

LAA Closure With the Watchman Device

A review of techniques and clinical studies.

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Atrial fibrillation (AF) is one of the most common cardiac arrhythmia conditions. The estimated burden of patients with AF in 2010 was 5.5 million in the United States and is projected to increase to 15 million in the next 40 years.^{1,2} Nonvalvular AF increases the risk for stroke 5.6 times, while valvular heart disease is associated with a 17-fold increased risk of stroke.³ Ninety-one percent of the emboli in nonvalvular AF originate in the left atrial appendage (LAA).⁴ The use of systemic anticoagulation or antiplatelet agents based on the pre-existing risk factors has been shown to decrease the risk of thromboembolism in studies.⁵ Noncompliance and bleeding from anticoagulation are the most common causes for discontinuation of anticoagulation. Warfarin discontinuation is as high as 38% per year, whereas 14% to 44% of the patients have at least one contraindication to anticoagulation therapy.⁶

There has been a growing interest in LAA exclusion techniques to offset the limitations of oral anticoagulants in an effort to minimize the risk of stroke in patients with AF. Several LAA exclusion strategies and devices exist, including surgical ligation, the AtriClip (AtriCure, Inc., West Chester, OH), the Amplatzer cardiac

plug (St. Jude Medical, Inc., St. Paul, MN), the Watchman LAAC device (Boston Scientific Corporation, Natick, MA), the Lariat (SentreHeart, Inc., Redwood City, CA), the WaveCrest (Coherex Medical, Inc., Salt Lake City, UT), and several others that are in the incubator. The Watchman device is an endovascular LAA closure device that is being studied extensively. The strategy of LAA closure has recently been included in the European Society of Cardiology guidelines for patients with a high risk of stroke and contraindications to oral anticoagulants.⁷ In the United States, the Watchman device is currently under consideration for approval by the US Food and Drug Administration (FDA).

THE WATCHMAN LAAC DEVICE

The Watchman is a parachute-shaped device that can be percutaneously implanted in the LAA. It is made up of a metallic frame that is covered by a polyester mesh membrane.⁸ The metallic frame is made from nitinol, which is an alloy of nickel and titanium that has unique memory and superelastic properties. These properties of nitinol allow the Watchman device to configure to the contours of the

LAA after deployment. The frame has 10 fixation anchors that allow it to anchor inside the LAA chamber.⁸ The mesh membrane covering the frame on the atrial side prevents clots from escaping into the left atrium (Figure 1). The Watchman device is currently available in five sizes: 21 mm, 24 mm, 27 mm, 30 mm, and 33 mm.⁹ The delivery mechanism has three components: the Watchman device, the delivery catheter,

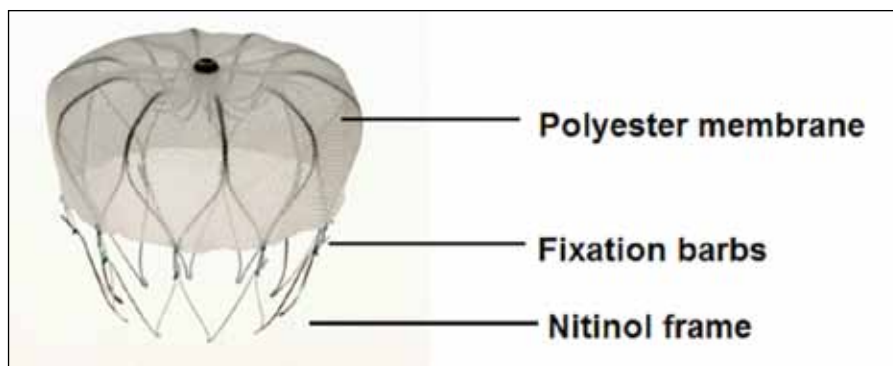


Figure 1. Image of the Watchman device showing the parachute-like metal frame with fixation bars and a polyester membrane covering the frame.



Figure 2. Diagram illustrating the optimal position for Watchman device deployment in the LAA (center). TEE images illustrating the optimal position of the Watchman device in the LAA (right and left). LA, left atrium; WM, Watchman device.

and a transseptal access sheath. The Watchman device has been described to be MRI conditional.¹⁰ At present, the Watchman device is available for investigational use only in the United States.

IMPLANTATION TECHNIQUE

The Watchman device is implanted percutaneously into the LAA using fluoroscopy and transesophageal echocardiography (TEE) for guidance. The procedure can be done under local or general anesthesia.¹¹ It is important to carefully select the appropriately sized device, which will allow adequate sealing of the LAA and prevent embolization of the device. It is recommended to select the size of the Watchman device such that after deployment, the device is compressed by approximately 8% to 20% of its original size.¹¹ The size of the LAA is measured by TEE in four different angles (0°, 45°, 90°, and 135°) to accurately assess the size of the LAA orifice and also to rule out thrombus in the LAA.

To implant the device, a transseptal catheter is advanced into the right atrium from the femoral vein. The transseptal puncture is made, and access to the left atrium is achieved under TEE guidance. The transseptal catheter is then exchanged with the Watchman access sheath over the guidewire, and a pigtail catheter is advanced through this access sheath into the left atrium. The access sheath is then advanced into the LAA over the pigtail catheter. The size of the LAA is again confirmed under TEE and fluoroscopic guidance. The pigtail catheter is then removed, and an appropriately sized Watchman delivery system (consisting of a delivery catheter and a preloaded Watchman device) is advanced into the LAA via the access sheath. The access sheath and delivery catheter are then withdrawn, and the device is deployed in the LAA.¹²

The position, anchoring, size, and seal (PASS) of the device are then checked. The ideal position of the Watchman device should be at or slightly distal to the orifice of the LAA (Figure 2).¹² The interventionist must be

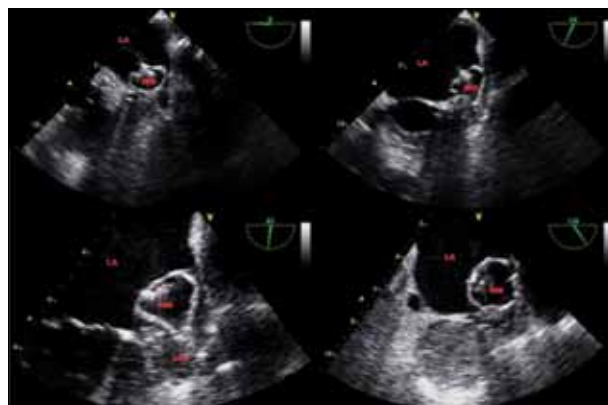


Figure 3. TEE images illustrating proximal deployment of the Watchman device. The device is located proximal to the orifice of the LAA and is projecting into the LA chamber. LA, left atrium; LAA, left atrial appendage; WM, Watchman device.

cautious not to deploy it too proximal or too distal to the orifice (Figure 3). The device should be properly secured in the LAA, and it should move in unison with the LAA.¹² Eight percent to 20% device compression is confirmed with TEE measurements. There should be adequate sealing of the device with no leaks around it. A leak of ≤ 3 mm is acceptable, and such leaks are almost always eccentric in location (Figure 4). The delivery catheter is subsequently detached from the Watchman device and withdrawn. At this point, the PASS device release criteria should be met (Table 1), confirmed by both TEE and fluoroscopy. Endothelialization of the surface of the Watchman device typically takes 45 to 60 days; until that time, oral anticoagulation is continued.¹²

CLINICAL STUDIES INVOLVING THE WATCHMAN LAA CLOSURE DEVICE

In the United States, the FDA currently has classified the Watchman device for investigational use only. It is currently available only to select physicians at select centers who are conducting clinical trials/registries with the device.

TABLE 1. THE PASS LAA EXCLUSION DEVICE RELEASE CRITERIA USING ENDOCARDIAL DEPLOYMENT

Feature	Details
Position	Device is distal to or at the ostium of the LAA
Anchor	Fixation of barbs engaged/device is stable with initial tug test
Size	Device is compressed 8% to 20% of original size
Seal	Device spans ostium, all lobes of LAA are covered; a ≤ 3 mm peri-device leak is acceptable

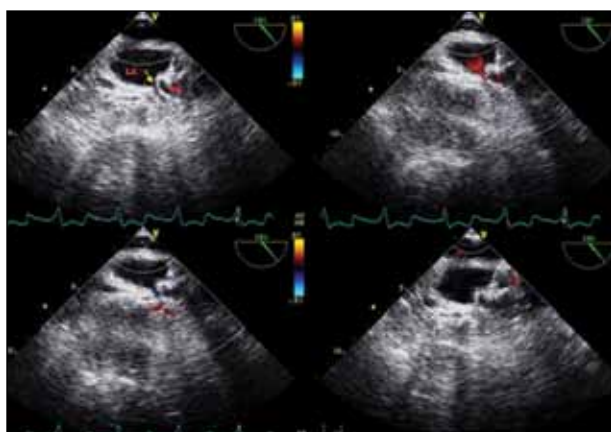


Figure 4. TEE image demonstrating eccentrically located peri-device leak (yellow arrow) around the Watchman device. Color Doppler demonstrates flow across the leak. LA, left atrium; WM, Watchman device.

PROTECT-AF

PROTECT-AF is a prospective, multicenter, randomized clinical study done across 59 centers in the United States and Europe.¹³ A total of 707 patients with a CHADS₂ score ≥ 1 were enrolled in a 2:1 ratio to a Watchman device arm and a control arm. Successful implantation of the device was seen in 89.5% of the subjects.¹⁴ After implantation, subjects were continued on oral anticoagulation therapy for 45 days. If adequate sealing (peri-device leak ≤ 5 mm) was noted on TEE at 45 days, they were switched to a combination of aspirin and clopidogrel for 6 months, after which only aspirin was continued. The cumulative follow-up period was 1,588.4 years. The primary efficacy endpoint (comprising stroke, thromboembolism, and death) showed that the Watchman device was noninferior to anticoagulation with warfarin (3% and 4.3%/100 patient-years; RR ratio, 0.7%). The primary procedure-related 7-day (safety event rate) event rate was higher in the Watchman group (5.5% vs 3.6% per year).¹³ The higher safety event rate in this group was due to a higher occurrence of periprocedural events

in the first half of the study, such as pericardial effusion and stroke and was attributed to the learning curve of the operators.¹⁵ In addition to noninferiority to warfarin, it was shown at 1 year that the quality of life was better in the Watchman group.¹⁶

More recently, the PROTECT-AF investigators have presented the long-term follow-up results from this study at the Heart Rhythm Society 2013 meeting. After a mean follow-up period of 45 months and an aggregate of 2,578 patient-years, the primary endpoints were 2.3 and 3.8 per 100 patient-years for the Watchman and the control group, respectively.¹⁷ More interestingly, all-cause mortality (3.2 vs 4.9 per 100 patient-years), cardiovascular mortality (1 vs 2.4 per 100 patient-years), and hemorrhagic stroke (0.2 vs 1 per 100 patient-years) were lower in the Watchman group.¹⁷ The relative risk reduction of 40% in primary endpoints, a 60% reduction in cardiovascular mortality, and a 34% reduction in all-cause mortality in the Watchman group make it superior to warfarin.¹⁷

The CAP Registry

Because of the higher rate of periprocedural events noted during the PROTECT-AF study, the FDA has allowed a subset of the PROTECT-AF investigators to gain additional information with regard to the safety and efficacy of the Watchman device. In this nonrandomized study of 460 patients with a protocol similar to that of PROTECT-AF, successful implantation was seen in 95% of the subjects.¹⁴ The safety event rates were remarkably lower in the CAP registry and had decreased to 3.7% from 7.7% in the PROTECT-AF study.¹⁴

PREVAIL

PREVAIL is a prospective, randomized study with a trial design similar to that of PROTECT-AF and was done to confirm the safety and efficacy results of PROTECT-AF and the CAP registry. PREVAIL enrolled 407 patients in 41 centers in the United States. The primary safety endpoint of death, stroke, thromboembolism, and device- or procedure-related complication requiring major endovascular or cardiovascular intervention at 7 days was 2.2%.¹⁸ The occurrence of all serious device-related vascular complications was also similar to the results from the CAP registry (4.4% and 4.1%, respectively) and was approximately half the complication rates seen in PROTECT-AF.¹⁸ Additionally, the number of patients with cardiac perforations needing surgical repair was also low in the PREVAIL study at 0.4% compared to 1.6% in PROTECT-AF.¹⁸

The ASAP Study

The ASAP study was done to evaluate the safety and efficacy of the Watchman device in patients who have

contraindications to anticoagulation therapy.¹⁹ ASAP was a multicenter, nonrandomized study and included patients with nonvalvular AF and a CHADS₂ score ≥ 1 . After device implantation, patients were continued on aspirin and either clopidogrel or ticlopidine for 6 months, after which only aspirin was continued. After a cumulative follow-up period of 176.9 patient years, the ischemic stroke rate was observed to be 1.7%.¹⁹ The ASAP study demonstrated that patients could be safely transitioned to antiplatelet therapy without being bridged with warfarin immediately after the procedure.

PERIPROCEDURAL COMPLICATIONS

The Watchman device has demonstrated noninferiority to warfarin in decreasing stroke risk in patients with AF; however, it does have short- and long-term complications.

Periprocedural Stroke

In the PROTECT-AF study, 0.9% of the subjects were noted to have a periprocedural stroke.¹⁴ Of the five patients observed with this complication, three were confirmed to have had a stroke due to air embolism from air escaping through the transseptal access sheath. The stroke manifestation in all of these patients was within the first 48 hours of the procedure. Subsequently, in the CAP registry and ASAP studies, this complication was not observed, likely due to improved operator experience and adeptness at handling the catheters and sheaths.^{14,19}

Pericardial Effusion

In the PROTECT-AF study, 5.2% of the subjects were noted to have pericardial effusion, and this complication rate decreased to 2.2% in the CAP registry.¹⁴ The cumulative rate of occurrence of pericardial effusion for both studies was 3.8% (34 patients had hemodynamic compromise, and four patients had their hospital stays prolonged by 4 days).¹⁴ In the ASAP study, pericardial effusion was noted in 2%, and tamponade was observed in 1.3% of the subjects.¹⁹

Incomplete Sealing of the LAA

The LAA has a variable size and shape; therefore, using an endovascular device with a fixed size and shape placement can become tricky and may result in incomplete sealing of the LAA. In the PROTECT-AF study, peri-device flow leak was noted in 40.9%, 33.8%, and 32.1% of the subjects at 45 days, 6 months, and 12 months, respectively.²⁰ In PROTECT-AF, the investigators did not observe a difference in the primary endpoints of stroke, systemic embolism, or cardiovascular or unexplained death in patients with and without peri-device leaks.²⁰ Furthermore, they also did not find any association between the severity of peri-device leaks and the primary

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endpoints, and the occurrence of primary endpoints was also not different if patients were on or off anticoagulation 45 days after implantation.²⁰ Due to continued remodeling of the LAA and the tissue around the device, the location and size of the peri-device leak continues to evolve even 12 months after implantation. Some leaks improve, and some worsen. Therefore, appropriate follow-up TEE is important to assess the leaks from time to time.²¹ One hundred percent exclusion of the LAA may not be possible with any of the existing technologies unless it is excised and oversewn. Because these small leaks do not have any major impact on the risk of stroke, it may still be an acceptable end result.

Device Embolization

Embolization of the device was observed in 0.6% of subjects in the PROTECT-AF study, and no embolization was noted in the CAP registry.¹⁴ In one patient, embolization was noticed immediately during the procedure and required cardiac surgery for explantation. In another two patients, embolization was noticed at 45-day follow-up; one patient required surgery, and in the other patient, the device was explanted percutaneously via a femoral approach.¹⁴ In one of these patients who had device embolization, the device migrated to the aortic valve and caused extensive damage to the aortic valve needing replacement with a prosthetic valve.²² The embolization rate in the ASAP study was slightly higher at 1.3%.¹⁹

Device Thrombus Formation

Thrombus formation on the device was noted in 4.2% and 4% of the subjects in the PROTECT-AF and ASAP studies, respectively.^{14,19} The estimated risk of stroke from device-associated thrombus was 0.3% per 100 patient-years.¹⁴ The long-term implications of thrombus on the device are not clear. However, appropriate anticoagulation, if not contraindicated, will help address this problem.

Device Infection

There has been one case report of Watchman device infection.²³ The patient was noted to have vegetation on the atrial side of the device and needed surgical explantation followed by a prolonged course of antibiotics.

Other Complications

Additional complications include those that are procedure-related, such as hematoma formation, pseudoaneurysms, arteriovenous fistula, esophageal tear, and hemopericardium. Despite the number of complications associated with this procedure, the overall disability and death rates were favorable in the Watchman group.¹⁴

CONCLUSION

The science of LAA exclusion for stroke prophylaxis is new and is evolving with the emergence of both endovascular and epicardial approaches. The results from clinical studies evaluating the Watchman device appear to be promising. Some concerns remain regarding the safety of the procedure and the long-term complications related to the device. However, it is becoming clear that with improved operator experience, the rate of complications is decreasing.

Operator experience and expertise continue to improve with time and seem to significantly minimize periprocedural complications and success of implantation. FDA clearance of the Watchman device will begin a new chapter in the science of LAA and will allow access to a therapeutic tool that is much needed in addressing the risk of stroke in patients with AF. Currently, a next-generation Watchman device, which, unlike the current device, can be fully recaptured and redeployed, is being studied. This device is designed to allay some of the concerns regarding peri-device leaks and embolization. ■

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