Combination of catheter ablation for non-valvular atrial fibrillation and left atrial appendage occlusion in a single procedure

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Abstract. Patients with atrial fibrillation (AF) have an increased risk of stroke and systemic embolism. Catheter ablation (CA) is increasingly applied for the treatment for drug-refractory AF; however, its long-term success rate is <50%. It has been proved that percutaneous left atrial appendage occlusion (LAAO) exerts the same efficacy as novel oral anti-coagulants [(N) OACs] in reducing thromboembolic events. The present study investigated whether a combined procedure of AF ablation and LAAO may be feasible and efficacious. CA was performed for patients with AF and a high risk of stroke according to their $CHADS_2$ or CHA_2DS_2-VASc score, and LAAO was performed using the Watchman device. A total of 25 patients (40% females; mean age, 64.2±3.5 years) who were treated between July 2016 and June 2017 were included in the present study. The median CHA2DS2-VASc score was 4.5 (range, 2-6) and the median HAS-BLED score was 3.17 (range, 1-7). Successful CA and LAAO were performed in 100% of cases. All patients met the criteria for successful LAAO. At the 6-month follow-up, complete sealing of the LAA was achieved in 23 patients (92%), while a minimal residual flow (<5 mm) was detected in 2 patients (8%). In 24 patients (96%), the administration of (N) OACs was terminated and aspirin administration was initiated at the 6-month follow-up. (N)OAC treatment was maintained in 1 patient (4%) on the basis of transient ischemic attack. During the 6-month follow-up period, 3 patients who had a recurrence of AF received a repeated ablation. In conclusion, the combination of CA and LAAO in a single procedure is feasible, safe and efficacious for patients with non-valvular AF at a high risk of stroke, and a contraindication regarding the use of (N)OACs.

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Introduction

As a common type of arrhythmia, atrial fibrillation (AF) occurs in 1-2% of individuals (1-3). In patients with non-valvular AF, the risk of ischemic stroke and systemic embolism is 5-fold increased compared with that in the general population (4), leading to a yearly incidence of ischemic stroke of 5% in patients with non-valvular AF and 15% in high-risk patients (5). In patients with AF, stroke is mainly caused by atrial thrombi formed in the left atrial appendage (LAA), and according to a previous study, ~90% of the thrombi formed in patients with AF were arising from the LAA (6). According to the European Society of Cardiology (ESC) guidelines, all AF patients with a high risk of thrombosis are required to take oral anti-coagulants (OACs) to prevent thromboembolic events (7). Although it is well established that patients with AF at a high risk of stroke benefit from warfarin or the recently introduced novel (N)OACs, these medications have several disadvantages, including severe hemorrhage and non-compliance (8-10). While catheter ablation (CA) for the treatment of AF is recommended by the 2016 ESC guidelines and is efficacious in rhythm control, its long-term efficacy is poor, and its role in stroke prevention remains unproven. Randomized clinical trials have demonstrated that percutaneous mechanical LAA occlusion (LAAO) is effective in preventing thromboembolism in AF patients (11-13). Combining CA and LAAO in a single procedure is an efficacious strategy for the treatment of patients at high risk of stroke. The present study reported on the rationale and feasibility of the technique of combining of CA and percutaneous LAAO in a single procedure, which is a novel procedure compared to various previous approaches, providing an optimized surgical route.

Materials and methods

Study group. Patients aged ≥18 years with documented paroxysmal or (longstanding) persistent, non-valvular AF, a $CHADS_2$ score (14) of ≥1 and/or a CHA_2DS_2-VASc score (15) ≥2, a HAS-BLED score (16) ≥1, who were subjected to CA and percutaneous LAAO in a single procedure at Yantai Yuhuangding Hospital (Yantai, China) between July 2016 and June 2017 were included in the present study (Table I).

Written informed consent was obtained from all participants included in the study. The Ethics Committee of Yantai Yuhuangding Hospital (Yantai, China) approved the protocol of the present study.

Pre-procedure preparation. Patients with an international normalized ratio of 2.0-3.0 were required to take vitamin K antagonist prior to the procedure or to take (N)OACs, which was discontinued from the day of the procedure. Prior to the procedure, a transesophageal echocardiogram (TEE) was recorded to exclude thrombi within the LAA, assess the anatomy of the LAA and to determine the appropriate occlusion device size (Fig. 1). All of the procedures were performed without general anesthesia.

Electrophysiological and CA procedure in AF patients. Local anesthesia was performed by administration of lidocaine in the groin and left subclavian region, and fentanyl was given as an analgesic. Through the left subclavian venous access, a decapolar catheter was placed in the coronary vein. Two transseptal punctures were performed through the right femoral vein using a Brockenbrough (BRK) needle (Baylis Medical Company Inc., Sainy-Laurent, Canada) to ensure co-axial alignment with the appendage. One inferior and posterior transseptal puncture was required. An unfractioned heparin bolus of 7,500 international units (IU) was given after transseptal puncture, and thereafter 1,000 IU were administered at 1-h intervals. Angiography of LAA and pulmonary veins (PVs) was performed via the sheath. A circular mapping catheter (Lasso NAV; Biosense Webster; Johnson & Johnson, New Brunswick, NJ, USA) was used to map PV potentials and construct the model of the left atrium and PVs. PV isolation was guided by a 3-dimensional mapping system (CARTO3 system; Biosense Webster; Johnson & Johnson) and performed point-by-point using a ThermoCool Smart Touch Catheter (Biosense Webster; Johnson & Johnson) with the power and temperature limited to 30-35 W and 43˚C, respectively. Bidirectional conduction block between the LA and PVs was the end-point of catheter ablation. Only PV isolation was performed for patients with paroxysmal AF. A roofline was also performed for patients with persistent AF (Fig. 2).

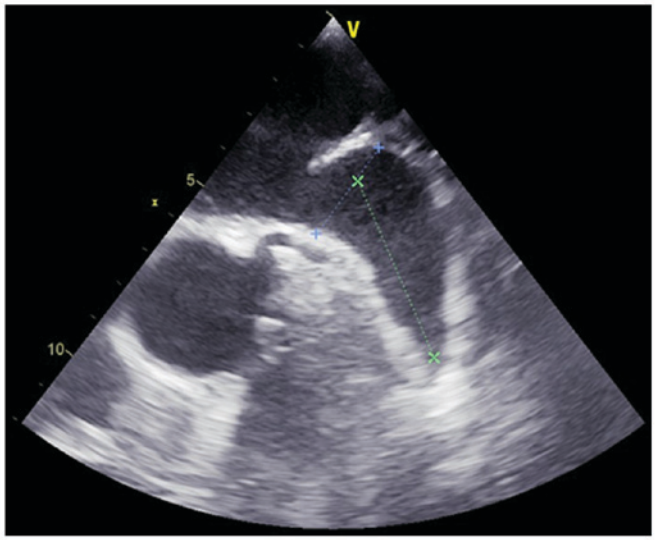

Figure 1. Transesophageal echocardiogram of the LAA to document the absence of thrombi within the LAA and to assess features and type of LAA. LAA, left atrial appendage.

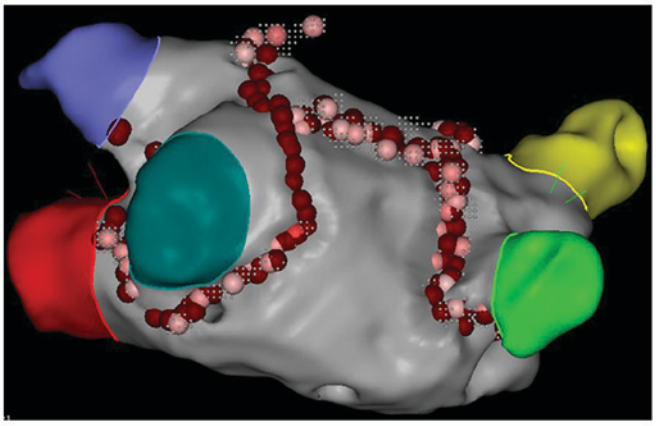

Figure 2. Schematic of the atrial fibrillation ablation. Electrophysiological and atrial fibrillation catheter ablation procedure visualized using Carto 3. Gray represents the left atrium, green, yellow and purple represent pulmonary veins and red represents the left atrial appendage.

LAAO with Watchman device. Immediately after the ablation procedure, the implantation of a Watchman device was performed by using fluoroscopy and TEE guidance.

Cefazolin sodium pentahydrate was administered as a prophylactic antibiotic at the end of the ablation procedure. A Watchman device (Boston Scientific, Marlborough, MA, USA) was then implanted using the following procedure: A 14F transseptal access sheath for delivering the pigtail catheter replaced the more inferior and posterior transseptal sheath. A pigtail catheter was positioned in the LAA to perform an angiography of the LAA at a right anterior oblique angle of 20-30° and a caudal angle 20-30°, delineating the shape and size of the LAA (Fig. 3). The device size was selected to be 10-20% larger than the largest diameter of the LAA measured by angiography and TEE guidance was applied for stable positioning.

The access sheath for delivering the Watchman device was carefully advanced over the pigtail catheter. The pigtail was then slowly removed. The device was deployed by retraction of the access sheath. Before the device was released, it was ensured that it was properly positioned, with minimal (leak of ≤5 mm) or no residual lateral flow past the device (confirmed by angiography and TEE; Fig. 4), and a sustained tug test for stability was performed.

Statistical analysis. The patients' characteristics were reported by descriptive statistics. The results were expressed as the mean ± standard deviation or the median (25-75th percentiles). Categorical variables were reported as n (%). All statistical data were analyzed by using SPSS software 19.0 (IBM Corp., Armonk, NY, USA).

Results

Between July 2016 and June 2017, all 25 patients (40% females; mean age, 64.2±3.5 years) successfully underwent a

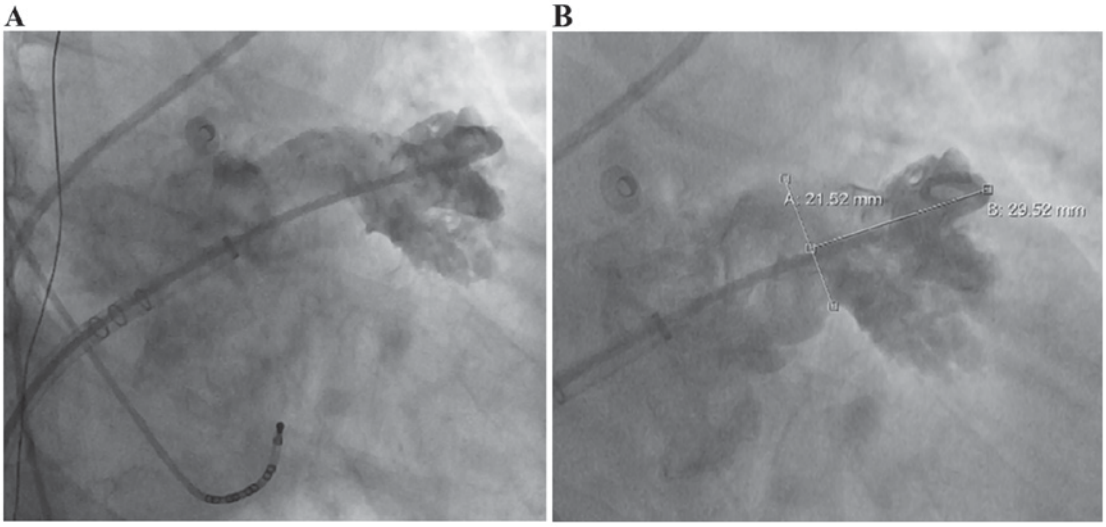

Figure 3. Angiogram and measurements of the LAA. (A) Angiogram of the LAA at a right anterior oblique of 30˚ and caudal 20˚. (B) Angiographic measurements of the length and width of the LAA for the selection of an appropriately sized Watchman device. LAA, left atrial appendage.

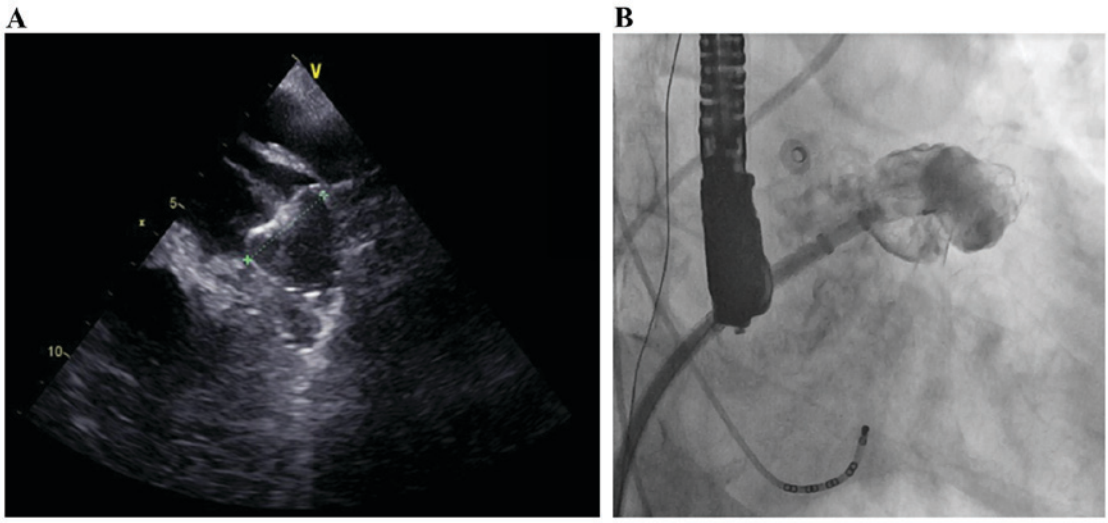

Figure 4. Evaluation of the LAA following Watchman deployment. (A) Echocardiographic evaluation of the LAA. (B) Immediate follow-up angiogram of the LAA after left atrial occlusion using a Watchman device. LAA, left atrial appendage.

combination of CA and LAA occlusion with Watchman device (short-term success rate, 100%). In 1 patient, due to the large residual lateral flow (leak of >5 mm), the device required replacing with a larger-diameter one, which was successfully deployed in this second procedure. The LAAO procedure was therefore completed using a mean of 1.04±0.20 devices per patient in the present cohort. After implantation, 3 patients had a small peri-device leak (≤5 mm), while complete closure of the LAA was achieved in all other cases. The median time for the combined procedure was 185.58 min (85.67 min for LAAO; Table II). No serious complications occurred during the procedure, and afterwards, only 2 patients had minor complications, including a slightly elevated temperature and a small groin hematoma, and no intervention was performed. No serious peri-procedural complications, including cardiac tamponade, dislodgement of the LAA closure, thrombus formation on the Watchman device and coronary artery air embolism occurred in any of the patients.

On the day after the procedure, all patients were discharged from hospital (Table III). The median hospital stay was 7.67 days (range, 2-13 days).

Follow-up. All of the 25 patients (100%) underwent TEE at 60 days after the procedure and an optimal sealing performance of the LAA was observed in 92% of the cases. Complete sealing of the LAA was achieved in 23 patients (92%) at the 6-month follow-up. A minimal residual flow (leak size, <5 mm) was detected in 2 patients (8%). In 24 patients (96%), the administration of (N)OACs was discontinued and aspirin treatment was initiated at the 6-month follow-up. (N)OACs treatment was maintained in 1 patient (4%) on the basis of transient ischemic attack (Table IV). During the 6-month follow-up, 3 patients who had a recurrence of AF received a repeated ablation. In this second ablation, the Watchman device was stable and did not interfere with the procedure. Furthermore, no thrombus formation on the device was detected during the follow-up. Prior to

Table I. Baseline characteristics of the study population (n=25).

Characteristics	Value
Mean age (years)	64.2±3.5
Females	10 (40)
Hypertension	18 (72)
Type of AF	
Paroxysmal	3 (12)
Persistent	8 (32)
Long-standing persistent	14 (56)
CHADS2 score	
1	0 (0)
2	3 (12)
3	8 (32)
4	11 (44)
5	3 (12)
CHA2DS2-VASc score	4.5 (2-6)
HAS-BLED score	3.17 (1-7)
Drug use	
Vitamin K antagonist	14 (56)
NOAC	9 (36)
Aspirin	2 (8)
Stroke during use of (N)OAC	19 (76)

Values are expressed as the mean ± standard deviation, n (%) or the median (25-75th percentiles). AF, atrial fibrillation; NOAC, novel oral anti-coagulant.

Table II. Procedural characteristics in the study population (n=25).

Characteristics	Value
Successful implantation of LAA occlusion device	25 (100)
LAA measurements (mm)	
Width	28.76 (21.4-31.9)
Length	30.98 (26.29-34.1)
Morphology type of LAA	
Chicken wing	5 (20)
Cauliflower	14 (56)
Wind sock	6 (24)
Device size (mm)	
27	4 (16)
30	14 (56)
33	7 (28)
LAA occlusion time (min)	85.67 (60-120)
Total procedural time (min)	185.58 (123-295)
Total contrast dose (ml)	162 (80-260)
Mean no. of devices deployed per patient	1.04±0.20
Hospitalization time (days)	7.67 (2-13)

Values are expressed as n (%) or the median (25-75th percentiles). LAA, left atrial appendage.

the paper being finished, a 1-year follow-up was performed for 18 patients (Table V). During the 1-year follow-up, 17 patients (95%) achieved a complete sealing and only 1 patient (5%) had minimal residual flow (<2 mm). The NOACs was interrupted in all patients and aspirin was taken. No mortality, stroke or transient ischemic events occurred. A total of 4 patients (22%) who had a recurrence of AF received a redo-ablation successfully.

Discussion

The present study reports that the combination of LAAO and CA is a feasible and safe strategy for the treatment of AF in patients at high risk of stroke.

The Watchman device has been proved to be safe and effective in numerous randomized clinical trials. A previous multicenter randomized clinical trial, the 'PROETCT AF' trial, evaluated the efficacy and safety of LAAO with a Watchman device compared with warfarin treatment (17). This trial reported that LAAO with the Watchman device was not inferior compared with standard warfarin therapy in patients with non-valvular AF.

Furthermore, the 'PREVAIL' trial (18) proved that compared with the PROETCT AF study, complications associated with the LAAO procedure were infrequent, providing a significant improvement. The PREVAIL trial also indicated that LAAO with the Watchman device for the prevention of stroke was not inferior to standard warfarin therapy.

Alli *et al* (19), performed a quality of life (QOL) assessment in the cohort of the PROTECT AF trial, revealing that in non-valvular AF patients treated with LAAO with the Watchman device, the QOL was improved compared to that in patients treated with warfarin.

CA is a well-established treatment to prevent recurrent AF (20,21), and in maintaining the sinus rhythm, it is more effective, while the complication rate is similar compared with that associated with anti-arrhythmic drugs (22,23). The optimal surgical outcome for CA is complete bidirectional conduction block between the LA and PVs (24-26), which is achieved by lesions encircling PVs caused by radiofrequency ablation or cryoballoon ablation (27,28). Reynolds *et al* (29) reported that the risk of stroke and transient ischemic attack is decreased more significantly in patients treated with ablation than in those receiving anti-arrhythmic drug therapy. The efficacy of the hybrid procedure of CA and LAAO with the Watchman device to maintain the sinus rhythm and prevent stroke in patients with AF is supported by the data of previous studies (30,31). Certain studies reasoned that the longer duration of the procedure and fluoroscopy, as well as the application of general anesthesia are disadvantages of the combined procedure (30,32). In the present study, all of the procedures were performed under local anesthesia for the first time. In the present cohort, the Watchman device was successfully implanted in 96% of patients under local anesthesia on the first attempt.

Apart from the abovementioned limited single-center studies, a consensus statement from the European Heart Rhythm Association/European Association of Percutaneous

Table III. Procedure-associated complications and post-procedure TEE results.

Characteristics	Value
Complications	
Catheter thrombus	0 (0)
Hematoma	1 (4)
Pericardial effusion	0 (0)
Post-procedure TEE observations	
Successful implantation	25 (100)
Minimal residual flow	3 (12)
Hospitalization time (days)	7.67 (2-13)

Values are expressed as n (%) or the median (25-75th percentiles). LAA, left atrial appendage; TEE, transesophageal echocardiography.

Table IV. Characteristics of the patients (n=25) at 6-month follow-up.

Characteristics	Value
TEE observations	
Minimal residual flow	2 (8)
Device embolism	0 (0)
Thrombus on device	0 (0)
No atrial fibrillation recurrent	11 (44)
(N)OAC use	1 (4)
Repeated ablation	2 (12)
Complications during follow-up	
Stroke	0 (0)
Transient ischemic attack	1 (4)
Major bleeding	0 (0)

Values are expressed as n (%). TEE, transesophageal echocardiography; (N)OAC, novel oral anti-coagulant.

Cardiovascular Interventions (33) suggests that the hybrid procedure of CA and LAAO is beneficial for patients with a contraindication for OACs and a high risk of thromboembolic events.

The feasibility and techniques of combining CA and LAAO with the Watchman device in a single procedure have been reported by few studies (30,31). The avoidance of a second vascular access and transseptal puncture may make the combined strategy safer. It is important to note that a combined procedure of Watchman placement and CA does not interfere with the electrical isolation of the LAA. Di Biase *et al* (34) revealed that in 27% of patients with recurrent AF after initial ablation, foci arising from the LAA were observed, and electrical isolation of the LAA should ideally be performed in these patients. LAA may be more thrombogenic due to LAA stasis caused by electrical isolation of the LAA. LAAO may be particularly beneficial for these patients.

Table V. Characteristics at 1-year follow-up (n=18).

Characteristics	Value
TEE observations	
Minimal residual flow	1 (5)
Device embolism	0 (0)
Thrombus on device	0 (0)
No atrial fibrillation recurrent	9 (50)
(N)OAC use	0 (0)
Redo ablation	4 (22)

No causes of mortality, stroke, transient ischemic attack or major bleeding occurred. Values are expressed as n (%). TEE, transesophageal echocardiography; (N)OAC, novel oral anti-coagulant.

In the present study, 100.0% of the patients had a successful occlusion, and 12.0% (3/25) had small residual leak immediately after the release of the device. During the 6-months follow-up, the stroke rate in the present study was 0. However, 1 patient had a transient ischemic attack at 3 months after the procedure. Device-associated thrombus formation remains a concern, but was not observed in the present study. A limitation of the present study is that there is no other treatment that the group was compared with.

In conclusion, the present study indicated that combination of CA and LAAO in a single procedure is feasible, safe and efficacious for patients with non-valvular AF at a high risk of stroke, and a contraindication regarding the use of (N)OACs.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

XL and JL contributed to the conception and design of the study and wrote this manuscript. HC, LW and LS collected and analyzed clinical data. GW and XW contributed to the patient follow-ups and revised the manuscript for intellectual content. The final version of the manuscript has been read and approved by all authors, and each author believes that the manuscript represents honest work.

Ethical approval and consent to participate

Written informed consent was obtained from all participants included in the study. The Ethics Committee of Yantai

Yuhuangding Hospital (Yantai, China) approved the protocol of the present study.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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