



Left atrial appendage closure with Watchman device: Insights from the first-ever Tunisian experience and six-year follow-up.

La fermeture percutanée de l'auricule gauche par le dispositif de Watchman: aperçus de la toute première expérience tunisienne et suivi de six ans.

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RÉSUMÉ

Introduction : L'accident vasculaire cérébral (AVC) est une complication majeure de la fibrillation auriculaire non valvulaire (FA). Malgré son efficacité prouvée dans la prévention des AVC, l'anticoagulation orale (ACO) est associée à une augmentation significative des complications hémorragiques. De nouvelles techniques telles que la fermeture percutanée de l'auricule gauche (AG) ont été développées.

Objectif : Evaluer les résultats immédiats, à moyen et à long terme après la fermeture percutanée de l'AG chez des patients tunisiens présentant une FA non valvulaire.

Méthodes et Résultats. Dix-neuf patients atteints de FA non valvulaire ont été recrutés de manière prospective pour une fermeture percutanée de l'AG entre février 2013 et juin 2014. Le dispositif Watchman a été utilisé dans toutes les procédures de fermeture de l'AG. Un suivi clinique et échocardiographique a été réalisé à 1, 6, 12 mois et à 6 ans chez tous les patients. L'âge moyen était de $68,4 \pm 7,5$ ans. Treize patients étaient des femmes, 16 souffraient d'hypertension, 12 de diabète sucré et sept avaient des antécédents d'AVC ou d'accident ischémique transitoire (AIT). Le score moyen CHA2DS2VASc (insuffisance cardiaque congestive / dysfonctionnement ventriculaire gauche, hypertension, âge ≥ 75 , diabète sucré, accident vasculaire cérébral / accident ischémique transitoire / événement thromboembolique, maladie vasculaire, âge ≥ 65 ans, catégorie de sexe) était de $4,2 \pm 1,5$ et HAS-BLED (hypertension, Fonction rénale / hépatique anormale, accident vasculaire cérébral, tendance hémorragique, INR labile, âge ≥ 65 ans, score médicamenteux) était de $3,5 \pm 1$. Dix patients avaient des antécédents d'hémorragie sévère. Le succès de la procédure a été obtenu chez tous les patients. Un épanchement péricardique avec tamponnade a été rapporté dans un cas. Aucun décès postopératoire n'a été signalé. Un suivi régulier à 1, 6 et 12 mois puis tous les ans jusqu'à 6 ans n'a rapporté aucun AVC, aucun événement thromboembolique, aucune thrombose du dispositif Watchman et trois cas de décès dus à un problème respiratoire et des cancers.

Conclusion. Selon cette étude, la fermeture de l'AG avec le dispositif Watchman est efficace pour prévenir les AVC chez les patients atteints de FA non valvulaire et contre-indication à l'OAC.

Mot clés : l'auricule gauche, fermeture percutanée, fibrillation auriculaire, accident vasculaire cérébral, anticoagulation

SUMMARY

Background. Stroke is a major complication of nonvalvular atrial fibrillation (AF). Despite its proven efficacy in stroke prevention, oral anticoagulation (OAC) is associated to a significant increase in bleeding complications. New techniques such as percutaneous left atrial appendage (LAA) closure were developed.

Aim: To evaluate immediate, mid- and long-term outcomes after percutaneous LAA closure in Tunisian patients presenting with nonvalvular AF.

Methods and Results. Nineteen patients with nonvalvular AF were prospectively enrolled for percutaneous LAA closure between February 2013 and June 2014. The Watchman device was used in all LAA closure procedures. Clinical and echocardiographic follow-up were carried-out at 1, 6, 12 months and six years in all patients. Mean age was 68.4 ± 7.5 years. Thirteen patients were female, 16 had hypertension, 12 had diabetes mellitus and seven had a history of stroke or transient ischemic attack (TIA). Average CHA2DS2VASc (Congestive Heart Failure/Left Ventricular Dysfunction, Hypertension, Age ≥ 75 , Diabetes mellitus, Stroke/Transient Ischemic Attack/Thromboembolic event, Vascular disease, Age ≥ 65 , Sex category) score was 4.2 ± 1.5 and HAS-BLED (Hypertension, Abnormal renal/liver function, Stroke, Bleeding tendency, Labile INR, Age ≥ 65 , Drugs) score was 3.5 ± 1 . Ten patients had a history of severe bleeding. Procedural success was achieved in all patients. Pericardial effusion with tamponade was reported in one case. No post-procedural death was reported. Regular follow-up at 1, 6 and 12 months then every year up to 6 years reported no stroke, no thromboembolic event, no Watchman device thrombosis and three cases of death caused by a respiratory problem and cancers.

Conclusion. According to this study, LAA closure with Watchman device was safe and effective in preventing stroke in patients with nonvalvular AF and contra indication to OAC.

Keywords: Left atrial appendage, percutaneous closure, atrial fibrillation, stroke, anticoagulation

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INTRODUCTION

Nonvalvular atrial fibrillation (AF) is the most common arrhythmia (1) with a prevalence of 1% in the general population (2). AF is associated to a significant increase in short- and long-term morbidity and mortality (3-6). Thromboembolic events, on top of which stroke, represent the major complication of AF and anatomical studies showed that left atrial appendage (LAA) is the site of predilection for causative thrombus formation (7-8). Oral anticoagulation (OAC) has broadly proven its efficacy in reducing the occurrence of thromboembolic events in this setting and is recommended as the first line treatment for thromboembolism prevention (9-10). Yet, OAC is associated to a significant increase in minor and major bleeding events and when it comes to OAC with vitamin-K antagonists (VKAs), serial blood tests are needed to reach and maintain an international normalized ratio (INR) in the therapeutic range. Furthermore, in some patients, OAC is contra-indicated due to a very high bleeding risk. Percutaneous techniques for LAA occlusion were suggested as a surrogate to OAC for thromboembolism prevention in patients presenting for nonvalvular AF. The Watchman (Boston Scientific, St. Paul, Minnesota) LAA occlusion device has been tested in some trials with acceptable safety and very encouraging mid-term results in terms of thromboembolic events in comparison to OAC. In this study, we report immediate and long-term outcomes from the first single center Tunisian series of LAA closure with the Watchman device in patients presenting with nonvalvular AF.

METHODS

This is a prospective study carried-out in a Tunisian tertiary care center. Nineteen consecutive patients aged ≥ 18 years and eligible for LAA closure who presented to our cardiology department with nonvalvular AF between February 2013 and June 2014 were enrolled. Inclusion criteria were: nonvalvular AF, CHA₂DS₂VASc (Congestive Heart Failure/ Left Ventricular Dysfunction, Hypertension, Age ≥ 75 , Diabetes mellitus, Stroke/Transient Ischemic Attack/ Thromboembolic event, Vascular Disease, Age ≥ 65 , Sex category)score ≥ 1 , HAS-BLED (Hypertension, Abnormal renal/liver function, Stroke, Bleeding tendency, Labile INR, Age ≥ 65 , Drugs)score ≥ 3 and intolerance or contraindication to OAC. Exclusion criteria were any significant valvular heart disease including prosthetic valve, formal indication

for OAC other than AF, LAA thrombus and any history of inter-atrial septum defect repair. All patients underwent a thorough clinical examination, routine blood tests, and electrocardiogram, transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE). LAA depth and diameter were measured using TEE on 0°, 45°, 90° and 135° multiplan views. The procedure was explained to all patients. Informed and written consent was obtained from all patients for procedure and subsequent follow-up. The Watchman device was used in all cases. It is a parachute shaped implantable device consisting of a self-expanding nitinol frame structure with ten fixation anchors and a polyethylene terephthalate fabric membrane cap that faces LAA inside after placement. The device is available in several diameters (21, 24, 27, 31, and 33 mm). Usually, the device size should be 8-20% larger than the LAA ostium diameter to ensure sufficient compression against the LAA wall for stability. LAA access is achieved by a 14-French trans-septal access sheath via the femoral vein approach. After confirmation of suitable device position by cine-angiography and TEE, the device is deployed by retracting the covering sheath. Once deployed, the implant can be retrieved and repositioned if needed.

In post-procedural, all patients were monitored for 48 hours. TTE and TEE were performed before discharge. Double Antiplatelet therapy including aspirin (100 mg o.i.d.) and clopidogrel (75 mg o.i.d.) was initiated before discharge and maintained for up to 6 months. Aspirin was maintained indefinitely thereafter. Follow up was obtained at one, six and 12 months after the procedure using TTE and TEE. A final clinical follow-up was obtained at six years.

RESULTS

Nineteen patients were included in the present study. Mean age was 68.4 \pm 7.5 years. Thirteen (68.4%) patients were female. Prevalence of hypertension, diabetes mellitus and stroke/transient ischemic attack were 84%, 63% and 36% respectively. Average CHA₂DS₂VASc score was 4.2 \pm 1.5 and that of HAS-BLED score was 3.5 \pm 1. Ten (53%) patients had a history of severe bleeding. Mean left ventricle ejection fraction (LVEF) was 60%. Mean LAA depth was 28.0 \pm 5.2 mm and orifice diameter was 20.1 \pm 3.1 mm. Clinical and echocardiographic features of the study population are presented in tables 1 and 2.

Table 1. Clinical characteristics of the study population.

	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13	P14	P15	P16	P17	P18	P19
Age (years)	60	65	65	78	65	76	66	76	71	63	81	51	65	64	65	75	78	64	73
CHA ₂ DS ₂ -VASC Score	3	4	4	4	4	6	4	3	5	3	7	2	6	2	4	5	6	2	6
HAS-BLED Score	3	3	5	4	5	3	4	4	4	2	5	1	4	2	4	3	3	3	4
Contra-indication to OAC	Cerebral bleeding	None	Digestive bleeding	Digestive bleeding	Digestive bleeding	None	Epistaxis	Digestive bleeding	None	0	Digestive bleeding	Type B Aortic dissection	0	Cerebral bleeding	Cerebral bleeding	0	0	Cerebral bleeding	0

OAC : oral anticoagulation

Table 2. Echocardiographic characteristics of the study population.

	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13	P14	P15	P16	P17	P18	P19
LVEF	67 %	65%	50%	60%	58%	60%	55%	60%	40%	70%	65%	60%	60%	65%	57%	60%	45%	70%	76%
LAA Length (mm)	24	29	27	27	19	30	42	26	28	30	32	30	29	20	30	36	25	24	25
LAA orifice diameter (mm)	17	21	23	18	14	24	22	17	18	24	23	25	21	15	22	22	20	18	19

LAA : Left atrial appendage, LVEF : Left ventricular ejection fraction

Table 3. Watchman device sizes and periprocedural complications.

	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13	P14	P15	P16	P17	P18	P19
Watchman device size (mm)	21	21	27	24	21	27	30	21	24	27	27	30	33	21	21	33	27	30	27
Periprocedural complication	No	No	No	No	No	No	No	No	Yes	No	No	Yes	No	No	No	No	No	No	No
Type of complications	-	-	-	-	-	-	-	-	Pulmonary edema	-	-	Tamponade	-	-	-	-	-	-	-

Table 4. Short, mid- and long term follow-up after left atrial appendage closure.

	P1	P2	P3	P4	P5	P6	P7	P8	P9	P 10	P 11	P12	P13	P14	P15	P16	P17	P18	P19
Stroke, bleeding, death or device complication at 1 month	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Stroke, bleeding, death or device complication at 6 months	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Stroke, bleeding, death or device complication at 12 months	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Stroke, bleeding, death or device complication at 6 years	0	0	0	0	0	death	0	0	0	0	death	0	0	0	0	0	death	0	0

The procedure was feasible in all patients. Mean duration of LAA closure procedure was 58 ± 26 minutes. In 9 (47.4%) patients, the procedure took less than 50 minutes. Procedural success could be obtained in all patients. In one case, pericardial effusion with tamponade occurred during device positioning. The case was successfully managed by pericardiocentesis and autotransfusion achieving complete recovery in 24 hours. No periprocedural death or need for emergent surgery was reported. Table 3 recapitulates the different sizes of Watchman devices used and periprocedural complications.

All patients had TTE and TEE to control the Watchman device position in LAA and to eliminate the device complications such as thrombosis. All patients were discharged on double anti-platelet therapy with aspirin and clopidogrel for a total duration of 6 months then aspirin was kept lifelong. No patient received any OAC.

All patients had clinical and echocardiographic follow-up at 1, 6, 12 months and six years. No case of stroke or bleeding was reported during 6 years after LAA closure. TTE and TEE did not show any device complication (figure 1). Three cases of death caused by an acute respiratory disease and cancers were reported. Table 4 shows short, mid and long term follow up after LAA closure.

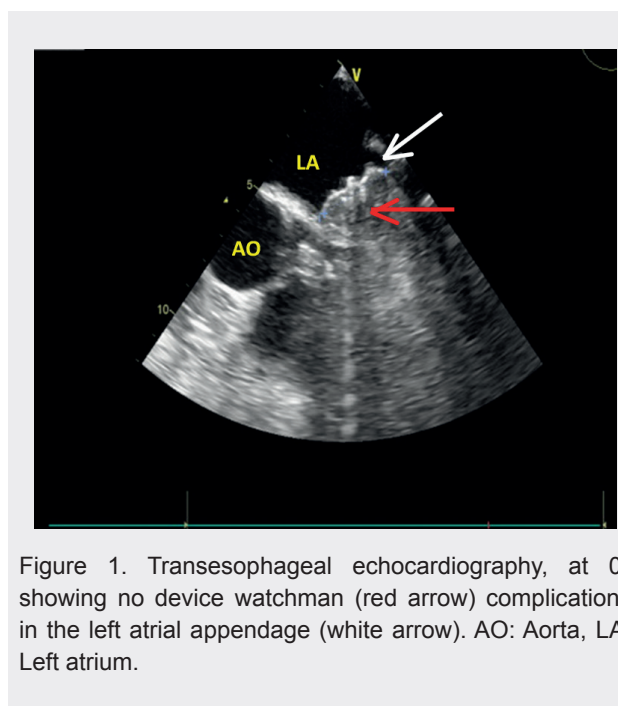


Figure 1. Transesophageal echocardiography, at 0° showing no device watchman (red arrow) complications in the left atrial appendage (white arrow). AO: Aorta, LA: Left atrium.

DISCUSSION

This is the first published study evaluating LAA closure with Watchman device in the Tunisian context. According to this study, percutaneous LAA closure was feasible and safe with favorable short and long-term outcomes in our context. It showed 100% procedural success of implantation in patients presenting for nonvalvular AF with intolerance or contraindication for OAC. Short, mid- and long-term follow-up confirms positive results of LAA closure with Watchman device showing no death, stroke/transient ischemic attack and no device complications

such as thrombosis. These results are in accordance with those from the PROTECT AF study which demonstrated non inferiority of percutaneous closure of the LAA by Watchman device compared to warfarin. PROTECT AF was a randomized, prospective, multicenter study that enrolled 707 patients with nonvalvular AF, recruited between 2005 and 2008. LAA closure with Watchman device reduced ischemic or hemorrhagic stroke, cardiovascular or unexplained death, and systemic embolism compared to warfarine in nonvalvular AF. In post-procedural, warfarine was maintained during 45 days then dual anti platelet therapy was administered for 6 months (11-16). Five-year outcomes of the PROTECT AF and PREVAIL trials demonstrate that LAA closure with Watchman provided stroke prevention in nonvalvular AF comparable to warfarin (HR=0.82, 95% CI 0.58-1.17, p=0.27) with additional reductions in hemorrhagic stroke, fatal stroke, cardiovascular/unexplained death, all-cause death, and post-procedure bleeding favoring LAA closure (17).

In our experience, time needed for LAA closure was 58±26 minutes. In 9 patients (47.4%), this procedure took less than 50 min. In Continued Access Protocol (CAP) registry, the time required for LAA closure was 67±36 minutes compared to 50±21 minutes in the PROTECT AF study (p<0.001) (18). The CAP registry enrolled 437 patients implanted by the Watchman device. Compared to PROTECT AF, implantation success rate was better in the CAP registry (95% vs. 89.5%, p=0.001) and the incidence of peri-procedural complications within 7 days was lower (3.7% vs. 7.7%, p=0.007). Moreover, there has been no device thrombosis or stroke after LAA closure (18).

In our series, post-procedural treatment was dual antiplatelet therapy with aspirin and clopidogrel for 6 months followed by lifelong aspirin. It was the therapeutic protocol adopted in ASA Plavix Feasibility Study With Atrial Appendage Closure Watchman Left Technology (ASAP) study. ASAP is a nonrandomized study in which device implantation success reached 94.7%. No patient received any OAC. The study reported a 2.3% incidence of stroke (ischemic and hemorrhagic) at a mean follow-up of 14.4 months in patients receiving the LAA occlusion Watchman device (19).

Study limitations. The study we present here is indeed the first published Tunisian report on the matter. Although with a small population size, the study is both informative

and encouraging in regards to the efficacy and safety of Watchman LAA occlusion device in our context. Yet, study population size and the single center character do not permit to draw definitive conclusions regarding possibilities of adoption of the technique in other Tunisian centers. Likewise, neither medico-economic analysis nor randomization versus OAC could be done in the aim to assess the actual input of such a technique in our context.

CONCLUSION

According to this study, LAA closure with Watchman device is safe and effective in preventing stroke in a small population of patients with nonvalvular AF not taking OAC. This therapeutic option seems to be a good surrogate to OAC in patients with high bleeding risk. Other studies are needed in our Tunisian context to better define its definitive positioning in the therapeutic arsenal for nonvalvular AF.

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The authors have no financial or nonfinancial conflict of interest to declare.

Competing interests

Nothing to declare.

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