Ablation for Atrial Fibrillation Combined With Left Atrial Appendage Closure

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ABSTRACT

OBJECTIVES The study sought to determine long-term clinical effects of combining catheter ablation (CA) and left atrial appendage (LAA) occlusion (LAAO) in a single procedure.

BACKGROUND CA relieves symptoms in atrial fibrillation (AF), but freedom from AF is not assured. Thus, oral anticoagulation (OAC) remains necessary in high stroke risk patients. LAAO has proved a viable alternative for preventing thromboembolic complications.

METHODS Symptomatic patients with drug-refractory AF (CHADS2 =1) and indications for LAAO were included. Transesophageal echocardiography was performed to assess LAA size/anatomy/thrombus. After CA, LAAO was performed using the Watchman device (Atritech, Inc., Plymouth, Minnesota, Minnesota). At 3 months, OAC was switched to aspirin/clopidogrel if LAAO criteria were met.

RESULTS From September 2009 to October 2013, 62 patients (22 female, 64 ± 8 years of age, CHADS2 2.5) underwent combined procedures. Indications for LAAO included history of stroke despite OAC (29.0%), contraindications for OAC (24.2%), high stroke risk (24.2%), and miscellaneous reasons (22.6%). LAAO resulted in complete acute closure in all, with a median number of 1 device. After a median follow-up of 38 (range: 25 to 45) months, 95% of the patients met the criteria for successful sealing and 78% could discontinue OAC, while recurrence of AF was documented in 42%. During long-term follow-up, 3 ischemic strokes were observed with an annual stroke risk of 1.7%, which is lower than the expected annual risk of 6.5%.

CONCLUSIONS LAAO combined with CA for AF can be performed successfully and safely in a single procedure, with a lower than expected stroke rate. Further studies are necessary to determine which patients benefit from the combined therapy. (J Am Coll Cardiol EP 2015;1:486–95) © 2015 by the American College of Cardiology Foundation.

Atrial fibrillation (AF) is the most common arrhythmia with tremendous expenditure of health resources (1–3). Various antiarrhythmic drugs (AAD) are used, often accompanied by side effects while rarely resulting in complete freedom of AF. The RACE (Rate Control versus Electrical Cardioversion) (4) and AFFIRM (Atrial Fibrillation Follow-up Investigation of Rhythm Management) (5) trials have shown that neither rate or rhythm control by AAD can eliminate AF or prevent adverse events. Catheter ablation (CA) is more effective than AAD to reduce the burden of AF (6). However, the actual freedom of AF is lower than initial studies suggested, especially in patients with...
Stroke is the most devastating complication of AF, accounting for 15% to 20% of all strokes (7). According to guidelines, oral anticoagulation (OAC) is indicated to prevent thromboembolic events in patients with high stroke risk based on CHADS2 or CHA2DS2-VASc scores (1). Vitamin K antagonists have several disadvantages including (major) bleedings, intolerance, noncompliance, and a narrow therapeutic range (8-10). The novel factor IIa and Xa inhibitors (novel oral anticoagulations [NOACs]) have advantages over vitamin K antagonists, but may still lead to bleeding, and also have limitations such as the absence of antidotes in case of bleeding, limited long-term data, limited cardiovascular outcome data, and high medication cost (11-14).

The left atrial appendage (LAA) may be the source of thrombi in >90% of patients with nonvalvular AF (15). Randomized clinical trials have shown that percutaneous mechanical occlusion of the left atrial appendage (LAAO) can be an effective alternative to OAC (16-18). In the 2012 ESC guidelines, LAAO has received a Class IIb recommendation in high stroke risk patients that are contraindicated for long-term use of OAC (1).

The combination therapy of AF ablation with LAAO would avoid the added risk of multiple procedures, while providing a permanent reduction in stroke risk, and abolishing the need for OAC. Specifically in patients with contraindications for OAC, LAAO has proven safe and successful (19). Previously, our group has published short-term data showing that combining CA and LAAO is feasible and safe (20). In this prospective registry study, we now show procedural data for a larger group of patients, with long-term follow-up data on bleeding, stroke, and the need for OAC.

METHODS

PATIENT SELECTION. The study was designed as an open-label, nonrandomized, prospective registry. From September 2009 to September 2013, patients who were eligible for both CA and LAAO were included. All patients were seen by an electrophysiologist in the outpatient clinic to evaluate eligibility. They signed a written consent form. The hospital’s ethics committee approved the study. All procedures were done in accordance with the hospital’s ethics standards and the Helsinki Declaration of 1975 (revised in 2008). As LAAO is not reimbursed in the Netherlands, the procedures were financed by a Research Funding grant by the St. Antonius Hospital, up to a maximum of 30 procedures per year.

The indication for ablation was documented symptomatic and recurrent paroxysmal or (longstanding) persistent AF, despite at least 1 AAD and cardioversion in accordance with international guidelines. The indications for concomitant LAAO were an increased risk of stroke (CHADS2 score ≥1), with a (relative) contraindication for and/or failure of OAC. The risks of stroke and bleeding were determined according to the CHADS2 and the HAS-BLED scores. To assess LAA anatomy, and exclude LAA thrombus and significant structural cardiac abnormalities, transesophageal echocardiography (TEE) was carried out in all patients within 1 week of the procedure. All data were collected prospectively by means of a web-based database.

ABLATION PROCEDURE. All procedures were performed in patients under general anesthesia, preferably under continued OAC use, aiming at therapeutic international normalized ratio (INR) levels of 2 to 3. AAD were continued.

Ablation was performed with the Phased radiofrequency catheter system (Medtronic/Ablation Frontiers, Inc., Carlsbad, California) as described before in detail by our group (20-23). The filter settings of the EP system (Bard, Inc., Lowell, Massachusetts) for the phased radiofrequency catheters were set from 100 to 500 kHz for the pulmonary vein (PV) ablation catheter (PVAC), with signal amplification at 5,000. PV isolation was performed with PVAC, while in patients with longstanding persistent AF complex-fractionated atrial electrogram ablation was performed with the multiarray catheters, multiarray septal catheter (septum), and multiarray ablation catheter (LA roof, free wall, mitral isthmus, mitral annulus, and posterior wall) (23). Electrodes 1 and 10 of the PVAC were disconnected as these may induce silent cerebral ischemias by interaction.

A 7-F sheath was introduced through the right femoral vein. A quadripolar catheter was introduced into the coronary sinus for pacing purposes. A standard transseptal puncture was performed with a radiofrequency Brockenbrough needle (Baylis Medical Company Inc., Montreal, Quebec, Canada) with a 12.5-F outer diameter/9.5-F inner diameter steerable sheath (Channel, Bard, Lowell, Massachusetts). After transseptal puncture, angiography was performed.

ABBREVIATIONS AND ACRONYMS

AAD = antiarrhythmic drugs
AF = atrial fibrillation
CA = catheter ablation
CHADS2 = congestive heart failure, hypertension, age ≥75 y, diabetes mellitus, prior stroke or TIA
CHADS2-VASc = CHADS2 score + vascular disease
CHF = congestive heart failure
CHF-VASc = CHADS2 score + vascular disease
CT = computed tomography
CTA = contrast-enhanced computed tomography
CTIA = computed tomography
DCS = deflectable common carotid sheath
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via the sheath to delineate the PVs and LAA. A single heparin IV bolus of 10,000 IU was administered through the sheath to accompany the first hour of ablation with a repeated bolus of 5,000 IU after each additional half-hour. After successful transseptal puncture the PVAC was used for antrum ablation in all PVs. In all PVs, the guidewire was consecutively positioned in different side branches to allow the ablation catheter to enter the antrum from different angles. The applications were made as proximal as possible, trying to reach away from the ostium toward the antrum as far as possible. The right middle vein was cannulated separately, regardless of whether this was a separate vein or a side-branch. In patients with a left common antrum, ablation was performed as proximal as possible while still achieving sufficient contact for adequate tissue temperature. The guidewire was consecutively positioned in the upper and lower PV to allow complete circumferential ablation of the common antrum.

The endpoint with PVAC ablation (PV isolation) was confirmed by the absence of local potentials with PVAC mapping inside each vein combined with pacing maneuvers from the CS, and/or the PV to distinguish local potentials from far field potentials (20–22). The endpoint for multiarray septal catheter ablation was elimination of all septal complex fractionated atrial electrograms (CFAEs) within reach of the array in a 360° circle. For the multiarray catheter ablation this was elimination of LA roof, free wall, mitral annulus, and posterior wall (23). CFAEs were defined visually as local continuous deflections with multiple components crossing the baseline.

LAAO. Watchman (Atritech, Inc., Plymouth, Minnesota/Boston Scientific, Marlborough, Massachusetts) implantation was carried out immediately subsequent to the ablation procedure under 2D or 3D TEE guidance. Details of the Watchman device and procedure have been described elsewhere (20,24,25). The initial 12.5-F sheath was replaced by a 14-F transeptal access sheath (Atritech, Inc.), which was positioned in the LAA. With a pigtail catheter, additional angiograms were made to determine size and shape of the LAA. This access sheath serves a conduit for the delivery catheter, which contains the device, a self-expanding nitinol frame with fixation barbs and a permeable polyester fabric cover. There are 5 device sizes (21, 24, 27, 30, and 33 mm) to accommodate varying LAA anatomy and size. A device size 10% to 20% larger than the largest diameter of the LAA body (as measured by angiography and TEE) was chosen, to have sufficient compression for stable positioning. The device deploys by retracting the access sheath. Before releasing it from the delivery catheter, several release criteria had to be fulfilled, including proper LAA position, no or minimal (<5 mm) residual lateral flow past the device, and a tug test for stability. If all these device release criteria were confirmed, the device was released and its position reconfirmed by angiography and TEE. Patients were discharged the following day after a chest x-ray to verify the Watchman position in the heart. Vitamin K antagonists were either continued or started as standard of care after CA and LAAO with INR between 2 and 3, if necessary with bridging low-molecular-weight heparin until INR was >2.0. In patients with an absolute contraindication for OAC, low-molecular-weight heparin was given for at least 3 weeks, as this period constitutes the highest risk period (26). In these patients aspirin, clopidogrel, or both were also started.

FOLLOW-UP. Patients were seen by their treating electrophysiologist in the outpatient clinic 90 days after the procedure. Before this visit, TEE imaging was performed at approximately 60 days to evaluate LAAO, thrombus formation, device position, and residual flow. Sealing was considered successful when there was either no flow (complete), or the presence of a remaining jet <5 mm (24,25). Patients using OAC were then switched to aspirin indefinitely. In the OAC contraindicated group, aspirin was also continued indefinitely while clopidogrel (75 mg daily) was prescribed for 6 months unless contraindicated. If criteria for successful sealing were not met, TEE was repeated at 3 to 6 months. A yearly follow-up was done by examining the electronic hospital charts, and/or contacting the treating cardiologist, and/or contacting the patients to provide information on their evolution.

Long-term rhythm follow-up was left at the discretion of the referring cardiologist or treating electrophysiologist as needed. In all patients, a 12-lead electrocardiogram was routinely obtained at the 3 months outpatient clinic appointment and Holters were performed in the first year after the index procedure. Adverse event monitoring focused on bleeding complications, and stroke or systemic embolism. Ischemic stroke was defined as the sudden onset of a focal neurological deficit in the distribution of a single brain artery with symptoms and/or signs persisting ≥24 h, or when ≥24 h if accompanied by the evidence of tissue loss without hemorrhage based on computed tomography or magnetic resonance brain imaging (27).
STATISTICS. Descriptive statistics were used to report patient characteristics. Continuous variables with normal distribution were reported as mean ± SD. Median (25th to 75th percentiles) were used when normal distribution was absent. Percentages were used to report categorical variables. All statistical analyses were performed in SPSS software (version 22.0, SPSS Inc., Chicago, Illinois).

RESULTS

BASELINE CHARACTERISTICS. A total of 62 patients (22 female, 64 ± 8 years of age) underwent CA combined with LAAO in a single procedure. The baseline characteristics are described in Table 1. The majority of patients had a history of paroxysmal AF. The median CHADS2, CHA2DS2-VASc, and HAS-BLED scores were 2.5 (2.0 to 3.0), 3.0 (2.75 to 4.00), and 2.0 (2.0 to 3.0), respectively. A total of 77.4% of patients had a history of stroke or transient ischemic attack. Anticoagulation therapy with OAC or NOAC was used in 80.6% of patients, while 5 patients used only aspirin due to major bleeding in their history. Seven patients used a combination of aspirin and P2Y12 inhibitors (Figure 1).

The indication to perform LAAO was stroke under OAC with proper INR in 18 patients. Fifteen patients had a contraindication for OAC (13 bleedings under OAC, 1 at risk of falling, and 1 with unstable INR values). The third group (n = 15) was eligible for OAC but was offered LAAO due to high CHADS2 score and all with a history of stroke with a CHADS2 score ≥2, while in another 14 patients miscellaneous practical reasons from either the physician or patient led to LAAO. These included loss of job in case of OAC use/INR control issues (n = 4: 1 police officer, 1 pilot, 1 businessman who was abroad often, and 1 patient had inadequate variable INR values), and refusal to use OAC (n = 9), while 1 patient wanted to make a journey around the world.

PROCEDURAL AND IN-HOSPITAL RESULTS CHARACTERISTICS. Ablation by PVAC was performed in 44 patients, while additional CFAE ablation by the multiarray septal catheter and multiarray ablation catheters was carried out in the remaining 18 patients with longstanding persistent AF. The mean total procedure time was 99 ± 24 min including a mean 39 ± 11 min for LAAO. At the end of the procedure, 8 patients had accepted minimal residual flow (flow ≤5 mm), while in all other cases complete LAAO was documented on TEE. There were no major, and only 5 minor periprocedural complications: 1 patient developed a small tongue hematoma (likely due to either intubation or TEE probe manipulation), and 4 patients developed a small groin hematoma managed conservatively. All patients were discharged the next day after X-ray confirmation of the Watchman positioned in the LAA (Table 2).

SHORT-TERM 90 DAYS AND LONG-TERM FOLLOW-UP AFTER THE PROCEDURE. TEE data 60 days after the procedure overall successful LAAO 59 (95%) patients (50% complete sealing and 45% minimal residual flow of <5 mm). Flow >5 mm was observed in 2 patients, with asymptomatic device embolization in 1 patient observed after 2 months. Additional imaging showed that the device had embolized to the abdominal aorta, allowing it to be successfully retrieved by an uneventful percutaneous femoral technique.

After a median follow-up of 38 (25 to 45) months, 36 (58.1%) patients (23, 11, and 2 patients with

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<th>TABLE 1 Baseline Characteristics in 62 Patients With the Combined Procedure of AF Ablation and Watchman LAAO</th>
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Values are mean ± SD, n (%), or median (25th to 75th percentile). *According to the Vaughan-Williams classification.

AF = atrial fibrillation; (N)OAC = (novel) oral anticoagulation; LAA = left atrial appendage; VKA = vitamin K antagonist.
paroxysmal, persistent, and longstanding persistent AF, respectively) had neither documented AF recurrences nor symptoms suggestive for AF (Table 3). A redo ablation was performed in 9 patients while 5 patients underwent a (mini)-MAZE surgical procedure. The latter patients had persistent or longstanding persistent AF and severely enlarged left atrium. These reasons including other important factors as informed patient choice, application of ESC guidelines, and results of the FAST (Atrial Fibrillation Catheter Ablation versus Surgical Ablation Treatment) trial (28) led to a surgical procedure rather than a percutaneous one.

During follow-up, 11 of the 62 patients (18%) either remained on, or restarted the use of, (N)OAC due to recurrent AF as determined by their treating physician. In 50 patients who were on (N)OAC before the procedure, 39 were switched to aspirin. Another 9 patients used a combination of aspirin and a P2Y12 inhibitor due to myocardial infarction, or did not use any anticoagulation at all (Table 3).

Two patients died: 1 due to pneumonia with septic shock (while on aspirin) and the other due to extensive multiorgan hemorrhage resulting from Rendu-Osler-Weber (ROW) disease, despite not using any form of anticoagulation.

Three major bleedings were recorded in the follow-up period. The first patient (using aspirin) suffered major bowel bleeding caused by a carcinoma. The second (using no anticoagulation or antiplatelet drug) suffered major bowel bleeding due to ROW disease. The third patient (using aspirin) had major recurrent lung bleeding due to pathological bronchiectasis, which had been the indication for LAAO instead of OAC in the first place.

STROKE DURING FOLLOW-UP. During follow-up, 2 patients had an episode of possible neurological symptoms that were nonwitnessed, without neurological disabilities during physical exam nor signs of neurological damage on computed tomography/magnetic resonance (Table 4).
Three ischemic strokes were observed during the median and mean follow-up periods of 38 and 35 months, respectively, all confirmed by a neurologist. During follow-up, none of these strokes were accompanied by lasting disabilities and full recovery occurred. Interestingly, in 2 patients, the strokes occurred still in the first 4 months after the procedure, 1 of them (with ROW disease) while still even on OAC with an appropriate INR. The third stroke occurred much later—almost 3 years after the procedure. TEE showed complete LAA sealing in 1, and small residual flow <5 mm in the other 2 patients, all without evidence of thrombus on the device. In 1 patient with a history of myocardial infarction resulting in dyskinesia of the left ventricle apex, a new LV apical thrombus was observed on MRI, which could be related to the stroke. Neurological analysis showed that all 3 patients had plaque formation in the carotid arteries, with >50% stenosis in both carotids in 1 patient. Interestingly, 2 of the 3 patients had a compelling contraindication for OAC due to a history of significant and recurrent bleeding, 1 as a result of ROW disease. In 2 of the 3 patients, ECG monitoring documented recurrence of AF, while the last patient was asymptomatic and had no AF documented even on continuous rhythm monitoring by an implantable loop recorder.

There were no hemorrhagic strokes. The real time annual stroke risk for the group was 1.7%, compared to a CHADS2-based expected annual risk of 6.5% (if untreated by OAC). This translates into 74% fewer strokes observed than expected if no anticoagulation would be used.

**Discussion**

To our knowledge, this is the first prospective study of combined LAAO and radiofrequency ablation of AF with a median follow-up of more than 3 years in patients with high stroke risk and/or contraindication(s) for OAC. During follow-up, adequate LAA sealing was achieved in 95% of patients, 58% of patients had neither documented AF recurrence nor symptoms, while 78% of patients could discontinue OAC therapy. The results show that the strategy of ablation and LAAO combined in a single procedure can be performed safely and successfully, with a long-term annual rate of stroke that was 74% lower than expected based on CHADS2 score.

**Efficacy of AF Ablation.** The efficacy of a single ablation procedure ranges from 50% to 60% in general at 1 year (6, 22, 23, 29), to 47% for long-term...
freedom from paroxysmal AF (30). Weerasooriya et al. (31) have shown that success rate decreases dramatically toward 29% after 5 years in patients with mixed types of AF. Although Holter monitoring was not systematically performed, 58% of patients became asymptomatic and had no AF documented on any type of recording during the complete follow-up period. Such a long-term efficacy is in line with the literature, especially given that 37% of our patients had nonparoxysmal AF with significant comorbidity. If anything, in our population the true AF recurrence would be underestimated, which only strengthens the case for indefinite stroke prevention in high-risk patients even after ablation. Finally, there is increasing appreciation that while ablation certainly has a dramatic favorable effect on patient symptoms, freedom from recurrent AF does not assure freedom from cardioembolic events. Despite maintaining sinus rhythm, there remains a high stroke risk in patients with extensive atrial scar related to both/either pre-existing disease progression and/or ablation-related damage (32).

Another LAAO device mainly used in the United States is the LARIAT device (SentreHEART, Inc., Redwood City, California). It relies on elimination of the LAA by an epicardial string around the neck of the appendage. This does not only close the LAA cavity, but may also lead to elimination of electrical activity. This may be beneficial in patients where the LAA is a source for ectopic triggers or part of the AF substrate. Indeed, Di Biase et al. (33) have shown that in a selected patient group with recurrent AF after an initial ablation, 27% showed foci arising from the LAA. Recent data have shown that complete LAAO by LARIAT device resulted in a reduction of AF burden specifically in patients with proven LAA ectopy (34). Whether other LAA devices result in a similar devitalization and arrhythmic effects has not been published so far. There is only 1 study comparing the Watchman device to LARIAT (35). The LARIAT device showed a lower rate of residual leaks at 1-year follow-up, but no significant clinical impact was observed, especially not for cerebrovascular accidents. However, procedural safety may be an issue as a recent systemic review showed a significant amount of serious adverse events consisting of cardiac tamponade and bleeding needing urgent surgery, and even 1 death (36).

### EFFICACY AND SAFETY OF STROKE PREVENTION IN THE COMBINED APPROACH

After the median follow-up of 38 months, 3 ischemic strokes were found, translating into an annualized stroke rate of 1.7%. When compared to the expected CHADS2 calculated annual risk of 6.5% and taking into consideration that most patients were able to discontinue (NOAC) therapy, these real-life data suggest that the combined procedure may significantly reduce the rate of both stroke and bleeding. However, in line with long-term follow-up data of PROTECT-AF (The Watchman Left Atrial Appendage System for Embolic Protection in Patients With AF) and PREVAIL (Prospective randomized evaluation of the Watchman Left Atrial Appendage Closure device in patients with atrial fibrillation versus long-term warfarin therapy) (16,17), neither OAC nor LAAO can completely eradicate strokes. The most recent published 4-year PROTECT-AF data showed significantly lower event rates in the Watchman group versus warfarin group, though the outcome was mainly driven by fewer hemorrhagic strokes and cardiovascular deaths while the stroke rate did not differ (18). In our heterogeneous study population with significant comorbidities and mean age of 68 years, embolic strokes could also have developed from noncardiac origins such as atheromatous plaque in the thoracic aorta or carotid arteries (37,38). Carotid artery echocardiography indeed showed plaque formation or stenosis >50% in the 3 patients that developed stroke during the follow-up period. However, the observed annual stroke rate of 1.7% was still higher than desired after combining an ablation meant to cure AF, and adding LAAO to prevent stroke. In the 3 patients with stroke, no common explanatory denominator was apparent and their CHADS2 score was even fairly low. AF was
documented in the 2 patients with stroke within 4 months of the procedure, while continuous rhythm monitoring with implantable loop recorder showed no AF recurrence in the patient with stroke after 3 years. In 2 patients, sealing was incomplete but still acceptable with <5 mm. Although prior retrospective analysis of the PROTECT-AF trial did not establish a relation between minimal residual flow and thromboembolism (39), this cannot be completely ruled out.

The acute safety profile of the combined procedure was very good, with only 5 minor and no major procedural complications. The few procedural complications observed were not device related but resulted mostly from femoral access. Using a fixed team of skilled implanters with optimal echocardiographic imaging facilitates a good safety record. The benefit of experience is supported by even shorter procedural times compared to our previously published data (20). The fact that 95% of implants showed acute successful LAAO, is also in line with the data published in the PROTECT-AF and PREVAIL trials (16,17). During the follow-up period, 3 device implants did not result in sufficient LAA sealing. Two patients had a malposition of the Watchman with >5 mm residual flow, and OAC therapy was therefore maintained. In 1 patient (the third implant in our center in 2010), asymptomatic device embolization to the abdominal aorta occurred, with uneventful retrieval from the groin.

**STUDY LIMITATIONS.** The population in the study is heterogeneous, including patients with failed OAC, and with bleeding and/or strict contraindication to OAC, but also high stroke risk patients who were included for miscellaneous and/or practical reasons despite eligibility for OAC. This makes the history of these patients highly variable, as well as their ability to use any form of anticoagulation after LAAO. Some patients underwent repeated CA or surgical ablation with LAA removal. This makes it challenging to estimate the expected stroke risk in this population. Although the study population has doubled compared to our first feasibility study (21), the number of patients remains limited. However, the relatively long follow-up time makes the data solid to interpret on key events. Our prospective study is purely observational without a conventional control group. For patients with a contraindication for OAC, such control data are not readily available; such a trial seems ethically problematic. As this was a practical observational trial aiming at proof of principle, there was no systematic long-term rhythm follow-up with Holter or implantable loop recorder to establish freedom from AF. With our strategy we were able to show that at least 42% of patients had recurrence of AF. This may underestimate the absolute recurrence of AF, specifically in asymptomatic patients who were even unwilling to undergo further testing. With the pragmatic strategy we describe the need for the long-term intense rhythm follow-up actually becomes less relevant as patients are protected by their Watchman LAAO. Larger (randomized) trials are needed with more stringent criteria and dedicated arrhythmia detection.

Finally, we cannot rule out asymptomatic cerebral emboli. In early publications (40,41) in small registries it was observed that PVAC ablation was accompanied by a substantially higher rate of asymptomatic cerebral emboli up to 40%. By performing an elaborate root cause analysis in an animal model, Haines et al. (42) observed several possible mechanisms for asymptomatic cerebral emboli including air introduction from the transseptal sheath, and overlap of electrodes 1 and 10 of the array, leading to overheating and coagulum formation. In response, several changes were made to procedure workflow, the generator, and the PVAC array. The ERACE (Evaluation of Reduction of Asymptomatic Cerebral Embolism) trial (43) showed that with adequate INR >2.0 and activated clotting time >350 s, underwater loading of the PVAC to avoid microbubbles, disconnecting either pair 1 or pair 5 of the array to avoid overlap, and using the new GENius CONTACT-IQ generator (Medtronic, Carlsbad, California), resulted in a decrease of asymptomatic cerebral emboli rate to 1.7%, which is on the low end of reported asymptomatic cerebral emboli rates of other techniques.

**CONCLUSIONS**

LAAO combined with ablation for AF can be performed successfully and safely in a single procedure. Long-term follow-up shows a lower than expected stroke rate compared to the expected baseline CHADS2 score. However, this stroke rate is higher than desirable after combined therapy to prevent stroke at both ends. Further studies are needed to illuminate the patient phenotype, which benefits the most from the combined therapy.

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COMPETENCY IN MEDICAL KNOWLEDGE: The 2 competencies describing the best implications of the study for current practice are patient care and medical knowledge. Patient care comprises that the best suitable and effective care is the out-of-the-box combined therapy for the individual patients with severe comorbidity and with symptomatic drug-refractory AF at high risk of bleeding. Sufficient medical knowledge of both therapies would eventually promote health for the specific AF patient with severe comorbidity.

TRANSLATIONAL OUTLOOK: Besides reducing discomfort, the long-term success rate was at least reasonable with 58% of patients with no documented AF recurrence nor symptoms after 38 months of follow-up. Overall, high-risk patients need to remain on OAC even after ablation in line with the Consensus statement by the Heart Rhythm Society/European Heart Rhythm Association/European Cardiac Arrhythmia Society, as we cannot prove that AF is 100% cured, and even long-term recurrence may occur. By adding LAAO in these patients, their thromboembolic risk is effectively reduced without having to continue (N)OAC, which is especially important in those at high risk of (recurrent) bleeding. In the randomized clinical trials PROTECT-AF and PREVAIL trials, Watchman LAAO showed a complication risk of 5% to 20%. Ablation of AF also carries a significant risk of complications of 5% to 10%. Many of these risks are similar, such as groin bleeding, tamponade, and stroke, simply due to the fact that these procedures require access to the left atrium. It is therefore only logical that combining these procedures limits the inherent risks and patient discomfort of 2 separate procedures. Whether this is cost-effective depends on reimbursement policies in each country, actual reduction in stroke, and long-term freedom of AF after ablation. The latter has been found to be lower than expected in studies with long-term rhythm monitoring. Translating our clinical study into care of individual patients with symptomatic drug-refractory AF and high risk of bleeding means that oral anticoagulation can be stopped, regardless of the long-term outcome of ablation for AF.

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KEY WORDS atrial fibrillation, left atrial appendage closure, stroke