

Fourth-Generation Cryoablation Based Left Atrial Appendage Isolation for the Treatment of Persistent Atrial Fibrillation: First Case Report

Authors' Contribution:
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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Patient: Male, 67-year-old
Final Diagnosis: Atrial fibrillation
Symptoms: Palpitations
Medication: —
Clinical Procedure: Left atrial appendage isolation
Specialty: Cardiology • Rhythmology





Objective: Unusual or unexpected effect of treatment
Background: Pulmonary vein isolation (PVI) is an effective treatment strategy for patients with paroxysmal atrial fibrillation (AF), yet it is associated with limited success rates in patients with persistent AF (PersAF). The left atrial appendage (LAA) was recently identified as a target of catheter ablation especially in PVI non-responders and LAA-isolation (LAAI) by cryoballoon or radiofrequency was shown to be effective. Recently the fourth-generation cryoballoon (CB4) was introduced to clinical practice. Here we are demonstrating the first case report of CB4-based LAAI followed by LAA-closure in a patient with PersAF.

Case Report: A 67-year-old male patient presented with symptomatic PersAF and thromboembolism due to LAA-thrombus. After resolving the LAA-thrombus cryoballoon based PVI and empirical LAAI was successfully performed. To prevent further thromboembolism LAA-closure was successfully performed after 6 weeks. On short-term follow-up (12 weeks) the patients stayed in stable sinus rhythm.

Conclusions: Fourth-generation cryoballoon based ablation seems to be an effective treatment strategy for LAAI.

MeSH Keywords: Ablation Techniques • Atrial Appendage • Atrial Fibrillation

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Background

Although pulmonary vein isolation (PVI) is an effective treatment strategy for patients with paroxysmal atrial fibrillation (AF) [1,2]. It is associated with limited success rates in patients with persistent AF (PersAF) [3]. Current research has focused on additional ablation strategies, yet recent findings have been controversial [4]. In this context, the left atrial appendage (LAA) was recently identified as a target for catheter ablation especially in PVI non-responders. Recent trials have demonstrated increased clinical success after electrical isolation of the LAA (LAAI) using radiofrequency (RF) current in addition to PVI. Although effective, this strategy might cause electromechanical dissociation and thus is assumed to be associated with an increased risk of thrombus formation and thromboembolism despite oral anticoagulation (OAC) [5,6]. Therefore, subsequent LAA closure has been suggested to prevent thromboembolism. Second-generation cryoballoon (CB2, Arctic Front Advance, Medtronic Inc., Minneapolis, MN, USA) based ablation is safe and effective for PVI, which has been shown to be non-inferior to RF ablation in paroxysmal AF [7]. Since RF based LAAI showed increased rates of thromboembolism, and because stable LAAI is difficult to achieve in some cases, CB2-based LAAI might offer a valuable option to achieve safe and durable LAAI. However, due to the relatively long distal tip of the CB2, this approach needs high operator caution: the LAA has a very thin wall and might be prone to perforation either by the tip or the spiral mapping catheter (Achieve,

Medtronic). Recently the fourth generation cryoballoon (CB4, Arctic Front Advance Pro, Medtronic) was introduced and first reports have shown it is safe and feasible for PVI [8]. Compared to the CB2, the CB4 offers a 40% shorter distal tip aiming to improve time-to-effect based ablation strategies by positioning the Achieve catheter in a more proximal position near the balloon surface [9]. Additionally, the shorter tip potentially increases the safety profile of CB-based LAAI. Here we are demonstrating the first case report of CB4-based LAAI followed by LAA-closure in a patient with PersAF.

Case Report

A 67-year-old male patient presented to our emergency care unit with first diagnosis of symptomatic AF (CHA₂DS₂-VASc score of 4 and HASBLED score of 2) and an acute ischemia of the arteria mesenteric superior as well as the left arteria popliteal. After immediate abdominal surgery with thromboembolctomy a percutaneous transluminal angioplasty was successfully performed. To evaluate the source of simultaneous ischemic events a transesophageal echocardiography (TEE) was conducted and a large LAA-thrombus was detected. To dissolve the LAA-thrombus OAC with phenprocoumon (INR 2–3) was initiated, and rate control by metoprolol (95 mg 1-0-1) and digoxin (0.1 mg 1-0-0) was prescribed. The patient was scheduled for a further TEE after 6 weeks. The following TEE showed normal flow within the LAA (90 cm/s) and no LAA-stroke or

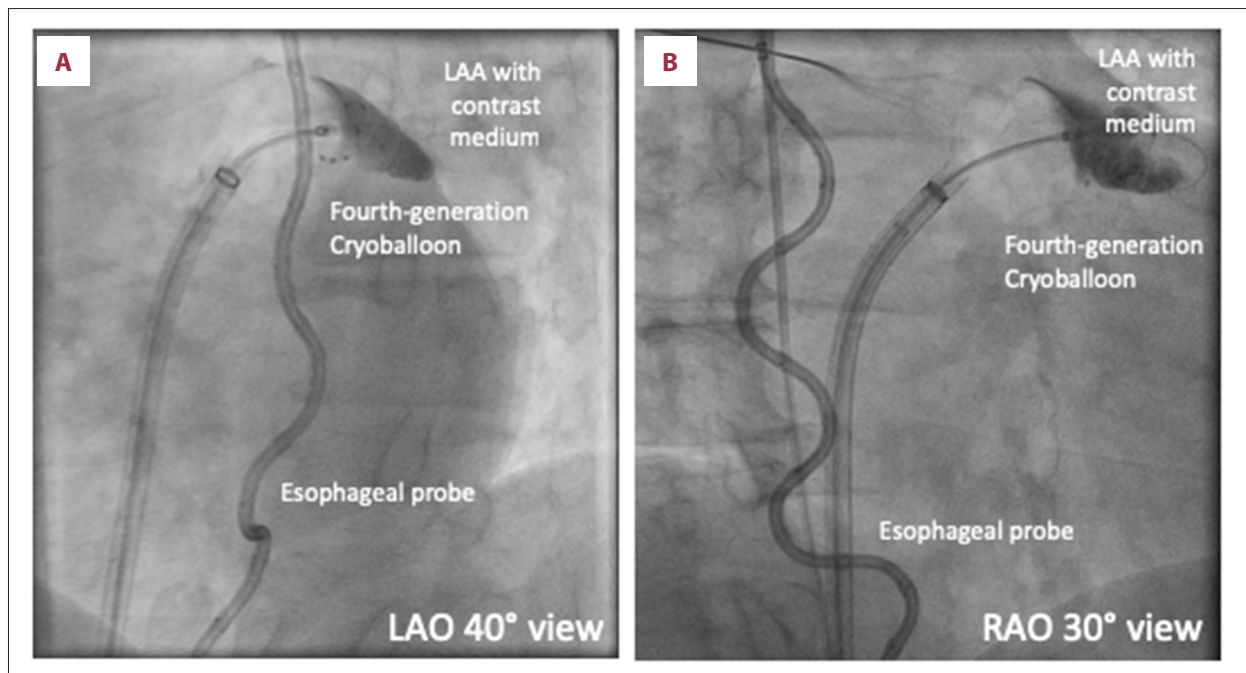
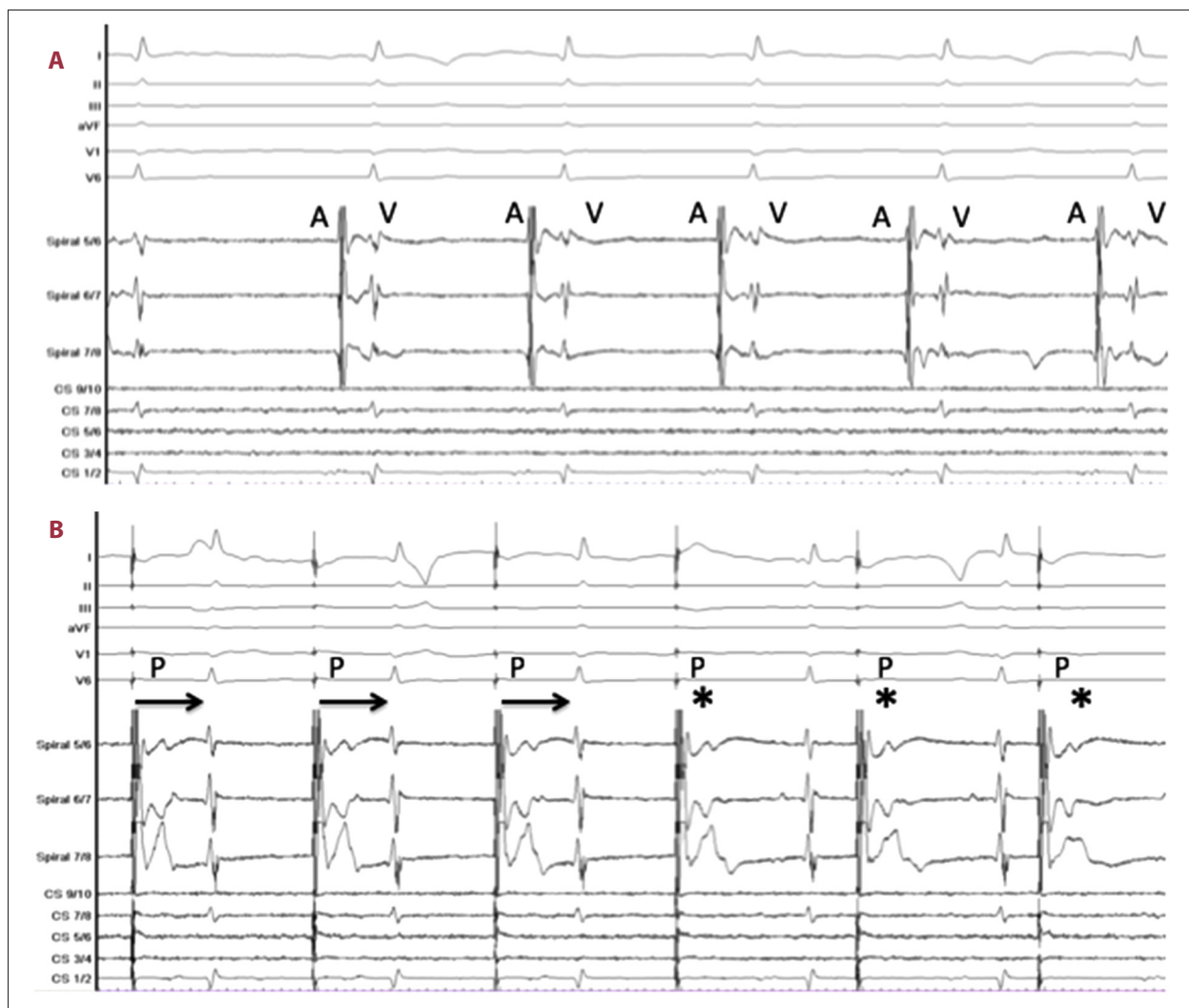


Figure 1. Fourth-generation Cryoballoon based isolation of the left atrial appendage. Fluoroscopic image in LAO 40° view (A) and RAO 30° view (B) showing contrast medium verified complete occlusion of the left atrial appendage by the fourth-generation cryoballoon. Achieve spiral catheter is placed inside the left atrial appendage.

thrombus formation. Direct current (DC) cardioversion was performed to treat symptomatic AF but failed despite amiodarone therapy. Therefore, the patient was scheduled for catheter ablation. Due to failed DC cardioversion and previous LAA-thrombus a CB4-based PVI as well as empirical LAAI followed by LAA-closure to prevent further thromboembolism was suggested and the patient consented to this treatment strategy.

Preprocedural TEE found normal flow within the LAA (90 cm/s) and no LAA-smoke or thrombus formation. The patient was scheduled for the ablation procedure on the next day. The INR on the day of the procedure was 2.4. During the procedure an ACT-level of >300 seconds was reached by heparin administration. All PVs were successfully isolated by a single freeze approach with applications of 180 seconds utilizing the CB4 in combination with a 20 mm Achieve catheter. Time to effect was measured during treatment of every PV. After verified isolation of all PVs the LAA was targeted and electrically isolated during the first CB4 application after 190 seconds (Figures 1, 2).

Due to low temperature the first cryo application was stopped at a minimum temperature -61°C after 211 seconds. Afterwards a bonus-freeze application of 300 seconds was applied with a minimal temperature of -59°C . LAAI was confirmed by entrance- and exit-block. Left phrenic nerve stimulation was performed via the Achieve catheter placed in the LAA during the CB4 applications to detect and prevent injury of the left phrenic nerve. No periprocedural complications occurred. Phenprocoumon (INR 2–3) was continued at 6 hours following the procedure. The patient was discharged on amiodarone therapy and scheduled for LAA-closure 6 weeks after ablation. Repeat TEE revealed no evidence of LAA-thrombus with low flow within the LAA (10 cm/s). An invasive electrophysiological study using a spiral-mapping catheter demonstrated persistent LAAI and LAA-closure using a 24 mm Watchman-Device (Abbott, Chicago, IL, USA) was performed (Figures 3, 4). No periprocedural complications occurred and no leakage or device dislocation was observed, and the patient was discharged after 2 days. Phenprocoumon therapy and amiodarone was administered for 6 additional weeks post



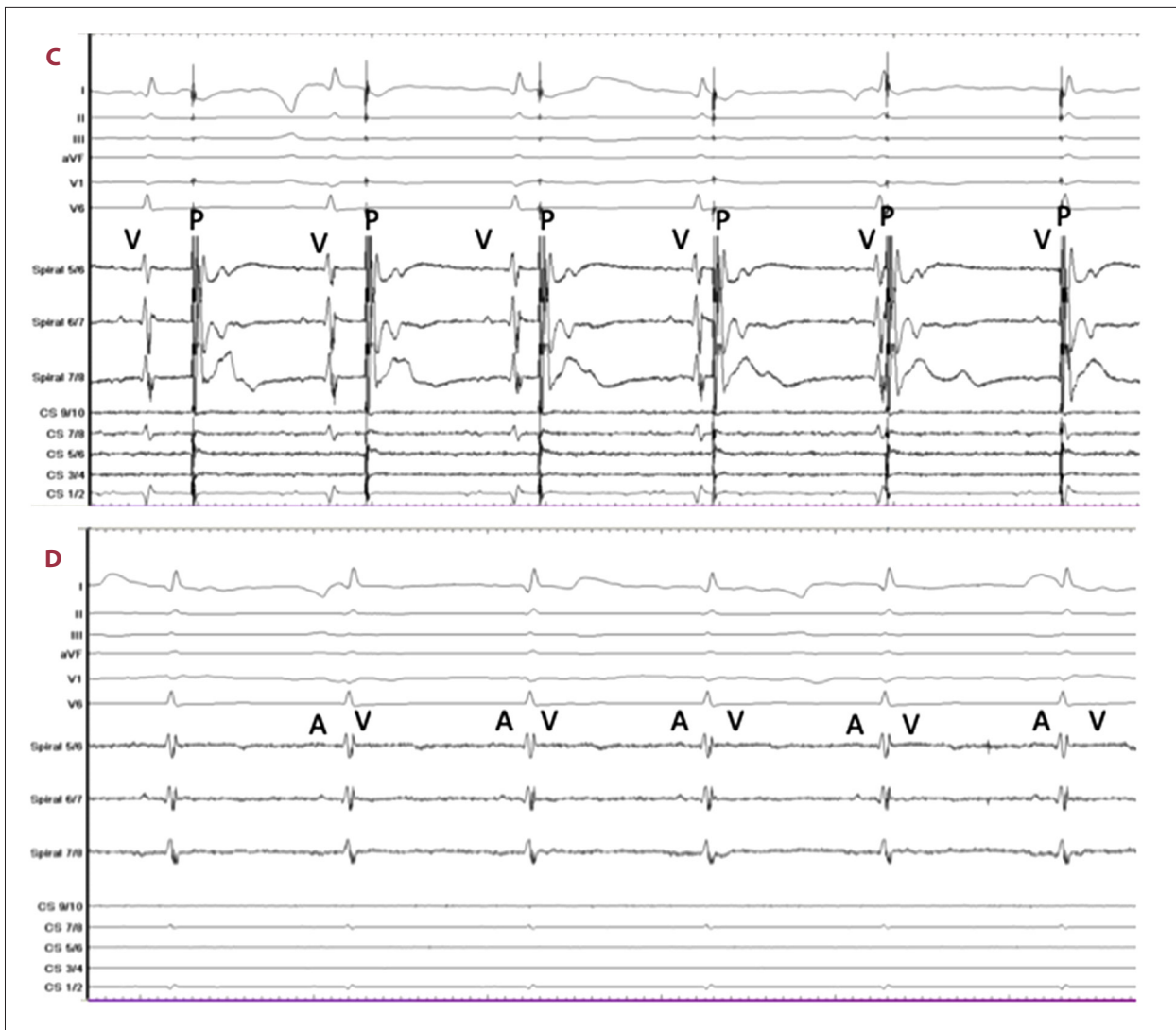


Figure 2. Electrocardiogram recordings during left atrial appendage isolation. (A) Surface and intracardiac electrocardiograms at baseline. The spiral mapping catheter is placed inside the left atrial appendage showing reconduction into the left atrial appendage. (B) Surface and intracardiac electrocardiograms during left atrial appendage isolation with pacing from the spiral mapping catheter inside the left atrial appendage and evidence of conduction dissociation (exit block) between the left atrial appendage and the ventricular signal. Arrows: conduction from the spiral mapping catheter to ventricle. Asterisks: dissociation between the left atrial appendage and the ventricular signal. (C) Surface and intracardiac electrocardiograms 15 minutes after left atrial appendage isolation with pacing from the spiral mapping catheter inside the left atrial appendage and evidence of conduction dissociation (exit block) between the left atrial appendage and the ventricular signal. (D) Surface and intracardiac electrocardiograms after left atrial appendage isolation. During sinus rhythm no conduction into the left atrial appendage (entrance block). A – atrium; V – ventricle; P – paced beat.

device implantation. Afterwards acetylsalicylic acid (100 mg/day) was prescribed. On short-term follow-up (12 weeks), no recurrence of AF or thromboembolism occurred.

Discussion

Catheter ablation is an effective treatment strategy for patients with paroxysmal AF [2]. However, results of catheter

ablation in patients with PersAF and long-standing PersAF are relatively mediocre and novel ablation strategies aiming at improved outcome are under evaluation [10]. Recent studies identified the LAA as an important triggering source and substrate in PersAF and LAAI as adjacent therapy to PVI seems to be a valuable therapeutic option [6]. Since this patient suffered from previously detected LAA thrombus and acute ischemia we discussed the potential benefit of PVI plus LAAI plus LAAC with this individual patient. In our opinion LAAC seems to be a

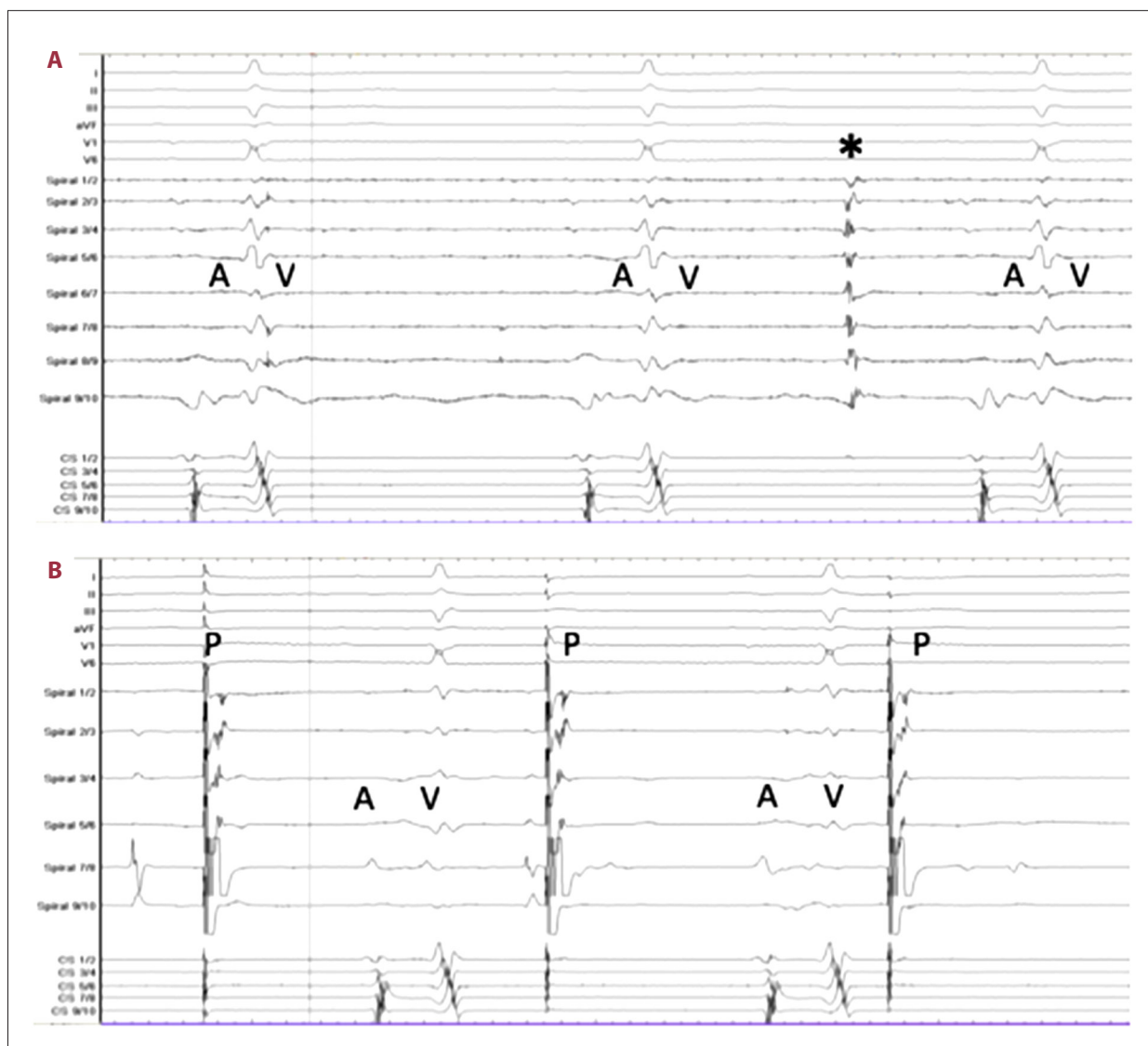


Figure 3. Electrocardiogram recordings during left atrial appendage closure. **(A)** Surface and intracardiac electrocardiograms 6 months after left atrial appendage isolation. The spiral mapping catheter is placed inside the left atrial appendage. During sinus rhythm no conduction into the left atrial appendage (entrance block) has been observed. Asterisk shows automaticity from the left atrial appendage with no conduction to the atrium (exit block). **(B)** Pacing from the spiral mapping catheter inside the left atrial appendage and evidence of conduction dissociation (exit block) between the left atrial appendage and the atrium. A – atrium; V – ventricle; P – paced beat.

good option to prevent recurrence of LAA thrombus with high risk of stroke, TIA, and embolism. Since the LAA was recently identified as a potential source of AF triggers by LAAC might be a valuable strategy LAAI followed for this patient to treat AF as well as recurrence of LAA thrombi [5,6,11].

Although LAAI seems to be effective for AF treatment, the optimal technique and strategy for LAAI remains unclear and there is paucity of data directly comparing different strategies [5,11,12]. Radiofrequency based LAAI might be a suboptimal approach. The procedure is technically challenging and

reported rates of periprocedural complications such as cardiac tamponade during RF-based LAAI are relatively high (7%) [12]. Furthermore, the rate of failed LAAI was reported to be 12.9% to 18%, and the rate of durable LAAI assessed during redo procedures was only 58% to 73% [11–13]. Of note, the aforementioned studies of RF-based LAAI were conducted in highly experienced centers, suggesting that conduction of this ablation strategy might be difficult to implement in routine clinical practice in less experienced hands. In this context cryoballoon based LAAI might offer an effective and safe treatment option. Yorgun et al. recently evaluated CB-based LAAI in addition

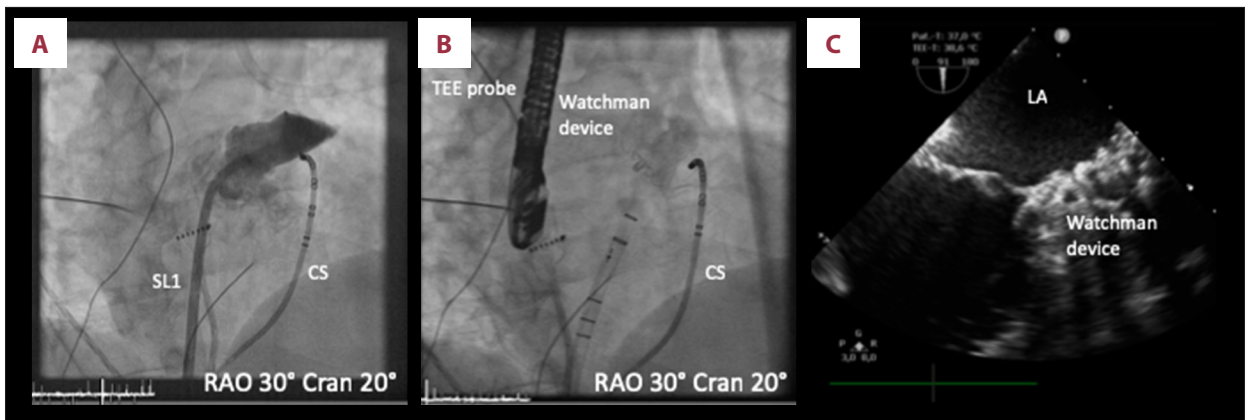


Figure 4. Left atrial appendage closure. (A) Fluoroscopic image in RAO 30° CRAN 20° view with angiography of the left atrial appendage. (B) Fluoroscopic image in RAO 30° CRAN 20° view showing the final image after left atrial appendage closure utilizing a 24 mm Watchman device. (C) Transesophageal echocardiographic image after left atrial appendage closure. LAA-closure via 24 mm Watchman device.

to PVI and observed 0% of pericardial effusion and tamponade and a 100% LAAI durability assessed during repeat procedures [14]. Loss of LAA mechanical contraction after LAAI was suggested to potentially increase thromboembolic risk [6]. While DiBiase et al. [11] and Yorgun et al. [14] found no increased rate for LAA thrombus and thromboembolism after RF-based circular LAAI and CB-based LAAI, Rillig et al. [5] and Heeger et al. [6] found an increased rate of post-procedural LAA-thrombus and thromboembolism after RF-based LAAI despite sufficient OAC. Reasons for this disparity are unclear. LAA flow velocity was preserved in about 44% and 66% after circular RF LAAI and CB-based LAAI [11,12], which is in contrast to results from follow-up TEE investigations after RF-based LAAI reported by Rillig et al. [5] and Heeger et al. [6], which showed highly impaired LAA flow velocities in the majority of patients after LAAI.

For CB2-based LAAI no postprocedural LAA thrombus and no increase of thromboembolism has been observed [14]. Although recently a case reported on CB2-based empirical LAAI and subsequent LAA-thrombus formation despite sufficient oral anticoagulation was published, cryoballoon based LAAI might be favorable concerning thromboembolism [15]. Using the cryoballoon a more distal, circular LAA-isolation is performed compared to RF based wide-area LAA-isolation [11,14]. Therefore, the isolated area might be smaller, which potentially reduces the risk of thrombus formation. In this case report no postprocedural LAA thrombus was detected, successful LAA-closure was performed after 6 weeks and no thromboembolism was detected within 3 months of follow-up which is supporting the cryoballoon-based strategy of LAAI.

Since the left phrenic nerve might be injured by the fast and intense temperature drop utilizing the CB4 for LAAI, continuous left phrenic nerve stimulation was performed via the Achieve

catheter placed in the LAA. In this case no phrenic nerve injury was observed.

Since the LAA is a very thin-walled, vulnerable structure high operator cautiousness is necessary to prevent LAA perforation by positioning of the cryoballoon catheter to the LAA [14]. Due to the 40% shorter distal tip of the CB4 compared to the CB2 the operator may be able to prevent LAA perforation by positioning the cryoballoon tip or the circular mapping catheter too deep inside the LAA. To the best of our knowledge this is the first case of reporting on the acute results of CB4-based LAAI. Proven LAAI was achieved during the first CB4 application after 190 seconds as recorded on the spiral mapping catheter. To possibly improve durability a bonus-freeze application of 300 seconds was applied. Furthermore, no device dislocation or other complications occurred, no LAA reconduction was found as assessed during LAA-closure and no AF recurrence was detected within 3 months of follow-up. Although recent studies evaluated efficacy and safety of LAAI, latest data is controversy, preliminary and off label [5,6,11,15]. Furthermore, CB-based LAAI is an off label, non-approved and investigational use, of a device not commercially available in the USA. Therefore, LAAI might be utilized only in individual patients and will need further evaluation in randomized controlled trials.

Conclusions

Our findings on efficacy of CB4-based LAAI are in line with recent literature of CB2-based LAAI [14]. Due to its shorter distal tip compared to the CB2 the CB4 potentially provides improved safety with an identical acute efficacy for PVI and LAAI. Nevertheless, more studies are needed to determine the optimal strategy in the management of PersAF and whether additional LAAI can reduce AF recurrence in this population.

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