

Left atrial appendage thrombus formation less than 24 hours after empirical cryoballoon-based left atrial appendage isolation: A serious warning



Roland Richard Tilz, MD, FESC, FEHRA, FHRS, Spyridon Liosis, MD, Julia Vogler, MD, Jan C. Reil, MD, Charlotte Eitel, MD, Christian-H. Heeger, MD

From the Department of Cardiology, Angiology and Intensive Care Medicine, University Heart Center Lübeck, Medical Clinic II, Lübeck, Germany.

Introduction

Pulmonary vein isolation (PVI) is an effective treatment strategy for patients with paroxysmal atrial fibrillation (AF).^{1,2} However, in patients with persistent AF (PersAF) and long-standing PersAF, PVI is associated with limited success rates, often requiring multiple procedures for those not responding to PVI.³ More extensive ablation strategies, including ablation of complex fractionated atrial electrograms, linear lesions, and rotors, have been performed with the aim of improving clinical outcome. However, recent findings remain controversial.^{4–7} Therefore, current research is focusing on ablation strategies that potentially enhance procedural success, particularly in nonresponders to PVI. In this context, additional targets outside the PVs have been suggested.^{8,9} Di Biase and colleagues^{8,10} demonstrated that ectopic beats from the left atrial appendage (LAA) are able to initiate and perpetuate AF, and empirical electrical isolation of the LAA (LAAI) using radiofrequency (RF) current in addition to PVI has been shown to increase clinical success. Although potentially effective, this strategy may cause electromechanical dissociation of the LAA and therefore was assumed to be associated with an increased risk for LAA thrombus formation and subsequent thromboembolic events despite oral anticoagulation.¹¹ However, available data are limited, vary across a wide range, and lack long-term assessments.^{10–12} Although data on the

KEY TEACHING POINTS

- Empirical electrical isolation of the left atrial appendage (LAAI) using radiofrequency (RF) current in addition to pulmonary vein isolation has been shown to increase clinical success. Although potentially effective, this strategy may be associated with an increased risk for left atrial appendage (LAA) thrombus formation and subsequent thromboembolic events.
- LAA thrombus formation is possible after empirical LAAI using a second-generation cryoballoon (CB2).
- Although we report the case of a single patient, our finding highlights the importance of screening patients for LAA thrombi after RF- or CB2-based LAAI.
- LAA closure seems to be a reasonable strategy to prevent LAA thrombus formation after LAAI.

KEYWORDS Atrial fibrillation; Catheter ablation; Cryoballoon; Left atrial appendage isolation; Stroke; Thrombus formation (Heart Rhythm Case Reports 2019;5:124–127)

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thrombogenicity of RF-based LAA isolation are conflicting, no increased risk for LAA thrombus or thromboembolism has been reported after second-generation cryoballoon (CB2, Arctic Front Advance, Medtronic, Minneapolis, MN)-based LAAI.¹³ Here we report a case of LAA thrombus formation occurring less than 24 hours after CB2-based LAAI despite oral anticoagulation.

Case report

A 74-year-old male patient (CHA₂DS₂-VASc score 2, HAS-BLED score 2) suffered from recurrent PersAF after CB2-based PVI in July 2015 despite antiarrhythmic drug therapy with flecainide (2 × 100 mg) and oral anticoagulation with apixaban (2 × 5 mg). The patient was scheduled for a second ablation procedure. He was unwilling to take oral anticoagulation. Because of PersAF after initial PVI, an empirical

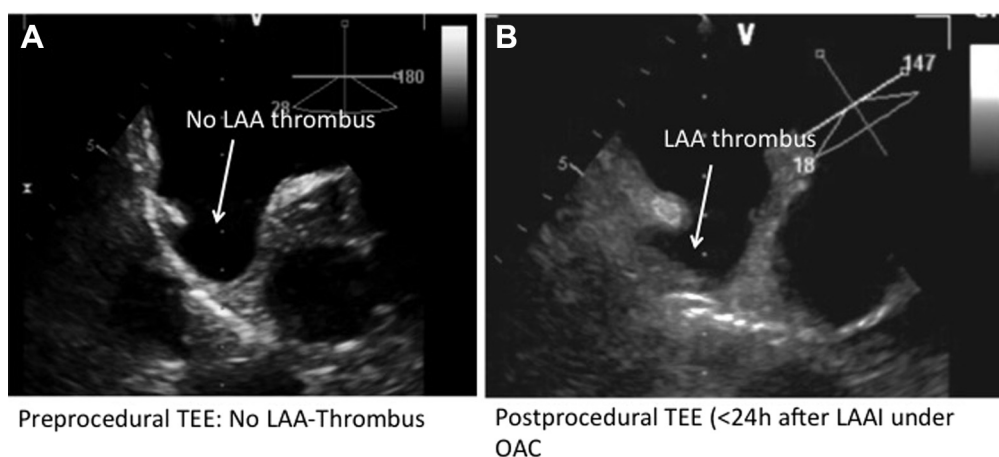


Figure 1 Transesophageal echocardiographic (TEE) images of the left atrial appendage (LAA). **A:** Preprocedural analysis with no evidence of thrombus formation within the LAA. **B:** Postprocedural analysis <24 hours after LAA isolation (LAAI) with evidence of an LAA thrombus. OAC = oral anticoagulation.

isolation of the LAA before LAA closure was suggested, and the patient consented to this treatment strategy.

Preprocedural transesophageal echocardiography (TEE) revealed normal flow within the LAA (90 cm/s) and no LAA smoke or thrombus formation (Figure 1A). The ablation procedure was scheduled for the next day. Only the morning dose of apixaban was withheld. When the procedure started, the patient was in stable sinus rhythm. During the procedure, an activated clotting time >300 seconds was maintained using heparin. All PVs showed durable PVI. Ostial potentials were ablated around the left common pulmonary vein. Using the 28-mm CB2 in combination with a 20-mm Achieve catheter, the LAA was isolated during the first CB2 application after 240 seconds. Cryoapplication time was 300 seconds, and minimum temperature was -50°C (Figure 2). Afterward, a bonus freeze application of 300 seconds was applied with a minimal temperature of -49°C . LAAI was confirmed by entrance and exit block. Left phrenic nerve stimulation was performed during the CB2 applications to prevent phrenic nerve injury. Apixaban 2.5 mg was started 6 hours after the procedure and increased to 5 mg twice per day on the next day.

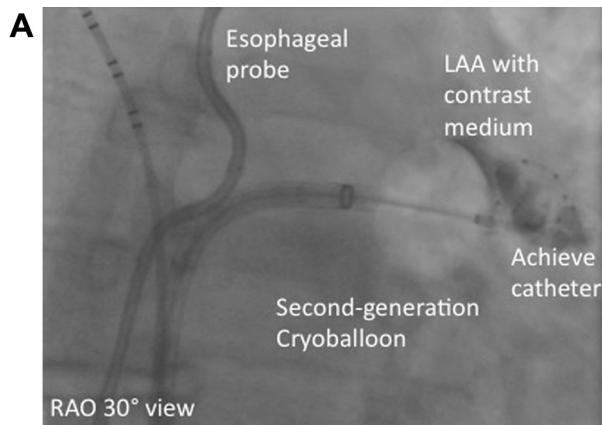
Contrast-enhanced computed tomography of the heart scheduled on day 1 after the procedure to plan epicardial LAA closure revealed a thrombus at the distal LAA. TEE confirmed the LAA thrombus and revealed LAA flow of 60 cm/s (Figure 1B). To dissolve the LAA thrombus, oral anticoagulation with phenprocoumon (international normalized ratio 2–3) was initiated. The patient was in stable sinus rhythm with flecainide 100 mg twice per day until discharge. Follow-up TEE 6 weeks later revealed evidence of a persistent LAA thrombus. Repeat TEE 12 weeks postablation revealed no evidence of LAA thrombus. To prevent further LAA thrombus formation, an LAA closure procedure was planned. The epicardial LAA ligation device features a snare with a maximum snare expansion diameter of 45 mm. Because the ostium of the LAA was measured as 47 mm by computed tomography, an endocardial approach was scheduled. An invasive electrophysiological study using a spiral mapping catheter demonstrated persistent LAAI. LAA closure using

a 28-mm Amplatzer Amulet device (Abbott, Chicago, IL) was performed (Figure 3). Antiplatelet therapy with clopidogrel and aspirin was administered for 6 weeks after device implantation. No recurrence of AF or thromboembolism occurred during short-term follow-up of 3 months.

Discussion

Here we report a case of rapid LAA thrombus formation that occurred <24 hours after CB2-based LAAI. Loss of LAA mechanical function after LAAI was previously suggested to potentially increase thromboembolic risk.^{9,11} Although possibly effective, the optimal ablation strategy for LAAI remains unclear, and assessments of postprocedural LAA thrombus formation are inconsistent.^{10–12} In the BELIEF (Effect of Empirical Left Atrial Appendage Isolation on Long-term Procedure Outcome in Patients With Persistent or Longstanding Persistent Atrial Fibrillation Undergoing Catheter Ablation) trial¹⁰ and in a study by Bordignon and colleagues,¹² no increased rates of LAA thrombus formation and thromboembolism were observed for LAAI patients. However, Heeger and colleagues¹⁴ found an increased rate of postprocedural LAA thrombus and thromboembolism after LAAI. Although different ablation strategies might explain this discrepancy, the mechanism of electrical LAAI with consecutive loss of mechanical contraction resulting in thrombus formation presumably occurs regardless of the strategy.¹¹

Using the CB2, 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 might reduce the risk of thrombus formation. Yorgun and colleagues¹³ recently evaluated CB2-based LAAI in addition to PVI. In their study, a favorable outcome compared to the PVI-only strategy without any postprocedural LAA thrombus formation and no increase in thromboembolism was observed in the LAAI group.¹³ In contrast to the previous study, we identified LAA thrombus formation in the first patient with CB2-based LAAI at our clinic.



Cryoballoon based LAA-Isolation

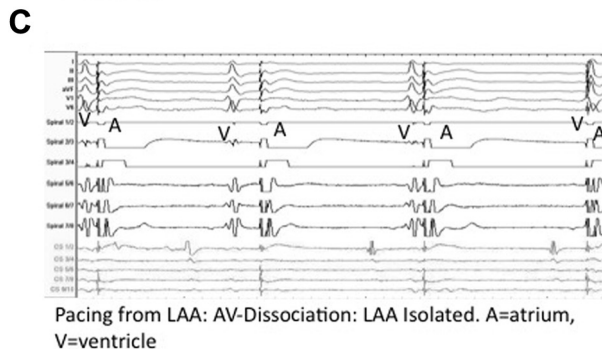
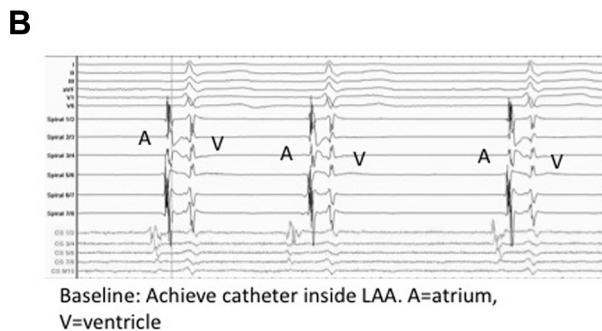
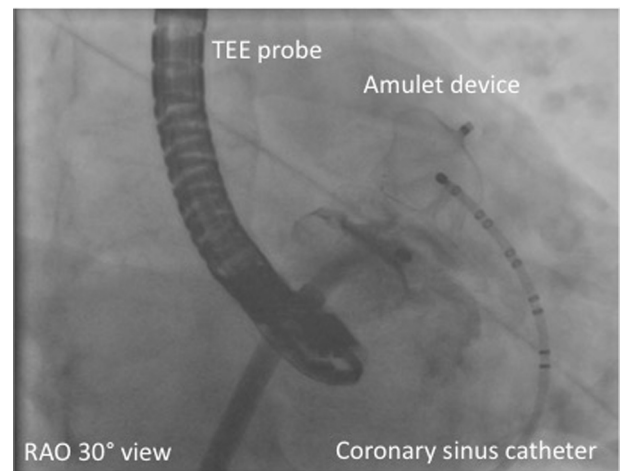


Figure 2 Second-generation cryoballoon-based isolation of the left atrial appendage (LAA). **A:** Fluoroscopic image in right anterior oblique (RAO) 30° view showing contrast medium-verified complete occlusion of the LAA by the second-generation cryoballoon. The Achieve spiral catheter is placed inside the LAA. **B:** Surface and intracardiac electrocardiograms at baseline showing reconnection into the LAA. **C:** Surface and intracardiac electrocardiograms after LAA isolation with pacing from the Achieve catheter inside the LAA and evidence of conduction dissociation between the LAA and the ventricular signal. A = atrium; V = ventricle.

Although this might be a remarkable coincidence, the tremendous clinical relevance of potential iatrogenic cerebral thromboembolism after LAAI underlines the need to evaluate this controversial finding in large multicenter trials. As a result of our observation, the protocol for postprocedural oral anticoagulation after CB2-based LAAI was changed at our institution so that full-dose novel oral anticoagulants are started after 6 hours (not half-dose as reported in this case report).

Closure of the LAA after LAAI may be a viable option to reduce the risk for thromboembolic complications without



LAA-closure via 28mm Amulet device

Figure 3 Left atrial appendage closure. Fluoroscopic image in the right anterior oblique (RAO) 30° view showing the final image after left atrial appendage closure using an Amulet device. TEE = transesophageal echocardiography.

the need for lifelong oral anticoagulation and its potential consequences.¹⁵ For this purpose, LAA closure was performed in our patient to prevent recurrent LAA thrombus formation and potential thromboembolism.

Conclusion

Here we present a case of CB2-based empirical LAAI and subsequent LAA thrombus formation despite sufficient oral anticoagulation. Although we report the case of a single patient, our finding highlights the importance of screening patients for LAA thrombi after RF- or CB2-based LAAI. Clinical trials and registries are necessary to draw final conclusions.

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