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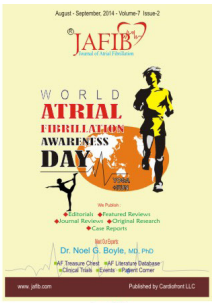

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Watchman Device: Left Atrial Appendage Closure For Stroke Prophylaxis In Atrial Fibrillation

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Abstract

A concerning proportion of patients with atrial fibrillation (AF) with indications for oral anticoagulation (OAC) discontinue OAC or are never prescribed OAC therapy and many AF patients with the highest risk for embolic events off OAC also have the greatest risk for hemorrhagic complications on OACs. Medium-term efficacy and safety data provide evidence that the WATCHMAN device, the most studied device and the only one with randomized and medium-term follow-up data, may be a viable alternative to chronic warfarin therapy in nonvalvular AF patients. In addition to presenting key data pertaining to LAA closure techniques including the WATCHMAN device, this review will discuss crucial WATCHMAN implantation technical points.

Introduction

A concerning proportion of patients with atrial fibrillation (AF) with indications for oral anticoagulation (OAC) discontinue OAC or are never prescribed OAC therapy because of current, perceived or potential concerns pertaining to side effects or bleeding concerns.[1] Additionally patients' decisions related to quality of life may also contribute to non-utilization of OACs. The recently published RELY trial reported, 17% treated with warfarin stopped warfarin at 2 years.[2] Similarly 21% of patients treated with dabigatran 150 mg discontinued therapy at 2 years. In the ROCKET-AF trial, 24% and 22% of patients discontinued OAC therapy with rivaroxaban and warfarin, respectively.[3] In the ARISTOTLE trial, 28% and 25% discontinued warfarin or apixaban, respectively.[4]

Embolic events in a majority of patients with AF result from thrombus formation in the left atrial appendage (LAA).[5] Risk scores (e.g., $CHADS_2$) have been developed to determine whether OAC therapy should be prescribed for prevention of embolic events.[6] The opposing risk of bleeding can be determined also using risk scores (e.g., HAS- BLED[7]). However many AF patients with the highest risk for embolic events off OAC also have the greatest risk for hemorrhagic complications on OACs. Nevertheless, in almost all patients, the risk of embolic stroke without OAC is higher than the risk of intracranial bleeding with OAC.[8] Although risk scores identify patients recommended for OACs and evidence strongly supports OAC, numerous factors, including contra-indications, physician preference based on clinical circumstances (bleeding risk, drug-drug interaction, poor patient compliance, labile INR) and patient preference has led to development of LAA occlusion techniques (percutaneous and surgical). Although several techniques have been described including endovascular percutaneous occlusion of the LAA, suture during concomitant cardiac surgery and epicardial ligation by stapling or clipping the LAA, all studies have limitations that place them as techniques lacking strong recommendations with absence of resolved long-term clinical evidence. Studies regarding surgical closure are small and lack/are pending long-term follow up. Initial data pertaining to the LARIAT (SentreHEART Inc, Redwood City, CA) device, which utilizes a technique that is intermediate between the surgical approach and the transcatheter approach has reported a 96% implant success, and 98% complete LAA closure at 1 year.[9]

Although Four devices with an endocardial approach have been reported - the percutaneous LAA transcatheter occlusion (PLAATO) system (eV3, Plymouth, MN), the Amplatzer cardiac plug (St. Jude Medical, Minneapolis, MN), the WATCHMAN device (Boston Scientific, Maple Grove, MN) and the Wavecrest System (Coherex Medical, Salt Lake City, UT),[10] this review will discuss the WATCHMAN, which has the only randomized study on an endovascular LAA closure device, reporting on safety and efficacy outcomes in a relatively large-scale trial (i.e., the WATCHMAN Left Atrial Appendage System for Embolic Protection in Patients with Atrial Fibrillation - PROTECT-AF).

The Evidence For The WATCHMAN Device

The PROTECT-AF trial demonstrated the efficacy of percuta-

Key Words:

Left Atrial Appendage, Non-Valvular Atrial Fibrillation, Atrial Fibrillation, Watchman, Left Atrial Appendage Occlusion, Stroke, Warfarin, Protect-Af.

Disclosures:
None.

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neous closure of the LAA as non-inferior to warfarin therapy.[11] At 1065 patient-years of follow-up, the primary efficacy (a composite endpoint of stroke, cardiovascular death, and systemic embolism) event rate was 3.0 per 100 patient-years in the intervention group and 4.9 per 100 patient-years in the control group (rate ratio [RR] 0.62, 95% Credible Interval (CrI) 0.35-1.25). In the warfarin control group, the therapeutic INR range was achieved 66% of the time despite close INR follow-up. Arguably a comparative study with novel OACs (NOACs) may not definitively demonstrate such a benefit.

Medium-term follow-up data of the PROTECT-AF trial (4-year follow-up) reported a 40% relative risk reduction (combined endpoint of all strokes, cardiovascular, or unexplained death and systemic embolism) in the WATCHMAN group compared to the warfarin group with a primary efficacy event rate of 2.3% and 3.8%, respectively.[12] Superiority in all-cause mortality (34% relative risk reduction) and cardiovascular mortality (60% relative risk reduction) was also reported.[12] There was a significantly higher risk of complications, predominantly pericardial effusion and procedural stroke related to air embolism in PROTECT AF. However, there was a significant improvement in the safety of implantation with increased operator experience.[13]

The WATCHMAN device frame is constructed of nitinol (nickel/titanium alloy). It is composed of 10 fixation anchors around the device perimeter designed to secure the device into the LAA. A fabric cap, constructed of polyethyl terephthalate serves as a 160-micron filter preventing emboli from exiting during the device endothelialization process. The PROTECT-AF study randomized 707 patients with non-valvular AF from 59 sites worldwide in a 2:1 distribution. Patients were >18 years of age with paroxysmal, persistent, or permanent non-valvular AF and had a $CHADS_2$ risk score >1. Exclusion criteria included contraindications to warfarin, co-morbidities other than AF that required chronic warfarin use, LAA thrombus, patent foramen ovale with atrial septal aneurysm and right-to-left shunt, mobile aortic atheroma, and symptomatic carotid artery disease. Patients allocated to the intervention group were treated post-implant with warfarin for 45 days. Warfarin was discontinued if the transesophageal echocardiogram (TEE) at 45 days post-implant showed either complete LAA occlusion or small residual peri-device flow (jet <5 mm in width). After warfarin treatment was stopped, clopidogrel (75 mg) and aspirin (81–325 mg) were prescribed until completion of 6-month follow-up visit, then aspirin alone was continued indefinitely. Patients in the control group received warfarin for the duration of the study. The safety end-points of the study included bleeding and procedure-related events (pericardial effusion, stroke, device embolization), which have been shown to typically occur in the periprocedural period and significantly decrease with operator experience.[13]

The preliminary data from the Prospective Randomized Evaluation of the WATCHMAN LAA Closure Device In Patients with Atrial Fibrillation Versus Long Term Warfarin Therapy (PREVAIL) reported an implant success of 95%, and safety events (defined as acute (i.e., within 7 days) occurrence of death, ischemic stroke, systemic embolism, and procedure- or device-related complications requiring major cardiovascular or endovascular intervention) occurred in only 2.2% of patients.[14]

The ASA Plavix Registry (ASAP) (n=150 with non-valvular AF, $CHADS_2$ >1 with a mean 2.8+/-1.2), enrolled patients with contraindications to warfarin treatment.[15] Following WATCHMAN implant, patients were discharged taking clopidogrel for 6 months and aspirin lifelong. At mean follow-up of 14.4+/-8.6 months, there were 4 strokes, 6 instances of device-related thrombus by TEE (1 resulted in a ischemic stroke), and 5 pericardial effusions (2 with tamponade requiring percutaneous drainage). The rate of ischemic stroke was 1.7%, compared to an expected rate of 7.3% if treated with aspirin alone (i.e., 77% reduction from the expected event rate) versus a 5% rate if treated with aspirin and lifelong clopidogrel. Thus WATCHMAN implantation without warfarin transition is arguably safe and effective in patients with an absolute contraindications to even short-term OAC.

Medium-term efficacy and safety data from PROTECT-AF, PREVAIL, ASAP and CAP[13] provide evidence that the WATCHMAN device, the most studied device and the only one with randomized and medium-term follow-up data, may be a viable alternative to chronic warfarin therapy in nonvalvular AF patients.

Clinical Use

The WATCHMAN device can be considered a reasonably safe and effective alternative to OAC, when OAC is contraindicated or when OAC may place patients at a high-predicted risk for major bleeding.

The following clinical scenarios would reasonably warrant LAA occlusion;

1. Non-valvular AF with a high CHA_2DS_2VSc (>2) and high bleeding risk (HASBLED >3).
2. Non-valvular AF with a high CHA_2DS_2VSc (>2) and recurrent bleeding on OAC.
3. Non-valvular AF with a high CHA_2DS_2VSc (>2) and contraindications/intolerance to OAC.
4. Non-valvular AF with a high CHA_2DS_2VSc (>2) and patient preference based on non-compliance or unwillingness to take OAC.
5. Patients who have had a major bleed or hemorrhagic stroke but have a high thromboembolic risk.

Key Implantation Technical Points

The WATCHMAN access system is available in double or single curve styles (14F Outer Diameter and 12F Inner Diameter). The WATCHMAN device comes preloaded within the delivery catheter. The device comes in 5 different sizes: 21, 24, 27, 30, 33 mm. The device size is selected such that following deployment, the device is compressed by approximately 8% to 20% from its original size. Implantation of an oversized device risks encroachment of adjacent structures and perforation and under-sizing risks device embolization and inadequate sealing of the LAA.

Transoesophageal echocardiographic (TEE) assessment is currently the main modality used to screen suitable candidates. 3D TEE can provide additional information to identify unusual LAA morphology. TEE is used to assess LAA morphology, ostial dimension, and maximum length of the LAA dominant lobe. Prior to the procedure, TEE should also document the absence of thrombi within the LAA. Measurements of the LAA ostium in at least 4 TEE views are required (0, 45, 90 and 135 degrees) to provisionally establish device size. The maximum LAA ostial size should be >17mm and <31mm. Cardiac CT can be utilized to assess LAA morphology though LAA dimensions have been reported to be under-estimated compared to 2D TTE.[16]

Most LAA can be categorize as 'Wind-sock Type, 'Chicken-wing Type' or 'Broccoli Type'. The Windsock type represents one dominant lobe and the implantation procedure in most cases is straightforward. The Chicken-wing type features a sharp bend in the dominant lobe.

If the proximal part (prior to the bend) is shorter than the maximum width of the orifice, the procedure may be complicated. The Broccoli type features limited LAA length with complex internal architecture. Since there are several lobes to cover and the length of the LAA is limited the device can be difficult to implant in the Broccoli type.

Peri-procedural TEE should rule out LAA thrombus and re-confirm LAA characteristics and size prior to transeptal access. Peri-procedural TEE is crucial for safe delivery and deployment of the device and is the imaging modality widely used. However, intra-cardiac echocardiography (ICE) with colour Doppler is also a viable alternative.[17, 18] ICE imaging however is reportedly less sensitive compared to TEE for LAA thrombus identification.[18] Once transeptal access is gained with TEE/ICE and fluoroscopy guidance, an activated clotting time of 250-350 seconds should be maintained. Left atrial pressure should be measured and fluids infused if pressure <10mmHg to accurately assess LAA dimensions. The WATCHMAN access sheath and dilator can then be introduced into the LA. A pigtail catheter is exchanged for the dilator and utilized to position the access sheath safely in the distal LAA with fluoroscopy and contrast guidance. If subsequent repositioning of the access sheath is required during the procedure the pigtail catheter should always be re-inserted into the access sheath prior to re-positioning.

It is paramount to prepare the sheaths and catheters carefully to minimize the potential for introducing air and allow bleed-back prior to introducing catheters via the access sheath. It is also important to prepare the device with care eliminating air by flushing the device submerged in normal saline.

The appropriate WATCHMAN device size based on the TEE measurements should be selected. Under fluoroscopic guidance the WATCHMAN delivery catheter is then advanced through the access sheath into position (aligning the distal tip of the delivery catheter with the marker band on the access sheath) and snapped onto the access sheath. The most distal marker band for the 21mm, the middle marker for the 27mm and the proximal marker for the 33mm device indicate the WATCHMAN landing zone. The 24mm and 30mm device landing zones are in between markers. The device is deployed by slowly retracting the access sheath/delivery catheter assembly. Once the device has been deployed fluoroscopy and TEE is utilized to confirm the device Position, Anchoring, Size and Seal (PASS).

The device is properly positioned when the plane of maximum diameter of the device is at or just distal to the LAA orifice spanning the entire LAA ostium. The device is properly anchored when the access sheath/delivery catheter assembly is 1 - 2 cm from the face of the device and gentle retraction and release of the deployment knob corresponds to device and LAA movement in unison as viewed with fluoroscopy and TEE (i.e., tug test). The device is properly sized when the deployed device is 80-92% of the original size, measured in the plane of the maximum diameter of the device-using TEE in the standard 4 views. Device seal is confirmed using colour Doppler to ensure that all lobes distal to device is sealed. A small gap (<5mm) is between the LAA wall and the device requires no repositioning. If there is a gap >5 mm, the device should be repositioned (initial distal implant) or fully recaptured and replaced (initial proximal implant). If all release criteria are met the Device can be released from the access sheath/catheter assembly and sheath/catheter assembly removed.

Avoiding Complications

The risk of pericardial effusion/tamponade can be minimized by TEE/ICE guided transeptal access, care during access into the LAA with the access sheath always via the pigtail catheter. A posterior transeptal puncture site appears to assist in accurate delivery and positioning of the device into the LAA. Great care should also be undertaken during device positioning within the access sheath and deployment and recapture. Air embolism and strokes can be minimized by adequate anticoagulation pre-procedure, peri-procedure and post procedure and meticulous detail to 'de-airing' of the sheath and device. In-appropriate device placement requiring recapture can be minimized with careful positioning of the access sheath and device positioning within the sheath and deployment guided by TEE and fluoroscopy. Device sizing is crucial to ensure device stability and proper LAA sealing. Peri-procedural TEE is also critical to ensure the axis of the device is in alignment with the major axis of the LAA. Encroachment of the device to adjacent anatomical structures (e.g., disruption of mitral valve function or pulmonary vein flow or left circumflex coronary artery compression) should be noted prior to final irretrievable device deployment). Screening for haemopericardium throughout procedure should be undertaken. Early detection of cerebral/systemic embolism should be screened for post procedure and during recovery.

Conclusion:

In patients who cannot tolerate or who have a contra-indication to OAC, occlusion of the LAA by the WATCHMAN device is a reasonable alternative with encouraging short and medium term data. However there is a lack of large randomized trials on truly long-term outcomes.

Further clinical data with longer follow-up is expected and is likely to reinforce the safety and efficacy profile of the WATCHAM device. Further studies are required reporting on the efficacy and safety of LAA occlusion in comparison to NOACs.

References:

1. Nieuwlaat R, Capucci A, Camm AJ, Olsson SB, Andresen D, Davies DW, Cobbe S, Breithardt G, Le Heuzey JY, Prins MH, Levy S, Crijns HJ, European Heart Survey I. Atrial fibrillation management: a prospective survey in ESC member countries: the Euro Heart Survey on Atrial Fibrillation. Eur Heart J. 2005;26:2422-2434.
2. Connolly SJ, Ezekowitz MD, Yusuf S, Eikelboom J, Oldgren J, Parekh A, Pogue J, Reilly PA, Themeles E, Varrone J, Wang S, Alings M, Xavier D, Zhu J, Diaz R, Lewis BS, Darius H, Diener HC, Joyner CD, Wallentin L, Committee R-LS, Investigators. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med. 2009;361:1139-1151.
3. Patel MR, Mahaffey KW, Garg J, Pan G, Singer DE, Hacke W, Breithardt G, Halperin JL, Hankey GJ, Piccini JP, Becker RC, Nessel CC, Paolini JF, Berkowitz SD, Fox KA, Califf RM, Investigators RA. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med. 2011;365:883-891.
4. Granger CB, Alexander JH, McMurray JJ, Lopes RD, Hylek EM, Hanna M, Al-Khalidi HR, Ansell J, Atar D, Avezum A, Bahit MC, Diaz R, Easton JD, Ezekowitz JA, Flaker G, Garcia D, Geraldes M, Gersh BJ, Golitsyn S, Goto S, Hermosillo AG, Hohnloser SH, Horowitz J, Mohan P, Jansky P, Lewis BS, Lopez-Sendon JL, Pais P, Parkhomenko A, Verheugt FW, Zhu J, Wallentin L, Committees A, Investigators. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2011;365:981-992.
5. Beinart R, Heist EK, Newell JB, Holmvang G, Ruskin JN, Mansour M. Left atrial appendage dimensions predict the risk of stroke/TIA in patients with atrial fibrillation. J Cardiovasc Electrophysiol. 2011;22:10-15.
6. Fang MC, Go AS, Chang Y, Borowsky L, Pomernacki NK, Singer DE, Group AS. Comparison of risk stratification schemes to predict thromboembolism in

people with nonvalvular atrial fibrillation. J Am Coll Cardiol. 2008;51:810-815.
7. 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;138:1093-1100.
8. Friberg L, Rosenqvist M, Lip GY. Net clinical benefit of warfarin in patients with atrial fibrillation: a report from the Swedish atrial fibrillation cohort study. Circulation. 2012;125:2298-2307.
9. Bartus K, Han FT, Bednarek J, Myc J, Kapelak B, Sadowski J, Lelakowski J, Bartus S, Yakubov SJ, Lee RJ. Percutaneous left atrial appendage suture ligation using the LARIAT device in patients with atrial fibrillation: initial clinical experience. J Am Coll Cardiol. 2013;62:108-118.
10. Cruz-Gonzalez I, Yan BP, Lam YY. Left atrial appendage exclusion: state-of-the-art. Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions. 2010;75:806-813.
11. Holmes DR, Reddy VY, Turi ZG, Doshi SK, Sievert H, Buchbinder M, Mullin CM, Sick P, Investigators PA. Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial. Lancet. 2009;374:534-542.
12. Reddy V, Doshi S, Sievert H. Long term results of PROTECT-AF: the mortality effects of left atrial appendage closure versus warfarin for stroke prophylaxis in AF. Heart Rhyth Society Scientofic sessions. May 09, 2013, Denver, Colorado. 2013.
13. 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;123:417-424.
14. Holmes D. Randomized Trial of LAA Closure vs Warfarin for Stroke/ Thromboembolic Prevention in Patients with Non-valvular Atrial Fibrillation (PREVAIL). . CIT. CNCC, Beijing, China. 20 March 2013. Interventional Innovation Summit Lecture. 2013.
15. Reddy VY, Mobius-Winkler S, Miller MA, Neuzil P, Schuler G, Wiebe J, Sick P, Sievert H. 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). J Am Coll Cardiol. 2013;61:2551-2556.
16. Budge LP, Shaffer KM, Moorman JR, Lake DE, Ferguson JD, Mangrum JM. Analysis of in vivo left atrial appendage morphology in patients with atrial fibrillation: a direct comparison of transesophageal echocardiography, planar cardiac CT, and segmented three-dimensional cardiac CT. J Interv Card Electrophysiol. 2008;23:87-93.
17. Ho IC, Neuzil P, Mraz T, Beldova Z, Gross D, Formanek P, Taborsky M, Niederle P, Ruskin JN, Reddy VY. Use of intracardiac echocardiography to guide implantation of a left atrial appendage occlusion device (PLAATO). Heart Rhythm. 2007;4:567-571.
18. Saksena S, Sra J, Jordaens L, Kusumoto F, Knight B, Natale A, Kocheril A, Nanda NC, Nagarakanti R, Simon AM, Viggiano MA, Lokhandwala T, Chandler ML, Group I-CIS. A prospective comparison of cardiac imaging using intracardiac echocardiography with transesophageal echocardiography in patients with atrial fibrillation: the intracardiac echocardiography guided cardioversion helps interventional procedures study. Circ Arrhythm Electrophysiol. 2010;3:571-577.