Journal of Arrhythmia 32 (2016) 119–126

Contents lists available at ScienceDirect

Journal of Arrhythmia

journal homepage: www.elsevier.com/locate/joa

Original Article

Combined catheter ablation for atrial fibrillation and Watchman® left atrial appendage occlusion procedures: Five-year experience

Karen P. Phillips, MBBS*, Daniel T. Walker, B. Appl. Sci., Julie A. Humphries, MBBS

HeartCare Partners, GenesisCare, Greenslopes Private Hospital, Newdegate St, Greenslopes, Brisbane, QLD 4120, Australia

ARTICLE INFO

Article history:
Received 25 August 2015
Received in revised form
16 October 2015
Accepted 4 November 2015
Available online 8 December 2015

Keywords:
Left atrial appendage
Device occlusion
Catheter ablation
Atrial fibrillation
Watchman

ABSTRACT

Background: Patients with atrial fibrillation (AF) may benefit from undergoing concomitant interventions of left atrial catheter ablation and device occlusion of the left atrial appendage (LAA) as a two-pronged strategy for rhythm control and stroke prevention. We report on the outcome of combined procedures in a single center case series over a 5-year timeframe.

Methods: Ninety-eight patients with non-valvular AF and a mean CHA_2DS_2-VASc score 2.6 ± 1.0 underwent either first time, or redo pulmonary vein isolation (PVI) procedures, followed by successful implant of a Watchman® device.

Results: All procedures were generally uncomplicated with a mean case time of 213 ± 40 min. Complete LAA occlusion was achieved at initial implant in 92 (94%) patients. Satisfactory LAA occlusion was achieved in 100% of patients at 12 months, with a complete LAA occlusion rate of 86%. All patients discontinued oral anticoagulation. Persistent late peri-device leaks were more frequently associated with device angulation or shoulder protrusion, and were associated with a significantly lower achieved device compression of $12 \pm 3\%$ vs. $15 \pm 5\%$ ($p < 0.01$) than complete occlusion. One ischemic stroke was recorded over a mean follow-up time of 802 ± 439 days. Twelve months' freedom from detectable AF was achieved in 77% of patients.

Conclusions: Combined procedures of catheter ablation for AF and Watchman® LAA implant appear to be feasible and safe, with excellent rates of LAA occlusion achieved and an observed stroke rate of 0.5% per year during mid-term follow-up. Incomplete occlusion was associated with lower achieved device compression and was more frequently associated with suboptimal device position.

1. Introduction

Left atrial appendage (LAA) occlusion with the Watchman® device (Boston Scientific, Natick, USA) has demonstrated efficacy in long term stroke prevention for patients with non-valvular atrial fibrillation (AF) with a $CHADS_2$ score ≥ 1 and a demonstrated mortality benefit compared with warfarin [1]. Catheter ablation therapy for AF is an efficacious rhythm control strategy for patients with symptomatic, drug-refractory AF [2], but its role in long-term stroke prevention remains unproven. Evidence suggests that longer term AF recurrence rates, following initially successful catheter ablation are significant [3], and that oral anticoagulation cannot be safely stopped in patients with a CHA_2DS_2-VASc stroke risk score of ≥ 2 [4]. Both procedures require percutaneous catheter instrumentation of the left atrium. Therefore, a subset of patients with symptomatic AF may benefit from undergoing concomitant intervention of catheter ablation and device occlusion of the LAA [5] as a two-pronged strategy for rhythm control and stroke prevention. We report on the outcome of combined procedures with the Watchman® device in a single center over a 5-year timeframe.

2. Material and methods

In December 2009, following Therapeutic Goods Administration approval of the Watchman® device in Australia, patients with a $CHADS_2$ score of 1 or greater (PROTECT AF inclusion criteria [1]), seeking to undergo left atrial catheter ablation for symptomatic, drug-refractory non-valvular AF at a single center, were offered concomitant implant as an alternative to taking long-term oral anticoagulation. Subsequent to the updated ESC Clinical Guidelines for the Management of Atrial Fibrillation in 2010 [6], a

* Correspondence to: Suite 212, Ramsay Specialist Centre, Newdegate St, Greenslopes, Brisbane, QLD, 4120, Australia. Tel.: +61 7 3394 3100; fax: +61 7 3394 3118.
E-mail address: kphillips@heartcarepartners.com.au (K.P. Phillips).

http://dx.doi.org/10.1016/j.joa.2015.11.001

CHA_2DS_2-VASc score of 2 or greater was used for eligibility. This retrospective study was approved by the institutional review board for human research and complies with the Declaration of Helsinki. Informed consent was obtained from all participants.

2.1. Procedural planning

Patients underwent screening transesophageal echocardiography (TOE) and a contrast 64-slice cardiac CT scan within 7 days of the planned procedure. Three-dimensional reconstruction of the left atrium and LAA was performed from the CT scan using Ensite Verismo software (St. Jude Medical, St. Paul, USA), to assist with planning of the ablation and anatomical analysis of the LAA takeoff and morphology [7]. Pre-procedural TOE was utilized to exclude LAA thrombus and to assess suitability of the ostial dimensions for closure with the Watchman® device [8].

2.2. Procedure

Antiarrhythmic drug (AAD) therapy was stopped 3 days prior. Therapeutic warfarin therapy was continued uninterrupted. After June 2013, dabigatran and rivaroxaban were continued uninterrupted for patients with persistent AF. Procedures were performed under general anesthesia using a bifemoral venous approach. Intracardiac echocardiography was utilized to guide double transseptal puncture and the ablation phase of the procedure. Intravenous heparin was administered prior to the first transseptal puncture with a target ACT of ≥ 350 s [5].

Ensite NavX cardiac navigational system (St. Jude Medical, St. Paul, USA) with image integration of the segmented cardiac CT scan was utilized. A 20 mm decapolar circular mapping catheter and an irrigated-tip ablation catheter were utilized for mapping and radiofrequency ablation. Left and right-sided pulmonary vein antral ring electrical isolation was performed in all patients to an endpoint of complete pulmonary vein entrance and exit conduction block. Additional complex fragmented atrial electrogram (CFAE) guided or linear left or right atrial ablation was individualized according to requirements for persistent forms of AF or for redo ablation procedures. Patients undergoing ablation for persistent AF were cardioverted back to sinus rhythm following pulmonary vein isolation $\pm$ CFAE or linear ablation.

After completion of the ablation phase, TOE imaging was commenced. The LAA was assessed for ostial width and depth, once a mean left atrial pressure measurement of ≥ 10 mmHg was obtained. The more favorable transseptal sheath location was retained and the second sheath withdrawn to the venous circulation. Implant of a Watchman® device was then performed as previously described [7], using the post-ablation maximum LAA ostial width for device sizing. Patients were observed overnight in a coronary care unit and discharged within 24 h of the procedure.

2.3. TOE imaging assessment

Multidimensional assessment of the LAA ostium and body was performed intraprocedurally and at subsequent follow-up using approximate TOE angles of 0°, 45°, 90°, and 135° (see Fig. 1). Peri-device leaks were quantified in millimeters jet size from color flow imaging, and the location of the leak described according to which quadrant of the ostium was affected. In each case, for the vertical plane, a 'superior' and 'inferior' quadrant of the ostium was identified; and for the horizontal plane, the other 2 quadrants were termed 'anterior' and 'posterior.' It should be noted, however, that the correct anatomical description of the horizontal plane would depend on whether the LAA projects in an anterior or lateral orientation i.e., if the LAA projected anteriorly, the 2 quadrants would be identified as medial and lateral; for a laterally projecting LAA, the 2 quadrants would be orientated anterior and posterior.

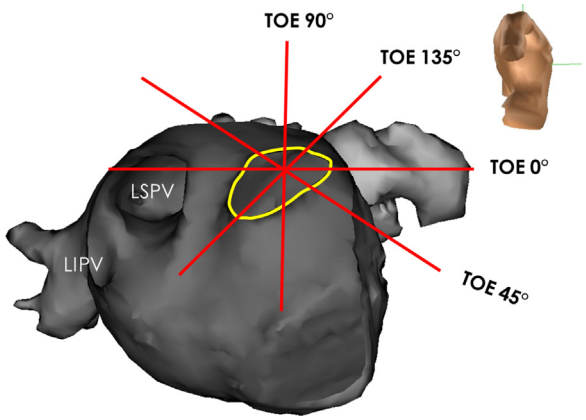

Fig. 1. Internal view of LAA ostium (outlined in yellow) from cardiac CT reconstruction (right lateral view) with schemata of approximate measurement angles during multiplane TOE for 0°, 45°, 90° and 135°. Labels indicate LSPV (left superior pulmonary vein) and LIPV (left inferior pulmonary vein).

2.4. Patient follow-up

Recurrent persistent early atrial tachyarrhythmias lasting ≥ 48 h were generally treated with electrical cardioversion, guided by TOE imaging. Follow-up TOE imaging was performed at 6 weeks to reassess the Watchman® appearances and efficacy of LAA ostial occlusion, the persistence of any interatrial septal shunt and to exclude pulmonary venous stenosis. At 3 months, if satisfactory TOE follow-up study had been confirmed, anticoagulation was discontinued and antiplatelet therapy (aspirin 100 mg + clopidogrel 75 mg) commenced for a further 3 months. Satisfactory LAA occlusion was defined as satisfactory positioning of the device at the ostium covering all trabeculated portions of the LAA with peri-device flow < 5 mm [1,7]. Further TOE assessment was performed at 6, and then 12 months, if any peri-device leak into the LAA was noted at 6 weeks, or if clinically required. Clinical follow-up for arrhythmia recurrence was performed at 3, 6, and 12, months (and every 6 months thereafter). Arrhythmia recurrence was assessed by patient symptom reporting, 12 lead ECG, and implanted cardiac-rhythm device interrogation, where applicable. Holter monitoring was performed at 12 months, and as required, to assess symptom recurrence. Antiarrhythmic drug therapy was ceased at or after 3 months, according to physician and patient discretion.

2.5. Statistical analysis

Results were analyzed using SPSS software and expressed as mean $\pm$ standard deviation. Unpaired t tests and Chi-square calculations were performed. A p value < 0.05 was considered to be statistically significant.

3. Results

3.1. Patient demographics

Ninety-eight patients underwent combined left atrial catheter ablation and implant of a Watchman® device between February 2010 and March 2015. An additional 4 patients were excluded – 2 patients had LAA ostium dimensions > 31 mm and proceeded with catheter ablation alone; 2 patients were found to have persistent LAA thrombus despite appropriate anticoagulation, of whom 1 proceeded to surgical excision and oversew of the LAA.

Table 1
Demographic and clinical variables for patient group.

	$n=98$
Age (yrs)	65(±7)
Females (*n*)	31(32%)
Paroxysmal AF (*n*)	56(57%)
Duration of AF (yrs)	7(±7)
EHRA Score (*n*)	3.7(±0.5)
CHA_2DS_2VASc (*n*)	2.6(±1.0)
HAS-BLED (*n*)	1.9(±0.8)
Diabetes (*n*)	16(16%)
Hypertension (*n*)	64(65%)
IHD (*n*)	14(14%)
CHF (*n*)	8(8%)
CVA (*n*)	28(29%)
EF(%)	61(±8)

AF: Atrial Fibrillation, EHRA score: European Heart Rhythm Association score of AF-related symptoms, HAS-BLED: score for major bleeding risk, IHD: Ischemic Heart Disease, CHF: Congestive Heart Failure, CVA: prior stroke / TIA, EF: Ejection Fraction.

Table 2
CHA_2DS_2-VASc and HAS-BLED scores for patient group.

CHA_2DS_2-VASc score	$n=98$	HAS-BLED score	$n=98$
0	0	**0**	1
1	12	**1**	30
2	39	**2**	45
3	32	**3**	21
4	10	**4**	1
5	4	**5**	0
6	1	**6**	0

Sixty-seven males and 31 females were included with a mean age of 65 ± 6 years (range 43–81) (Table 1). The group included 56 patients with paroxysmal, 27 with persistent, and 15 with long-standing persistent forms of AF. The mean EHRA Score for AF-related symptoms [7] was 3.7 ± 0.5. Eighty-seven patients were undergoing a first time ablation procedure for AF and 11 patients were undergoing a redo. The mean $CHADS_2$ score was 1.5 ± 1.0 (range 0–4) and mean CHA_2DS_2-VASc score was 2.6 ± 1.0 (range 1–6) (Table 2), with 28 patients (29%) having a prior history of cerebral or systemic thromboembolism. The mean HAS-BLED score was 1.9 ± 0.8 (range 0–4). All patients had been on established anticoagulation prior to the procedure with 37 patients on warfarin, 34 on dabigatran, and 27 on rivaroxaban. The indications for LAA device occlusion were relative contraindications to long-term oral anticoagulation in 29 (31%) (requirement for concomitant antiplatelet therapy in 8, previous major bleeding in 8, comorbid liver or renal disease in 2, alcohol abuse in 1, hazardous occupation in 1, HAS-BLED score ≥3 for other reasons in 10), systemic thromboembolism or documented LAA thrombus despite therapeutic oral anticoagulation in 5 (5%), and patient preference as an alternative to indefinite oral anticoagulation in 63 (64%).

3.2. Acute procedural success

Successful acute ablation endpoints were achieved in all patients, including pulmonary vein electrical isolation and return to sinus rhythm. Successful Watchman® implantation was achieved in all patients. The mean total procedure time was 213 ± 40 min (range 120–330). The mean fluoroscopic time was 36 ± 11 min (range 17–65) and radiation dose area product (DAP) 16 ± 13 Gy cm^2 (range 3–77). The procedure was performed on uninterrupted warfarin therapy in 37 patients, uninterrupted rivaroxaban in 22, and uninterrupted dabigatran in 14. In the remaining 25 patients, dabigatran (12/25) and rivaroxaban (13/25) were discontinued 1 day prior to the procedure and recommenced 4 h post-procedure.

3.3. Acute procedural complications

Two patients were noted to have transient ST segment elevation on ECG during Watchman® implantation, indicative of probable air embolism, but no hemodynamic instability or subsequent clinical sequelae were detected. Five patients were noted to develop simple hematomas at the site of vascular access before discharge, which resolved with conservative management. There were no other acute procedural complications, in particular, no pericardial effusion, stroke, or device embolization. All patients were discharged within 24 h of the procedure. One patient on uninterrupted rivaroxaban was readmitted within 5 days with minor bleeding from the vascular access site, which settled with conservative management.

3.4. LAA ostial assessment

In patients undergoing first-time pulmonary vein isolation, edema of the proximal ridge, between the left pulmonary veins and LAA opening, was typically noted on TOE following ablation, as compared with the pre-procedural study (Fig. 2). Ostial dimensions at the planned level of LAA device occlusion differed in 31 of 98 patients from the pre-procedure to post-ablation TOE. In 15 of the 31 patients, the maximal LAA ostial dimension was smaller post-ablation (range 1–8 mm), and in 16 patients, the dimension was larger post-ablation (range 1–3 mm).

3.5. Acute LAA device occlusion

Complete occlusion of the LAA was achieved with the Watchman® device in 92 patients, and a small peri-device leak ranging from 1 to 4 mm accepted in 6 patients at implant. The location of the leak was posterior in 5 patients (best viewed in TOE 135° or 45° angle), and inferior in 1 patient (TOE 90° angle). The leak was associated with device angulation that could not be corrected for in 2 patients and with device 'shoulder' protrusion in 4 patients. The mean maximal LAA ostium diameter at the time of implant was 20.6 ± 3 mm (range 14–28), and mean deployed device size 24 ± 3 mm (range 21–30). The mean minimum device compression measurement was 15 ± 5% (range 8–24%). The mean number of devices used per procedure was 1.03 ± 0.2 (1 device used in 95 patients, 2 devices required in 3).

3.6. TOE follow-up

All patients had satisfactory Watchman® appearances and occlusion of the LAA (peri-device leak < 5 mm) [1,7] at 6 weeks' follow-up. Thirty-two of the 98 patients had further TOE studies at 6 months, and 10 patients at 12 months, to re-evaluate the progress of peri-device leaks. No pulmonary venous stenosis was detected. The interatrial septum had healed with no residual detectable interatrial shunt in 82% (80/98) at the 6-week follow-up. Incidental, asymptomatic device-associated thrombus was detected in two patients: one at the routine 6-week study and another 1-week post-implant at a TOE study performed to guide a proposed DC cardioversion. In both cases, the seating of the device appeared appropriate and no peri-device leak was detected. The thrombus was demonstrated to resolve without clinical sequelae on continued rivaroxaban therapy over the next 4 months in the first case, and on continued dabigatran therapy by 6 weeks post-implant in the second case.

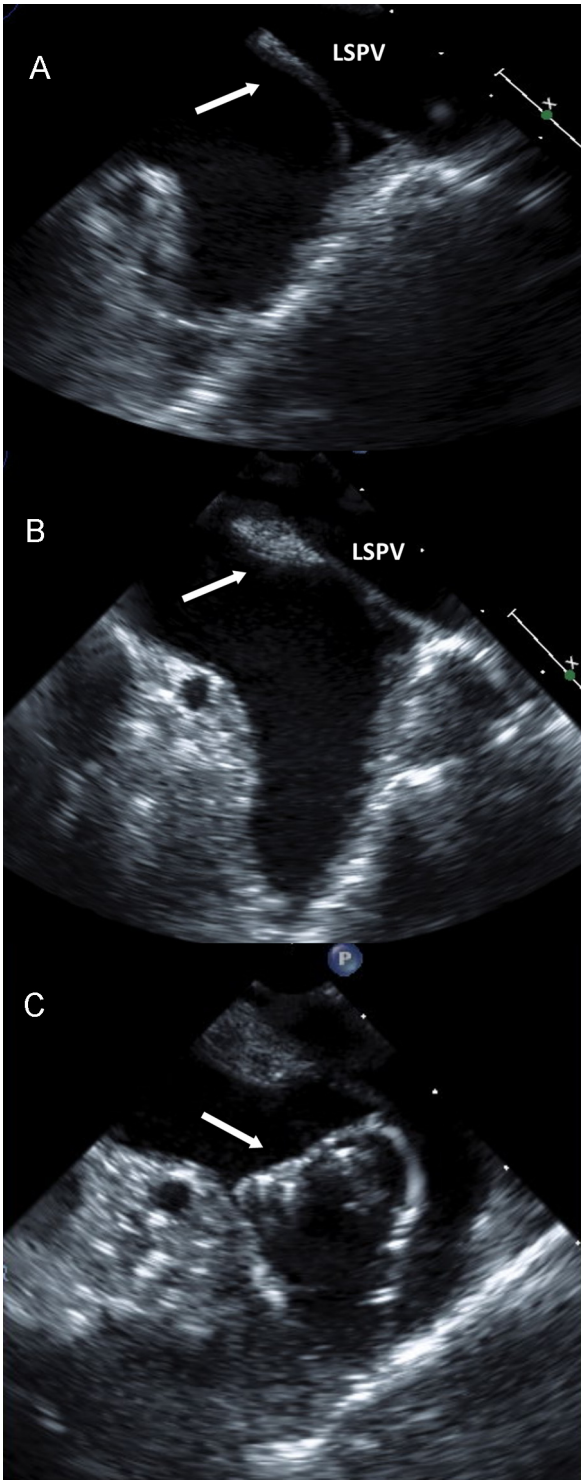

Fig. 2. Panel of images showing appearances of ridge between left superior pulmonary vein and left atrial appendage (arrowed) before ablation in panel A and edematous after ablation in panel B. In panel C the position of the Watchman® device (arrowed) after deployment is distal to the edematous region. Labels indicate LSPV (left superior pulmonary vein).

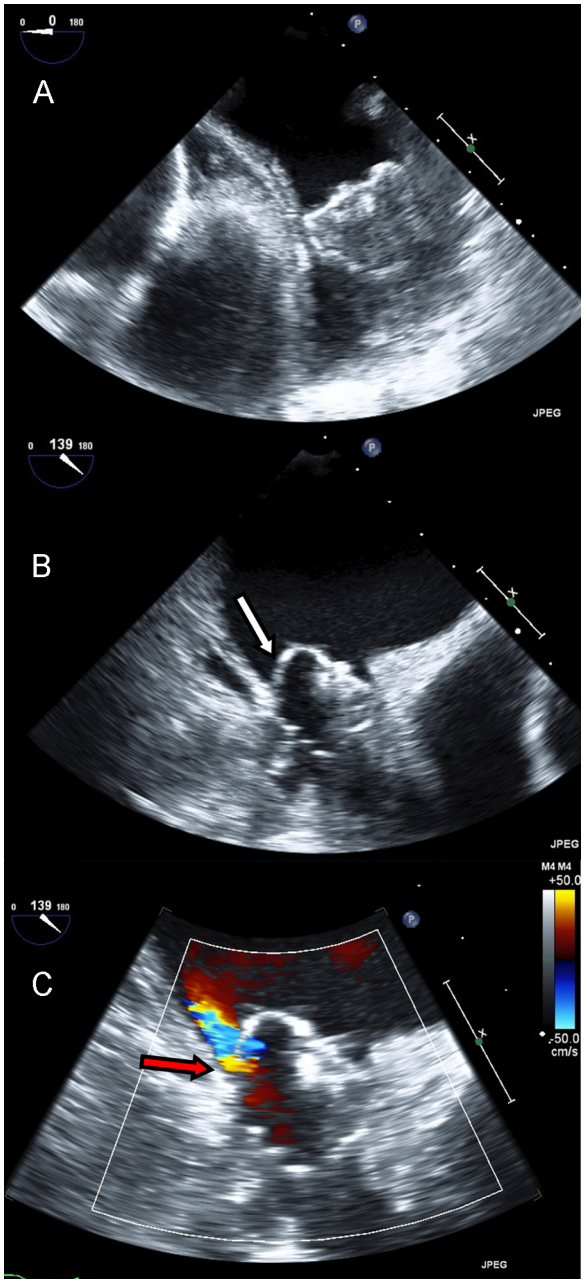

Fig. 3. Panel of images showing Watchman® device seating issues that were associated with late persistent peri-device leaks. Panel A shows angulation of the Watchman® device in relation to the long axis of the LAA; panel B shows significant device 'shoulder' protrusion above the ostium (arrowed); panel C demonstrates with color flow imaging a 2 mm peri-device leak (arrowed) associated with the 'shoulder' protrusion.

3.7. Peri-device leaks

3.7.1. Persistent peri-device leaks from implant

The peri-device leaks from implant resolved in 2 patients and persisted in 4 patients at follow-up, either reducing in size or remaining consistent. The location of the persistent leaks was posterior in all (best viewed in TOE 135° or 45° angle). The persistent leaks from implant were associated with device angulation in 2 patients, and device 'shoulder' protrusion in 2 (Fig. 3).

3.7.2. New peri-device leaks at follow-up

Twenty-eight new peri-device leaks were detected at the 6 week TOE (range 1–3 mm), with 18 of the leaks resolving again by the 6 month follow-up, and 10 having a small persistent leak (1–2 mm) at 12 month follow-up. The anticoagulation regimen in the 28 patients with new peri-device leaks at the 6-week follow-up was warfarin in 29%, dabigatran in 39% and rivaroxaban in 32%. The location of the new peri-device leaks were posterior in 79% (best viewed in TOE 135° angle), inferior in 18% (TOE 90° angle), and anterior in 4% (TOE 45° angle) ($p < 0.0001$) (Fig. 4). New peri-

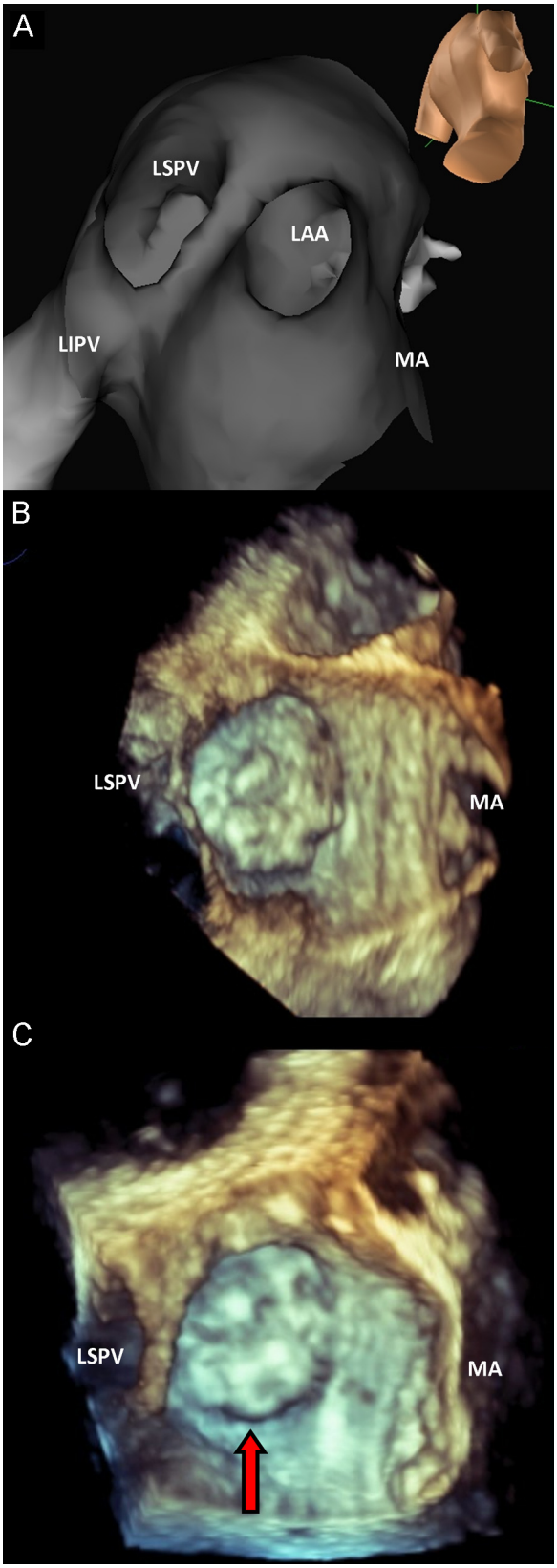

Fig. 4. Panel of images from a patient who developed a transient peri-device leak at 6-week follow-up TOE study. Panel A is an internal view of LAA ostium from cardiac CT reconstruction demonstrating elliptical orifice; panel B is a 3D TOE image of Watchman® device at time of implant showing complete occlusion of ostium; panel C is a 3D TOE image of Watchman® device at 6 week follow-up showing crescentic 2 mm leak at inferior margin (red arrow) associated with the largest LAA dimension. Labels indicate LSPV (left superior pulmonary vein), LIPV (left inferior pulmonary vein), LAA (left atrial appendage), and MA (mitral annulus).

device leaks were associated with device angulation in 14% (inferior and posterior locations) and device 'shoulder' protrusion in 32% (posterior location in 8, anterior location in 1), but in the remainder, the device appeared well seated. In 5 of the 28 patients with a new peri-device leak, a measurement discrepancy was found between the screening and post-ablation TOE ostial diameter: in 2 patients, the dimensions were larger than the screening TOE (range 1–3 mm) and in 3 patients, the dimensions were smaller (range 1–3 mm).

The location of the persistent late leaks from the 'new peri-device leak' group was posterior in 70%, inferior in 20%, and anterior in 10%. Persistent late leaks from the 'new peri-device leak' group were associated with device angulation in 40% (inferior and posterior locations) and/or device 'shoulder' protrusion in 60% (posterior and anterior locations). This contrasted with the group with transient 'new peri-device leaks' (in whom the leak subsequently resolved), whereby device angulation was only detected in 6% and shoulder protrusion seen in 17% ($p=0.004$ vs. persistent leaks).

3.7.3. Device compression

The mean device compression achieved in all patients with all persistent late leaks ($n=14$) was $12 \pm 3\%$, as compared with $15 \pm 5\%$ ($p < 0.01$) in patients with complete LAA occlusion.

3.7.4. Twelve month LAA occlusion

The 12-month complete LAA occlusion rate was 86% (84/98) for the group, with satisfactory results achieved in the remainder, with peri-device leaks ranging from 1 to 2 mm.

3.8. Clinical follow-up

No patient was lost to follow-up. The mean follow-up time for the series was 802 ± 439 days (range 88–1932). One female patient, on warfarin, was transferred back from a regional hospital, with progressive congestive cardiac failure (dyspnea and marked peripheral edema) 37 days after the procedure following early, severe pericarditis symptoms. She was found to have a large pericardial effusion, which required pericardiocentesis. She was diagnosed with effusive pericarditis (presumed due to the cardiac ablation) [9], and also received a course of prednisone and colchicine, subsequently making an uneventful recovery.

3.8.1. Arrhythmia events

Ninety-five of 98 patients were in sinus rhythm at the 3 months' follow-up, and anticoagulation was discontinued in 94 of 95 patients at this time, with 1 patient remaining on rivaroxaban until 6 months because of device-associated thrombus. Three of 98 patients were in persistent AF at 3 months follow-up and continued oral anticoagulation for the purposes of repeated electrical cardioversion. Two of the three patients with recurrent persistent AF subsequently accepted permanent AF. Oral anticoagulation was subsequently discontinued and substituted with antiplatelet agents in all 98 patients. Beyond 6 months' follow-up, 90 patients were prescribed aspirin only and 8 patients remained on dual antiplatelet therapy, due to drug-eluting coronary stents or history of recurrent myocardial infarction on aspirin.

At 3 months' follow-up, absence of detectable atrial tachycardias/atrial fibrillation (AT/AF) was noted in 75/98 (76%). For patients with at least 12 months follow-up, the 1-year rate of freedom from detectable AT/AF was 62/80 (77%). The 1 year rate of freedom from detectable AT/AF for patients with paroxysmal AF was 38/46 (83%), with 13/46 electing to remain on AAD, 17/23 (74%) for patients with recent persistent AF (15/23 patients remained on AAD), and 7/11 (64%) patients with longstanding persistent AF (10/11 patients remained on AAD). The mean EHRA score at follow-up was 1.3 ± 0.5. Eleven patients subsequently

underwent redo catheter ablation for atrial tachyarrhythmia recurrence (recommencing oral anticoagulation peri-procedure), with subsequent freedom from arrhythmia in 9. For patients with at least 2-years clinical follow-up (50/98), the late freedom from detectable AT/AF was maintained in 32/50 (64%) at a mean follow-up time of 1143 ± 307 days.

3.8.2. Electrical cardioversion

Over the period of follow-up, 13 patients underwent electrical cardioversion for recurrent, persistent atrial tachyarrhythmia, ranging from 9 days to 18 months after the index procedure. Patients were continued on, or recommenced, on oral anticoagulation for 4 weeks, following electrical cardioversion. TOE guidance was performed if the cardioversion was planned prior to the initial 6-week follow-up imaging study. Seven patients underwent TOE guided 'early' electrical cardioversion within the first 6 weeks with no detectable dislodgement of the Watchman® device at the time of the procedure or at subsequent follow-up.

3.8.3. Stroke events

One patient (CHA_2DS_2-VASc score of 5) represented 24 months post-implant with a left frontal cortical acute ischemic stroke confirmed on serial CT scans of the brain. Pacemaker interrogation confirmed that the patient remained free of atrial tachyarrhythmia since the procedure. TOE study showed satisfactory appearance of the Watchman® device, with a 2 mm peri-device leak unchanged since implant. Complex aortic atheroma was noted on TOE and moderate carotid atheroma was detected on carotid ultrasound. The patient had a prior history of myocardial infarction and reported having stopped atorvastatin therapy six weeks prior. The attending neurologist judged the stroke to be atherothrombotic in cause. Oral anticoagulation was not recommenced. Routine neuroradiological evaluation was not performed to examine for subclinical events in other patients. The observed ischemic stroke rate for the group was 0.5% per year.

3.8.4. Deaths

One patient was deceased at 5 months post-procedure from suicide. The coronial report did not implicate the procedure in the cause of death. The post-mortem findings showed no cardiac thrombus, with almost complete endothelialization of the device surface (Fig. 5).

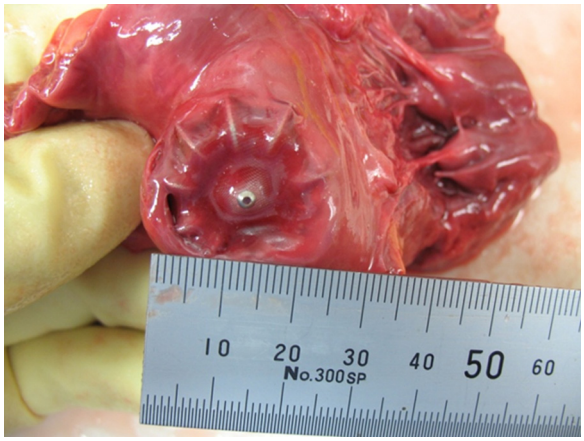

Fig. 5. Post-mortem photo of Watchman® device 5 months post-implant subsequent to concomitant catheter ablation and implant procedure. Complete occlusion of the LAA ostium was noted with almost complete endothelialisation of the device surface (small gap in endothelialisation noted at 8 o'clock).

4. Discussion

The results of this retrospective study demonstrate the feasibility and safety of combined left atrial catheter ablation and Watchman® implant procedures with satisfactory LAA occlusion maintained at follow-up. The rates of successful device implantation and complete LAA occlusion at follow-up in the current study compare favorably with results from the larger randomized controlled trials evaluating Watchman® implantation versus warfarin therapy [1]. The rates of successful device implantation were 91% in PROTECT-AF [7] and 95% in PREVAIL [10] as compared with 100% in our series. The 12 month rates of complete LAA occlusion on TOE studies in PROTECT-AF was 68% [11] as compared with 86% in this study.

Ablation-induced tissue injury at the ostium of the LAA following left pulmonary vein isolation was frequently observed on TOE during the procedures. However, the level of occlusion with the Watchman® device was always distal to any observed edematous change. Variation in the maximal measured LAA ostial dimension between the pre-procedure and the post-ablation TOE was observed in around one third of patients. However, this did not impact appropriate device sizing or rates of incomplete occlusion.

The development of 'new,' small peri-device leaks at the initial follow-up TOE has also been observed in 12–13% of patients in other Watchman® series [12,13], although, the rate was significantly higher in our study. The phenomenon is possibly related to a mismatch between the circular device and typical elliptical orifice of the LAA, that might be partially masked by an edema response at the time of implant. In the current series, the most common location for new leaks was at the posterior margin of the LAA ostium (best viewed in TOE angle 135°), which is commonly the largest dimension of the ostium (Fig. 1). Reassuringly, the majority of these new leaks were observed to resolve at follow-up, and the 12-month complete occlusion rate of 86% in our study was comparable to that in the other small series (93% and 66%). In our series, late persistent leaks were more frequently associated with device angulation or shoulder protrusion, suggesting that suboptimal device seating or apposition with the LAA walls is implicated. A statistically significantly lower amount of device compression was also noted for persistent late leaks as compared with complete occlusion (12 ± 3% vs. 15 ± 5%), suggesting that, where feasible, oversizing of the device by ≥ 15% may be preferred.

Concern has been raised that residual peri-device leaks have the potential to further enlarge with time in patients with untreated AF [13]. Progressive atrial dilatation as a consequence of AF is widely recognized [14] – progressive dilatation of the LAA ostium may also occur [6]. Reversal of left atrial dilatation in patients maintaining sinus rhythm following successful catheter ablation is also well documented [15]. This may be beneficial for patients undergoing the combined procedure with Watchman® device implantation, with the potential for reverse remodeling to shrink the LAA ostium around the implanted device. Further study is required to evaluate the effects of longer term atrial remodeling in different AF populations undergoing LAA device occlusion procedures. Fortunately, the evidence to date suggests that small residual peri-device leaks are unlikely to compromise the efficacy of LAA occlusion devices [16,17].

A significant number of the procedures were performed on patients on uninterrupted warfarin with a therapeutic INR. The safety of this approach has been documented for patients undergoing catheter ablation procedures for AF [18]. This series suggests this is also a safe approach for patients undergoing percutaneous LAA device occlusion. A small number of procedures were also performed on uninterrupted, novel oral anticoagulants. Further experience with performing catheterization procedures on the novel oral anticoagulants is required before drawing conclusions about the safety of this approach. Asymptomatic, early device-

associated thrombus was also noted in 2 patients (2%) in this study – both on novel anticoagulants (1 on dabigatran and 1 on rivaroxaban). However, the incidence was not significantly different from that reported in the PROTECT AF trial (3%) using warfarin [16]. Overall, the current experience supports the use of the novel anticoagulants with the Watchman® prosthesis as safe.

The results from catheter ablation in this cohort were comparable to previously reported outcomes [2,3]. The majority of patients with persistent or longstanding persistent AF, however, did not discontinue antiarrhythmic drug therapy post-procedure as an adjunctive measure to improve long-term maintenance of sinus rhythm. This strategy is aimed at reducing the significantly elevated long-term late recurrence rates associated with persistent AF [3]. The strategy is informed by demonstration of the relative safety of antiarrhythmic drug use in a patient populations receiving appropriate stroke prevention [19]. The presence of the Watchman® implant did not appear to impact the subsequent left atrial ablation procedure in patients requiring a redo, although, the repeat procedure was deferred at least 6 months to allow for implant healing [20].

In this case series, no clinical thromboembolic events were detected in a cohort with a mean CHA_2DS_2-VASc score of 2.6 $\pm$1 over a follow-up time of up to 5 years. The overall stroke rate was 0.5% per year. The authors concede that the very low stroke rate could have been the outcome of successful ablation and freedom from AF in the majority of patients. A body of evidence now points to catheter ablation therapy for AF conferring stroke risk reduction [21,22]. However, AF recurrence, cardiovascular morbidity, and stroke, are still observed to correlate with CHA_2DS_2-VASc score of 2 or greater over long-term follow-up [21–23]. The stroke rate in the current study compares similarly with the 0.72% event rate at mid-term follow-up of a large cohort of patients on anticoagulants with a mean CHA_2DS_2-VASc score of 2.1 $\pm$ 1.4 from the Leipzig Heart Center AF Ablation Registry [22] and contrasts with a much higher reported event rate of 5.1% for patients with CHA_2DS_2-VASc score of 2 who did not receive anticoagulation over a follow-up period of 39 months following catheter ablation [23]. This suggests that the two-pronged strategy may provide long-term cardiovascular benefits to patients with non-valvular AF, that is at least equivalent to ongoing oral anticoagulation strategy for patients with a CHA_2DS_2-VASc score of 2 or greater.

While the long-term follow-up of Watchman®-implanted patients in the PROTECT-AF randomized -controlled trial demonstrated superiority over warfarin for all cause stroke and mortality [1], concern has been raised over sub-analysis of the more recently conducted PREVAIL trial which showed a relatively higher rate of ischemic strokes during follow-up in the Watchman® group [10]. The single case of late ischemic stroke in the current study points to the difficulty of judging the mechanism of stroke in a patient group that frequently also has risk factors for atherothrombotic or hypertensive occlusive events. The authors are encouraged by the patient outcomes of the current series, and believe that catheter ablation for AF and LAA device occlusion will be complementary to a multi-faceted approach to long-term stroke prevention. However, further randomized controlled trials are required to define their respective roles.

4.1. Study limitations and future directions

One of the limitations of the current study, and other Watchman® implant series, is the lack of longer-term longitudinal imaging follow-up of all Watchman® implants. It is currently presumed that once complete occlusion (and tissue ingrowth over the prosthesis) is achieved, that complete occlusion will be indefinitely maintained. Further studies using TOE or contrast CT scan are required to document extended outcomes.

5. Conclusions

Combined procedures of catheter ablation for atrial fibrillation and percutaneous closure of the left atrial appendage with the Watchman® device were efficacious and safe in our single center experience with excellent rates of LAA occlusion achieved and an observed stroke rate of 0.5% per year during mid-term follow-up. Incomplete occlusion was associated with lower achieved device compression, and was more frequently associated with suboptimal device position, such as angulation and shoulder protrusion.

Conflict of interest

Dr. Karen Phillips and Dr. Julie Humphries have received consultancy fees from Boston Scientific. No financial disclosures for the other author.

References

[1] Reddy VY, Sievert H, Halperin J, et al. Percutaneous left atrial appendage closure vs warfarin for atrial fibrillation: a randomized clinical trial. JAMA 2014;312:1988–98.

[2] Wilber DJ, Pappone C, Neuzil P, et al. Comparison of antiarrhythmic drug therapy and radiofrequency catheter ablation in patients with paroxysmal atrial fibrillation: a randomized controlled trial. JAMA 2010;303 333–40l.

[3] Steinberg JS, Palekar R, Sichrovsky T, et al. Very long-term outcome after initially successful catheter ablation of atrial fibrillation. Heart Rhythm 2014;11:771–6.

[4] Chao TF, Lin YJ, Chang SL, et al. Can oral anticoagulants be stopped safely after a successful atrial fibrillation ablation? J Thorac Dis 2015;7:172–7.

[5] Meier B, Blaauw Y, Khattab A. EHRA/EAPCI expert consensus statement on catheter-based left atrial appendage occlusion. Europace. 2014. http://dx.doi.org/10.1093/europace/euu174 August 29 Advance Access.

[6] European Heart Rhythm Association, et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). Eur Heart J 2010;19:2369–429.

[7] Holmes DR, Reddy VY, Turi ZG, et al. 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;374:534–42.

[8] Walker DT, Humphries JA, Phillips KP. Anatomical analysis of the left atrial appendage using segmented three- dimensional cardiac CT: a comparison of patients with paroxysmal and persistent forms of atrial fibrillation. J Interv Card Electrophysiol 2012;34:173–9.

[9] Cappato R, Calkins H, Chen SA, et al. Delayed cardiac tamponade after radiofrequency catheter ablation of atrial fibrillation: a worldwide report. J Am Coll Cardiol 2011;58:2696–7.

[10] Holmes DR, 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. J Am Coll Cardiol 2014;64:1–12.

[11] Viles-Gonzalez JF, Kar S, Douglas P, et al. The clinical impact of incomplete left atrial appendage closure with the Watchman device in patients with atrial fibrillation: a PROTECT AF (Percutaneous Closure of the Left Atrial Appendage Versus Warfarin Therapy for Prevention of Stroke in Patients With Atrial Fibrillation) substudy. J Am Coll Cardiol 2012;59:923–9.

[12] Swaans MJ, Post MC, Rensing BJ, et al. Ablation for atrial fibrillation in combination with left atrial appendage closure: first results of a feasibility study. J Am Heart Assoc 2012;1:e002212.

[13] Bai R, Horton RP, Di Biase L, et al. Intraprocedural and long-term incomplete occlusion of the left atrial appendage following placement of the WATCHMAN device: a single center experience. J Cardiovasc Electrophysiol 2012;23:455–61.

[14] Sanfilippo AJ, Abascal VM, Sheehan M, et al. Atrial enlargement as a consequence of atrial fibrillation. A prospective echocardiographic study. Circulation 1990;82:792–7.

[15] Jeevanantham V, Ntim W, Navaneethan SD, et al. Meta-analysis of the effect of radiofrequency catheter ablation on left atrial size, volumes and function in patients with atrial fibrillation. Am J Cardiol 2010;105:1317–26.

[16] Viles-Gonzalez JF, Reddy VY, Petru J, et al. Incomplete occlusion of the left atrial appendage with the percutaneous left atrial appendage transcatheter occlusion device is not associated with increased risk of stroke. J Interv Card Electrophysiol 2012;33:69–75.

[17] Pillarisetti J, Reddy YM, Gunda S, et al. Endocardial (Watchman) vs epicardial (Lariat) left atrial appendage exclusion devices: understanding the differences in the location and type of leaks and their clinical implications. Heart Rhythm 2015;12:1501–7.

[18] Santangeli P, Di Biase L, Horton R, et al. Ablation of atrial fibrillation under therapeutic warfarin reduces periprocedural complications: evidence from a meta-analysis. Circ Arrhythm Electrophysiol 2012;5:302–11.
[19] Steinberg BA, Hellkamp AS, Lokhnygina Y, et al. ROCKET AF Steering Committee and Investigators. Use and outcomes of antiarrhythmic therapy in patients with atrial fibrillation receiving oral anticoagulation: results from the ROCKET AF trial. Heart Rhythm 2014;11:925–32.
[20] Walker DT, Phillips KP. Left atrial catheter ablation subsequent to Watchman® left atrial appendage device implantation: a single centre experience. Europace 2015 May 21. pii: euv037. [Epub ahead of print].
[21] Tran VN, Tessitore E, Gentil-Baron P, et al. Thromboembolic events 7–11 years after catheter ablation of atrial fibrillation. Pacing Clin Electrophysiol 2015. http://dx.doi.org/10.1111/pace.12588 [Epub ahead of print].
[22] Jacobs V, May HT, Bair TL, et al. The impact of risk score (CHADS2 versus CHA2DS2-VASc) on long-term outcomes after atrial fibrillation ablation. Heart Rhythm 2015;12:681–6.
[23] Chao TF, Lin YJ, Tsao HM, et al. CHADS2 and CHA2DS2-VASc scores in the prediction of clinical outcomes in patients with atrial fibrillation after catheter ablation. J Am Coll Cardiol 2011;58:2380–5.