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ORIGINAL PAPER

Bailout left atrial appendage occluder for pulmonary vein isolation and electrical cardioversion in patients with atrial fibrillation and left atrial appendage thrombus: a pilot study

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Abstract

Background Cardioversion and catheter-based circumferential pulmonary vein isolation (CPVI) are established rhythm control treatment strategies for patients with atrial fibrillation (AF). However, these treatments are contraindicated for AF patients with a left atrial appendage (LAA) thrombus.

Methods We conducted the first-in-man case series study to evaluate the feasibility and safety of performing cardioversion or CPVI in AF patients with LAA thrombus immediately after implantation of LAA Occluder (LAAO) in a combined procedure. In our multi-center LAAO registry of 310 patients, 27 symptomatic and drug-refractory AF patients underwent a combined procedure of LAAO and CPVI, among whom 10 (mean age 68 ± 16 years, 6 men) having anticoagulant-resistant LAA thrombus received a bailout procedure of LAAO implantation first then CPVI, and the other 17 patients without LAA thrombus received CPVI first then LAAO for comparison.

Results The mean CHA_2DS_2-VASc score and HAS-BLED score were comparable between these two groups. In patients with LAA thrombus, we put carotid filters and did a no-touch technique, neither advancing the wire and sheath into the LAA nor performing LAA angiography. After LAAO implantation, the connecting cable was still connected to the occluder when cardioversion was performed. During CPVI, the occluder location was registered in the LA geometry by three-dimensional mapping to guide the catheter not to touch the LAAO. The procedure was successful in all the patients without intra-procedural complications. After a mean follow-up of 1.7 ± 0.7 years, there was no device embolization, peri-device leak ≧ 5 mm or stroke event in both groups. The AF recurrence rate was also similar between the two groups ($P = 0.697$).

Conclusion We demonstrated that cardioversion or CPVI is doable in symptomatic AF patients with LAA thrombus if LAA was occluded ahead as a bailout procedure.

Keywords Left atrial appendage occluder · Left atrial appendage thrombus · Circumferential pulmonary vein isolation · Electrical cardioversion

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Abbreviations

AF	Atrial fibrillation
CPVI	Circumferential pulmonary vein isolation
ECG	Electrocardiogram
LAA	Left atrial appendage
LAAO	Left atrial appendage occlusion
TEE	Trans-esophageal echocardiography

Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in clinical practice [1, 2]. AF is associated with a fivefold increased risk of ischemic stroke and systemic thromboembolism and is responsible for approximately 25% of ischemic strokes [3, 4]. Long-term oral anticoagulation treatment is the mainstay therapy to prevent stroke, and direct-acting oral anticoagulants are now preferred over warfarin, primarily due to a lower risk of intracranial bleeding [5]. However, a significant proportion of patients who had contraindications or experienced a bleeding or ischemic event during anticoagulation treatment, may not be eligible for long-term anticoagulants therapy. In the non-valvular AF population, approximately 90% of thrombi were found in the left atrial appendage (LAA) [6]. Percutaneous LAA occlusion (LAAO) or closure has emerged as an alternative therapeutic option for the prevention of embolic stroke in high-risk patients with non-valvular AF. Among high-risk AF patients, LAAO in comparison with oral anticoagulants may have similar stroke prevention efficacy but lower risk of major bleeding and mortality in randomized trial and registry [7–12]. LAAO may reduce the bleeding risk associated with long-term anticoagulants use while still providing a continuous protection from stroke.

For symptomatic AF patients, rhythm control treatment strategy by electrical or pharmacological cardioversion, or catheter ablation therapy, is recommended to relieve symptoms and improve cardiac performance according to recent clinical guidelines (class I indication) [5]. Previous studies have shown that pharmacologic cardioversion is less effective than electrical cardioversion and catheter ablation therapy [13–15]. However, catheter ablation and direct current cardioversion carry the risk of peri-procedural thromboembolism and stroke, around 0.3% to 0.5% [16]. A documented LAA thrombosis is even considered as a contraindication to electrical cardioversion and catheter ablation therapy because of the associated high peri-procedural risk of thromboembolic events in AF patients [17, 18]. Unfortunately, LAA thrombosis could still be found in AF patients who have received full therapeutic anticoagulation [19, 20].

Therefore, rhythm control continues to be a great challenge in symptomatic AF patients with persistent LAA thrombus under adequate oral anticoagulation. Recently, several studies have shown that percutaneous LAAO implantation, when performed with some technical modifications by experienced operators, is feasible and effective in patients with persistent LAA thrombus [21]. Theoretically, the risk of LAA thrombus dislodgement during cardioversion or catheter ablation may become low if the LAA is closed by an occluder. Therefore, our study sought to investigate the feasibility, safety, and efficacy of performing electrical cardioversion or circumferential pulmonary vein isolation (CPVI) immediately after LAA closure as a bailout procedure in symptomatic AF patients with persistent LAA thrombus despite adequate anticoagulation therapy. We also describe this delicate procedure in detail.

Methods

Study population and follow-up

Of the 310 patients enrolled in an Asian long-term follow-up study and a multi-center LAAO registry in Taiwan since Aug. 2013, 27 consecutive symptomatic AF patients (mean age 70 ± 11 years, 16 men) and refractory to drug therapy were recruited to receive a combined procedure of LAAO implantation and cardioversion and/or CPVI with three-dimensional mapping. Among them, 10 patients had an oral anticoagulants-resistant LAA thrombus and received cardioversion or CPVI immediately after implantation of LAAO under general anesthesia and trans-esophageal echocardiography (TEE) guidance. It has been reported that direct-acting oral anticoagulants could dissolve the LAA thrombus within a wide range of treatment duration (less than 2 weeks to 30 weeks) [22–25]. All the patients were given either dabigatran 150 mg twice a day, apixaban 5 mg twice a day, or edoxaban 60 mg once a day for at least 8 weeks before the decision was made to undergo the bailout procedure.

In 9 of these 10 patients, carotid filter wires were put in bilateral internal carotid arteries to decrease the risk of intra-procedural embolic stroke. Two FilterWire EZ carotid filter wires (Boston Scientific) designed to fit 3.5–5.5 mm diameter vessels were advanced to the bilateral internal carotid arteries through bilateral femoral approach consecutively. The common carotid artery was first cannulated with a 6F right Judkins coronary guiding catheter and extracranial and intracranial angiographies were first done to rule out severe obstruction. Then the filter wire was advanced to the internal carotid artery for carotid protection. The other 17 patients without an LAA thrombus received CPVI first and then LAAO implantation. The study was approved by our Institutional Review Board and all patients provided written informed consent for these procedures.

After the combined procedure, an oral anticoagulant plus one antiplatelet or dual anti-platelets were prescribed for

at least 45 days in all patients and then a single antiplatelet drug was prescribed for lifelong use. Clinical follow-up was arranged at 1 week, 1–2 months, and then every 3 months after device implantation to assess the clinical outcomes, whereas a follow-up TEE was scheduled at 2, 6, and 12 months after the procedure to evaluate LA/LAA thrombus, peri-device leakage and flow, device embolization, pericardial effusion, and thrombus formation on the device. To detect AF recurrence, an electrocardiogram or Holter monitoring, or both were arranged at 1 week, 1–2 months, and then every 3 months or when symptoms of AF developed. Primary outcome events included death (cardiovascular or non-cardiovascular), stroke, transient ischemic attack, and systemic embolism.

No-touch LAAO implantation procedure

During LAAO implantation, a no-touch technique was used to prevent iatrogenic thrombus dislodgement (Fig. 1). We neither advanced the wire into the LAA nor did LAA angiography beforehand. Because contrast was not injected, the whole procedure was predominantly guided by TEE (Fig. 1). We also did not inject echo contrast in cases with a suspicious LAA thrombus because of the fear of possible thrombus dislodgement, and we treated them as thrombosis cases. We put the stiff wire in the left superior pulmonary vein and first introduced the large LAAO sheath into the left superior pulmonary vein (Fig. 1B). Then the wire was withdrawn, and the sheath tip was manipulated and guided to the vicinity of the LAA ostium under the TEE guidance (Fig. 1C). Then the Amulet lobe was first partially deployed here (Fig. 1D) and then slowly moved into the LAA neck or landing zone (Fig. 1E) under the TEE guidance and then the lobe and disk were fully deployed (Fig. 1F). In all of the cases, we did not try a second time because manipulation of the LAAO device in the LAA ran the risk of thrombus dislodgement. After LAAO deployment, LAA angiography was performed to check if there was significant peri-device leakage (Fig. 1H).

In the early stage of this study, we also tried to implant the Watchman device in the presence of an LAA thrombus. Unlike that of the Amulet, the sheath system of the Watchman had to be advanced into the distal LAA before deployment. We first put the Watchman sheath system in the left superior pulmonary vein, and not injecting dye and under TEE guidance, we gently guided and advanced the sheath system into the LAA by counterclockwise rotation. Under TEE guidance, we tried our best not to touch the thrombus. Once the sheath was deep enough in the LAA, we rapidly deployed the Watchman occluder. Because the implanting Watchman procedure was riskier than the Amulet procedure, we used the Watchman in only two cases and the majority of the patients received Amulet implantation.

Acute procedural success was defined as proper and stable LAAO device placement in the landing zone of the LAA without significant peri-device leak (≥ 5 mm), and impingement on surrounding cardiac structures, and no signs of device embolization or migration. The upper part of the Amulet disk was predominantly positioned within the LAAO neck to expose the Coumadin ridge for later left side pulmonary vein isolation (Fig. 2).

Pulmonary vein isolation and electrical cardioversion

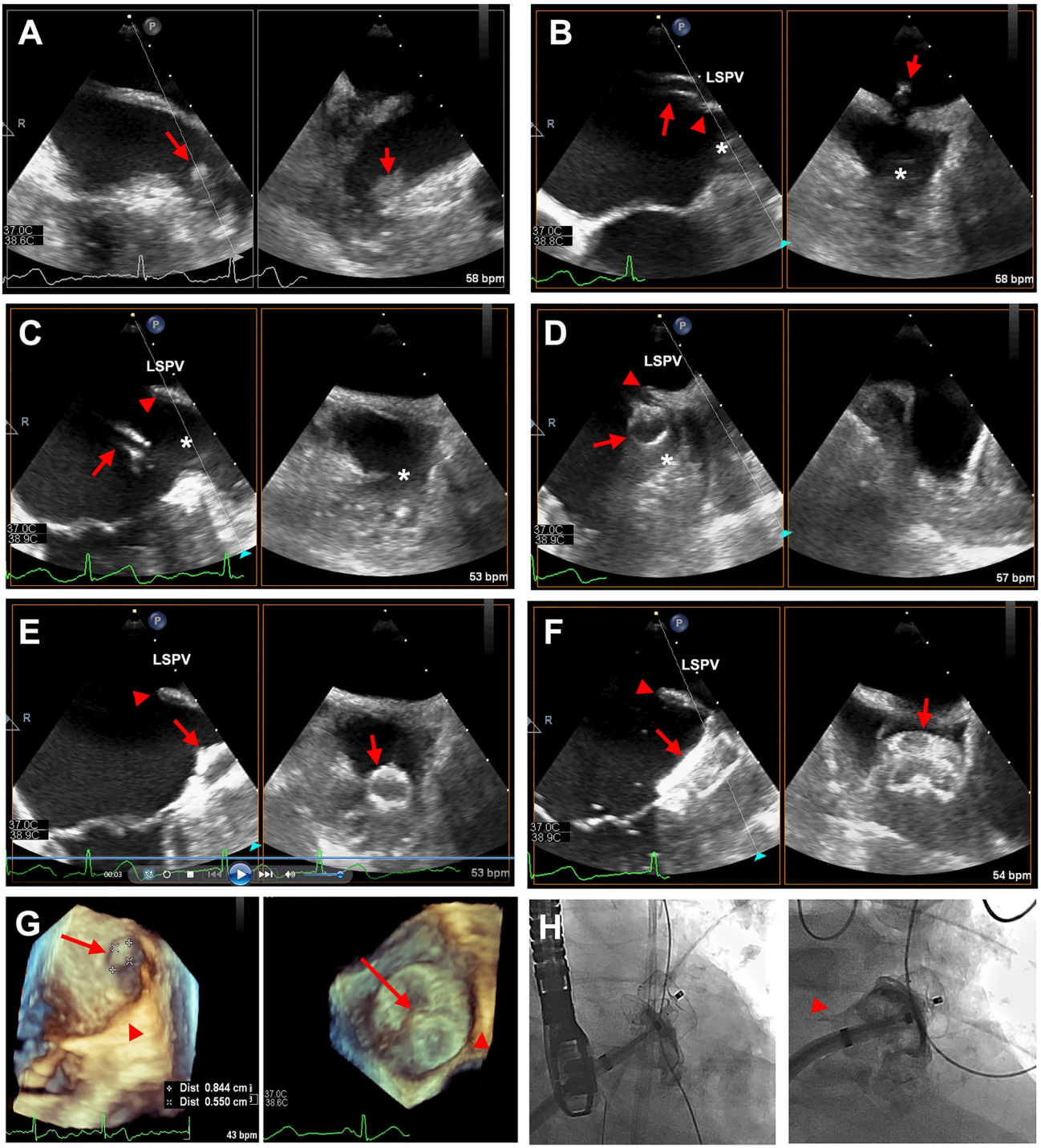
The three-dimensional mapping was performed using the Rhythmia HDx (Boston Scientific Corp., Maple Grove, MN, USA) or EnSite Precision (Abbott Cardiovascular, Plymouth, MN USA) system with the assistance of integrated LA multi-slice computer tomography images. The LAAO location was registered in the three-dimensional LA shell to avoid catheter touching the LAAO during pulmonary vein isolation (Fig. 2). When the catheter touched the LAAO device, there would be much noise on the local electrogram (Fig. 2B) and also the sound of a low-impedance alarm.

After mapping the anatomical structure and electrical signals of the LA, circumferential pulmonary vein isolation was performed using an irrigation catheter. The ablation energy setting was 30 watts at the posterior LA and 35 watts at the other sides. We did not perform other linear ablation procedures, such as roof line creation or substrate modification. To keep activated clotting time greater than 300 s, heparinization was performed after trans-septal puncture until the end of the procedure.

For those receiving cryoablation, the Arctic Front Advance Cardiac Cryoablation Catheter (Medtronic) was inserted into the LA. The three-dimensional mapping was also performed using the EnSite Precision mapping system (Abbott Cardiovascular, Plymouth, MN USA) and the Achieve mapping catheter (Medtronic). The LAAO location was also registered in the three-dimensional LA shell to avoid catheter touching the LAAO during cryoablation. The catheter was inserted into the four pulmonary veins consecutively. Two cryoballoon applications, each 3 min in duration, were delivered to each pulmonary vein. Pulmonary vein isolation was confirmed by entrance block and exit block by pacing within the pulmonary veins. Electrical cardioversion was performed by delivering shocks of 100 J up to 300 J in a biphasic waveform. The LAAO cable was connected to the disk when cardioversion was performed.

Statistics

Because of the small case number, we used non-parametric methods for our statistical analyses. Continuous data are



expressed as median and range. The comparison between groups was conducted by the Mann–Whitney U test for continuous variables, and Fisher's exact test for categorical variables. All statistical significances were set at $p < 0.05$ and statistical analyses were carried out by SPSS 23.0 (SPSS Inc. USA).

Results

Characteristics of patients with LAA thrombus receiving both LAAO and CPVI or cardioversion

The baseline characteristics and procedural details of each patient with LAA thrombus are shown in Table 1. Because it was difficult to do a complete no-touch technique in

◂**Fig. 1** Implantation of Amulet in the presence of a thrombus by a no-touch technique guided by transesophageal echocardiography. **A** The whole procedure is guided by transesophageal echocardiography (TEE) and no contrast is injected into the left atrial appendage (LAA) before the occluder is implanted. Pre-procedural TEE X-plane image shows a thrombus (arrow) in the neck of the LAA. **B** The Amulet sheath (arrow) is put into the left superior pulmonary vein (LSPV) above the Coumadin ridge (arrowhead) not touching the LAA (asterisk). **C** The Amulet sheath (arrow) is then manipulated and oriented crossing the Coumadin ridge (arrowhead) and down to the left atrial area close to the LAA ostium (asterisk). **D** The Amulet lobe (arrow) is then partially deployed in this area. **E** The partially deployed lobe (arrow) is advanced into the landing zone of the LAA quickly. **F** The lobe and disk (arrow) are then rapidly deployed. **G** Left panel, three-dimensional TEE looking from the ostium of the LAA shows a thrombus (arrow) in the neck of the LAA measuring 0.84 cm × 0.55 cm. Right panel, after implantation of the Amulet, the Amulet disk (arrow) covers the whole ostium of the LAA and thus the thrombus cannot be visualized. **H** After implantation of the Amulet, we can inject contrast and do LAA angiography without the fear of thrombus dislodgement, which shows no significant peri-device leak and complete closure of the LAA. Left panel and right panel, caudal and cranial views, respectively. In all the figures, the arrowhead indicates the Coumadin ridge

implanting the Watchman device, we implanted the Amulet in 8 patients and the Watchman in only 2. In these 10 patients, although LAAO or CPVI or cardioversion was contraindicated, we evaluated the feasibility of LAAO implantation first as a bailout procedure for subsequent CPVI or cardioversion in all of the 10 patients. We found CPVI or cardioversion after LAAO did not move or damage the implanted LAAO if it was performed carefully, and there was no thrombus dislodgement or intra-procedural development of stroke in any case. All the patients with LAA thrombus had persistent AF, and cardioversion was done in all of these patients. Although the whole chest moved abruptly during electrical cardioversion, (see online video 1 [fluoroscopic recording] and 2 [TEE] for Amulet under electrical cardioversion and online video 3 for Watchman under electrical cardioversion), the LAAO device remained in place if the connecting cable remained connected to the LAAO device (Fig. 3, the ECG artifact indicates the timing of cardioversion [red arrow]). After cardioversion, there was not any case of thrombus dislodgement or intra-procedural stroke development. After confirming that the LAAO position was optimal, the device was then released.

The device was successfully implanted in all of the cases without the occurrence of intra-procedural or peri-procedural complications or stroke events. The occluders in all the patients were in the final optimal LAAO position and the pulmonary veins were completely isolated. In one of the patients who received a Watchman implantation, a small debris was found in the carotid filter wire, but the patient did not have any symptom or sign of stroke during the intra-operative period and follow-up.

Long-term follow-up

We compared the long-term outcomes of our patients with LAA thrombus with those without LAA thrombus both receiving LAAO implantation and CPVI in a combined procedure. As mentioned, in the LAA thrombus group we implanted LAAO first and then performed CPVI. In the group without LAA thrombus, we performed CPVI first and then implanted LAAO. All the patients received the same anti-thrombotic regimen with oral anticoagulant plus one antiplatelet or dual anti-platelets drugs after the procedure for at least 45 days and then a single antiplatelet drug for life-long.

The baseline characteristics of these two groups are shown in Table 2. There was no significant difference in clinical variables, except a trend that there were more hypertensive patients in the group without LAA thrombus ($P = 0.081$). Unexpectedly, the mean CHA_2DS_2-VASc score was not higher in the group with LAA thrombus than the group without LAA thrombus. Nine patients had persistent AF in the group without LAA thrombus and all of them also received cardioversion before LAAO implantation.

Follow-up TEE 45–60 days and 6 months after the procedure showed no significant peri-device leakage and no thrombus formation on the device in every patient in both groups. After a mean follow-up of 1.7 ± 0.7 years, there was also no LAAO-related complications, such as device embolization or stroke event, developed in any patient and the AF recurrence rate was also similar between the two groups (1/10 vs 2/17, $P = 0.697$). Regarding the cardiovascular outcome, one patient in the group with an LAA thrombus died of end-stage renal disease and sepsis 9 months later and one patient in the group without LAA thrombus died suddenly of unknown causes 3 weeks after the procedure (1/10 vs 1/17, $P = 0.613$).

Discussion

We reported the outcomes of a case series of rhythm control strategy immediately after percutaneous LAA closure as a bailout procedure in AF patients with a known LAA thrombus. Previous studies showed a still high rate (up to 10%) of LAA thrombus persistence despite adequate anticoagulation and similar rate between patients taking warfarin and direct-acting oral anticoagulants [23, 26]. A persisting LAA thrombus would prohibit these patients from receiving electrical cardioversion or catheter ablation for rhythm control of AF because of the risk of systemic thromboembolism due to dislodgement of an LAA clot by a catheter or shock current.

However, evidence has accumulated that rhythm control strategy improves long-term outcome in symptomatic AF patients with multiple co-morbidities [27–29]. Pulmonary

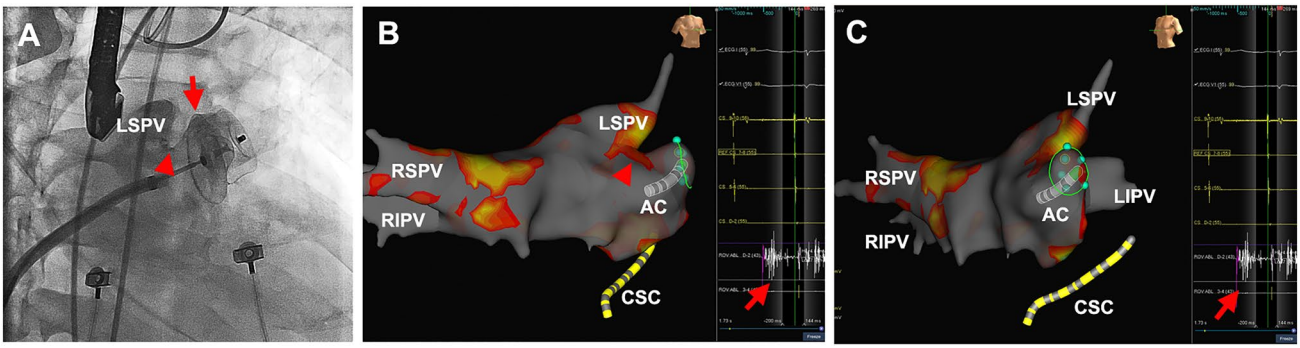


Fig. 2 Placement of the upper rim of the Amulet disk in the neck of the left atrial appendage to facilitate subsequent pulmonary vein isolation. **A** On implantation of the Amulet device, the Amulet disk is inserted deeper into the neck of the left atrial appendage (LAA). LAA angiography shows the upper rim of the Amulet disk (arrow) localized in the neck of the LAA and the Coumadin ridge is clearly exposed (arrowhead). **B** After implantation of the Amulet, we then create a three-dimensional (3D) shell of the whole left atrium with four pulmonary veins using the Ensite 3D mapping system for pulmonary vein isolation. This is the right anterior oblique view. The green circle indicates the periphery of the Amulet disk, the upper rim of the disk is deep in the neck and the Coumadin ridge is clearly exposed without any device on it (arrowhead). When the ablation catheter tip touches the Amulet disk, because the tip directly contacts a metal part, huge artifacts appear in the local electrogram tracing (arrow) and the 3D mapping system alarm is triggered. The green dots indicating where the ablation catheter tip touches the disk with an alarm are tagged. During pulmonary vein isolation, especially when the ablation catheter is on the Coumadin ridge, we avoid touching the disk of the Amulet under the guidance of 3D mapping (avoid getting close to the green circle or dots). LSPV, left superior pulmonary vein; LIPV, left inferior pulmonary vein; RSPV, right superior pulmonary vein; RIPV, right inferior pulmonary vein; CSC, coronary sinus catheter. **C** The left anterior oblique view of the LA in Ensite 3D mapping system

vein isolation is the cornerstone of AF rhythm control strategy and can be achieved either by radiofrequency or cryoballoon ablation, which is more effective than antiarrhythmic drug therapy for maintaining sinus rhythm, particularly in patients with paroxysmal AF [14, 30, 31]. Besides, electrical cardioversion is frequently performed to relieve AF symptoms, improve cardiac performance, and is usually necessary during pulmonary vein isolation. However, the presence of an LAA thrombus is currently a contraindication to these rhythm-control procedures. Thus, it is very important to seek a solution to the problem of rhythm control and alleviate the risk of thromboembolism in the presence of an LAA thrombus. Our report is the first to provide insight into the feasibility of electrical cardioversion or pulmonary vein ablation in symptomatic AF patients with a persistent LAA thrombus immediately after LAA closure as a bailout procedure. Although doable, the procedure may be complicated and should be performed carefully, be reserved only for very symptomatic patients with an LAA thrombus, not become a routine procedure, and require shared decision-making between the doctor and patient.

As mentioned, any interventional procedure in the LA when an LAA thrombus is present runs the risk of thrombus dislodgement and embolization during the procedure. We thought that LAA occlusion before the procedure might be a solution to this problem. After LAA is occluded, the thrombus is trapped in the LAA and there is no risk of thrombus dislodgement in the subsequent procedure. However, performing LAAO in the setting of an LAA thrombus is also risky. In such scenarios, any procedures involving the LAA might need modifications to minimize interventions within the LAA. Until now, there have been limited data on the outcomes of LAA closure in patients with AF who have LAA thrombus [21].

The risk of LAA touching and embolization might be higher with the Watchman device because the Watchman delivery sheath has to be advanced into the LAA until its marker aligns with the ostial plane of the LAA. By design, the Amulet device consisting of a lobe and disk may be more suitable as it can be safely implanted without advancing the delivery sheath into the LAA distally. Furthermore, the disk covering the ostium is good for LAA thrombus trapping. Thus, owing to the above-mentioned characteristics, we mostly used the Amulet as the LAA closure device. Furthermore, it is more possible to achieve good device positioning on one trial in implanting the Amulet [32].

We also used a modified no-touch technique that avoided contrast injection into the LAA and manipulation of the sheath, catheters, or guidewire in the LAA [33]. We also used a cerebral protection device in most of our patients [34]. Besides, as mentioned, we could not have the second trial and therefore TEE was routinely performed by trained physicians during the whole procedure in all cases. Our study did not disclose any peri-procedural device-related complications, and follow-up TEE also showed no significant peri-device leaks and no thrombus formation on the device. Therefore, our study proved again that LAAO was

Table 1 Clinical and procedural characteristics and outcomes of patients with a persistent LAA thrombus undergoing LAAO implantation and PVI

Case number	Age (years)	Gender	AF type	CHA2DS2-VASc score	HAS-BLED score	Device type	PVI Mode	Procedural characteristics	Antithrombotics before procedure	Antithrombotics after procedure	Longterm outcome event
1	66	M	Persistent	5	4	Watchman	RF	CBP+; TEE guided advancing sheath into LAA rapid deploy	Full dose DOAC	SAPT+DOAC	–
2	83	F	Persistent	7	5	Amulet	RF	CBP+; TEE guided partial lobe into LAA rapid deploy	Full dose DOAC	SAPT+DOAC	–
3	64	M	Persistent	3	2	Watchman	RF	CBP+, sludge+; TEE guided advancing sheath into LAA rapid deploy	Full dose DOAC	DAPT	–
4	65	M	Persistent	4	4	Amulet	Cryo	CBP+; wire inadvertently pushed into LAA TEE guided partial lobe into LAA rapid deploy	Full dose DOAC	DAPT	–
5	79	F	Persistent	6	5	Amulet	RF	CBP+; TEE guided partial lobe into LAA rapid deploy	Full dose DOAC	SAPT+DOAC	–
6	67	M	Persistent	4	3	Amulet	Cryo	CBP+; TEE guided partial lobe into LAA rapid deploy	Full dose DOAC	DAPT	–
7	64	M	Persistent	3	1	Amulet	RF	CBP+; TEE guided partial lobe into LAA rapid deploy	Full dose DOAC	DAPT	–
8	62	F	Persistent	6	5	Amulet	RF	CBP -; TEE guided partial lobe into LAA rapid deploy	Full dose DOAC	SAPT+DOAC	–
9	73	M	Persistent	4	3	Amulet	RF	CBP+; TEE guided partial lobe into LAA rapid deploy	Full dose DOAC	SAPT+DOAC	–
10	53	F	Persistent	2	1	Amulet	RF	CBP+; TEE guided partial lobe into LAA rapid deploy	Full dose DOAC	DAPT	–

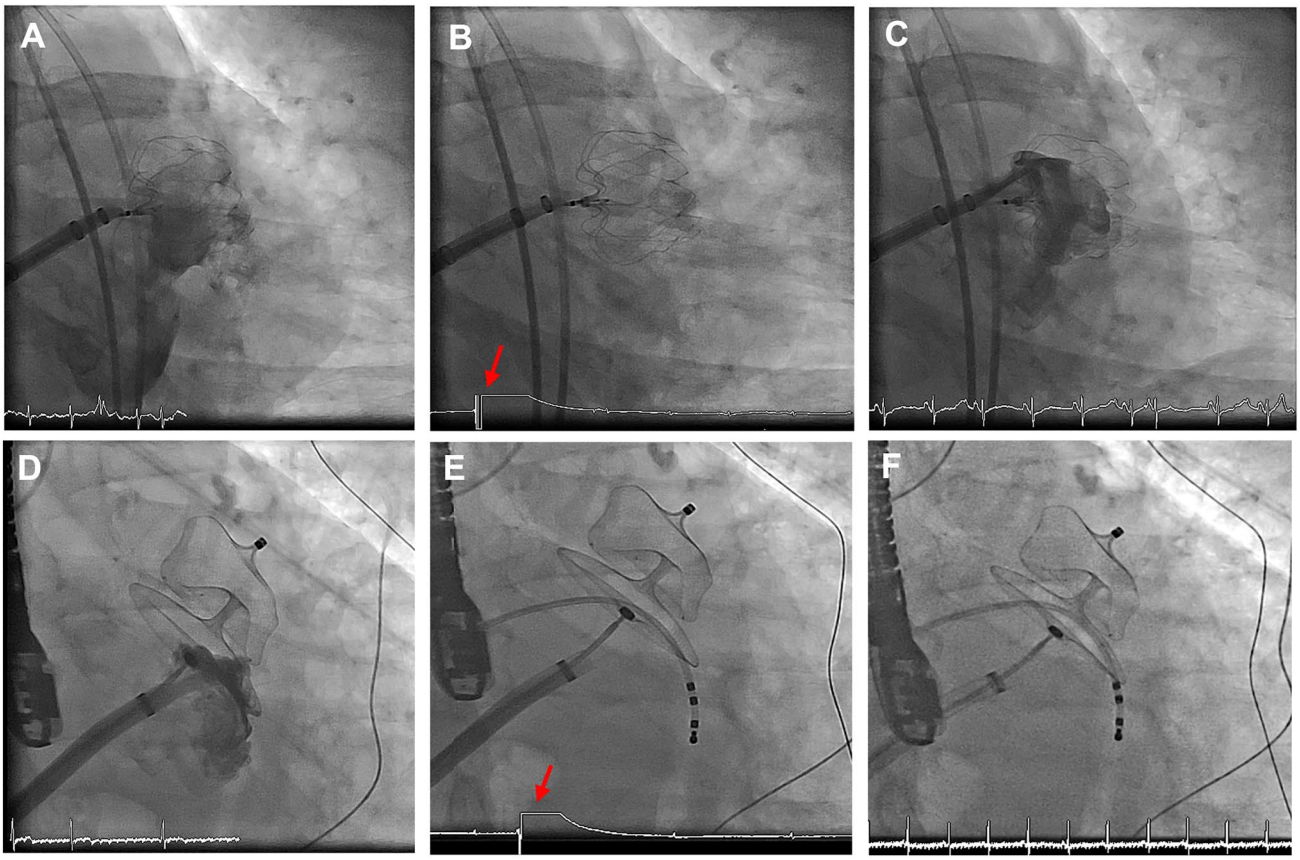


Fig. 3 Electrical cardioversion in patients with a newly implanted Amulet or Watchman and the connecting cable still attached to the device during cardioversion. **A** The location of the Watchman in the left atrial appendage (LAA) before cardioversion. **B** During electrical cardioversion, the location of the Watchman remains unchanged. The electrocardiogram tracing (at the bottom of each angiogram) shows that electrical cardioversion creates a large artifact (arrow). **C** After cardioversion, the Watchman device remains in the same location. **D** The location of the Amulet in the LAA before cardioversion. **E** During electrical cardioversion, the location of Amulet remains unchanged. Electrical cardioversion creates a large artifact in the electrocardiogram (arrow). **F** After cardioversion, the Amulet remains in the same location

safe and effective when performed with some procedural modifications in patients with persistent LAA thrombus.

In the present study, we were lucky and did not encounter situations in which the LAAO had to be repositioned or resized due to a large peri-device leak or the too shallow placement of the device in the LAA. As a bailout procedure, occluding the large leak with another device such as a vascular plug may be considered. If the device is too shallow and risk of device embolization is high, recapture of the device and re-implantation is needed. Because we employ a cerebral protection device during the procedure, at least we can prevent the most devastating complication (cerebral embolization). For thrombi embolized to other organs, they could be retrieved on-site or later when symptoms develop. To sum up, these are very difficult situations, and the treatment should be tailored to each patient's condition.

Catheter ablation for AF several months after LAAO in two consecutive procedures has been shown to be feasible and safe [35]. However, because these two percutaneous interventions share similar procedural issues and technical requirements (e.g., atrial trans-septal procedure), the combined procedure in a single session has also been reported as a technically feasible and safe strategy [36, 37]. However, in these studies, pulmonary vein isolation was performed before LAAO implantation in AF patients without LAA thrombus and the chosen LAAO devices were predominantly Watchman devices. In the present study, we implanted the Amulet device first before carrying out catheter ablation and/or electrical cardioversion in a combined procedure in patients with LAA thrombus, which has never been reported before. The reason for doing LAAO first was for thrombus trapping by the LAAO and preventing the catheters from inadvertently getting into the LAA and dislodging the thrombus during catheter ablation. Besides, we did it in a combined procedure because these patients with an LAA thrombus might had a high burden of thrombosis and we could not anticipate whether there would be a device-related thrombus that would preclude doing pulmonary vein

Table 2 Clinical characteristics and comparison between patients undergoing combined procedure with left atrial appendage thrombus and those without thrombus

Variable	Patients with thrombus ($n=10$)	Patients without thrombus ($n=17$)
Clinical parameters		
Age (year) (median, range)	67 (53–83)	69 (56–85)
Men	6 (60%)	10 (59%)
Indication		
Bleeding on anticoagulant	5 (50%)	14 (82%)
Patient refusal	2 (20%)	0 (0%)
Cerebrovascular event despite OAC	3 (30%)	5 (29%)
CHA_2DS_2-VASc score (median, range)	4 (2–7)	4 (2–7)
HAS-BLED score (median, range)	3 (1–5)	3 (1–5)
Diabetes mellitus	4 (40%)	8 (47%)
Hypertension	5 (50%)	16 (94%)
Congestive heart failure	5 (50%)	5 (29%)
Previous history of TIA/stroke	3 (30%)	8 (47%)
Vascular disease (CAD/PAOD)	3 (30%)	7 (41%)
Device parameters		
Device type		
Watchman	2 (20%)	4 (24%)
Amulet/ACP	8 (80%)	13 (76%)
Implant (mm) (median size, range)	22 (18–31)	24 (18–34)
Mode of pulmonary vein isolation		
Cryo-ablation	2 (20%)	4 (24%)
Radiofrequency ablation	8 (80%)	13 (76%)

ACP Amplatzer cardiac plug, *CAD* coronary artery disease, *OAC* oral anticoagulants, *PAOD* peripheral arterial occlusive disease, *TIA* transient ischemic accident

isolation or electrical cardioversion in future. Therefore, we did pulmonary vein isolation and cardioversion immediately after LAAO implantation.

In this combined procedure, we mostly used the Amulet device because it provided the possibility of not touching the LAA and its disk totally covered the LAA ostium to prevent thrombus dislodgement during cardioversion or catheter intrusion into the distal LAA. However, using the Amulet before pulmonary vein isolation also raised some technical issues. First, ablation in the area surrounding the Amulet device may carry risks of device dislodgement, disk perforation, and thrombus formation when energy is directly applied to the metal disk. Second, pulmonary vein isolation may not be complete if the disk of the Amulet blocks the access to the Coumadin ridge between the left superior pulmonary vein and LAA. There are also reports on the safety of AF ablation procedures in the presence of a previously implanted Watchman device [38] and on the possibility of creating a peri-device leak by performing catheter ablation in a pre-existing Watchman device [39]. There was only one case report demonstrating that radiofrequency ablation is a feasible and safe method of pulmonary vein isolation in patients with preexisting Amulet devices [35]. Therefore, in the present study, we provide the largest series of patients who underwent a combined procedure of Amulet device implantation followed immediately by pulmonary vein isolation.

Although the rationale for exposing the Coumadin ridge by placing the Amulet predominantly into the LAA neck to facilitate CPVI is reasonable, leaving an overhang of the ridge on the disk at an angle $<90°$ may pose a risk toward developing a device-related thrombus [40]. Although no device-related thrombus developed in any of the patients in our study, which might be due to the low case number, device-related thrombus might develop and pose a relevant clinical problem if the procedures were performed more often or in more patients. Therefore, the patients should be followed up more closely for device-related thrombus.

There have been concerns about increasing LA pressure and LAA size after saline infusion in pulmonary vein isolation using irrigation catheters, which may create an LAA and LAAO size discrepancy when LAAO is implanted after catheter ablation. Studies also demonstrate that intra-procedural volume loading with saline increases the LAA orifice dimensions and depth during the LAA closure [41]. In our study, we implanted LAAO before irrigation-based catheter ablation which might preclude the possibility of an LAA and LAAO size discrepancy. Furthermore, we also were the first to find that there was no significant peri-device leakage at the end of the procedure, demonstrating that saline infusion did not increase LAA size much if the LAA was closed during saline infusion. Another concern is potential under-sizing of the LAAO with subsequent peri-device leakage because of ablation-related tissue edema when in the combined procedure (CPVI is done before LAAO). We measured the size of the LAA after completing ablation to correctly size the LAAO device. Similar to previous studies showing that this combined treatment (CPVI first, then LAAO) approach appears to be a safe and effective procedure [42], our study (LAAO first, then CPVI) detected no device embolization or peri-device leak at a mean follow-up of 1.7 ± 0.7 years.

Sharma et al. recently demonstrated that electrical cardioversion several months after LAAO implantation is feasible and not associated with complications [43]. However, the efficacy and safety of the electrical cardioversion following on-site LAAO implantation in patients with an LAA thrombus is unknown. In the present study, we found that electrical cardioversion is doable immediately after the implantation of the LAAO if the cable is connected to the LAAO device. We disconnected the connecting cable only after successful electrical cardioversion of AF to sinus rhythm.

Limitations

There are limitations in the present study. The case number is too low and there may be a learning curve for those tasked with performing a no-touch technique combining LAAO with CPVI. Therefore, our proposed procedure could not be generalized to a routine procedure and only serves as a bailout procedure. We did not arrange for cerebral magnetic resonance imaging studies and complete neurological evaluations, and thus we could not rule out the possibility of very subtle neurological sequelae that were neglected by the patients and the physicians. Finally, this is a risky procedure, and one may consider giving patients oral anticoagulants for a longer time before the procedure or adding on an anti-platelet agent, although there are reports and guidelines addressing the use of oral anticoagulants for as short a period as 2 weeks to dissolve the LAA thrombus [22–25].

Conclusion

In conclusion, this is the first-in-man report of a hybrid strategy of rhythm-control either by electrical cardioversion or by pulmonary vein isolation immediately following implantation of LAAO in a single procedure, which is feasible as a bailout procedure in symptomatic AF patients already on anticoagulants but with a persistent LAA thrombus.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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