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Left atrial appendage closure after cryoballoon ablation in patients with atrial fibrillation

Background

Nonvalvular atrial fibrillation (AF) is a common clinical cardiac arrhythmia [1]. Catheter ablation, whether by radiofrequency catheter ablation (RFCA) or by cryoballoon ablation (CBA), is an effective management tool for patients with drug-refractory symptomatic AF. According to expert consensus [1], life-long oral anticoagulation (OAC) therapy should be continued even after a successful catheter ablation outcome when treating a patient with AF and a high risk of stroke (CHA_2DS_2-VASc score >1). However, some patients with AF and a high risk of bleeding cannot tolerate life-long OAC treatment, and others have severe acute contraindications to OAC therapy. More recently, left atrial appendage (LAA) closure (LAAC) emerged as a feasible management strategy to replace OAC therapy (when necessary) for patients with a high risk of bleeding and stroke, on the basis of updated guidelines for the management of patients with AF [2].

Our previous study demonstrated that CBA, which is effective in managing patients with AF and improving their AF-related symptoms [3], especially using the second-generation cryoballoon [4], has a lower complication rate ranging from 2.8% [3] to 8.8% [4]. Additionally, the LAAC procedure is useful in managing patients with OAC intolerance who have a high risk of stroke, transient ischemic attack (TIA), and bleeding [5], and is associated with a lower complication rate of 2.7–8.7% [6].

In this study, we investigated whether the concomitant usage of CBA and LAAC is feasible (safe and effective) in a cohort of patients with AF and a high risk of stroke and bleeding.

Methods

Study population

Informed consent was obtained from all patients enrolled in the study from 1 May 2017 to 30 June 2018. The study examined consecutive patients with nonvalvular symptomatic drug-refractory AF who elected to undergo a concomitant procedure of CBA for pulmonary vein (PV) isolation (PVI) and LAAC via insertion of an occlusion device. More specifically, patients were refractory to class I or III antiarrhythmic drugs (AADs), but they were excluded from the study if they had undergone a previous catheter ablation for any atrial arrhythmia or they had a prior history of heart valve disease. This study was approved by the institutional research ethics committee of Fuwai Hospital, Beijing, China.

Before catheter ablation, all patients underwent transesophageal echocardiography (TEE) and computerized tomography (CT) imaging to rule out the presence of an atrial thrombus and to assess the left atrial (LA) and LAA anatomy. The LA diameter and left ventricular ejection fraction were measured by transthoracic echocardiography, and AF type (paroxysmal or persistent) was classified according to expert consensus [1].

Cryoballoon ablation

Details of the CBA procedure and electrophysiological study by our laboratory have been previously described [3, 4]. In brief, patients were sedated with general anesthesia or local anesthesia. Following left femoral vein puncture, a 6-Fr decapolar and a 5-Fr bipolar diagnostic catheter were individually inserted into the coronary sinus and right ventricular apex. After a successful single transseptal puncture with a BRK-1 needle and standard 8.5-Fr SL1 long sheath, selected PV angiography was completed with the left superior PV and left inferior PV captured in a left anterior oblique projection. Similarly, a right anterior oblique projection was utilized to view the right superior PV and right inferior PV.

Abbreviations

AAD	antiarrhythmic drug
AF	atrial fibrillation
AFL	atrial flutter
AT	atrial tachycardia
CBA	cryoballoon ablation
CT	computerized tomography
LA	left atrium
LAA	left atrial appendage
LAAC	left atrial appendage closure
LAAI	left atrial appendage isolation
OAC	oral anticoagulation
PV	pulmonary vein
PVI	pulmonary vein isolation
RFCA	radiofrequency catheter ablation
TEE	transesophageal echocardiography
TIA	transient ischemic attack

A 15-Fr steerable sheath (FlexCath Advance; Medtronic Inc. USA) was exchanged with a stiff guidewire and inserted into the LA. Next, a second-generation 28-mm cryoballoon (Arctic Front Advance; Medtronic Inc. USA) with a 20-mm octopolar circular mapping catheter (Achieve; Medtronic Inc. USA) was advanced to each PV ostium, and PV potentials were continuously recorded. Phrenic nerve pacing was conducted during CBA of the right-sided PVs, and freezing was immediately terminated at any sign of weakened diaphragmatic contraction. The acute endpoint of cryoablation was PVI at each PV by confirmed high-output testing for entrance and exit block. After CBA, direct-current cardioversion was administered to any patient who was not in sinus rhythm.

Left atrial appendage closure

All patients were under general anesthesia during the LAAC procedure. Details of the LAAC procedure have been previously described by our group [5]. In summary, the procedure was performed from the right femoral vein under continuous guidance by TEE. Angiography of the LAA was completed with a 6-Fr pigtail catheter using a projection at 30° right anterior oblique and 20° caudal. The LAA ostium diameter and depth were measured by both chest x-ray and TEE imaging. Left atrial appendage closure was completed with one of the three inserted occlusion devices, including WATCHMAN (Boston Scientific, USA), Amplatzer Cardiac Plug (St. Jude Medical, USA), or LAmbre (Lifetech Scientific, China). The LAA anatomy, LAA dimensional measurements, and commercial device availability were used to determine the LAAC device selected in our study. During the "pre-release" occlusion testing, angiography and TEE examinations were conducted to determine the optimal location for the LAAC device deployment. After LAAC device release, a repeated series of angiography and TEE were used to assess LAA occlusion and the amount (diameter) of leakage around the LAA device (when present). The procedure success was defined as no leak >5 mm on color Doppler TEE, no device-related complication, exclusion of the LAA, and no procedure-related complications in accordance with the Munich consensus [7].

Clinical follow-up

All patients underwent regular clinical follow-up at intervals of 3 months, and all class I and III AADs were terminated during the "landmark" 90-day blanking period to evaluate the CBA efficacy. A 72-h Holter monitor was used at 3, 6, 9, and 12 months after the index CBA/LAAC procedure to systematically screen for episodes of atrial arrhythmia. Also, patients used a transtelephonic wireless electrocardiograph to record cardiac electrograms during any self-assessed episode of arrhythmia symptom(s) [8]. The efficacy of CBA was defined as the freedom from AF, atrial flutter (AFL), and/or atrial tachycardia (AT) of ≥30 s outside of the 90-day blanking period. The efficacy of LAAC was assessed by a TEE and CT scan conducted at 3 months after the index procedure to determine whether there was any peri-device leakage, and if leakage was present, the diameter of the leak was recorded as well.

Anticoagulation and antiplatelet drugs

All patients received OAC drugs for 3 months after the procedure. Thereafter, the OAC drugs were discontinued, and a dual anti-platelet therapy strategy (with aspirin and clopidogrel) was used for the next 3 months. After a further 6 months, single antiplatelet therapy (aspirin or clopidogrel) was used throughout the study duration, and the choice of aspirin or clopidogrel was based primarily on the patient's preference.

Complications

All complications were recorded throughout the duration of the study. Attention was given to known potential procedure-related complications, including: phrenic nerve palsy, pericardial effusion or tamponade, symptomatic PV stenosis, atrio-esophageal fistula, thrombosis, stroke, TIA, and major bleeding events [9], which were defined as Bleeding Academic Research Consortium (BARC; [10]) type 3a and life threatening or disabling according to the Munich consensus [7].

Statistical analysis

Continuous variables with normal distribution are reported as mean ± standard deviation and were compared using Student's *t* test. Continuous variables with non-normal distribution are reported as median (5% quartile, 95% quartile) and were analyzed with Wilcoxon's test. Discrete variables were compared with chi-square or Fisher's exact test, as appropriate. A Kaplan–Meier estimate was used to assess treatment success during long-term follow-up care, and a log-rank test was used to test for statistical differences between groups. Two-sided statistical tests were conducted, and p value of <0.05 was considered statistically significant. Statistical analyses were performed with SAS (Version 9.1, SAS Institute Inc. USA).

Results

Baseline data

A total of 27 patients were enrolled into this study, and their baseline characteristics are reported in **Table 1**. The average age of the study participants was 65 years, and the cohort was mostly male (74.1%), had mostly paroxysmal AF (63.0%), and was otherwise healthy (except for a high presence of hypertension; 92.6%). According to the study design, these patients had a high proportion of previous stroke/TIA and bleeding events. Eight patients (29.6%) had a history of bleeding, and 23 patients (85.2%) had a history of stoke/TIA. Consequently, the mean CHA_2DS_2-VASc score was 4.8 ± 1.4, and the average HAS-BLED scores was 3.6 ± 1.3.

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J. Liu · Y. Xia · H. Zhang · X. Li · S. Zhang · P. Fang

Left atrial appendage closure after cryoballoon ablation in patients with atrial fibrillation

Abstract

Background. Cryoballoon ablation (CBA) is effective for patients with drug-refractory symptomatic atrial fibrillation (AF). For patients with a high risk of stroke (CHA_2DS_2-VASc score ≥2), life-long oral anticoagulation therapy should be continued even after successful catheter ablation. We investigated the safety and efficacy of concomitant use of a second-generation CBA catheter for pulmonary vein isolation (PVI) and a left atrial appendage closure (LAAC) device in patients with AF.

Methods. We enrolled 27 patients (64.7 ± 6.3 years, 74% male, 63% paroxysmal AF, 37% persistent AF, 4.8 ± 1.4 CHA_2DS_2-VASc score, and 3.6 ± 1.3 HAS-BLED score). In total, 85% of the patients had a prior stroke or TIA, and 30% of patients had a clinical history of bleeding. Patients received a CBA for PVI and underwent occlusion of the LAA with an LAAC device. The efficacy of CBA was defined as lack of arrhythmia recurrence (AF, atrial flutter, and/or atrial tachycardia lasting ≥30 s) after a 90-day blanking period. The success of LAAC was determined by the rate of stroke, TIA, and/or bleeding events.

Results. The mean procedural time for CBA and LAAC was 80 ± 16 min and 44 ± 12 min, respectively. Acute PVI by CBA was achieved in 100% of the procedures, and 96% of patients obtained acute LAAC device placement during the procedure. Upon complete release of the LAAC device, only 62% patients (16/26) had no detectable leakage during intraprocedural transesophageal echocardiography. Three patients experienced an acute complication: a pericardial effusion and two phrenic nerve palsy events. Mean follow-up was 18 months (range 9–23 months), and freedom from AF recurrence was 74% (20/27).

Conclusion. The intraprocedural combination of CBA and LAAC is feasible in patients with non-valvular AF with a high risk of stroke, TIA, and/or bleeding. Larger long-term randomized studies are needed to judge the overall safety and efficacy of the combined procedure.

Keywords

Catheter ablation · Pulmonary vein isolation · Atrial flutter · Stroke · Bleeding

Verschluss des linken Herzohrs nach Kryoballonablation bei Patienten mit Vorhofflimmern

Zusammenfassung

Hintergrund. Die Kryoballonablation (CBA) ist bei Patienten mit medikamentenresistentem symptomatischem Vorhofflimmern („atrial fibrillation", AF) wirksam. Besteht ein hohes Risiko für einen Schlaganfall (CHA_2DS_2-VASc-Score ≥2), so sollte bei solchen Patienten die Antikoagulationstherapie lebenslang fortgeführt werden, auch nach einer erfolgreichen Katheterablation. Die Autoren untersuchten die Sicherheit und Wirksamkeit der gleichzeitigen Anwendung eines CBA-Katheters der 2. Generation für die Pulmonalvenenisolation (PVI) und eines Systems zum Verschluss des linken Herzohrs („left atrial appendage closure", LAAC) bei Patienten mit AF.

Methoden. In die Studie wurden 27 Patienten im Alter von 64,7 ± 6,3 Jahren einbezogen; 74% männlich; 63% paroxysmales AF; 37% persistierendes AF; CHA_2DS_2-VASc-Score (kongestive Herzinsuffizienz, Hypertonie, Alter >75 Jahre: 2 Punkte, Diabetes, Schlaganfall/TIA: 2 Punkte, vaskuläre Erkrankung, Alter: 65–74 Jahre, „sex"/Geschlecht: weiblich): 4,8 ± 1,4; HAS-BLED-Score (Hypertonie, abnormale Nierenfunktion, Schlaganfall, Blutung, labile INR-Einstellung, „elderly"/Alter, „drugs"/Medikamente): 3,6 ± 1,3. Anamnestisch gaben 85% der Patienten einen Schlaganfall oder eine TIA (transitorische ischämische Attacke) an, 30% eine Blutung. Bei den Patienten erfolgte eine CBA zur PVI und der Verschluss des linken Herzohrs mit einem LAAC-System. Die Wirksamkeit der CBA war als das Nichtwiederauftreten der Arrhythmie (AF, Vorhofflattern und/oder Vorhoftachkardie ≥30 s) nach einer Stabilisierungsphase („blanking period") von 90 Tagen definiert. Der Erfolg der LAAC-Intervention wurde anhand der Rate für Schlaganfall, TIA und/oder Blutungen ermittelt.

Ergebnisse. Die mittlere Interventionsdauer für CBA und LAAC betrug 80 ± 16 min bzw. 44 ± 12 min. In 100% der Eingriffe wurde eine akute PVI mit der CBA erzielt, und bei 96% der Patienten erfolgte die Platzierung des LAAC-Systems während des Eingriffs. Bei vollständiger Freigabe des LAAC-Systems war nur bei 62% der Patienten (16/26) keine Leckage in der intraprozeduralen transösophagealen Echokardiographie erkennbar. Eine akute Komplikation trat bei 3 Patienten auf: einmal ein Perikarderguss und 2 Fälle mit Parese des N. phrenicus. Im Mittel betrug die Nachbeobachtungsdauer 18 Monate (Spanne: 9–23 Monate), und die AF-Rezidivfreiheit lag bei 74% (20/27).

Schlussfolgerung. Die Kombination von CBA und LAAC in einem Eingriff ist bei Patienten mit nichtvalvulärem AF und hohem Risiko für Schlaganfall, TIA und/oder Blutung praktikabel. Es sind größere randomisierte Langzeitstudien erforderlich, um die Gesamtsicherheit und -wirksamkeit der kombinierten Intervention zu beurteilen.

Schlüsselwörter

Katheterablation · Pulmonalvenenisolation · Vorhofflattern · Schlaganfall · Blutung

Cryoballoon ablation and phrenic nerve complication

The procedure-related parameters, adverse events, and results of clinical follow-up are listed in **Table 2**. During the CBA procedure, all patients achieved acute PVI at entrance and exit block testing, and the mean CBA procedure time was 80.1 ± 15.6 min. The first 11 patients were sedated using general anesthesia, while the remaining 16 patients underwent ablation using local anesthesia. The change in sedation protocol was in response to acute phrenic nerve palsy during the CBA procedure. Specifically, two patients under general anesthesia had a procedure-related phrenic nerve interruption during CBA of the right-sided PVs, which led to the CBA freeze cycles being performed/monitored using continuous fluoroscopy during all right-sided PV ablations. In response, a decision was made to only conduct CBA while using local anesthe-

Table 1 Baseline characteristics of study patients (*N*=27)

Age (years)	64.7 ± 6.3
Male (*n*/%)	20/74.1
Body mass index (kg/m^2)	25.9 ± 3.7
Atrial fibrillation (AF) type	
Paroxysmal AF (*n*/%)	17/63.0
Persistent AF (*n*/%)	10/37.0
CHA_2DS_2-VASc Score	4.8 ± 1.4
Chronic heart failure (*n*/%)	5/18.5
Hypertension (*n*/%)	25/92.6
Diabetes (*n*/%)	12/44.4
Prior stroke/TIA (*n*/%)	23/85.2
Vascular disease (*n*/%)	19/70.4
HAS-BLED score	3.6 ± 1.3
History of bleeding (*n*/%)	8/29.6
Impaired liver function (*n*/%)	5/18.5
Impaired renal function (*n*/%)	2/7.4
Labile INR (*n*/%)	2/7.4
Drug abuse (*n*/%)	11/40.7
Alcohol abuse (*n*/%)	5/18.5
Left atrial diameter (mm)	40.3 ± 5.2
LVED (mm)	48.1 ± 5.1
LVEF (%)	61.2 ± 3.9

TIA Transient ischemic attack, *INR* International normalized ratio, *LVED* Left ventricular end-diastolic diameter, *LVEF* Left ventricular ejection fraction

Table 2 Procedural data, complications, and follow-up

Cryoballoon procedure (N = 27)	
Mean CBA duration (min)	80 ± 16
General anesthesia during CBA (*n*/%)	11/40.7
Local anesthesia during CBA (*n*/%)	16/59.3
Acute pulmonary vein isolation (*n*/%)	27/100.0
Attempted left atrial appendage closure (N = 27)[a]	
Mean LAA closure duration (min)	44 ± 12
General anesthesia during LAAC (*n*/%)	27/100.0
Acute LAA closure device placement (*n*/%)	26/96.3[a]
Type of LAA closure device used (N = 26)[a]	
Watchman device (*n*/%)	20/76.9
Amplatzer Cardiac Plug (*n*/%)	4/15.4
LAmbre LAA closure system (*n*/%)	2/7.7
Leak detection after release of LAAC device (N = 26)[a]	
Leak diameter <5 and >3 mm (*n*/%)	3/11.1
Leak diameter <3 mm (*n*/%)	7/26.9
No leak (*n*/%)	16/61.5
Acute complications (N = 27)	
Pericardial effusion (*n*/%)	1/3.7
Transient phrenic nerve palsy (*n*/%)	1/3.7
Phrenic nerve palsy at discharge (*n*/%)	1/3.7
Follow-up (N = 27)	
Mean duration (months)	18
Range (months)	9–23
Freedom from AF/AFL/AT (*n*/%)	20/74.1
Complications (N = 27)	
Stroke (*n*/%)	0/0
Transient ischemic attack (*n*/%)	1/3.7
Bleeding event (*n*/%)	0/0
Any other adverse event (*n*/%)	0/0

CBA cryoballoon ablation, *LAA* left atrial appendage, *LAAC* left atrial appendage closure, *AF* atrial fibrillation, *AFL* atrial flutter, *AT* atrial tachycardia
[a]In one patient there was complete failure to implant a left atrial appendage closure device

sia, and thus the next 16 patients were treated with administration of local anesthesia and phrenic nerve palsy was not observed in this group of patients. Of the two patients with phrenic nerve interruption, in one patient the complication resolved before hospital discharge, and in the other patient diaphragmatic paralysis resolved at the 1-month follow-up visit.

Left atrial appendage closure

As reported in **Table 2**, all LAACs were conducted under general anesthesia. In all 27 patients, an attempt was made to insert the LAAC device; however, in one patient there was failure in installing the LAAC device, which occurred after multiple attempts to occlude the LAA. Because of the patient's complex LAA anatomy, the device could not maintain a stable position within the LAA. In this patient, the LAAC device was withdrawn during the procedure. A total of 26 LAAC devices were installed, and a large proportion of patients were treated with the WATCHMAN occlusion device (20/26; 76.9%). During acute device placement and testing, "pre-release" occlusion was achieved in all but one patient (26/27; 96.3%), and the mean time of the LAAC procedure was 44 ± 12 min. However, upon complete LAAC device release and stabilization in the LAA, only 16 LAAC devices (16/26; 61.5%) remained leakage-free when examined via intraprocedural TEE using multiple angles of viewing. The remaining seven patients (7/26; 26.9%) had a small leak that was determined to be less than 3 mm in diameter, while three patients (3/26; 11.5%) had a leak that was between 3 and 5 mm in diameter.

Acute and long-term complications

In addition to the two previously mentioned phrenic nerve injuries, one patient suffered from a pericardial effusion without hemodynamic change during the in-hospital stay. This patient was treated conservatively and required no interventional drainage. Importantly, all three procedure-related complications resolved without further surgical intervention and continuing sequelae. During

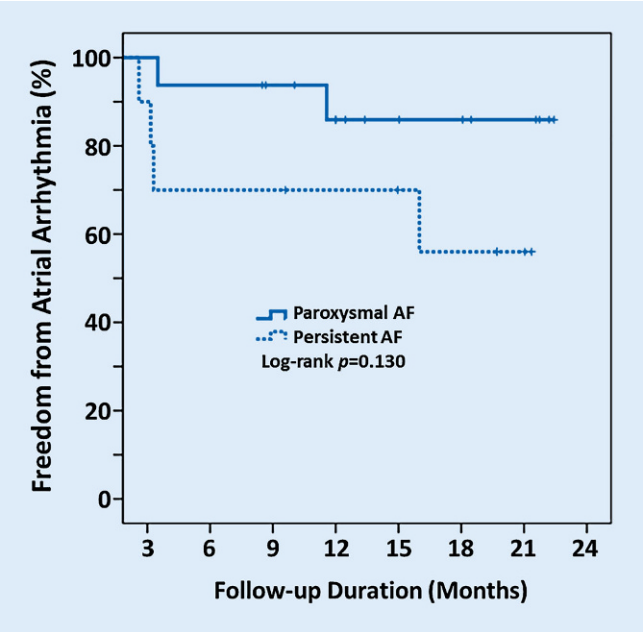

Fig. 1 ◀ Kaplan–Meier estimate for patients undergoing cryoballoon ablation for pulmonary vein isolation and left atrial appendage closure device installation. The freedom from atrial arrhythmia was 74.1% at a mean of 18 months of follow-up with no statistical difference in outcomes between patients with paroxysmal or persistent atrial fibrillation (*AF*; $p = 0.130$)

long-term follow-up, one additional patient suffered from a TIA, which required clinical follow-up but did not cause long-term debilitation (mental or physical).

Follow-up outcomes: CBA and LAA for AF

After a mean follow-up period of 18 months (range, 9–23 months), 20 patients (20/27; 74.1%) observed complete freedom from AF/AFL/AT without AAD usage. Patients with paroxysmal AF had better outcomes than did patients with persistent AF (87.5% vs 60%); however, this difference in clinical outcomes was not statistically significant (**Fig. 1**; log-rank $p = 0.130$). With regard to the LAAC (based on the TEE examination at 3 months); 15 patients (15/26; 57.7%) had no leakage, five patients (5/26; 19.2%) had a leak smaller than 3 mm, and six patients (6/26; 23.1%) had a leak that was between 3 and 5 mm in diameter. When comparing acute and longer-term LAAC outcomes (among the 16 patients without a leak detected after the intraprocedural device release), five patients did go on to develop a leak at the 3-month follow-up visit. Conversely, among the ten patients with an acute intraprocedural LAAC leak, four were completely free of leakage at the 3-month follow-up TEE imaging visit. Additionally, all patients had their OAC drug discontinued and no thrombosis was detected by TEE. All patients were able to manage a single antiplatelet therapy strategy; however, one patient suffered from a non-debilitating TIA. Importantly, there were no strokes or bleeding events during the study.

Discussion

Our study had two major findings: (1) the concomitant usage of CBA for PVI and LAAC by occlusion device placement is a feasible procedure (safe and effective) in patients who have non-valvular AF and a high risk of stroke and bleeding; and (2) the CBA procedure can be conducted with local anesthesia while changing over to general anesthesia during the LAAC procedure, which may help to minimize phrenic nerve injury.

There are two important objectives in managing patients with AF: to decrease the risk of stroke while managing bleeding events, and to relieve the patient from both symptomatic and asymptomatic AF attacks. To this end, both RFCA and CBA have been effective for managing AF symptoms and are presently the gold standard for catheter ablation [1, 2]. Additionally, OAC therapy is recommended for patients with AF and a high risk of stroke. Furthermore, OAC therapy should not be discontinued even when a patient is able to maintain long periods of sinus rhythm following catheter ablation [1, 2, 9]. However, with OAC therapy, there is an increasing risk of severe bleeding. And more recently, LAAC was shown to have a similar stroke prevention profile as OAC therapy for patients with non-valvular AF [2]. Consequently, in patients with a high risk of stroke and bleeding, the concomitant usage of CBA and LAAC may be an effective and safe alternative treatment for patients with AF.

Previously published studies have reported on the combined usage of RFCA and LAAC [2, 9, 11–13]. Swaans et al. [11] first reported an observation of 30 patients who underwent RFCA and concomitant WATCHMAN device occlusion. At 60 days, all patients met the study criteria for successful LAAC, and at 12 months, there was a 30% recurrence of AF. Phillips et al. [13] reported on a multicenter registry of RFCA and WATCHMAN implantation during 30 days of post-procedural follow-up. They reported a 100% success rate of LAAC device installation, and at 30 days, there was an 8.7% event rate for serious complications. Wintgens et al. [12] published a longer-term follow-up study from a large multicenter registry of RFCA and WATCHMAN implantation. At 35 months of mean follow-up, 51% of patients had recurrence of AF, and a total of nine ischemic strokes were reported, resulting in an annualized stroke rate of 0.9% (compared with an expected stroke rate of 3.2% without intervention). These studies summarized the feasibility and expected outcome when using RFCA and LAAC in a combined procedure.

Recently, studies reporting the usage of CBA and LAAC have been published [14–17]. Fassini et al. [14] first published the feasibility of CBA and LAAC in a cohort of 35 patients. The first ten patients were treated with the first-generation cryoballoon and the following 25 patients underwent ablation with the second-generation balloon. The mean time of CBA was 114 ± 32 min, and at a mean follow-up of 24 months, atrial arrhythmia recurrence was observed in 28% of patients. Importantly, 86% of patients had a complete LAAC at 1 year on TEE exami-

nation, and there was no reporting of device-related complications or thromboembolic events. In a second study of 49 patients, Fassini et al. [15] reported on the exclusive usage of the second-generation cryoballoon with CBA for PVI and concomitant LAAC. At 24 months, the overall freedom from atrial arrhythmia was 60%, and 92% of patients were off anti-thrombotic drugs. At 8 weeks and 6 months of follow-up, 82 and 86% of patients demonstrated a complete LAAC, respectively. Importantly, the observed annualized stroke and bleeding rates were 1 and 2%, respectively. There was a 71% reduction in stroke and a 60% reduction in bleeding compared with the predictive cohort rates from their respective CHA_2DS_2-VASc and HAS-BLED scores.

In a single-patient case report, Bordignon et al. [16] took an extension of the aforementioned published work (on CBA and LAAC) and asked whether the cryoballoon catheter could be used for both PVI and left atrial appendage isolation (LAAI) with LAAC "followed up" in a staged approach 6 weeks later. Bordignon et al. [17] then followed this study design in a larger cohort of 32 patients. In the first procedure, CBA was used to establish PVI and LAAI, and in 91% of patients it was possible to establish acute LAAI by CBA. The mean procedure time was 61 ± 29 min; however, one patient suffered from a left-side phrenic nerve injury. During the study, the staged approach for the LAAC was completed in 25 patients, and within this cohort, 16 patients (73%) were found to have a durable LAAI from the previous CBA. Both the Fassini et al. [14, 15] and the Bordignon et al. [16, 17] series of studies found CBA and LAAC to be safe and effective. However, a left-sided phrenic nerve palsy occurred during LAAI [17].

Our study results (although based on a small population size) demonstrated a lack of phrenic nerve injury when using local anesthesia approach during CBA, and in China, most catheter ablations for AF are conducted under local anesthesia. One potential explanation is that (under local anesthesia administration) there is less broad-spectrum muscle relaxation, and the diaphragmatic weakening during CBA-induced phrenic nerve interruption may be caught earlier when the diaphragmatic muscle is not exposed to sedative drugs (general anesthesia). However, one cannot ignore the possibility that in our small series of patients this progressive reduction in phrenic nerve injury may have been a simple response to the CBA learning curve. Simply, phrenic nerve injury subsided with more cryoballoon usage. Further study is warranted before a definitive causal relationship is known.

Limitations

Our study comprised a single-arm and single-center observational data set that did not set out to test a specific hypothesis. Additionally, the study was designed to enroll consecutive patients who had CBA and LAAC. Consequently, it is heard to draw any definitive conclusions because of the small size of the study cohort (27 patients) and the employment of three different LAAC devices. Finally, longer-term TEE was not used to examine LAAC leakage beyond 3 months.

Conclusion

The intraprocedural concomitant usage of cryoballoon ablation for pulmonary vein isolation and left atrial appendage closure is feasible in patients with non-valvular atrial fibrillation and a high risk of stroke, transient ischemic injury, and/or bleeding. However, larger long-term comparative studies are needed to judge the overall safety and efficacy of the combined procedure.

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Compliance with ethical guidelines

Conflict of interest J. Liu, Y. Xia, H. Zhang, X. Li, S. Zhang, and P. Fang declare that they have no competing interests.

For this article no studies with human participants or animals were performed by any of the authors. All studies performed were in accordance with the ethical standards indicated in each case.

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