Original Article
Transcatheter closure of the left atrial appendage: initial experience with the WATCHMAN device

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Abstract: Background: Atrial fibrillation (AF) is the most commonly encountered clinical arrhythmia, accounting for approximately one third of hospitalizations for cardiac rhythm disturbance. In patients with non-valvular AF, approximately 90% of thrombi are thought to arise from the left atrial appendage (LAA). Anticoagulation with warfarin has been the mainstay of therapy to reduce stroke risk in these patients; however, it is not without its complications including bleeding and drug interactions. Percutaneous left atrial appendage closure can be an alternative to warfarin treatment in patients with AF at high risk for thromboembolic events and/or bleeding complications. Methods: Patients with atrial fibrillation and CHADSVASc score ≥ 2, not eligible for anticoagulation, were submitted to left atrial appendage closure using the WATCHMAN device. The procedure was performed under general anaesthesia, and was guided by fluoroscopy and transoesophageal echocardiography. Results: Percutaneous LAA closure with the WATCHMAN device was performed in all patients. At 45-day follow-up no recurrent major adverse events and especially no thromboembolic events occurred. Conclusions: Transcatheter closure of the LAA with the WATCHMAN device is generally safe and feasible. Long-term follow-up will further reveal the risk and benefits of this therapy.

Keywords: Atrial fibrillation, left atrial appendage, WATCHMAN device

Introduction

Atrial fibrillation (AF) is the most common arrhythmia encountered in clinical practice [1, 2]. It is a disease of older individuals, affecting up to 15% of people aged 80 years and older, and its prevalence is expected to increase with the overall aging of the population worldwide [1, 3]. According to conservative estimates, the AF population in China is currently over 8 million [2].

AF is associated with a fivefold increased risk for stroke, mostly secondary to thromboembolic events [4, 5]. Most importantly, compared with the other causes of stroke, AF-related stroke had longer hospitalization, more recurrent stroke, higher morbidity and mortality [5, 6]. It imposed a huge social and economic burden. Warfarin, the predominant oral anticoagulant, was shown to reduce AF-related stroke by 60% in standardized treatment, but is difficult to be used safely and conveniently. Some patients at risk of thromboembolic stroke due to AF have a number of contraindications for traditional anticoagulation, because of the risk

of bleeding, especially in the elderly in whom the risk of stroke is highest. Aspirin, although generally better tolerated, is clearly less effective at stroke prevention [7]. The newer anticoagulants such as dabigatran, rivaroxaban and apixaban have been shown to be non-inferior, if not superior, to warfarin [8, 9]. They have helped overcome some of the drawbacks of warfarin therapy. However, these agents are still associated with potential bleeding complications, high cost, and unlike warfarin; there are no currently available antagonists.

As an alternative to systemic anticoagulant therapy, the PROTECT AF (Watchman Left Atrial Appendage System for Embolic Protection in Patients with AF) clinical trial examined the hypothesis that the "local" therapy of left atrial appendage (LAA) closure could recapitulate the benefits in stroke prevention observed with warfarin [10, 11].

This study reported our initial experience with WATCHMAN device implantation for patients with non-valvular AF at high risk for stroke in our centers.
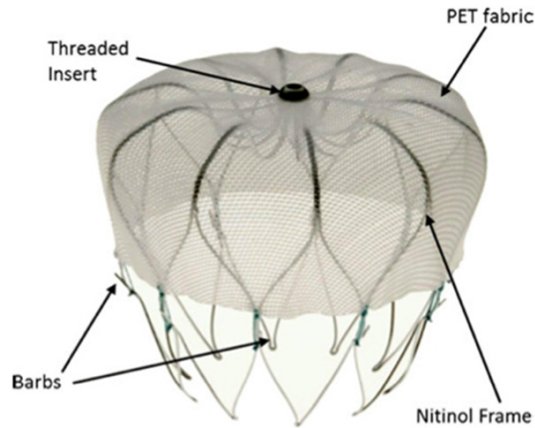
Figure 1. The WATCHMAN device, a self-expanding nitinol frame structure with fixation barbs and a permeable polyester fabric that covers the atrial facing surface of the device.

Methods

Study population

The criteria for patient selection included presence of chronic or nonvalvular AF, CHA2DS2-VASc score > 2, previous thromboembolic events, presence of thrombus in the LAA in spite of adequate anticoagulation (but with resolution before the intervention), and limitations to anticoagulation due to clinical contraindications or due to social, cultural, or educational factors that prevented the prescription. Informed patient consent obtained after an extensive discussion regarding procedural details, benefits and potential complications.

WATCHMAN device

Left atrial appendage occlusion was performed with the use of the WATCHMAN device. The WATCHMAN device (Boston Scientific Corporation, Natick, MA) is a parachute-shaped device, percutaneously deployed in the LAA. It consists of a self-expanding nitinol metal frame, which is covered by a polyester mesh (**Figure 1**). The physical properties of nitinol allow the device to adapt to the contours of the LAA after implantation. The structure has ten anchors that help it to attach inside the LAA. The polyester membrane covering the device on the atrial side prevents the escape of blood clots to the left atrium. The WATCHMAN Device is currently available in five sizes (21, 24, 27, 30, and 33 mm) and allows the occlusion of LAA measuring up to 31 mm in diameter. The delivery system has three components: the 14 F access sheath, the delivery catheter preloaded with the device, and a transeptal puncture sheath.

### WATCHMAN device implantation procedure

Before the procedure, patients received acetylsalicylic acid (ASA) at a dose of 100 mg/day and clopidogrel at a dose of 75 mg/day. However, patients with image of thrombus in the LAA received warfarin (international normalized ratio [INR] of 2 to 3) and ASA for at least 15 days before the procedure and were then submitted to transesophageal echocardiography (TEE) one day prior to implantation, to verify the presence of thrombi. Under general endotracheal anesthesia and TEE monitoring, the LAA was measured, as well as its inlet orifice and depth.

Stage I: Vascular access. Vascular access was obtained with 6 F and 5 F introducers in the right femoral vein and left radial artery, respectively.

Stage II: Transseptal puncture. Transseptal puncture was performed using standard equipment including the Brocken-brough needle and an 8 F SL0 St. Jude Medical transseptal sheath. The puncture was guided by TEE and left atrial pressures and performed in the middle lower part of the septum. This puncture site is recommended for both safety reasons and the ease of reaching LAA with the guiding system. In echocardiography, the septum was imaged in two perpendicular planes, a bicaval view and an aortic short-axis view (**Figure 2**). After transseptal puncture and introduction of the system to the left atrium, unfractionated heparin was administered in an initial dose of 1000 U/10 kg of body weight to increase the activated clotting time (ACT) to at least 250 s.

Stage III: Fluoroscopic and TEE LAA measurements. After transseptal puncture, a stiff 0.035-in. J-tipped wire can be positioned into the left upper pulmonary vein and the sheath exchanged for the access sheath. Then, the access sheath is slightly withdrawn from the pulmonary vein and a pigtail catheter advanced into the LAA followed by advancement of the access sheath over the pigtail catheter. With the help of a pigtail catheter, manual angiograms were obtained in the right anterior oblique view (20° to 30°) with cranial (10° to 20°) and caudal
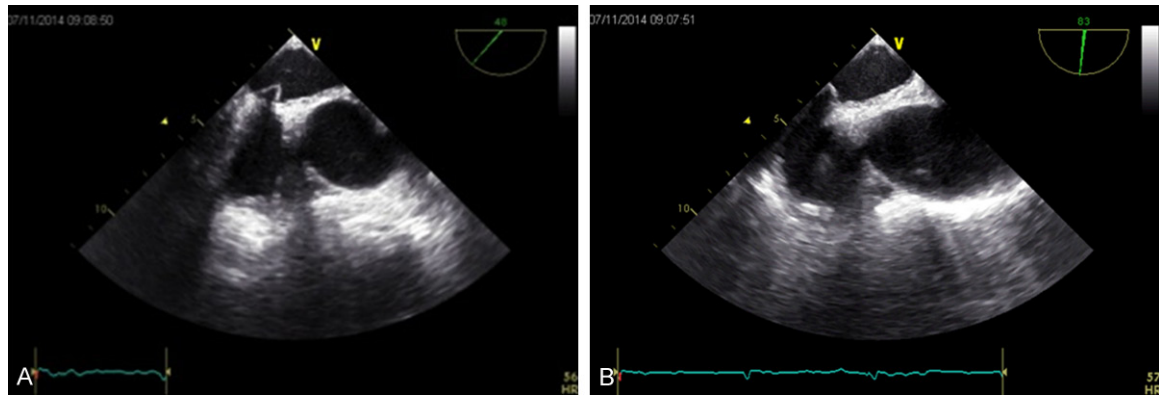
Figure 2. Echocardiographic selection of the transseptal puncture site-images obtained in an aortic short-axis view (A) and a bicaval view (B).
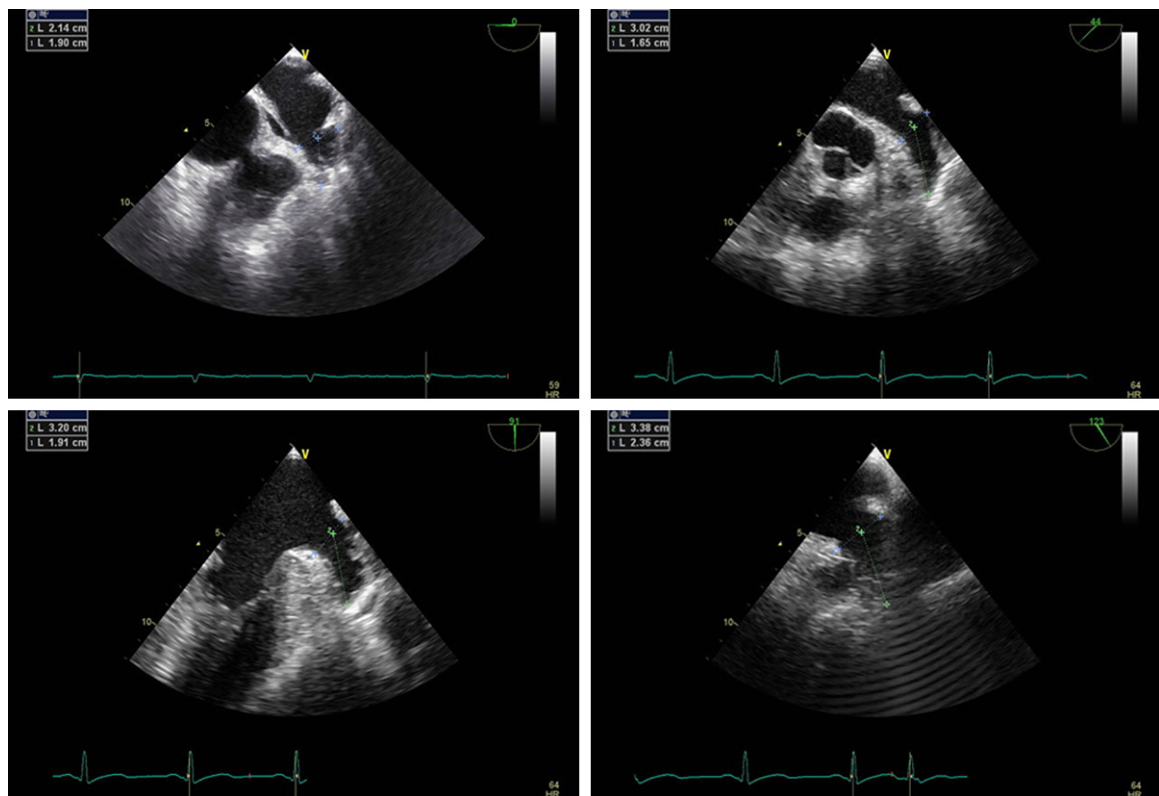
Figure 3. The inlet orifice of the LAA and its depth were evaluated: echocardiographic measurement.

(20° to 30°) angulation for anatomic delineation and measurement of structures. Simultaneously, guided by TEE, the widest LAA ostium (anatomic orifice measured from the circumflex artery inferiorly to a point superiorly 1 to 2 cm within the pulmonary vein ridge) and the available depth of the LAA (from ostium to apex of LAA) were evaluated at cuts of 0°, 45°, 90°, and 135° (**Figure 3**). The device was selected in accordance with the table provided by

the manufacturer and based on the inlet orifice and the depth of the LAA primary lobe.

Stage IV: Access sheath advancement. The 14 F double-curve sheath was advanced into the dominant lobe of the LAA under the pigtail catheter, until the corresponding radio-opaque marker band for the device size is aligned with the LAA ostium. Once in position, the pigtail is removed, and often a moderate degree of cath-

Figure 4. Angiography images showing the final position of the WATCHMAN device before and after device release.
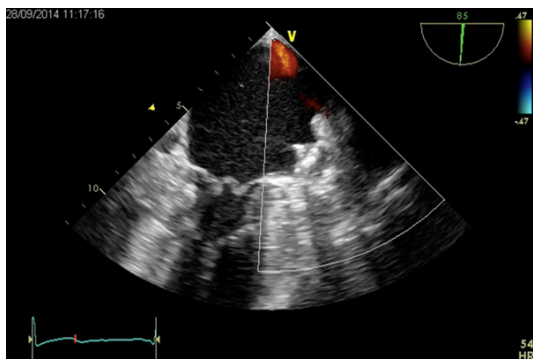
Figure 5. Color Doppler echocardiography images show the absence of residual shunt within the left atrial appendage.

eter torque is required to maintain sheath position in the distal lobe.

Stage V: Implantation steps. Once the desired depth was achieved with the double-curve sheath, the device, which was preloaded in the 12 F delivery catheter, was advanced up to its extremity and the cable was pushed to align the radiopaque markers of the delivery catheter and of the 14 F sheath. Then, the 14 F catheter was slowly retracted, keeping the delivery system fixed inside the LAA. While holding the cable, the delivery system was slowly withdrawn along the 14 F sheath, thus exposing and configuring the prosthesis in the LAA. Before device release, the 4 "PASS" criteria should be met: (1) position (device distal or at

LAA ostium, protrusion of shoulder by < 40% to 50% of device depth is acceptable); (2) anchor (testing stability by retracting the deployment knob and letting go, to assess return to original position); (3) size (device shoulder compressed 8% to 20% of original size on TEE); and (4) seal (assess TEE for any residual flow, must be < 5 mm before release). When these criteria are met, the device may be released with counterclockwise rotation of the core wire for 3 to 5 turns (**Figure 4**). Final angiographic and TEE images showing the absence of residual shunt in the LAA are shown in **Figure 5**.

Post implantation procedure

The day following the procedure a transthoracic echocardiography showed the correct position of the device and the absence of pericardial effusion. The patient was then discharged with warfarin associated with aspirin (100 mg/day) for 45 days, followed by aspirin (indefinitely) and clopidogrel (six months) as antithrombotic treatment, A TEE performed at 45 days after the procedure showed no changes, and no events were observed at follow-up. If the TEE criteria for successful sealing of the LAA were met (LAA completely sealed or a minimal residual flow (< 5 mm jet) around the device) the physician was allowed to discontinue the warfarin while the aspirin was continued indefinitely and clopidogrel was started (75 mg daily) for 6 months. If these echocardiographic criteria for

Table 1. Characteristics of the study group

Patient	Age [years]	Sex	Number of points in the CHA2DS2VASc score	Number of points in the HAS-BLED score
1	59	M	5	5
2	73	M	4	3
3	68	F	6	4
4	66	M	3	2
5	87	F	4	3
6	68	F	6	3
7	74	M	3	3
8	80	M	7	5
9	73	F	4	3

Table 2. Shows comorbidities in the study group

Patient	CHD	HP	CKD	History of stroke/TIA	DM	History of bleeding	CHF
1	+	+	-	+	+	+	-
2	+	+	+	-	+	-	-
3	+	+	-	+	-	-	-
4	-	-	-	+	-	-	-
5	+	+	+	-	-	+	-
6	+	+	-	+	-	-	-
7	+	+	-	-	-	-	-
8	+	+	+	+	-	+	-
9	-	+	-	-	-	-	-

CAD = coronary artery disease; HP = hypertension; CKD = chronic kidney disease; DM = diabetes; CHF = congestive heart failure.

successful sealing where not met, TEE was repeated at 6 months.

Major adverse events

Major adverse events were defined as death, stroke, systemic embolism, device embolization, pericardial bleeding requiring an intervention (cardiac tamponade) or other major bleeding requiring invasive treatment or blood transfusion.

Statistical analysis

Descriptive statistics were used to report patient characteristics. Continuous variables with normal distribution are reported by mean ± standard deviation. Median and range were used when normal distribution was absent. Percentages were used to report categorical variables. All statistical analyses were performed using SPSS software (SPSS Inc., version 17.0 for Windows).

Results

Patient characteristics

9 patients (mean age 72 years, 44.4% female) were treated. All patients had documented AF and a CHA2DS2VASc score of > 3 that necessitated the use of oral anticoagulation. The median CHA2DS2VASc score was 4.67 (range 3-7) and HAS-BLED score was 3.44 (range 2-5) (**Table 1**).

Table 2 shows the risk factors of the study participants.

Procedural and in-hospital results

The success rate for this procedure was 100%, as complete occlusion was attained, as well as absence of residual flux in all cases. Characteristics of the procedure are shown in **Table 3**. All patients showed a favorable evolution after the procedure, with no immediate clinical events. The day following the procedure a transthoracic echocardiography showed the correct position of the device and no complications such as obvious thrombus or pericardial effusion. No events were observed at the 45-day follow-up and met TEE criteria in 4 patients and the patients were able to stop taking warfarin.

Follow-up results

At 45-day follow-up no recurrent major adverse events and especially no thromboembolic events occurred. TEE showed no peri-device leakage, pulmonary venous obstruction, thrombus formation on the implants, or delayed device embolization.

Discussion

This report shows the feasibility of LAA closure with WATCHMAN device, the WATCHMAN device in 9 patients with non-valvular AF who were unsuitable for warfarin therapy and who had high cardioembolic risk. No events were observed at the 45-day follow-up. Our results indicate that a high procedural success rate with a relatively low complication rate can be obtained.

The risk for stroke among patients with non-valvular AF is 5% per year, and when transient ischemic attacks (TIAs) and subclinical strokes

Table 3. Characteristics of the procedure

Patient	Ostium (mm)	Depth of LAA (mm)	Device size (mm)	Residual shunt (> 2 mm)	Total procedure duration (min)	Fluoroscopy time (min)
1	25	33	30	-	33	16.32
2	21	28	24	-	41	18.00
3	21	30	24	-	49	20.35
4	26	36	33	-	60	21.16
5	21	34	27	-	47	19.55
6	22	32	27	-	45	19.25
7	27	36	33	-	57	20.55
8	21	27	24	-	45	18.43
9	21	26	24	-	40	17.19

detected on brain imaging are included, this risk may exceed 7% per year [1]. International guidelines for the management of non-valvular AF recommend anticoagulation as the treatment of choice in the prevention of stroke in the case of CHA2DS2-VASc score > 2, which represents two-thirds of the population with AF [12], but, it has several disadvantages: (major) bleeding, non-tolerance, non-compliance, interactions with some foods and other medication and a narrow therapeutic range. It has to be shown that the LAA is the main location for left atrial thrombus formation in patients with non-valvular atrial fibrillation [1, 9, 10]. Echocardiographic and pathologic studies suggest that when a source can be identified, approximately 90% of such strokes can be attributed to thrombus in the left atrial appendage (LAA) [12].

The LAA is a long, tubular, hooked structure which is usually crenellated and has a narrow junction with the venous component of the atrium, and it's different from the fully developed left atrium. There are a lot of pectinate muscles and trabecular muscles in LAA. LAA thrombosis is rare while in sinus rhythm because of its normal contractility. The LAA flow velocity decreases when atrium filling and emptying in AF patients, resulting in deposition of blood in the LAA, and it's the pathological basis of thrombus formation in LAA. Thus, LAA closure to preventing thromboembolism has important theoretical basis in patients with AF. Over the last decade, several percutaneous LAA closure devices have been developed and tested in humans, such as PLAATO device, WATCHMAN device, Amplatzer Cardiac Plug (ACP) device and the Lariat device.

The critical role of the LAA in stroke pathogenesis was recently demonstrated by the use of the Watchman LAA closure device (Atritech, Plymouth, Minnesota) in the PROTECT AF (Percutaneous Closure of the Left Atrial Appendage Versus Warfarin Therapy for Prevention of Stroke in Patients with Atrial Fibrillation) study [11, 13]. The PROTECT-AF trial [13] was a non-inferiority trial, which randomly allocated 707 patients with non-valvular AF to undergo mechanical LAA occlusion with the Watchman device with subsequent temporary anticoagulation or to receive permanent pharmacological anticoagulation. At a mean follow-up of 18 months, the device was shown to be non-inferior to warfarin therapy (RR 0.62, 95% CI 0.35-1.25) with regard to the primary outcome, a composite of ischemic or hemorrhagic stroke, cardiovascular or unexplained death, or systemic embolism. In the Watchman group, the rate of ischemic stroke was higher (3.24 versus 2.46%; RR 1.34, 95% CI 0.60-4.29), but there was a significantly lower risk of hemorrhagic stroke (0.22 versus 2.46%; RR 0.09, 95% CI 0.00-0.45). The PROTECT-AF trial showed that percuteneous LAA closure with the WATCHMAN device was non-inferior to warfarin therapy in patients with non-valvular atrial fibrillation for the prevention of stroke, systemic embolism and cardiovascular death.

A subsequent analysis of the PROTECT AF trial by Reddy et al. addressed safety by investigating the influence of operator experience with the WATCHMAN device [14]. The continued access registry study was a prospective clinical trial that compared the outcomes in patients who received the WATCHMAN device (Continued Access Protocol [CAP]) with the PROTECT AF group [14]. The primary safety outcomes included bleeding and procedure related events such as pericardial effusion, stroke, and device embolization [14]. The authors showed a significant decline in the rate of procedure or device related safety events within 7 days of the procedure and a decrease in the rate of pericardial

effusions in the CAP Registry compared to the PROTECT AF group [14]. The authors concluded that there is significant improvement in the safety of the device with operator experience [14].

Recently the direct thrombin inhibitor dabigatran or the selective factor Xa inhibitors apixaban and rivaroxaban became available. A recent analysis of the RE-LY trial has suggested that in patients with atrial fibrillation at risk for stroke, the lower and the higher dose of dabigatran compared with warfarin had a lower risk of both intracranial and extracranial bleeding in patients aged, 75 years. In those aged $\geq$ 75 years, intracranial bleeding risk is lower, but extracranial bleeding risk is similar or higher with both doses of dabigatran compared with warfarin [15]. Advantages of dabigatran over OAC include: no need for routine laboratory monitoring, a fixed-dose regimen, and potentially fewer clinically important drug interactions. Although the results are promising, there are some concerns including higher incidences of dyspepsia and gastrointestinal bleeding and lack of effective antidote. Additional drawbacks include higher drug costs, accumulation in case of renal impairment, and high discontinuation rates due to adverse events [15, 16]. In patients with a high risk of bleeding or contraindication for OAC, LAA closure might still be a better option.

Vulnerability of the LAA and the wash-out of pre-existing thrombi are two main sources of severe complications of the LAA occlusion procedure: pericardial effusion and stroke. Fortunately, stroke remains a rare complication of manipulating within the left side of the heart. Nevertheless, causing a stroke with a procedure that aims to avoid it is frustrating. Although our small series reported 0% pericardial effusion rate, the larger European ACP series did report 6.6% of pericardial effusion (n = 9) after ACP implants and five out of those nine patients eventually required pericardiocentesis. In the PROTECT AF trial [13], pericardial effusion was related to the experience of the operator because it occurred in 7% of the first three patients at each site and in 4% of subsequent patients. It is hoped that the safety data of the two clinically available LAA occluders will continue to improve by more careful patient selection and comprehensive operator training prior to implantation [3].

Study limitations

The sample size of our study was small and the follow-up time was short, which limits the evaluation of clinical outcomes, but we are continuing to select patients for this treatment and will perform long-term follow-up regarding safety and efficacy. Otherwise, it is an observational study, not comparing the percutaneous technique with conventional treatment.

Conclusions

This study demonstrated that implantation of the WATCHMAN device is a generally safe and feasible method for percutaneously sealing the LAA. Long-term follow-up will further reveal the risk and benefits of this therapy.

Disclosure of conflict of interest

None.

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