One-stop strategy for treatment of atrial fibrillation: feasibility and safety of combining catheter ablation and left atrial appendage closure in a single procedure

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Abstract
Background: Catheter ablation is effective in restoring sinus rhythm and left atrial appendage closure (LAAC) is increasingly used for stroke prevention in patients with atrial fibrillation (AF). We aimed to observe the feasibility and safety of performing AF ablation and LAAC in a single (one-stop) procedure.

Methods: Consecutive AF patients who underwent the combined procedure of AF ablation and LAAC with WATCHMAN device between March 2017 and September 2018 were prospectively enrolled. Baseline and intra-procedural parameters were evaluated. Three-month and subsequent 1-year follow-up were performed in all and earlier-enrolled subjects, respectively.

Results: A total of 178 AF patients (94 males, 68.9 ± 8.1 years) underwent the one-stop procedure with CHA2DS2-VASc score 3.3 ± 1.5 and HAS-BLED score 1.6 ± 1.0, respectively. Pulmonary vein isolation was achieved in all patients while additional linear ablation was applied if the operator deemed necessary, yielding immediate ablation success rate of 98.9% (176/178). In the subsequent LAAC, satisfactory seal (residual leak < 5 mm) was achieved in all patients. One stroke and four cardiac perforations occurred peri-operatively. At 3-month follow-up, sinus rhythm and satisfactory seal were maintained in 153/178 (86.0%) and 178/178 (100%) patients, respectively. One stroke and one delayed cardiac tamponade occurred, while no device-related thrombus or device migration was observed. During the 1-year follow-up for the earlier enrolled subjects, 52/72 (72.2%) of the patients maintained sinus rhythm. There was no stroke or systemic embolism observed.

Conclusion: Combining catheter ablation and LAAC in a single procedure can be successfully and safely performed in non-valvular AF patients of Chinese population.

Keywords: Atrial fibrillation; Left atrial appendage closure; Catheter ablation; Stroke; WATCHMAN; One-stop procedure

Introduction
While catheter ablation of atrial fibrillation (AF) is effective in arrhythmic burden reduction and life quality improvement,[1-3] AF ablation per se has limited preventive effect on stroke and systematic embolism in the long-term follow-up, suggesting a need for post-ablation anti-coagulation in patients with high stroke risks.[6-8] However, a number of patients could not tolerate oral anti-coagulation (OAC) due to high bleeding risks or unwilling to receive long-term pharmacologic therapy.[9,10] Under such circumstances, left atrial appendage (LAA) closure (LAAC) has recently emerged as an acceptable non-pharmacologic approach for stroke prevention in non-valvular AF patients.[11-13] Clinical trials and real-world registries have demonstrated that LAAC with WATCHMAN device is comparable to warfarin in stroke prevention and may provide additional reduction in major bleeding and mortality.[14,15]

Combining catheter ablation for AF and LAAC in a single (one-stop) procedure has raised increasing attention recently. The rationale of the combined strategy is based on several shared operative approaches, including femoral venous catheterization, trans-septal puncture and peri-operative management. Despite previous studies reported promising results,[16,17] very limited Chinese population were included in those patient series. In the present study, we sought to address the safety and efficacy of the one-stop procedure in AF patients of Chinese population.
Methods

Ethical approval
This study was approved by the ethics board of Xinhua Hospital, Shanghai, China. Patients signed an informed written consent form.

Study population
We prospectively enrolled 178 Chinese patients with symptomatic drug-refractory AF who underwent catheter ablation and LAAC in a single procedure between March 2017 and September 2018 in Xinhua Hospital, School of Medicine, Shanghai Jiao Tong University, China. We included the patients who met the following criteria: (1) paroxysmal or persistent AF with electrocardiogram evidence; (2) between 18 and 85 years of age; (3) with contraindications or unwillingness to receive long-term OACs; and (4) signed informed consents. We excluded patients with severe valvular heart diseases and hyperthyroidism.

One-stop procedure
After admission, patients discontinued anti-arrhythmic and anti-thrombotic medications and were bridged with low-molecular-weight heparin. Patients with symptomatic rapid ventricular rates during AF were allowed to use β-blockers. After the evaluation of medical history and demographic characteristics, patients were subject to pre-operative examinations, including laboratory tests, thoracic echocardiography (TTE) and cardiac computed tomography (CT). Trans-esophageal echocardiography (TEE) was performed within 48 h prior to the procedure to exclude LAA thrombus.

Patients underwent successive catheter ablation of AF and LAAC. Standard pulmonary vein isolation was performed in all patients. Additional linear ablation was performed if the operator deemed necessary. The CARTO (Johnson & Johnson Medical, Irvine, CA, USA) or ENSITE (St. Jude Medical, Little Canada, MN, USA) electro-anatomical mapping systems were used for left atrial reconstruction and the guidance of AF ablation, with near-zero fluoroscopy approaches. Disappearance of pulmonary vein potential and bidirectional block of the ablation circles or lines were verified as the endpoint of ablation.

After AF ablation, LAAC was subsequently performed. WATCHMAN device (Boston Scientific Corporation, Natick, MA, USA) was implanted as previously described. The device size was selected according to the LAA angiography. The device was released only if PASS (Position-Anchor-Size-Seal) principle was fulfilled. Immediate intra-procedural TEE and/or angiography were further performed to re-verify the appropriate implantation of the device.

Post-operative management
The vital signs and post-operative complications were monitored, including cardiac perforation, bleeding, stroke, and femoral vascular access-site complications. Within 24-h post-operative period, all subjects received normal heparin unless with contraindications. Patients received either warfarin or novel oral anti-coagulants at the physician’s discretion at discharge.

Follow-up
Patients were followed-up at 3 months post-procedure. Holter monitoring and electrocardiogram were generally advised to detect any AF recurrence. N-terminal pro-B-type natriuretic peptide (NT-proBNP) and TTE were advised to evaluate the potential heart failure amelioration and cardiac reverse remodeling if the physician deemed necessary. TEE and/or cardiac CT were repeated for detection of peri-device leak and device-related thrombus. Patients with satisfactory seal (defined as jet size < 5 mm by TEE) were recommended to discontinue anti-coagulation and switch to anti-platelet therapy (aspirin 100 mg + clopidogrel 75 mg) until 6 months post-procedure, or at the discretion of the physicians. If unsatisfactory seal or device-related thrombus was detected, OAC was continued until satisfactory seal was achieved by the evaluation of TEE repeated every 3 months. For the earlier cases enrolled before March 2018, 1-year follow-up was performed to detect serious adverse events.

Statistics
Statistics were performed using SPSS 23.0 (IBM, Armonk, NY, USA). Continuous variables are presented as mean ± standard deviation and categorical variables as counts and percentages, unless mentioned specifically. The Kaplan-Meier method was used to describe rates of serious adverse events at follow-up. Paired Student t tests were used to compare variables obtained at two time points from the same subject. A two-sided P value < 0.05 was considered statistically significant.

Results

Demographics
A total of 178 AF patients (94 males and 84 females) were consecutively enrolled. All patients underwent the first-time attempt for LAAC device implantation. Redo procedure for AF ablation was performed in 11 patients. The mean CHA2DS2-VASc score and HAS-BLED score were 3.3 ± 1.5 and 1.6 ± 1.0, respectively. The primary AF pattern was persistent AF in 50.6% (90/178). Prior to the admission, patients were on anti-coagulation (78/178, 43.8%), anti-platelet (36/178, 20.2%) or not on any anti-thrombotic medication (64/178, 36.0%). The detailed demographics are listed in Table 1.

Procedural success
As shown in Table 2, ablation endpoint for pulmonary vein isolation with or without additional linear ablation was achieved in all patients, with immediate conversion to sinus rhythm in 176 patients (98.9%). Satisfactory seal (leak < 5 mm) was achieved in all patients with an attempt of a median number of one device. Minimal peri-device leak (< 5 mm) was observed in eight cases. The most frequently and infrequently selected device sizes were 27 mm (62/178, 34.8%) and 21 mm (8/178, 4.5%), respectively. Cauliflower-
er is the primary LAA morphology (139/178, 78.1%), followed by chicken wing (33/178, 18.5%), windsock (7/178, 3.9%), cactus (2/178, 1.1%), and reversed chicken wing (2/178, 1.1%). Additional peri-operative information is listed in Table 2.

Peri-operative complications

During the peri-operative period, one (0.6%) stroke occurred at 22 h post-procedure and was managed properly [patient 1 in Table 3, Figure 1A]. Four (2.2%) cases of cardiac perforation occurred and were resolved by pericardiocentesis. There was no peri-procedural coronary air embolism, device embolization, or death [Table 4].

Three-month follow-up

All patients completed 3-month follow-up. Sinus rhythm was maintained in 153 (86%) patients while AF recurrence was detected in 25 (14%) cases. The follow-up TEE found no major peri-device leak (>5 mm) and eight minimal residual leaks (<5 mm), including one new and seven persisting leaks. There was no device-related thrombus or prominent device migration. One stroke [patient 2 in Table 3 and Figure 1B] was observed in a 75-year female at 28 days post-procedure.

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Table 1: Demographic and baseline characteristics of the 178 AF patients receiving the combined procedure of ablation and left atrial appendage closure.

| Items                              | Results          |
|------------------------------------|------------------|
| Male                               | 94 (52.8)        |
| Age (years)                        | 68.9 ± 8.1       |
| AF types                           |                  |
| Paroxysmal AF                      | 88 (49.4)        |
| Persistent AF                      | 90 (50.6)        |
| CHA2DS2-VASc score                 | 3.3 ± 1.5        |
| HAS-BLED score                     | 1.6 ± 1.0        |
| Comorbidities                      |                  |
| Hypertension                       | 129 (72.5)       |
| Diabetes                           | 39 (21.9)        |
| Stroke/transient ischemic attack   | 50 (28.1)        |
| Periphery artery disease           | 16 (9.0)         |
| Smoking                            | 52 (29.2)        |
| N-terminal pro-B-type natriuretic peptide (pg/ml) | 1011.5 ± 1171.7 |
| Left ventricular ejection fraction (%) | 64.0 ± 5.9    |
| Left atrial diameter (mm)          | 42.5 ± 5.6       |
| Left ventricular diastolic diameter (%) | 50.3 ± 4.0   |
| NYHA classification                |                  |
| I                                  | 97 (54.5)        |
| II                                 | 57 (32.0)        |
| III                                | 23 (12.9)        |
| IV                                 | 1 (0.6)          |
| Anti-thrombotic drugs              |                  |
| Warfarin                           | 60 (33.7)        |
| Dabigatran                         | 10 (5.6)         |
| Rivaroxaban                        | 8 (4.5)          |
| Aspirin/ clopidogrel               | 36 (20.2)        |
| Not on long-term antithrombotic medication | 64 (36.0)       |
| Anti-arrhythmic drugs              |                  |
| Amiodarone                         | 25 (14.0)        |
| Propafenone                        | 13 (7.3)         |
| β-Blocker                          | 72 (40.4)        |
| Digoxin                            | 8 (4.5)          |
| ACEI/ARB                           | 78 (43.8)        |
| Statins                            | 53 (29.8)        |
| Diuretics                          | 28 (15.7)        |

Data are presented as mean ± standard deviation or counts and percentages. AF: Atrial fibrillation; NYHA: New York Heart Association; ACEI: Angiotensin converting enzyme inhibitor; ARB: Angiotensin II receptor blockers; CHA2DS2-VASc: congestive heart failure, hypertension, age ≥75 [doubled], diabetes, stroke [doubled], vascular disease, age 65 to 74, and sex category [female]; HAS-BLED: hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile INR [doubled], elderly [age ≥65 years], drugs/alcohol concomitantly.

Table 2: Procedure-related characteristics in 178 atrial fibrillation patients receiving the combined procedure of ablation and left atrial appendage closure.

| Characteristics                        | Results          |
|----------------------------------------|------------------|
| Mapping system                         |                  |
| Carto                                  | 79 (44.4)        |
| Ensite                                 | 99 (55.6)        |
| Intra-procedural conversion to sinus rhythm | 176 (98.9)    |
| PVI                                    | 88 (49.4)        |
| PVI + linear ablation                  | 90 (50.6)        |
| LAA morphology                         |                  |
| Cauliflower                           | 139 (78.1)       |
| Chicken wing                           | 33 (18.5)        |
| Windsock                               | 7 (3.9)          |
| Cactus                                 | 2 (1.1)          |
| Reversed chicken wing                  | 2 (1.1)          |
| LAA ostial width (mm)                  | 22.9 ± 3.3       |
| Device size selection (mm)             |                  |
| 21                                     | 8 (4.5)          |
| 24                                     | 26 (14.6)        |
| 27                                     | 62 (34.8)        |
| 30                                     | 36 (20.2)        |
| 33                                     | 46 (25.8)        |
| Median number of device per procedure  | 1                |
| No residual flow after occlusion       | 170 (95.5)       |
| Residual leak <5 mm                    | 8 (4.5)          |
| Residual leak >5 mm                    | 0                |
| Duration of hospitalization (days)     | 5.2 ± 2.9        |
| Anti-coagulation at discharge          |                  |
| Warfarin                              | 127 (67.4)       |
| Dabigatran                            | 35 (19.7)        |
| Rivaroxaban                           | 23 (12.9)        |
| Additional anti-platelet therapy      | 8 (4.5)          |
| Post-procedural use of anti-arrhythmic drugs |        |
| Amiodarone                            | 140 (78.7)       |
| Propafenone                           | 11 (6.2)         |
| β-Blocker                             | 68 (38.2)        |
| Digoxin                               | 4 (2.2)          |
| Post-procedural use of ACEI/ARB       | 93 (52.2)        |
| Post-procedural use of statins        | 73 (41.0)        |
| Post-procedural use of diuretics      | 45 (25.3)        |

Data are presented as mean ± standard deviation or counts and percentages. PVI: Pulmonary vein isolation; LAA: Left atrial appendage; ACEI: Angiotensin converting enzyme inhibitor; ARB: Angiotensin II receptor blockers.

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The patient had a TEE-detected LAA thrombus 2 years ago and started warfarin thereafter. However, she failed to maintain stable international normalized ratio (ranging from 1.3 to 6.2) and the pre-procedural TEE revealed moderate spontaneous echo contrast (smoke). The patient restarted warfarin and was on warfarin with international normalized ratio 2.6 when stroke happened. One case of delayed cardiac tamponade occurred. There was no death during the 3-month follow-up (Table 5).

Table 3: Two cases of stroke after the procedure in 178 atrial fibrillation patients receiving the combined procedure of ablation and left atrial appendage closure.

| Patient | Sex | Age (years) | CHA2DS2-VASc | Pre-procedural TEE | LAA morphology | Intra-procedural TEE | Time of stroke | Anti-coagulation when stroke | Heart rhythm | Stroke lesion |
|---------|-----|-------------|--------------|-------------------|----------------|----------------------|----------------|-------------------------------|--------------|--------------|
| 1       | Female | 84         | 6            | No smoke          | Cauliflower     | No leak              | 22 h           | Intra-venous heparin           | Sinus rhythm | Right cerebellum             |
| 2       | Female | 75         | 5            | Moderate smoke (thrombus 2 years ago) | Reversed chicken wing | No leak | 29 days | Warfarin | Atrial fibrillation | Right cerebellum |

TEE: Trans-esophageal echocardiography; LAA: Left atrial appendage; INR: International normalized ratios.
One-year follow-up
For patients (n = 101) underwent the procedure before March 2018, 72 patients were able to be followed for 1 year. Sinus rhythm was maintained in 52 (72.2%) patients. Redo ablation was performed in six patients with uncontrolled recurrent AF. Repeated TEE at 1 year was available in 4/6 patients with minimal residual peri-device leaks at 3 months, which detected a persisting leak in one patient. One gastrointestinal bleeding was observed on aspirin therapy. No stroke or other procedure-related complication was observed. One patient died due to stomach cancer.

Cardiac remodeling
The levels of NT-proBNP were significantly reduced at 3 months and 1 year follow-up, compared with those at baseline [Figure 2]. However, significant difference was not achieved in echocardiographic parameters, including left ventricular ejection fraction, left atrial diameter, and left ventricular end-diastolic and end-systolic diameters.

Discussion
Although the safety and effectiveness of AF ablation and LAAC in separate procedures have been elucidated, the concomitant performance of these two procedures remains controversial. Since both ablation and LAAC are associated with several procedure-related complications,[21,22] the major drawback of the one-stop strategy could be represented by the concerning of potentially increased peri-operative risks. In the present study, the rate of peri-procedural stroke and cardiac perforations were 2.2% and 0.6%, respectively, without any other major cardiovascular events or death. The low complication incidence, which was in consistency with the previous studies,[18,19,23,24] suggests no additional peri-procedural risks induced by the combined strategy. Another concern about the one-stop strategy is that the post-ablation atrial edema and stunning might mislead the device size selection, resulting in long-term peri-device leak and device migration. In the present study, satisfactory LAA seal was achieved intra-procedurally and at 3-month follow-up, which was comparable to the successful rates reported by previous studies.[18,19] Our results reinforce the concept that the one-stop procedure does not necessarily increase procedure-related complications or impair the success rate of both ablation and LAAC.

Compared with the previous investigation of the one-stop procedure,[17] the present study had larger cohort (178 vs. 139 cases), older patient ages (68.9 vs. 64.1 years) and longer follow-up period (1 year vs. 30 days). To the best of our knowledge, this was the largest cohort of the one-stop procedure in Chinese population. In the previous study, no post-operative stroke was observed during the 30 days of follow-up.[17] However, we observed two cases of strokes in the first month post-procedure. Both patients showed no peri-device leak in the intra-procedural TEE and were on oral anti-coagulants when strokes occurred. Of note, the lesions of both cases were at the right cerebellum. During the extended 1-year follow-up, no stroke or systemic embolism was further observed, suggesting the post-LAAC strokes might be likely to occur in the first month.

Previous literature reported opposite effects on left atrial volume changes between AF ablation and LAAC,[25,26]
that AF ablation led to decreased left atrial volume (reverse remodeling) while LAAC induced left atrial enlargement (remodeling). Therefore, LAAC with concomitant ablation might benefit patients by reversing LAAC-induced left atrial remodeling, which was supported by our previous study using cardiac CT-based evaluation. However, the reverse remodeling has not been detected by the TTE follow-up in the present study. This discrepancy might be due to the limited reproducibility and intra- and inter-operator’s variability among echocardiographic tests. Additionally, the reverse remodeling might be a long-term process which requires further follow-up. Nevertheless, NT-proBNP was significantly decreased after the procedure, suggesting heart failure alleviation.

We routinely performed LAAC after catheter ablation due to the following considerations. Firstly, the device might challenge the catheter manipulation and tissue contact at the crista of left pulmonary veins. Secondly, the device implantation makes arrhythmogenic foci within or at the base of LAA inaccessible by the catheter. In addition, catheter might potentially damage, dislodge and be entrapped by the device. Despite a previous study reporting similar outcomes as to performing ablation first or LAAC first, we recommend performing ablation prior to LAAC.

In the present study, cauliflower type is the predominant LAA morphology, which has been shown to be associated with highest stroke risk among all morphologies. In contrast, a study from the United States reported chicken wing type as the most common LAA morphology. Racial differences as well as selective bias might contribute to the discrepancy which needs further verification.

In addition, the one-stop procedure might be more cost-effective. It is estimated that the one-stop procedure might reduce the hospitalization cost by 20,000 RMB per patient than performing AF ablation and LAAC separately. The one-stop strategy also reduces the hospital stay by 3.5 days compared with performing ablation and LAAC in separate hospitalizations.

Limitations

First, since only WATCHMAN was used in this study, the feasibility and safety of the one-stop procedure using other LAAC devices were not addressed. Secondly, due to the nature of the single center observational study, we were not able to perform direct comparisons between the one-stop and the separated approaches of AF ablation and LAAC. Moreover, although we reported positive results of the short and intermediate-term follow-up, the long-term outcomes of the one-stop procedure need further investigation.

Conclusions

Combining catheter ablation and LAAC for AF treatment is feasible and safe in Chinese population. The one-stop approach might benefit AF patients who are at high stroke risks and intolerant or unwilling to receive long-term anticoagulation.

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Conflicts of interest

None.

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