present at the time of implantation. Subsequently, the patient was lost to follow-up. Videos 6 and 7 correspond to this figure.

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