Utility of Transesophageal Echocardiogram Surveillance after Watchman Device Placement

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Abstract

Background: In atrial fibrillation patients undergoing left atrial appendage occlusion with a Watchman device, surveillance imaging with a transesophageal echocardiogram (TEE) is typically performed at 45 days and 1 year to evaluate for device-related thrombus (DRT) and peri-device leak (PDL) before cessation of oral anticoagulation. The incidence of these complications is relatively low, and the ideal timing and duration of surveillance is unknown. We sought to evaluate the incidence of DRT and PDL after Watchman placement at 45 days and 1 year to determine the necessity of surveillance TEEs. Methods: We retrospectively analyzed 361 patients who received a Watchman device between January 2016 and January 2020. Baseline clinical and echocardiographic data, post-procedure antithrombotic therapy and surveillance echocardiographic data were collected from the NCDR LAAO Registry. Nested backward variable elimination regression was performed to derive independent predictors of the composite outcome of DRT and PDL. Results: A total of 286 patients who had post-procedure TEEs were included in the analysis. At 45 days, 9 patients had DRT (3.2%) and 44 patients had PDL (15.0%). At 1 year, 5 patients had DRT (5.6%) and 8 patients had PDL (8.9%). All DRT at 45 days was treated with continued anticoagulation while no change in protocol occurred with PDL. All DRT at 1 year occurred in new patients without prior thrombus. A history of prior transient ischemic attack (TIA) and thromboembolism were significantly associated with DRT or PDL at 1 year. Conclusions: We identified several patients with device-related complications at 45 days and 1 year despite appropriate device sizing and adequate use of antithrombotic therapy. The incidence of DRT increased from 45 days to 1 year and occurred in patients without prior thrombus. These findings highlight the importance of surveillance imaging and suggest the potential need for extended surveillance in select patients.

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Results: A total of 286 patients who had post-procedure TEEs were included in the analysis. At 45 days, 9 patients had DRT (3.2%) and 44 patients had PDL (15.0%). At 1 year, 5 patients had DRT (5.6%) and 8 patients had PDL (8.9%). All DRT at 45 days was treated with continued anticoagulation while no change in protocol occurred with PDL. All DRT at 1 year occurred in new patients without prior thrombus. A history of prior transient ischemic attack (TIA) and thromboembolism were significantly associated with DRT or PDL at 1 year.

Conclusions: We identified several patients with device-related complications at 45 days and 1 year despite appropriate device sizing and adequate use of antithrombotic therapy. The incidence of DRT increased from 45 days to 1 year and occurred in patients without prior thrombus. These findings highlight the importance of surveillance imaging and suggest the potential need for extended surveillance in select patients.

Keywords: Watchman, Surveillance, Transesophageal echocardiogram, Device-related thrombus, Peri-device leak

Background

It is well-established that patients with non-valvular atrial fibrillation and increased stroke risk benefit from anticoagulation with a vitamin K antagonist or a direct oral anticoagulant. However long-term oral anticoagulation increases risk of bleeding and therefore percutaneous left atrial appendage occlusion (LAAO), such as the Watchman device, has been incorporated into the guidelines as an alternative for patients with increased stroke risk and contraindications to anticoagulation.[1] In patients undergoing LAAO with a Watchman device, a transesophageal echocardiogram (TEE) is typically performed at 45 days and 1 year to assess for device-related complications including device-related thrombus (DRT) and peri-device leak (PDL).[2]

While DRT is an uncommon finding after Watchman implantation with studies reporting an incidence of 3-6%, it has been shown to be associated with an increased risk of thromboembolic events.[3,4] A single center study showed that a short course of warfarin successfully resolved all cases of DRT within 6 months without thrombus recurrence and with favorable clinical outcomes.[5] This highlights the importance of detection and treatment of DRT. The incidence of PDL is highly variable, ranging from 15 and 40%. PDL results in a persistent communication between the LAA and the left atrium and therefore the systemic circulation, potentially allowing thrombus within the LAA to be a source of embolic events. Clinical trials have used a threshold of 5mm as a meaningful leak requiring continued anticoagulation, however this is an arbitrary number with inconsistent clinical implications.[6] A recent study showed that PDL greater than 3mm detected

at 45 to 90 days was associated with an increased risk of the combined outcome of failure to stop anticoagulation, transient ischemic attack or stroke, DRT and need for PDL closure.[7] Additionally these complications continue to occur during long-term follow-up after 12 months, although the clinical implications of these findings are unclear.[8]

Amidst the ongoing coronavirus disease-2019 pandemic, the deferring of aerosolizing elective procedures such as TEE has been examined to prevent risk of viral transmission. In particular, the utility of 45-day TEE after Watchman implantation was examined and showed a very low rate of PDL and no DRT and therefore it was argued that it may be reasonable to defer the 45-day TEE during the ongoing pandemic and potentially in routine practice.[9] While TEE is an overall low risk procedure, it is still an invasive procedure and should only be performed if clinically necessary. We sought to evaluate the incidence of DRT and PDL after Watchman placement performed at a high-volume center at 45 days and 1 year to determine the necessity and utility of surveillance TEEs at these time points.

Methods

We retrospectively analyzed 361 patients who underwent Watchman device placement between 2016 and 2020 and received surveillance TEE imaging within 1 year. Baseline characteristics and echocardiographic data, post-procedure anticoagulation/antiplatelet use, and surveillance TEE data were collected from the NCDR LAAO Registry and patients' electronic medical records. Significant PDL was defined as >3mm color jet seen on post-procedure TEE, defined based upon a recent study showing higher risk of adverse outcomes with >3mm leak. Categorical variables were analyzed using chi-square statistics, as appropriate and continuous variables were analyzed using student T-test. Nested backward variable elimination of non-significant variables at an α-level >0.05 derived independent predictors of the composite of DRT and PDL. SAS version 9.4 (SAS Institute Inc., Cary, NC) was used for statistical analyses.

The Cedars-Sinai Institutional Review Board approved this retrospective study and waived the requirement for individual patient informed consent.

Results

A total of 286 patients who had post-procedure TEEs at 45 days were included in the analysis, of which 96 had 1-year TEEs. Patients who did not have 45-day follow-up with TEE were excluded (n=75). Demographic and clinical characteristics and baseline echocardiographic data are provided in **Tables 1A and 1B** . The mean age of the patient was 80 $\pm$ 8.7 years, 38% were female and 87% were white. The mean left ventricular ejection fraction was 56% and mean CHA_2DS_2-VASc score was 4.4 $\pm$ 1.5. Upon discharge after the Watchman procedure, 261 patients (92%) were discharged on at least 1 antiplatelet agent (92%) and 274 patients (96%) were discharged on an anticoagulation agent (**Table 2**).

The follow-up TEE findings are described in **Figure 1** . At 45 days, 44 patients had PDL [?]3mm (15%) and 9 patients had DRT (3%). At 1 year, 8 patients of 96 with TEE had PDL (8%) and 5 patients had DRT (5%). All patients with PDL had a leak size [?]5mm at both 45 days and 1 year and presence of leak did not change management or effect duration anticoagulation therapy. There was no progression of PDL at 1 year (no leak increased in size to >5mm) and 8 patients with PDL had improvement at 1 year. All DRTs at 45 days were treated with continued anticoagulation and all with follow-up TEE at 1 year demonstrated resolution. Of the available data at 1 year follow-up, 92 patients (96%) were documented to be on least 1 antiplatelet agent. The 5 DRTs demonstrated at 1 year occurred in patients who did not have prior thrombi on imaging. A history of prior transient ischemic attack (TIA) and prior thromboembolic event were independently associated with having DRT or PDL at 1 year (both p=0.04).

Discussion

In this retrospective analysis we identified several patients with device-related complications including DRT and PDL at 45 days and 1 year, despite appropriate use of antithrombotic therapy, suggesting that performance of a low-risk TEE at these time points is still indicated and can impact clinical management. The

rate of PDL decreased over time (15% to 8%) and there was no progression of PDL to >5mm at 1 year despite no targeted therapy at the time PDL was discovered.

The rate of DRT increased slightly between 45 days and 1 year (3% to 5%) and of note all cases of DRT at 1 year did not have thrombus at 45 days suggesting that continued surveillance at least to 1 year appears to be warranted. All DRTs were treated with continued anticoagulation at 45 days and resolved in those with follow-up imaging. All DRTs seen on 1 year TEE were in those without prior thrombus. Prior TIA and thromboembolism were associated with the presence of device-related complications at 1 year.

DRT is an important complication after percutaneous left atrial appendage closure and is associated with higher risk of ischemic events and the optimal postprocedural antithrombotic therapy and duration remains unknown. The current evidence reports a 3-4% incidence, which is consistent with our findings. Although the risk of DRT was thought to be highest during early endothelization, there is increasing recognition of late onset DRT with longer surveillance imaging which may be related to delayed or incomplete endothelization of the device.[10,11] We showed that with appropriate treatment of DRT detected at 45 days, there was complete resolution in those with follow-up, which highlights the importance of early surveillance imaging to guide appropriate therapy and prevent adverse events. Interestingly, at 1 year there was a higher rate of DRT compared to at 45 days, and all events occurred in patients without prior DRT. Importantly, none of the patients with delayed DRT had undersized watchman devices (all devices selected were 10-20% larger than the maximum width of the left atrial appendage measured by TEE). This finding supports that late device-related complications can occur despite appropriate antithrombotic therapy and appropriate device sizing, and questions whether surveillance imaging up to 1 year is sufficient. Staubach et al showed that new DRT continues to be detected on longer term follow-up (>12 months) and a sub-study of the PROTECT-AF trial also showed an increase in DRT at 5 months and 12 months, although early anticoagulation was not rigorously documented.[8,12]Delayed DRT may be related to incomplete endothelization which has been discovered after removal of device and in postmortem reports.[13,14] Further investigation is needed to determine patients who are at higher risk for incomplete endothelization of the device and thrombus formation and therefore would warrant extended surveillance imaging and anticoagulation therapy.

There is a wide range in the incidence of PDL, reported between 15-40%, which varies based upon the cutoff used to determine a clinically significant leak.[6] Delayed endothelization and device undersizing have been proposed as mechanisms for the occurrence of PDL.[15] The cutoffs used to discriminate significant leaks in the literature, usually >3mm or >5mm, have been selected arbitrarily and are not based upon clear data and the clinical importance of a persistent leak remains controversial. Our study showed a decrease in the incidence of PDL over 1 year follow-up, however there were 5 patients with new PDL detected at 1 year that were not seen at 45 days. The PROTECT AF study showed that over 30% of patients had major PDL (defined as >3mm) at 45 days and 1 year and presence of PDL was not associated with an increase in thromboembolic events, however interpretation of this is limited by the low event rate.[16] A more recent study showed that PDL, irrespective of size, was associated with a higher incidence of TIA or stroke, supporting the use of the lower cutoff of 3mm for our study.[7] Given the unclear consequence of persistent leaks and the availability of percutaneous PDL closure, further investigation of the implication of PDL is needed as well as determination of a significant cutoff.

Limitations

Several limitations to this study merit consideration. This is a retrospective single but high-volume center study, and our results may not be universally applicable, especially in centers with lower volumes of LAAO. Long-term follow-up clinical data was missing for many patients, therefore we cannot comment on clinical outcomes or TEE data beyond one year. We were unable to correlate international normalized ratio values with the presence or absence of DRT for patients taking warfarin. Antithrombotic therapy at 45 days and 1 year were obtained through the NCDR LAAO Registry, however adherence to therapy between these dates cannot be confirmed. Although all DRT at 45 days was treated with continued anticoagulation and all resolved by 1 year, the exact duration of treatment is unknown. The findings of this study are relevant only to the Watchman device and may not be applicable to other LAAO devices including the newer Watchman

FLX, therefore the rates of device-related complications in this study may not apply to other devices. Cardiac computed tomography, which has been shown to be a feasible alternative to TEE for detecting device-related complications after Watchman, was not used in this study.[15,17]Finally, we did not have outcomes data such as thrombo-embolic event rates.

Conclusion

Our study showed that surveillance imaging identified several device-related complications including DRT and PDL at 45 days and 1 year after Watchman placement, despite the appropriate use of antithrombotic therapy. The incidence of DRT was slightly higher at 1 year compared to 45 days and all DRT at 1 year were new cases, further highlighting the need for TEE surveillance at these two timepoints and potentially a need for even longer follow-up to identify delayed complications. Limited by sample size, we could not identify patients at high or low risk in whom TEE would definitely be needed or could be safely deferred, respectively. Further investigation is warranted to determine the optimal timing and duration of surveillance imaging after Watchman placement and further elucidate the clinical consequences and ideal treatment of device-related complications.

References

1. January CT, Wann LS, Calkins H, et al. 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(2).

2. Kuroki K, Doshi SK, Whang W, et al. Follow-up imaging after left atrial appendage closure. Heart Rhythm. 2020;17(11):1848-1855.

3. Dukkipati SR, Kar S, Holmes DR, et al. Device-related thrombus after left atrial appendage closure: incidence, predictors, and outcomes. Circulation. 2018;138(9):874-885.

4. Fauchier L, Cinaud A, Brigadeau F, et al. Device-related thrombosis after percutaneous left atrial appendage occlusion for atrial fibrillation. Journal of the American College of Cardiology. 2018;71(14):1528-1536.

5. 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;3(12):1380-1386.

6. Sahore A, Della Rocca DG, Anannab A, et al. Clinical Implications and Management Strategies for Left Atrial Appendage Leaks. *Cardiac Electrophysiology Clinics* . 2020;12(1):89-96. doi:10.1016/j.ccep.2019.11.010

7. Afzal MR, Gabriels JK, Jackson GG, et al. Temporal changes and clinical implications of delayed peridevice leak following left atrial appendage closure. JACC: Clinical Electrophysiology. 2022;8(1):15-25.

8. Staubach S, Schlatterbeck L, Mortl M, et al. Long-term transesophageal echocardiography follow-up after percutaneous left atrial appendage closure. Heart Rhythm. 2020;17(5 Pt A):728-733.

9. Tan BEX, Depta JP, Baibhav B, Bhatt DL. Necessity of 45-day transesophageal echocardiography after the watchman procedure amid the covid-19 pandemic. JACC Cardiovasc Imaging. 2020;13(11):2461-2462.

10. Asmarats L, Cruz-Gonzalez I, Nombela-Franco L, et al. Recurrence of device-related thrombus after percutaneous left atrial appendage closure. Circulation. 2019;140(17):1441-1443.

11. Lakkireddy D. Incomplete endothelialization of watchmantm device: predictors and implications from two cases. Journal of Atrial Fibrillation. 2019;11(5):2162.

12. Main ML, Fan D, Reddy VY, et al. Assessment of Device-Related Thrombus and Associated Clinical Outcomes With the WATCHMAN Left Atrial Appendage Closure Device for Embolic Protection in

Patients With Atrial Fibrillation (from the PROTECT-AF Trial). *The American Journal of Cardiology* . 2016;117(7):1127-1134. doi:10.1016/j.amjcard.2016.01.039

13. Schwartz RS, Holmes DR, Van Tassel RA, et al. Left atrial appendage obliteration. JACC: Cardiovascular Interventions. 2010;3(8):870-877.

14. Massarenti L, Yilmaz A. Incomplete endothelialization of left atrial appendage occlusion device 10 months after implantation. Journal of Cardiovascular Electrophysiology. 2012;23(12):1384-1385.

15. Saw J, Fahmy P, DeJong P, et al. Cardiac CT angiography for device surveillance after endovascular left atrial appendage closure. Eur Heart J Cardiovasc Imaging. 2015;16(11):1198-1206.

16. Viles-Gonzalez JF, Kar S, Douglas P, et al. The Clinical Impact of Incomplete Left Atrial Appendage Closure With the Watchman Device in Patients With Atrial Fibrillation. *Journal of the American College of Cardiology* . 2012;59(10):923-929. doi:10.1016/j.jacc.2011.11.028

17. Korsholm K, Jensen JM, Norgaard BL, Nielsen-Kudsk JE. Detection of device-related thrombosis following left atrial appendage occlusion: a comparison between cardiac computed tomography and transesophageal echocardiography. Circ: Cardiovascular Interventions. 2019;12(9):e008112.

Table 1. (A) Demographics and baseline clinical characteristics. (B) Baseline echocardiographic data.

A.

	All patients	Patients with DRT or PDL at 1 year	Patients without DRT or PDL at 1 yea
Age, years (SD)	80 (8.7)	78 (8.0)	79 (8.0)
BMI, kg/m2 (SD)	28 (6.4)	27 (3.2)	27 (5.4)
Creatinine, mg/dL (SD)	1.4 (1.2)	1.6 (1.0)	1.2 (0.8)
Female (%)	108 (38)	4 (33)	24 (31)
Race (%)			
White	248 (87)	10 (83)	67 (86)
Black	9 (3)	0	3 (3.9)
Asian	15 (5)	2 (17)	4 (5.1)
Paroxysmal AF (%)	105 (37)	3 (25)	29 (37)
Persistent AF (%)	49 (17)	2 (17)	10 (13)
Permanent AF (%)	132 (46)	7 (58)	39 (50)
Chronic lung disease (%)	28 (10)	1 (8.3)	8 (10)
OSA (%)	23 (8)	1 (8.3)	6 (7.7)
History of CAD (%)	110 (39)	4 (33)	29 (37)
CHA_2DS_2-VASc score (SD)	4.4 (1.5)	4.6 (1.6)	4 (1.3)
CHF (%)	57 (20)	1 (8)	17 (22)
Hypertension (%)	260 (91)	11 (92)	73 (94)
Diabetes (%)	89 (31)	1 (8)	21 (27)
Prior stroke (%)	70 (25)	4 (33)	17 (22)
Prior TIA (%)	19 (7)	3 (25)	4 (5)
Prior thromboembolism (%)	21 (7)	2 (17)	1 (1)
Vascular disease (%)	23 (8)	0	7 (9)

Values reported as mean (SD) or n (%).

AF, atrial fibrillation; BMI, body mass index; CAD, coronary artery disease; CHF, congestive heart failure; LV, left ventricular; OSA, obstructive sleep apnea; TIA, transient ischemic attack

B.

	All patients	Patients with DRT or PDL at 1 year	Patients without DRT
LVEF, % (SD)	56 (11)	59 (7.4)	57 (12)
LA area, cm^2 (SD)	26 (7.5)	27 (6.8)	26 (8.4)
Mod-severe or severe mitral regurgitation (%)	13 (5)	1 (8)	4 (5)
Spontaneous echo contrast (%)	51 (19)	3 (30)	12 (16)
LA appendage orifice area, cm^2 (SD)	22 (3.8)	23 (3.4)	22 (4.1)

Values reported as mean (SD) or n (%).

LA, left atrial; LVEF, left ventricular ejection fraction

Table 2. Post-procedural antiplatelet and anticoagulation therapy at 45 days.

	All patients	Patients with DRT or PDL at 1 year	Patients without DRT or PDL at 1 year	P-va
Antiplatelet (%)	261 (92)	12 (100)	76 (97)	0.5
Aspirin (%)	245 (86)	10 (83)	73 (94)	0.2
Clopidogrel (%)	29 (10)	2 (17)	9 (12)	0.6
Anticoagulation (%)	274 (96)	12 (100)	73 (94)	0.4
Warfarin (%)	182 (64)	8 (67)	52 (67)	1
Rivaroxaban (%)	17 (6)	0	6 (8)	1
Apixaban (%)	67 (24)	4 (33)	14 (18)	0.2
Dabigatran (%)	8 (3)	0	1 (1.4)	1

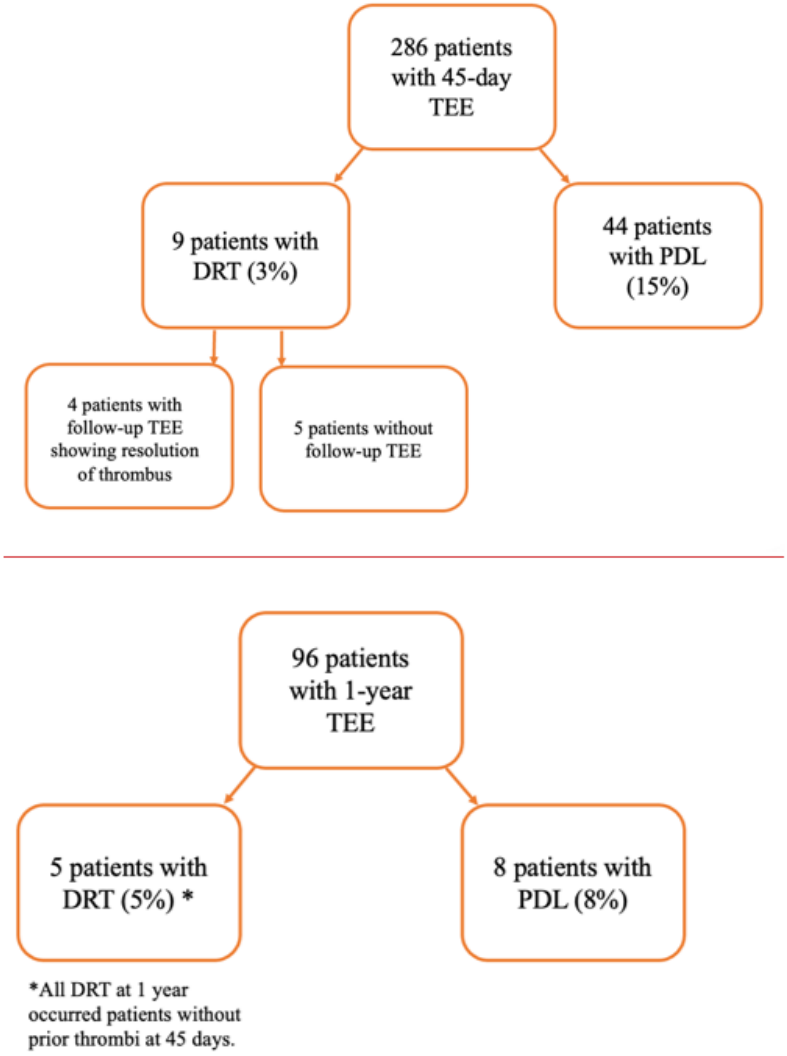

Figure 1. Post-watchman placement complications at 45 days and 1 year