

# Combining left atrial appendage closure and catheter ablation for atrial fibrillation: 2-year outcomes from a multinational registry

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## Aims

Clinical practice guidelines do not recommend discontinuation of long-term oral anticoagulation in patients with a high stroke risk after catheter ablation for atrial fibrillation (AF). Left atrial appendage closure (LAAC) with Watchman has emerged as an alternative to long-term anticoagulation for patients accepting of the procedural risks. We report on the long-term outcomes of combining catheter ablation procedures for AF and LAAC from multicentre registries.

## Methods and results

Data were pooled from two prospective, real-world Watchman LAAC registries running in parallel in Europe/Middle-East/Russia (EWOLUTION) and Asia/Australia (WASP) between 2013 and 2015. Of the 1140 patients, 142 subjects at 11 centres underwent a concomitant AF ablation and LAAC procedure. The mean CHA<sub>2</sub>DS<sub>2</sub>-VASc score was 3.4 ± 1.4 and HAS-BLED score 1.5 ± 0.9. Successful LAAC was achieved in 99.3% of patients. The 30-day device and/or procedure-related serious adverse event rate was 2.1%. After a mean follow-up time of 726 ± 91 days, 92% of patients remained off oral anticoagulation. The rates of the composite endpoint of ischaemic stroke/transient ischaemic attack/systemic thromboembolism were 1.09 per 100 patient-years (100-PY); and for non-procedural major bleeding were 1.09 per 100-PY. These represent relative reductions of 84% and 70% vs. expected rates per risk scores.

## Conclusion

The long-term outcomes from these international, multicentre registries show efficacy for all-cause stroke prevention and a significant reduction in late bleeding events in a population of high stroke risk post-ablation patients who have been withdrawn from oral anticoagulation.

## Keywords

Left atrial appendage • Device occlusion • Catheter ablation • Atrial fibrillation • Watchman

## Introduction

No randomized controlled trials to date have shown a reduction in the risk of thromboembolic events or ischaemic stroke following

catheter ablation therapy for atrial fibrillation (AF) as compared with standard medical therapy and oral anticoagulation.<sup>1</sup> The CHA<sub>2</sub>DS<sub>2</sub>-VASc risk score has been shown to correlate with both risk of AF recurrence and risk of thromboembolic events post-ablation,<sup>2</sup> and

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### What's new?

- This study reports on long-term outcomes from a subset of patients who underwent combined catheter ablation for atrial fibrillation and left atrial appendage closure procedures while enrolled in the large real-world WASP and EWOLUTION Watchman Registries.
- The results provide further multicentre evidence that the combined procedure provides efficacious long-term stroke prevention as well as reduced risk of major bleeding by allowing high-risk post-ablation patients to safely stop oral anticoagulation.

underscores the need for on-going stroke protection in high-risk patients. Accordingly, clinical practice guidelines recommend continuation of long-term oral anticoagulation in high stroke risk patients following catheter ablation therapy.<sup>3</sup>

Catheter-based left atrial appendage (LAA) occlusion, in contrast, has demonstrated efficacy for all-cause stroke prevention in non-valvular AF and can provide a mechanical alternative to long-term anticoagulation.<sup>4</sup> It has been suggested that combining the two left atrial interventions may be a valuable and practical approach.<sup>5</sup> We report on the 2-year outcomes of combined catheter ablation procedures for AF with LAA closure as studied in prospective international multicentre registries.

## Methods

The study design has previously been described in detail in the first report on peri-procedural outcomes.<sup>6</sup> Subgroup analysis was planned prospectively for patients undergoing concomitant catheter ablation of AF with Watchman (Boston Scientific Corporation; Natick, MA, USA) left atrial appendage closure (LAAC) during participation in either the EWOLUTION or WASP registries. The EWOLUTION and WASP registries were designed to collect real-world usage and outcomes data for patients implanted with the Watchman LAA closure device and were registered on ClinicalTrials.gov (NCT01972282 and NCT01972295, respectively).<sup>7,8</sup> Both registries used appropriate guidelines to determine device eligibility and were performed by trained implanters. The study was approved by the respective institutional review boards for human research and complies with the Declaration of Helsinki. Informed consent was obtained from all participants. A contract research organization monitored both studies and conducted multiple site visits to verify the accuracy and completeness of follow-up data.

## Procedure

Catheter ablation for AF was performed per physician discretion with the choice of ablation energy modality, ancillary catheters, and use of cardiac navigational system individualized to patients and physician preferences. The ablation endpoint was left and right-sided pulmonary vein electrical isolation, as well as any additional left or right atrial ablation, deemed necessary by the operator. After completion of the ablation phase, the transseptal sheath was exchanged for the Watchman access sheath. One centre reported using intracardiac echocardiography during the ablation phase of the procedure, however, all centres reported use of transoesophageal echocardiography (TOE) to guide LAA device closure. Implant of

the LAA closure device was then performed as previously described.<sup>7,8</sup> Peri-procedural oral anticoagulation (OAC), intravenous heparin, and target-activated clotting time were managed at the physician's discretion.

## Patient follow-up

The schedule of clinical follow-up was at the discretion of the physician and according to each institution's standard practice. Generally, clinical review was performed at 2–3 months post-procedure and then annually thereafter. Additional telephone contact was made with patients during the study.

Follow-up TOE imaging was recommended at 6 weeks to reassess device position and any residual jet flow around the device. Left atrial appendage occlusion was defined as satisfactory positioning of the device at the ostium covering all trabeculated portions of the LAA with peri-device flow  $\leq 5$  mm.<sup>4</sup> If satisfactory appearances on TOE follow-up study had been confirmed, anticoagulation discontinuation was recommended at the next follow-up visit and patients were then recommended for antiplatelet therapy (aspirin 81 – 325 mg + clopidogrel 75 mg) for 6 months post-implant or at the discretion of the physician.

## Data collection and event definition

All data collection and adverse event reporting were performed directly by the individual sites and captured in a standardized central database. All centres were monitored by an outside contract research organization on an ongoing basis with one or more site visits depending on the number of patients enrolled and compliance review.

Both trials required serious adverse events (SAEs) reporting per ISO 14155 and the MEDDEV 2.7/3 12/2010. Adjudication was performed by investigators with oversight by a Medical Safety Group. Events included procedure-related complications (e.g. serious pericardial effusion, device embolization, and procedure-related stroke) and events related to excessive bleeding (e.g. intracranial or gastrointestinal bleeding) scored according to the Bleeding Academic Research Consortium (BARC) criteria. The definition of various safety events and major bleeding align with reporting standards suggested by the consensus document.<sup>9</sup> Safety events were further classified as Watchman procedure-related, device-related or related to prescribed anticoagulation regimen.

Screening for recurrent atrial tachyarrhythmias and follow-up of rhythm outcomes was left to the physician's discretion. Data were not collected on rhythm outcomes in the central databases and is not reported on as part of these studies.

## Endpoints

Efficacy endpoints required reporting of any occurrence of stroke (including ischaemic or haemorrhagic stroke), death, or systemic embolism (SE). The primary endpoints of this study were efficacy of the procedure and device to prevent the combined endpoint of stroke, transient ischaemic attack (TIA), or SE over 2-year follow-up. Secondary endpoints included assessment of procedural success and safety, assessment of bleeding events, and all-cause mortality over 2-year follow-up.

## Statistical analysis

Continuous variables are summarized using the mean, standard deviation, range, and categorical variables with counts and percentages. Predicted risk of annual stroke (in the absence of therapy) and bleeding (during anti-coagulant therapy) was extrapolated for each individual subject based on CHA<sub>2</sub>DS<sub>2</sub>-VASc and HAS-BLED scores using published literature<sup>10,11</sup> and then the average risk for the study population was used to determine the expected rates for comparison to observed rates and risk reduction

calculations. Rates of stroke, TIA, SE, death, and bleeding events are calculated as number of events per 100 patient-years (100-PY) and estimates of rates and 95% confidence intervals for each subgroup are derived from a Poisson Model. The Kaplan–Meier method was used to describe SAE rates at specific time points in follow-up. The Fisher's exact test was used to compare binomial proportions, and *t*-test to compare continuous variables.

## Results

### Patient demographics

Enrolment in the EWOLUTION study included 1025 patients and spanned from October 2013 to May 2015 in 47 centres across 13 countries in Europe, the Middle East, and Russia. Enrolment in the WASP trial commenced in January 2014 and concluded in October 2015, resulting in 201 patients across seven countries including Australia, Asia, and the Middle East.

Of the 1140 patients from both registries, 142 subjects at 11 centres underwent a concomitant ablation and LAAC procedure and are included in the analysis. The majority of cases (97%) were performed by experienced AF catheter ablation proceduralists ( $\geq 50$  procedures per year). The results have previously been published in part as an initial report on 30-day procedural outcomes.<sup>6</sup> Subsequent to the initial publication site monitoring visits revealed three additional patients who had undergone concomitant catheter ablation procedures for AF but had been initially incorrectly classified in the database.

The mean age at time of consent was  $64.2 \pm 7.2$  years (range 39–85), and 54.2% of patients were male. Stroke risk scores (mean  $\pm$  standard deviation) for CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc were  $2.2 \pm 1.2$  and  $3.4 \pm 1.4$ , respectively, while the HAS-BLED score was  $1.5 \pm 0.9$ . The primary AF pattern was paroxysmal in 69%. A prior history of ischaemic stroke or TIA was recorded in 40.1% of patients, congestive heart failure in 33.8%, and left ventricular systolic dysfunction [left ventricular ejection fraction (LVEF)  $\leq 40\%$ ] in 2.1%. The indications for LAA device occlusion included labile international normalized ratios (INRs) in 25 (17.6%), requirement for concomitant drug therapy in 45 (31.7%), previous major bleeding in 14 (9.9%), recurrent anaemia due to gastrointestinal bleeding in 4 (2.8%), history of blood dyscrasia in 1 (0.7%), history of haemorrhagic tendency in 5 (3.5%), alcohol abuse in 8 (5.6%), senility in 1 (0.7%), job or lifestyle that prohibits warfarin use in 28 (19.7%), other contraindication, e.g. HAS-BLED score  $\geq 3$  in 20 (14.1%), and reason not recorded in 29 (20.4%). For a complete listing of all demographics, see Table 1.

### Procedural characteristics and success

The ablation modality used by the different operators included irrigated radiofrequency ablation in 106 patients, cryoballoon in one patient, non-irrigated phased radiofrequency multielectrode applications in 30 patients and modality not recorded in five patients. Ablation endpoints were not recorded in the registry dataset. Successful LAAC was achieved in 141/142 (99.3%) with one implant abandoned following the ablation phase of the procedure after recognition of a serious pericardial effusion which required pericardiocentesis. All implants achieved a satisfactory seal (residual leak  $< 5$  mm) per device release specifications<sup>4</sup> with 137/141 (97.2%)

**Table 1** Baseline characteristics

Characteristics	Summary statistics
Age at time of consent (years)	
Mean $\pm$ SD	64.2 $\pm$ 7.2
Range	39.0–85.0
Age $\geq 80$	0.7% (1/42)
Male	54.2% (77/142)
CHADS <sub>2</sub> score—continuous	
Mean $\pm$ SD	2.2 $\pm$ 1.2
Range	0.00–5.00
CHA <sub>2</sub> DS <sub>2</sub> -VASc score—continuous	
Mean $\pm$ SD	3.4 $\pm$ 1.4
Range	0.00–7.00
HAS-BLED score—continuous	
Mean $\pm$ SD	1.5 $\pm$ 0.9
Range	(0.00, 4.00)
Components of CHADS <sub>2</sub> and CHA <sub>2</sub> DS <sub>2</sub> -VASc scores	
CHF	33.8% (48/142)
Hypertension	80.3% (114/142)
Age $\geq 75$	9.2% (13/142)
Age 65–74	42.3% (60/142)
Diabetes	13.4% (19/142)
History of TIA/Stroke	40.1% (57/142)
Vascular disease	20.4% (29/142)
Female	45.8% (65/142)
Components of HAS-BLED scores	
Uncontrolled hypertension	15.5% (22/142)
Abnormal renal function	2.1% (3/142)
Abnormal liver function	0.7% (1/142)
History of ischaemic/haemorrhagic stroke	28.9% (41/142)
Prior major bleeding or predisposition to bleeding	4.9% (7/142)
Labile INRs	17.6% (25/142)
Concomitant use of drugs	31.7% (45/142)
Alcohol abuse	5.6% (8/142)
Age $> 65$	41.5% (59/142)
AF pattern	
Paroxysmal	69.0% (98/142)
Persistent	28.9% (41/142)
Long-standing persistent	1.4% (2/142)

Values presented are % (N/total) or mean  $\pm$  standard deviation, range (minimum–maximum).

AF, atrial fibrillation; CHF, congestive heart failure; INRs, international normalized ratios; SD, standard deviation; TIA, transient ischaemic attack.

achieving a complete seal and 4/141 (2.8%) accepting a small peridevice leak. The mean LAA diameter was  $20.8 \pm 2.8$  mm (range 14–28), resulting in final median device size of 24 mm.

### Oral anticoagulant regimen

Post-procedure, 92.9% of patients were prescribed an oral anticoagulant [54.2% non-vitamin K antagonist oral anticoagulants (NOAC),

38.7% warfarin], 5.6% were given anti-platelet (3.5% dual, 2.1% single), and the remainder received no therapy (1.4%).

### Peri-procedural safety

The 7-day device and/or procedure-related SAE rate was 1.4% (0.3–4.5%). The 30-day device and/or procedure-related SAE rate was 2.1% (0.6–5.6%). There were two serious pericardial effusions requiring pericardiocentesis (1.4%): one pericardial effusion was identified during the procedure following the ablation phase (therapeutic INR of 2.6 on warfarin) and required percutaneous drainage with uneventful recovery (but caused LAAC implant to be abandoned), while a second pericardial effusion with tamponade occurred on Day 12 post-procedure and was resolved with pericardiocentesis. There were four significant bleeding events within the first 30 days as previously described<sup>7</sup> including gastrointestinal bleeding on NOAC Day 1, frank haematuria on warfarin Day 5, secondary bleed from groin (vascular access) on warfarin on Day 13, and traumatic knee haematoma on NOAC on Day 28 post-procedure. The bleeding SAE rate at 30 days was 2.8% (0.9–6.6%). There were no peri-procedural strokes/TIAs, device embolization or deaths.

### Transoesophageal echocardiography follow-up

A first follow-up TOE in patients with a successful implant was performed at least 28 days post-procedure in 109/141 (77%) patients. Satisfactory LAA occlusion was noted in 107/109 (98.2%). Two patients had a jet size >5 mm determined to be due to device migration and were continued on OAC for the duration of the study due to unsuccessful LAA closure. Device-related thrombus (DRT) was detected during early follow-up TOE in three patients (2.1%) while still on OAC (Days 38, 45, and 45). There was no history of reduced LVEF or congestive cardiac failure in patients who developed DRT and all patients were identified to have appropriate positioning of the device (without malrotation) and with complete LAA seal. One patient had a history of paroxysmal AF and two patients had persistent AF prior to the index procedure with CHA<sub>2</sub>DS<sub>2</sub>-VASc scores ranging between 2 and 3. The rhythm at the time the thrombus was detected was sinus in two and unrecorded in one patient. Sessile thrombus across the atrial facing surface of the device was noted in one and mobile, pedunculated thrombus was attached to the inferior margin of the device in one, with no data available on the third patient. All patients were taking NOACs at the time of diagnosis which were continued until documented thrombus resolution (4 weeks to 4 months timeframe). All DRT patients were then successfully withdrawn from OAC. Device embolization was detected in one patient on Day 43 as part of investigations for difficulty walking. Radiological assessment detected the device at the distal bifurcation of the aorta. The device was retrieved surgically without complications.

### Antithrombotic therapy at follow-up

Subsequent to the first follow-up visit 132/141 (94%) of implanted patients were discontinued from or taking no oral anticoagulant. At 2-year follow-up the following rates of therapy were recorded in implanted patients: 8.0% OAC, 81.9% antiplatelet therapy (1.5% dual and 80.4% single), and 10.1% on no therapy (Figure 1).

**Table 2** Endpoint event rates

Events	Rate per 100 patients-years	95% CI
Death	0.36	0.05–2.53
Ischaemic stroke SAE	0.36	0.05–2.54
Ischaemic stroke/TIA/SE SAE	1.09	0.35–3.37
Major bleeding SAE	1.83	0.76–4.40
Non-procedure or device-related major bleeding SAE	1.09	0.35–3.38

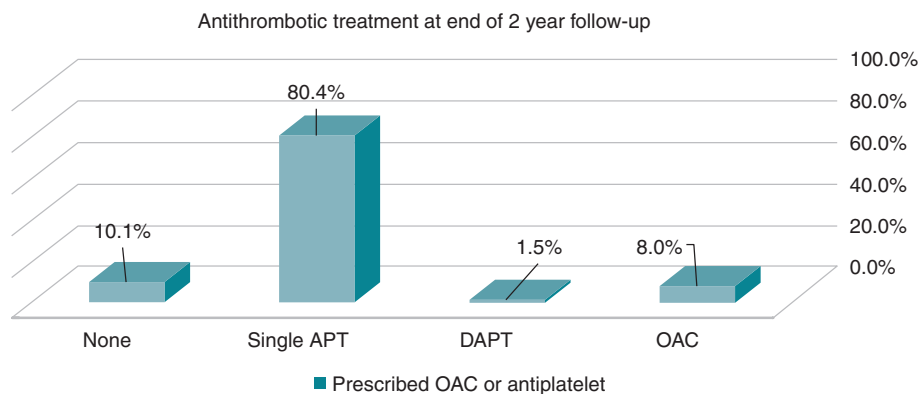
SAE, serious adverse event; SE, systemic embolism; TIA, transient ischaemic attack.

### Long-term follow-up

The mean follow-up time for the cohort who were successfully implanted was 726 ± 91 days (range 77–902). No patients were lost to follow-up. Two patients underwent cardiac surgery during which the surgeon chose to remove the LAA occlusion device and oversee the LAA in the absence of any documented adverse events related to the device. A total of five patients had bleeding events during 24 months of follow-up with four events clustered within the first 30 days and only one further event (gastrointestinal bleeding from acute diverticulitis while on Aspirin) at Day 199. The observed total major bleeding event rate was 1.83 per 100-PY; however, the non-procedural major bleeding rate was 1.09 per 100-PY. The expected rate of spontaneous major bleeding as predicted by HAS-BLED score if taking warfarin is 3.67 per 100-PY.<sup>11</sup> This represents a 70% relative risk reduction for non-procedural bleeding events (Figure 2).

One ischaemic stroke and five TIAs occurred in three patients during follow-up. One patient experienced a TIA Day 15 post-procedure on warfarin and aspirin therapy and was subsequently changed to warfarin and clopidogrel which was then prescribed long term. This patient was also identified to have device migration resulting in a peri-device leak of 5 mm on follow-up TOE and continued on OAC due to incomplete LAA closure. The same patient went on to suffer an ischaemic stroke on Day 458, and another TIA at day 610 (while still on warfarin and clopidogrel). Two patients experienced three TIAs: one patient at Day 246 on clopidogrel (and was changed to NOAC), a second patient at Day 262 while on warfarin (antiplatelet therapy added), and also on Day 707. The latter patient had a prior history of multiple TIA and strokes, and although had been initially withdrawn from OAC and changed to clopidogrel in early follow-up, he was subsequently recommenced on warfarin by the Neurologist when recurrent AF was detected 11 months post-procedure. There was no evidence for device thrombus in any of the patients who suffered TIA or stroke events. There was no correlation between cases of early detected device thrombus and later stroke/TIA events in the current study. There were no haemorrhagic strokes or intracranial bleeding events.

The expected rate of ischaemic stroke predicted by mean CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 3.4 without oral anticoagulation (and assuming aspirin use) is 4.86 per 100-PY,<sup>10</sup> however, the observed rate



**Figure 1** Anticoagulation drugs used by subjects at end of 2-year follow-up period. Single APT, single-antiplatelet therapy; DAPT, dual-antiplatelet therapy; OAC, oral anticoagulant (NOAC or warfarin).

for the study was 0.36 per 100-PY (Table 2). This represents a 93% relative risk reduction for stroke. When TIA and SE are added to the combined endpoint the predicted event rate is 6.81 per 100-PY,<sup>10</sup> with an observed rate for the study of 1.09 per 100-PY which translates to 84% relative risk reduction for stroke/TIA/SE (Figure 3).

There was one death over the follow-up period (patient found deceased in bathtub at day 104—cause of death unclear) resulting in a mortality event rate of 0.36 per 100-PY.

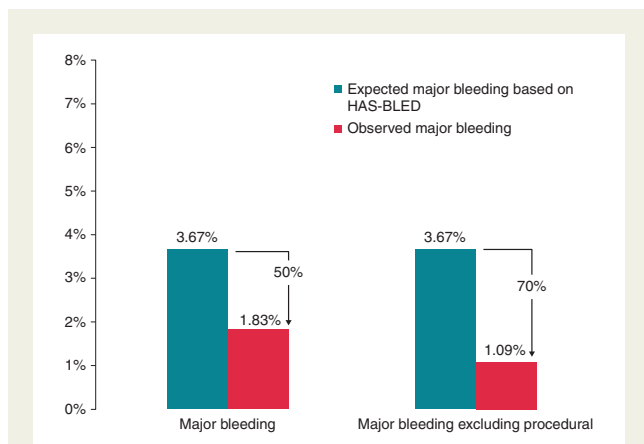
## Discussion

The current study provides long-term registry outcomes for a multinational cohort of patients with AF and high stroke risk who have undergone combined interventions of catheter ablation and LAAC. The study provides important observational data that points to significant lowering of expected stroke event rate despite 92% of patients discontinuing anticoagulation over the longer term. The results also show low rates of bleeding at long-term follow-up, again significantly lower than expected if the patient group had been consistently prescribed anticoagulation. Further the results show good periprocedural safety for high-volume ablation operators with procedural complication rates similar to those reported for catheter ablation therapy alone.<sup>12</sup> The results are consistent with two other multicentre reports of mid to long-term outcomes following combined ablation and LAAC procedures.<sup>13,14</sup> A multinational registry which followed up 349 patients with average CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 3.0 for a mean of 35 months off OAC documented an annualized stroke rate of 0.9% for the cohort (78% risk reduction vs expected) 0.13 A Chinese multicentre registry documented one ischaemic stroke during mean follow-up time of 20 months for a cohort of 50 patients off OAC with mean CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 3.7.<sup>14</sup> These long-term outcomes further support the acknowledgment that the combined procedure can be described as a 'valuable and practical approach' as stated in the 2015 EHRA/EAPCI expert consensus statement on catheter-based LAA occlusion.<sup>5</sup>

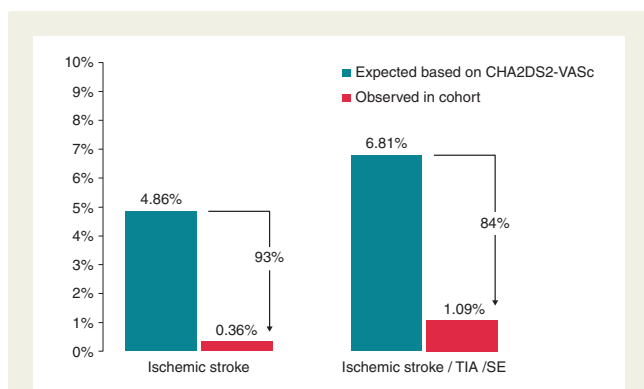
The ESC Guidelines for Management of Atrial Fibrillation acknowledge that several observational studies have suggested a relatively low stroke rate in the first few years after catheter ablation

of AF, but emphasize that the long-term risk of recurrent AF in ablated patients need to be considered.<sup>3</sup> While the guidelines continue to recommend anticoagulation after ablation based on stroke risk scores rather than rhythm outcome<sup>3</sup> the potential for serious bleeding events in post-ablation patients subjected to long-term anticoagulation has been raised by observational studies such as the Danish National Registry.<sup>15</sup> In the latter study, the incident rates of ischaemic stroke were demonstrated to be higher in the group who discontinued OAC than for those post-ablation patients who remained anticoagulated over the median follow-up time of 3.4 years, but the serious bleeding risks of OAC were suggested to 'outweigh' the potential small benefits of stroke risk reduction.<sup>15</sup> While the authors acknowledge that some degree of reduction in stroke risk over the current study timeframe is likely to have been conferred by catheter ablation the concomitant LAAC strategy has provided a proven long-term stroke prevention strategy that is equivalent to oral anticoagulation<sup>4</sup> but with removal of serious bleeding risks and without the ongoing requirement to carefully monitor for recurrent AF.

Global rates of catheter ablation treatment for AF have increased significantly over the last two decades.<sup>16</sup> Despite well-documented improvements in symptoms and quality of life scores catheter ablation has demonstrated few improvements in 'hard endpoints' in randomized trials with only the subset of patients with left ventricular systolic dysfunction and congestive cardiac failure showing reductions in mortality.<sup>17</sup> No randomized controlled trial of catheter ablation for AF to date has shown a reduction in long-term thromboembolic events or ischaemic stroke.<sup>1</sup> In contrast, the Watchman LAAC procedure is a catheter-based treatment which has been demonstrated in randomized controlled trials to reduce all-cause stroke and offers improved cardiovascular mortality when compared with warfarin anticoagulation.<sup>4</sup> The combination of LAAC (a proven stroke prevention therapy) with catheter ablation could thereby offer prognostically important outcomes from a single intervention. Further, the prognostic benefit from a 'bolt-on' LAAC intervention is likely to be widely applicable due to the prevalence of high stroke risk in the AF population seeking catheter ablation. While the usual decision-making process to arrive at LAAC procedure involves careful



**Figure 2** Calculated major bleeding risk based on HAS-BLED score, actual observed major bleeding rates and relative risk reduction (left), and observed major bleeding rate excluding procedural bleeding and relative risk reduction (right) after 2-year follow-up.



**Figure 3** Calculated stroke risk based on CHA<sub>2</sub>DS<sub>2</sub>-VASc score, actual observed stroke rate and the relative risk reduction (left), and calculated stroke/TIA/SE risk based on CHA<sub>2</sub>DS<sub>2</sub>-VASc score, actual observed combined endpoint of stroke/TIA/SE rate and the relative risk reduction (right) after 2-year follow-up. TIA, transient ischaemic attack; SE, systemic embolism. Effectiveness in stroke reduction vs. estimated in the absence of therapy for comparable CHA<sub>2</sub>DS<sub>2</sub>-VASc scores based on Friberg *et al.*<sup>10</sup>

consideration of procedural risks as compared with other long-term risks of continuing anticoagulation or the risks of no prophylaxis, patients undergoing catheter ablation for AF have already accepted procedural risk.

For patients with a high stroke risk who are already undertaking the procedural risks of catheter ablation a 'bolt-on' stroke prevention therapy with LAAC could represent a shift in the care paradigm. If the opportunistic LAAC can be performed at minimal extra cost/risk, the long-term benefits of mechanical stroke prevention (with ensured compliance) and reduction in bleeding events from discontinuation of oral anticoagulation may be considerable.

### Effect on long-term bleeding

The low rate of long-term (non-procedural) bleeding in the current study is notable and is likely explained by 92% of the cohort being

discontinued from oral anticoagulation. Long-term therapy with a novel anticoagulant confers an annual major bleeding risk of 2.13–3.6% in contemporary trials.<sup>18</sup> A link between spontaneous bleeding events and a significant increase in mortality has been demonstrated in multiple trials of patients with coronary artery disease.<sup>19</sup> Although the populations are not directly comparable, it may be important to understand the impact of spontaneous major bleeding events on prognosis/mortality in an aging population who are prescribed long-term OAC. PROTECT-AF and the wider meta-analysis of Watchman studies have already demonstrated a clinically and statistically significant reduction in cardiovascular mortality of Watchman LAAC over long-term warfarin anticoagulation<sup>4</sup> and it is intriguing to postulate whether this may be cumulative benefit from reduced major bleeding events in an aging cohort.

### Study limitations and future directions

Because these registries were designed as LAAC outcome studies, the datasets did not include arrhythmia outcomes and the authors acknowledge this as a limitation. There is no proof as yet that catheter ablation modifies the risk of thromboembolic stroke in high-risk patients with AF,<sup>1,20</sup> and long-term follow-up studies following catheter ablation have generally shown progressive arrhythmia recurrence, especially for patients with non-paroxysmal AF.<sup>20</sup> Accordingly Wintgens *et al.*<sup>13</sup> multicentre pooled registry experience of combined ablation and Watchman LAAC showed AF recurrence in 51% of patients by 35 months follow-up and similarly in the Chinese multicentre registry AF recurred at a rate of 36% by 20 months mean follow-up.<sup>14</sup>

Whether the concomitant LAAC procedure detrimentally affects the rhythm outcomes from ablation also cannot be answered by the current study. Larger randomized trials such as the currently enrolling OPTION study (NCT03795298) will be needed to assess for differences between performing the procedures separately vs. a combined approach and to specifically address any interaction with different ablation modalities.

Although registry data provides a beneficial real-world practice perspective, it does lead to variability in peri-procedural management (e.g. variation in ablation modality, anticoagulation regimen) and non-conformity of follow-up. Prospective collection of data into a central database with multiple monitoring visits has, however, enabled rigorous documentation of these variations.

The authors also acknowledge that the predictive accuracy of CHA<sub>2</sub>DS<sub>2</sub>-VASc and HAS-BLED scores for estimating expected stroke and bleeding rates in a post-catheter ablation cohort is unknown. The potential for overestimation of LAAC effect on stroke event rates, in particular, is considered likely.

The authors acknowledge that regulatory and reimbursement considerations in different regions around the world will have an impact on the ease with which physicians might adopt the combined approach.

### Conclusions

The outcomes from these international, multicentre registries support long-term safety and efficacy of a combined ablation and LAAC procedure for all-cause stroke prevention and a significant reduction

in late bleeding events in a population of high stroke risk post-ablation patients who have been withdrawn from long-term oral anticoagulation.

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