Outcomes in Patients Implanted With a Watchman Device in Relation to Choice of Anticoagulation and Indication for Implant

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Abstract

Background

Patients with atrial fibrillation are increasingly prescribed a direct oral anticoagulant (DOAC) over warfarin and seek to avoid anticoagulation even without a history of major bleeding. This study explores the outcomes of patients implanted with a Watchman device in relation to anticoagulation choice (warfarin versus DOAC) in the post-procedure period and a history of bleeding.

Methods

Patients implanted with a Watchman device at a single center were retrospectively analyzed. Characteristics including anticoagulation in the first 45 days and history of major bleed were assessed and efficacy (thromboembolism) and safety (bleeding) outcomes compared by Kaplan-Meier analysis.

Results

209 patients were implanted (57% male, age 74.6 ± 7.8 years) and followed for 23.5 ± 7.1 months. In the first half of patients, 98% were prescribed warfarin, which dropped to 51% in the second half ($p<0.0001$). A history of major bleed was present in 80.8% of the first half of patients and decreased to 60% in the second half ($p=0.001$). There were 16 safety and 4 efficacy events. There was no difference in safety outcomes according to history of major bleeding or anticoagulant choice in the first 45 days. There was no difference in efficacy outcomes over the duration of follow up according to anticoagulation choice in the first 45 days.

Conclusions

Patients implanted with a Watchman device were increasingly over time prescribed a DOAC and implanted without a history of major bleeding. Bleeding and thromboembolic events were infrequent and related neither to choice of anticoagulant nor to prior major bleeding.

Key words: left atrial appendage, Watchman, direct oral anticoagulant, stroke, thromboembolism, bleeding

Introduction

In March 2015, the Food and Drug Administration (FDA) approved the Watchman device for left atrial appendage closure (LAAC) based upon, two randomized trials (1) (2) and a registry (3,4). The FDA approval required that patients with non-valvular atrial fibrillation and at increased risk for stroke have an appropriate rationale to seek a non-pharmacologic alternative to warfarin. However, the subsequent Centers for Medicare & Medicaid Services (CMS) coverage decision memo of February 2016 went further by mandating that patients considered for Watchman implantation be deemed “unable to take long term oral anticoagulation”(5). This decision reflected the high bleeding risk in patients enrolled in the aforementioned studies. Since the CMS coverage decision, Watchman device implantations have grown substantially, with the recent National Cardiovascular Data Registry (NCDR) left atrial appendage occlusion registry(6) reporting 38,158 Watchman procedures performed between January 2016 and December 2018.

Over the past several years, there has been a shift in the prescription of oral anticoagulation favoring a direct oral anticoagulant (DOAC) over warfarin. In the NCDR outpatient Practice Innovation and Clinical Excellence registry from 2008 to 2014, DOAC use increased from 5 to 30% (7), and in the Veterans Health Administration, DOAC use increased from 2% in 2011 to 65% of new anticoagulation prescriptions in 2016 (8). This change in anticoagulation management raises important questions when considering the risks and benefits of left atrial appendage occlusion, as patients treated with a DOAC were not included in the Watchman randomized trials. Further questions

remain on how to manage patients that cannot tolerate any period of oral anticoagulation, which is used short term after device implantation. A non-randomized study suggested that Watchman implantation can be performed safely without a warfarin transition period(9), and the safety of deferring anticoagulation is under further investigation in a randomized controlled trial(10). Since the initial Watchman approval, device implant indications no longer require a formal bleeding risk assessment or documented history of a major bleeding event, leaving open how to interpret the CMS coverage requirement wording that the patient be unable to take an oral anticoagulant long-term. These changes are reflective of changing practice patterns as well as long-term data supporting the safety and efficacy of the device compared to ongoing anticoagulation therapy. In this study, we sought to determine safety and efficacy outcomes in patients implanted with a Watchman device and in relation to choice of anticoagulation used in the first 45 days and indication for implant in relation to a history of major bleeding.

Methods

Patient Selection

This was a retrospective observational study that included all consecutive patients with non-valvular atrial fibrillation who underwent left atrial appendage occlusion with a Watchman device at St Joseph's Hospital and Medical Center (Phoenix, AZ) between April 2015 and May 2018. Baseline characteristics included: patient demographic characteristics, choice of anticoagulation used in the first 45 days (warfarin or DOAC),

and history of a major bleeding event. De-identified data was collected by one author (MA) while employed at St Joseph's Hospital and Medical Center. This study was approved by the local Institutional Review Board (IRB) before data collection.

Procedure Protocol and Follow Up

Prior to the procedure, a transesophageal echocardiogram (TEE) was performed to assess left atrial appendage size to determine device size and to rule out left atrial thrombus. Procedures were performed under general anesthesia by interventional cardiologists or electrophysiologists. The device size was chosen to achieve a compression factor of 8-20%. Patients were on anticoagulation prior to the procedure, with DOACs held 48 hours prior to procedure and warfarin continued uninterrupted. Femoral vein cannulation was performed using ultrasound guidance and trans-septal access was obtained with intraoperative TEE guidance. Heparin was administered with a target activation clotting time greater than 250 seconds. Patients were monitored overnight in the hospital and then followed up in clinic in 1 week. DOACs were resumed the same day after the procedure. TEE was performed 45 days post procedure, and if there was no device related thrombus or peri-device leak of greater than 5mm, anticoagulation was discontinued and dual anti-platelet therapy with aspirin (81mg) and clopidogrel (75mg) daily was initiated for 4.5 months. A final TEE was performed at 6 months, and clopidogrel was discontinued with aspirin continued lifelong if there was no device related thrombus or significant peri-device leak.

End Points

The efficacy outcome was a composite of transient ischemic attack (TIA), ischemic stroke, or systemic thromboembolism. The safety outcome was a composite of major or clinically relevant non-major bleeding, as defined by the International Society of Thrombosis and Hemostasis (ISTH) (11). Major bleeding was defined as any fatal bleeding, bleeding in a critical organ such as intracranial, intraspinal, intraocular, retroperitoneal, intra-articular, pericardial, intramuscular with compartment syndrome, or bleeding episode leading to drop in hemoglobin of ≥2 g/dl and or transfusion of ≥2 units of whole blood or red cells. Clinically relevant non-major bleeding was defined as any sign or symptoms of hemorrhage, which led to hospitalization or increased level of care, required medical intervention by a healthcare professional or prompted a face-to-face encounter but did not meet criteria for major bleeding.

Data Collection and Statistical Analysis

Data on patient characteristics, procedural characteristics, follow up TEE reports, and outcomes were retrospectively collected. Patients were entered into the database and assigned a number (ID) sequentially over time. Data were reported as mean ± standard deviation for continuous variables and as median and interquartile range for discrete variables, and as proportion or frequency for categorical variables. Comparisons were performed between patients treated with warfarin versus a DOAC, and between patients with or without a history of a major bleed. Comparisons were assessed with a Student's t test or equality of medians test, as appropriate, for continuous variables and with a Fisher exact test for categorical variables.

The Kaplan-Meier method was used to assess time to outcome, with a log rank test to assess equality of survivor functions between patient groups. For the efficacy outcome, the entire period of follow up was assessed to compare patient groups according to history of major bleed and choice of anticoagulation employed in the first 45 days. For the safety outcome, the entire period of follow up was assessed to compare patients with and without a history of major bleeding, but restricted to the first 45 days to compare patients by choice of anticoagulation used in that time period. Significance was set at a $p<0.05$. All statistical analyses were performed with Stata/IC version 14.2 (College Station, TX).

Results

A total of 212 patients were referred and device implantation was successful in 209. Three patients were not successfully implanted due to left atrial appendage anatomy in two patients and unsuccessful groin access in a third patient and were excluded from the analysis. One patient, included in the analysis, had device embolization detected on day 32; the device was removed by a snaring technique but required left common iliac artery thrombectomy and was discharged home on warfarin.

Clinical and procedural characteristics of the cohort are described in Table 1. The mean age was 74.6 ± 7.8 years with 57% men. Warfarin was used in 152 patients (73%) and a DOAC in 57 patients (27%). Of the 57 patients treated with a DOAC, 28 received apixaban, 23 received rivaroxaban, 4 received dabigatran and 2 received edoxaban.

There was a history of a major bleeding event in 70.3% with the most common being a gastrointestinal (GI) bleed in 92 patients (44%). Other bleeding events included: falls with injuries (N=22, 10.5%), central nervous system bleeds (N=15, 7.1%), epistaxis (N=6, 2.8%), urological bleeds (N=5, 2.4%), hematoma (N=3, 1.4%), retroperitoneal bleed (N=2, 1.0%), corneal bleed (N=1, 0.5%), and one patient deemed high risk for bleeding due to sickle cell anemia. Over time, fewer patients had a history of a major bleed. In the first half of patients implanted, a history of a major bleed was present in 80.8%, while in the second half of patients implanted in this study this percentage was reduced to 60% (p=0.001). This is also reflected in a longer duration of follow up for patients with a history of a major bleed (24.2 ± 7.1 vs 21.7 ± 6.8 months, p=0.016). Patients with a history of a major bleed had a higher HAS-BLED score with a median value of 4, compared to 3 for those without a history of a major bleed (p<0.001). Patients with a history of a major bleed were also more likely to have coronary artery disease (29.9% vs 16.1%, p=0.039) and implanted with a larger device (25.6 ± 3.4 vs 24.5 ± 3.1 mm, p=0.032). No other characteristics were significantly different (Table 1).

Warfarin was prescribed more frequently in patients with chronic kidney disease and paroxysmal atrial fibrillation, while no other characteristics were significantly different between the anticoagulation groups (Table 1). Over time it was observed that physicians increasingly prescribed a DOAC over warfarin. In the first half of patients implanted, warfarin was prescribed to 98%, while in the second half of patients in this study warfarin was prescribed to 51% (p<0.0001), which in turn resulted in a longer follow-up time for warfarin treated patients (25.3 ±3.3 versus 18.6 ±4.3 months, p<0.0001) .

All patients underwent a TEE at 6 weeks following implant and then at 6 months. TEE performed at 6 weeks showed no device related thrombus or significant peri-device leak in any patient and therefore all patients were switched from anticoagulation to dual antiplatelet therapy (DAPT) at 45 days after implant. Patients were then switched to aspirin after the TEE performed at 6 months.

Efficacy Outcomes:

Efficacy outcomes of 1 TIA and 3 ischemic strokes occurred after 6 months while on low dose aspirin (Supplementary Table 1). A Kaplan-Meier analysis showed no significant differences between patients treated with warfarin versus a DOAC in the first 45 days after implant (Figure 1).

Safety outcomes

In the first 45 days after device implant, there were 9 safety events in 8 patients, that included non-major groin bleeding post procedure in 4 patients, of which 2 patients were on a DOAC (Supplementary Table 2). Major bleeding events included GI bleeding in 3 patients, a pericardial effusion requiring a pericardial window in 1 patient, and one death due to intracranial hemorrhage from uncontrolled hypertension. All major bleeding events occurred in warfarin-treated patients. A Kaplan-Meier analysis over the first 45 days showed no significant differences between patients treated with warfarin versus a DOAC (Figure 2).

After day 45, there were an additional 7 major bleeding events that occurred while on anti-platelet therapy, and with one death due to GI bleeding (Supplementary Table 2). A Kaplan-Meier analysis over the full duration of follow up showed no significant differences between patients with or without a history of major bleeding prior to implant (Figure 3).

Discussion

This investigation examined the outcomes of 209 patients that underwent left atrial appendage occlusion with the Watchman device and post-procedure anticoagulation with either warfarin (n=152) or a DOAC (n=57). We found that during the period of anticoagulation over the first 45 days, safety events were infrequent, with non-major bleeding in 4 patients (2 on warfarin and 2 on a DOAC) and major bleeding events in 5 warfarin-treated patients. After day 45 when patients had transitioned to anti-platelet therapy alone and over a mean follow up of 23.5 ± 7.1 months, there were 4 thromboembolic events and 7 major bleeding events. While adverse events were low in this cohort, there were no significant differences in a Kaplan-Meier analysis between patients treated with warfarin or a DOAC. These findings confirm the safety of DOACs when used in the first 45 days after left atrial appendage occlusion. Furthermore, the Watchman device was implanted successfully with no device related thromboses and no major (>5mm) leaks seen on follow-up TEE, which was performed both at six weeks and at six months after implant.

Occlusion of the left atrial appendage has procedural-related risks that include pericardial effusion, acute stroke, device embolization, and other procedure related major bleeding. The procedure-related complication rate in this cohort was low at 2.9%, including 4 groin-bleeds, 1 pericardial effusion and 1 device embolization. This procedure-related complication rate compares favorably with the recently reported in-hospital complication rate of 2.16% in the NCDR Left Atrial Appendage Occlusion Registry(6) . Additionally, the complication rate was considerably lower than reported in the PROTECT AF (Watchman Left Atrial Appendage System for Embolic Protection in Patients with Atrial Fibrillation) trial, (8.7%) (2), the PREVAIL (Prospective Randomized Evaluation of the Watchman LAA Closure Device in Patients with Atrial Fibrillation Versus Long Term Warfarin Therapy) trial (4.5%), and the Continued Access Protocol (CAP) registry (4.2%). In particular, procedure-related pericardial effusion has decreased considerably over time, which had comprised the majority of safety events in the PROTECT AF trial (3) . Our findings confirm that operators over time have gained experience and can perform this procedure with fewer complications.

In the past ten years, DOACs have become preferred over warfarin for the management of atrial fibrillation patients. In turn, DOACs have been more frequently prescribed over warfarin for the six-week post implant period. In a pilot study in Germany (12), 18 patients received a DOAC for the first 45 days and there was no device thrombus seen on TEE at 45 days. In a small study that included follow-up TEE up to 12 months, there were no device related thrombi or device leaks seen in 10 patients treated with rivaroxaban for the six weeks post implant (13). A cohort of 426 patients with 214 treated with a DOAC post procedure showed no difference in bleeding, device-related

thrombosis or thromboembolism over a follow up of up to 4 months(14). Our cohort that includes 57 patients treated with a DOAC in the 45-day post-procedure period, extends these findings and showed no major bleeding or thromboembolic events or device-related thrombosis in patients treated with a DOAC post –procedure, and confirmed by TEE performed at both 45 days and 6 months.

The landmark PROTECT AF trial established the non-inferiority of left atrial appendage occlusion compared to warfarin for the outcomes of ischemic stroke and systemic embolism(1,2) and confirmed in follow-up out to 5 years (15). Once anticoagulation is discontinued, the bleeding risks are reduced with the greatest impact seen with GI bleeding and hemorrhagic stroke compared to warfarin (16). However, it remains unknown how major bleeding risk compares between patients treated with a DOAC and patients that undergo left atrial appendage occlusion. In the landmark DOAC trials compared to warfarin, GI bleeding risk was higher with the 150mg dose of dabigatran(17) , rivaroxaban (18) and the 60mg dose of edoxaban (19), while GI bleeding risk was similar with apixaban (20). The risk of hemorrhagic stroke was lower with all of these DOACs (17-20). This is an important question that would require a randomized study, rather than observational cohorts, to answer.

Furthermore, there also remains the concern that residual leaks and device related thrombi may persist that could place the patient at continued risk for stroke and require reinstitution of anticoagulation. In the PROTECT AF and PREVAIL trials, device related

thrombus, while infrequent, was associated with a higher risk of stroke and systemic embolism(21) . A recently reported study of 63 patients that underwent TEE after a mean of 3.1 years showed an incidence of major device leak of 3% and device related thrombus of 13% although none suffered a stroke related to a thrombus(22,23) . The concern for a residual leak and device related thrombus is greater for patients who have undergone this procedure and deemed unsuitable for any period of anticoagulation. In the EWOLUTION registry, 73% of patients were discharged from the hospital on either anti-platelet therapy or no anti-thrombotic therapy, while 27% were discharged on a vitamin K antagonist or a DOAC(23). They reported a device related thrombus in 34 patients (4.1%) but this was not related to the chosen anti-thrombotic regimen(23) . The outcomes of patients with no period of anticoagulation is being investigated in the ongoing ASAP-TOO trial that is randomizing patients to undergo a Watchman implant with post-procedure aspirin and clopidogrel versus control therapy with a single antiplatelet or no therapy over a 5 year follow-up(10).

These questions of both short and long-term risk and benefit for patient populations not studied in the randomized controlled trials impact upon how such patients should be counseled. This is particularly important when considering patients where there may be uncertainty if they meet the language for the specified indications by the Centers for Medicare & Medicaid Services (CMS) national coverage determination that patients must be “deemed unable to take long-term oral anticoagulation” (5). It should be recognized, however, that the randomized trials, PROTECT AF(1) and PREVAIL(2), did not exclude patients based upon their ability to take long-term anticoagulation. In our

cohort, which represents a high-volume single center in a major US city, 29.7% of patients were without a history of a major bleeding event despite a median HAS-BLED score of 3, making it unclear if these patients would be unable to take long-term anticoagulation. Nonetheless, we have shown that our cohort had excellent outcomes followed clinically for a mean of about 2 years. We need more randomized trial data to determine long term risk and benefit questions that include patients on DOACs and regardless of ability to take long term anticoagulation to inform possible future revisions to the CMS coverage determination, and more importantly, our shared decision making process with the patient.

Limitations

Our study is limited by several factors. It is an observational cohort that is retrospectively analyzed. There may have been other unknown factors that could have driven physician preference to prescribe a DOAC versus warfarin, which in turn may have impacted upon our findings. Our study is also limited by a smaller number of patients prescribed a DOAC (n=57) compared to warfarin (n=152). As the choice of anticoagulant was not randomized, the apparent non-significant trends in procedure related bleeding events in warfarin patients may have been due to relative procedural inexperience, as warfarin was preferentially prescribed in the first half of this study. The INR value in warfarin treated patients was unknown, and thus bleeding events in warfarin treated patients may have been related to a supratherapeutic INR. Additionally, the follow-up duration was shorter for patients treated with DOACs (18.6 ±4.3 months),

but is still likely to have been sufficient to differentiate adverse events at intermediate durations of follow up (i.e. under one year).

Conclusions

In this single center observational cohort of 209 patients implanted with a Watchman device, adverse bleeding or embolic events were infrequent. Over time, patients were increasingly prescribed a DOAC in the first 45 days after implant and were referred with no documented prior major bleeding event. There was no difference in safety outcomes according to a prior history of major bleeding as the indication for implant and over the duration of follow up. For patients treated with warfarin or a DOAC there was no difference in safety outcomes while anticoagulated in the first 45 days or in efficacy outcomes over the duration of follow up.

References

1. Reddy VY, Doshi SK, Sievert H et al. Percutaneous left atrial appendage closure for stroke prophylaxis in patients with atrial fibrillation: 2.3-Year Follow-up of the PROTECT AF (Watchman Left Atrial Appendage System for Embolic Protection in Patients with Atrial Fibrillation) Trial. Circulation 2013;127:720-9.
2. Holmes DR, Jr., Kar S, Price MJ et al. Prospective randomized evaluation of the Watchman Left Atrial Appendage Closure device in patients with atrial fibrillation versus long-term warfarin therapy: the PREVAIL trial. Journal of the American College of Cardiology 2014;64:1-12.
3. 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;123:417-24.
4. Continued Access to PREVAIL (CAP2) - WATCHMAN Left Atrial Appendage (LAA) Closure Technology (CAP2). https://clinicaltrials.gov/ct2/show/NCT01760291. Accessed August 29, 2020.
5. Decision Memo for Percutaneous Left Atrial Appendage Closure (LAA) Closure Therapy (CAG-00445N). https://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=281&bc=AAAAAAAAQAAA&%20. Accesssed: July 20, 2020. .

6. Freeman JV, Varosy P, Price MJ et al. The NCDR Left Atrial Appendage Occlusion Registry. Journal of the American College of Cardiology 2020;75:1503-1518.
7. Katz DF, Maddox TM, Turakhia M et al. Contemporary Trends in Oral Anticoagulant Prescription in Atrial Fibrillation Patients at Low to Moderate Risk of Stroke After Guideline-Recommended Change in Use of the CHADS2 to the CHA2DS2-VASc Score for Thromboembolic Risk Assessment: Analysis From the National Cardiovascular Data Registry's Outpatient Practice Innovation and Clinical Excellence Atrial Fibrillation Registry. Circulation Cardiovascular quality and outcomes 2017;10.
8. Rose AJ, Goldberg R, McManus DD et al. Anticoagulant Prescribing for Non-Valvular Atrial Fibrillation in the Veterans Health Administration. Journal of the American Heart Association 2019;8:e012646.
9. Reddy VY, Mobius-Winkler S, Miller MA et al. Left atrial appendage closure with the Watchman device in patients with a contraindication for oral anticoagulation: the ASAP study (ASA Plavix Feasibility Study With Watchman Left Atrial Appendage Closure Technology). Journal of the American College of Cardiology 2013;61:2551-6.
10. Assessment of the WATCHMAN device in patients unsuitable for oral anticoagulation (ASAP-TOO). https://clinicaltrials.gov/ct2/show/NCT02928497. Accessed 8/29/20.
11. Kaatz S, Ahmad D, Spyropoulos AC, Schulman S. Definition of clinically relevant non-major bleeding in studies of anticoagulants in atrial fibrillation and venous

thromboembolic disease in non-surgical patients: communication from the SSC of the ISTH. J Thromb Haemost 2015;13:2119-26.

12. Bosche LI, Afshari F, Schone D, Ewers A, Mugge A, Gotzmann M. Initial Experience With Novel Oral Anticoagulants During the First 45 Days After Left Atrial Appendage Closure With the Watchman Device. Clinical cardiology 2015;38:720-4.

13. Gu ZC, Qiao ZQ, Hao ZY et al. Initial anticoagulation experience with standard-dose rivaroxaban after Watchman left atrial appendage occlusion. Annals of translational medicine 2020;8:105.

14. 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;14:19-24.

15. Reddy VY, Doshi SK, Kar S et al. 5-Year Outcomes After Left Atrial Appendage Closure: From the PREVAIL and PROTECT AF Trials. Journal of the American College of Cardiology 2017;70:2964-2975.

16. Price MJ, Reddy VY, Valderrabano M et al. Bleeding Outcomes After Left Atrial Appendage Closure Compared With Long-Term Warfarin: A Pooled, Patient-Level Analysis of the WATCHMAN Randomized Trial Experience. JACC Cardiovascular interventions 2015;8:1925-1932.

17. Connolly SJ, Ezekowitz MD, Yusuf S et al. Dabigatran versus warfarin in patients with atrial fibrillation. The New England journal of medicine 2009;361:1139-51.

18. Patel MR, Mahaffey KW, Garg J et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. The New England journal of medicine 2011;365:883-91.
19. Giugliano RP, Ruff CT, Braunwald E et al. Edoxaban versus warfarin in patients with atrial fibrillation. The New England journal of medicine 2013;369:2093-104.
20. Granger CB, Alexander JH, McMurray JJ et al. Apixaban versus warfarin in patients with atrial fibrillation. The New England journal of medicine 2011;365:981-92.
21. Dukkipati SR, Kar S, Holmes DR et al. Device-Related Thrombus After Left Atrial Appendage Closure: Incidence, Predictors, and Outcomes. Circulation 2018;138:874-885.
22. Staubach S, Schlatterbeck L, Mortl M et al. Long-term transesophageal echocardiography follow-up after percutaneous left atrial appendage closure. Heart rhythm 2020;17:728-733.
23. Boersma LV, Ince H, Kische S et al. Evaluating Real-World Clinical Outcomes in Atrial Fibrillation Patients Receiving the WATCHMAN Left Atrial Appendage Closure Technology: Final 2-Year Outcome Data of the EWOLUTION Trial Focusing on History of Stroke and Hemorrhage. Circulation Arrhythmia and electrophysiology 2019;12:e006841.

Figure Legends

Figure 1: Kaplan-Meier curves for efficacy outcomes according to anticoagulation choice utilized in the first 45 days after implant

Figure 2: Kaplan-Meier curves for safety outcomes according to anticoagulation choice utilized in the first 45 days after implant

Figure 3: Kaplan-Meier curves for safety outcomes according to history of major bleeding prior to implant