Left Atrial Appendage After Electrical Isolation
To Occlude or Not To Occlude, That Is the Question

Luigi Di Biase, MD, PhD, FHRS; Andrea Natale, MD, FESC, FHRS

The left atrial appendage (LAA) has been considered for years as a less relevant part of the left atrium. During the years, its function and role have been extensively studied.

The LAA is recognized as the major source (95%) of cardiac emboli in patients with nonvalvular atrial fibrillation (AF). In addition, the LAA has been shown to have important roles in atrial natriuretic peptide secretion and as an under-reported trigger site of AF. From an anatomic point of view, the LAA has a trabecular tubular shape with variable morphologies and derives from the embryonic left atrium as an outgrowth of the pulmonary veins.

Pulmonary vein (PV) isolation is the primary target for ablation. Procedural success rates vary depending on the experience of the operator and on the subtype of atrial fibrillation: higher in paroxysmal and lower in persistent and long-standing, persistent AF. Many patients continue to experience AF recurrences, despite permanent PV isolation. In such cases, several authors have identified additional targets for ablation outside the pulmonary veins, the so called non-PV triggers.

The most common non-PV trigger sites are the superior vena cava, the coronary sinus, the atrial septum, the posterior wall, the ligament of Marshall, and, more recently emphasized, the LAA. It is important to consider that the Cox-Maze III surgery data have demonstrated a 90% success rate at maintaining sinus rhythm and a low incidence of thromboembolic events, and this procedure excludes or excises the LAA.

The surgical data and the experience and lessons learned by burning guided our group to consider the LAA as a target for ablation. Catheter ablation of AF is a valid therapeutic option for the treatment of AF and has been shown to be superior to antiarrhythmic drugs for maintaining sinus rhythm.

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In our first series in 2010, we showed that LAA electric isolation rather than focal LAA ablation was the best strategy to maintain sinus rhythm at follow-up in a series of patients that failed previous procedures and showed sustained LAA firing. We also showed that after electric isolation of the LAA, in 50% of cases, lifelong anticoagulation is recommended to reduce the risk of thromboembolic complications. To eliminate the need for lifelong anticoagulation, LAA closure devices could potentially be used. It is also important to note that based on the current recommendations, discontinuation of oral anticoagulation (OAC) after successful ablation is allowed only in patients with a CHA2DS2-VASc score <2 and that the majority of patients with nonparoxysmal AF that may require LAA electric isolation have a CHA2DS2-VASc score ≥2.

In this issue of the Journal, Panikker et al sought to assess the feasibility, safety, and efficacy of concomitant LAA electric isolation and LAA occlusion with the Watchman closure device in 22 patients undergoing long-standing, persistent AF ablation. Outcomes were compared with a balanced (1:2 ratio) control group who had ablation for long-standing, persistent AF with the same lesion set without LAA electric isolation. LAA electric isolation was achieved in 20 of the 22 patients, and a Watchman closure device was successfully placed in all of these 20 patients without periprocedural complications. Imaging at 45 days and 9 months confirmed satisfactory device position in 19 out of 20 patients (95%), and these patients stopped warfarin 3 months post ablation. In 1 patient (5%), a gap >5 mm was detected into the LAA, and OAC was not discontinued. No major complications or effusions occurred periprocedurally or at follow-up. Importantly, no transient ischemic attacks or strokes occurred.

An important piece of information arising from the study is that freedom from AF/atrial tachycardia at 12-month follow-up after a single procedure off antiarrhythmic drugs was 60% in the LAA electric isolation group versus 40% in the control group (hazard ratio [95% confidence interval]=0.57 [0.26–1.28]; P=0.17). When considering only AF recurrences (defined as AF episodes longer than 30 seconds and excluding atrial tachycardia), the success rate at 12-month follow-up after a single procedure off antiarrhythmic drugs was 95% in the LAA electric isolation group and 63% in the control group (63%; hazard ratio=0.11 [0.02–0.87]; P=0.036). More interestingly, freedom from AF/atrial tachycardia after multiple procedures (mean of 1.3 procedures) in the LAA electric isolation group increased to 90%.

The authors should be commended for this excellent study and for the excellent outcome. Despite the absence of a formal randomization and the small sample size, this study is of interest and should be considered a pilot for future randomized studies.

Another interesting suggestion arising from the study is that in patients with long-standing, persistent AF, it is not...
necessary to demonstrate the presence of AF firing from the LAA to receive benefit from LAA electric isolation.21

The study clearly shows a better outcome after a single procedure and multiple procedures in patients with long-standing, persistent AF undergoing empirical LAA electric isolation. This observation may explain why series that required demonstration of firing in the LAA to justify ablation has reported a lower success rates.22,23 In addition, the study also shows that LAA electric isolation with radiofrequency energy is safe because no peri-procedural complications were reported.

These data are in line with the Belief randomized trial (NCT01362738) presented at the late breaking trial of the ESC 2015.24 The common belief that demonstration of a trigger from the LAA is necessary to justify that ablation in this structure is negated by both the Belief trial and by the study of Panikker et al.21,24 Similarly, for many years, we assumed that only the individual PV triggering AF had to be the target for ablation, and only later was it realized that empirical isolation of all PVs was a better approach. The same could be applied to long standing persistent AF patients and LAA electric isolation.

In the study by Panikker et al in addition to wide area pulmonary veins isolation, linear ablation at the left atrial roof, lateral mitral valve isthmus, and cavotricuspid isthmus were performed in all patients. Therefore, the higher success rate of the LAA electric isolation group needs to take into consideration the fact that the lesion set in both groups included more than just PV isolation.

The Amaze trial25 will enroll patients with persistent and long-standing, persistent AF undergoing Lariat LAA closure with mechanical electric isolation followed 3 weeks later by pulmonary vein isolation with radiofrequency energy and cavotricuspid isthmus. We feel that this study will probably support the relevance of the LAA as an important driver for AF, although in this author’s opinion, the fact that other non-PV triggers such as coronary sinus and posterior wall will not be ablated will weaken the overall long-term freedom from AF.

The main perceived drawback of LAA electric isolation is its potential thromboembolic risk. Our 2010 study12 and the preliminary data of the Belief trial24 show that ≈40% of patients have a flow velocity within normal range after LAA isolation and that with proper OAC no added stroke risk exists.

In contrast, Rillig et al26 reported an unexpectedly high incidence of LAA thrombus formation and stroke after LAA electric isolation despite OAC in a series of 50 patients, with 2 strokes and 1 TIA during a median follow-up of 6.5 months. In addition, LAA thrombus was identified on transesophageal echocardiography in 10 patients (21%). Several criticisms arise.

All the 3 patients had AF recurrence with 1 patient off OAC, 1 patient on warfarin with subtherapeutic international normalized ratio at the time of the event, and 1 patient was on dabigatran without verification of patient compliance. Similar concerns on OAC status could apply in the 10 patients with LAA thrombus. More recently, we reported data from 1854 consecutive AF patients (84% nonparoxysmal AF) receiving LAA isolation along with PV isolation.27 Transesophageal echocardiography at 6 months postablation follow-up showed impaired LAA mechanics in 58% of the patients. The overall thromboembolic event rate was 0.08% and 2.26% in on- and off-OAC populations, respectively (P<0.001). Of the 14 patients with stroke, 12 (85.7%) had subtherapeutic INR or discontinued their OACs for >5 days. These results provide more evidence that LAA isolation is not associated with a higher risk of thromboembolic events even in the presence of impaired LAA function as long as optimal anticoagulation is maintained.27 Another important difference that may explain the different outcome in stroke risk is the technique used to achieve LAA isolation. Rillig et al26 performed an extensive approach with a wider area of ablation after PV isolation followed by a mitral ishthus line and an anterior line in the majority of patients. This type of extensive ablation may compromise the overall atrial contraction and be prothrombotic. Our technique of LAA electric isolation is more conservative.10,11,24 In sinus rhythm, we place the circular mapping catheter at the antrum of the LAA (guided by the intracardiac echo), and the ablation targets the earliest activation signal on the circular mapping catheter. In addition, in our series, a transesophageal echocardiography is always performed 6 months post LAA isolation in patients with sinus rhythm with verification of flow velocity, A wave consistency, verification of LAA contraction, and its relation with the cardiac cycle before stopping OAC.

This is an expanding field, and more data are required to clarify the risks, benefits, hemodynamic impact, and best strategy of LAA electric isolation. The proposal to do LAA isolation and closure at the same procedure is interesting, but there are concerns. Although no complications occurred, it should be considered that the LAA ostium could be edematous from ablation, and this might affect the choice of the correct closure device size and create risks that emerge during follow-up. In addition, as with PV isolation, the LAA can reconnect, and repeat isolation may be more challenging with a closure device in place.24

The procedure cost and reimbursement should be also taken into account.

In view of these considerations, we think that after electric isolation of the LAA, occlusion should be performed at a later time, after ablation; after proper assessment of the LAA flow velocity and contraction, CHA2DS2-VASc score, and presence or absence of arrhythmia recurrence, and after considering patient compliance with OAC.28 More studies are required to assess whether we should occlude the LAA in all patients after its electric isolation.

Disclosures
Dr Di Biase is a consultant for Biosense Webster, Stereotaxis, and St. Jude Medical and has received speaker honorarium/travel from Boston Scientific, Medtronic, Janssen, EPiEP, Biotronik, and Pfizer. Dr Natale received speaker honorariums from Boston Scientific, Biosense Webster, St. Jude Medical, Biotronik, and Medtronic and is a consultant for Biosense Webster, St. Jude Medical, and Janssen.

References
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Circ Arrhythm Electrophysiol. 2016;9:
doi: 10.1161/CIRCEP.116.004372

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