Left atrial appendage electrical isolation and concomitant device occlusion: A safety and feasibility study with histologic characterization

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BACKGROUND Left atrial appendage (LAA) electrical isolation is reported to improve atrial fibrillation ablation outcomes. However, loss of mechanical function may increase thromboembolic risk.

OBJECTIVE The aim of this study was to evaluate the feasibility and safety of LAA occlusion after electrical isolation in a canine model.

METHODS Nine canines underwent LAA isolation with irrigated radiofrequency ablation after pulmonary vein (PV) isolation. Entrance and exit block were confirmed with intravenous adenosine after 30 minutes. The LAA was then occluded with a Watchman device. Device position was assessed at 10 days by using transthoracic echocardiography. At 45 days, LAA isolation was assessed epicardially. Hearts were then examined macroscopically and histologically.

RESULTS All 36 PVs and 8 of 9 LAAs (89%) were electrically isolated. Acute LAA reconnection occurred in 4 of 8 LAAs (50%). All were reisolated. The mean ablation time was 51 ± 19 minutes, including 24 ± 18 minutes for LAA isolation. LAA occlusion was successful in all cases. One animal died of a primary intracranial bleed due to anticoagulant hypersensitivity 36 hours after the procedure. Transthoracic echocardiography at 10 days confirmed satisfactory device positions and no pericardial effusion. At 45 days, 7 of 8 (88%) had persistent LAA electrical isolation. All devices were stable without evidence of erosion. Microscopy revealed complete device-tissue apposition and a mature connective tissue layer overlying the device surface in all cases.

CONCLUSION LAA electrical isolation and mechanical occlusion can be performed concomitantly in this animal model, with no displacement or mechanical erosion of the appendage at 45 days. This technique can potentially improve success rates and obviate the need for chronic anticoagulation. Future studies should address efficacy, safety, and feasibility in humans.

KEYWORDS Atrial fibrillation; Catheter ablation; Left atrial appendage; Occlusion; Anticoagulation; Thromboembolism

ABBREVIATIONS AF = atrial fibrillation; **LA** = left atrium; **LAA** = left atrial appendage; **LSPV** = left superior pulmonary vein; **PV** = pulmonary vein; **TEE** = transesophageal echocardiogram/echocardiography; **TTE** = transthoracic echocardiogram

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Introduction

Catheter ablation has revolutionized the treatment of atrial fibrillation (AF)[1,2]; however, the long-term outcomes in treating persistent AF are variable, often requiring multiple procedures to maintain long-term freedom from atrial arrhythmias.[3] While electrical isolation of the pulmonary veins (PVs) is central to catheter ablation strategies,[4] foci and/or substrate outside the PVs particularly in the left atrial appendage (LAA) have been found to play a key role in persistent AF.[5–7] LAA electrical isolation may improve freedom from AF.[5,7] There are, however, safety concerns regarding LAA ablation without subsequent LAA occlusion.[8] The combination of a standard AF ablation lesion set together with LAA electrical isolation and LAA occlusion may be synergistic in improving success rates of ablation for persistent AF while also mitigating stroke risk and reducing the bleeding risks from long-term anticoagulation in a single procedure. However, the feasibility and safety of concomitant endocardial electrical isolation and mechanical occlusion of the LAA are not known.

We therefore tested the hypothesis that concomitant electrical isolation of the LAA and its occlusion with a

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Watchman device after PV isolation is feasible and safe in a preclinical canine model.

Methods

The study protocol is presented in Figure 1. Full methodology details are given in the Online Supplemental data.

Animals

Nine healthy, purpose-bred, male mongrel dogs were studied. To reflect the human model of AF ablation and LAA occlusion, all dogs received warfarin to maintain an international normalized ratio of 2.5–3.0.

Catheter ablation

The aim of the catheter ablation procedure was to electrically isolate the PVs and LAA.[1,7,12] Circumferential ostial PV ablation was performed with an open-irrigated, 4-mm-tip ablation catheter (Blazer, Boston Scientific, Natick, MA), limiting power to 30 W.

Electrical isolation of the LAA incorporated a proportion of the lesions created during left superior pulmonary vein (LSPV) isolation. Higher power (35 W) was used to ablate at the LAA ostium owing to greater tissue thickness in this area (Figure 2A).

The end point of ablation was electrical isolation of all the PVs and the LAA. Electrical isolation was defined as bidirectional conduction block (Figure 2C).

After isolation of the LAA, a 30-minute observation period ensued to identify dogs with early LAA reconnection. Entrance and exit block were then reassessed before and after a 9-mg intravenous adenosine bolus.[9] Where reconnection was identified, ablation was performed to reisolate the LAA. Sites of reconnection and successful reisolation were recorded.

LAA device occlusion

The LAA was then occluded, as has previously been described in detail[10] (Figures 2E and 2F and Online Supplemental Figure 1; also see the Online Supplemental data).

Follow-up

Day 10 study

All animals underwent a transthoracic echocardiogram (TTE) under sedation at 10-day postprocedure. Further details are given in Figure 1.

Day 45 study

Under general anesthesia, transesophageal echocardiography (TEE) was performed, the left atrium (LA) was accessed via transseptal puncture, and an endocardial electrophysiology study was performed to assess PV conduction. The occlusion device caused mechanical obstruction to local endocardial testing at the LAA ostium. Therefore, LAA electrical activity was subsequently assessed epicardially. Entrance and exit conduction block were assessed relative to the endocardial Lasso catheter (Biosense Webster, Diamond Bar, CA) within the LA. Pacing was performed at 2 LAA sites at maximum output (25 V at 2 ms) to assess exit block (Figure 1).

Histologic analysis

After the assessment of LAA conduction, all animals were sacrificed. The brain, kidneys, liver, spleen, lungs, and local lymph nodes were inspected for evidence of infarction or other pathology. The LA was opened, and ablation lesions were identified. Histologic analysis was performed to assess

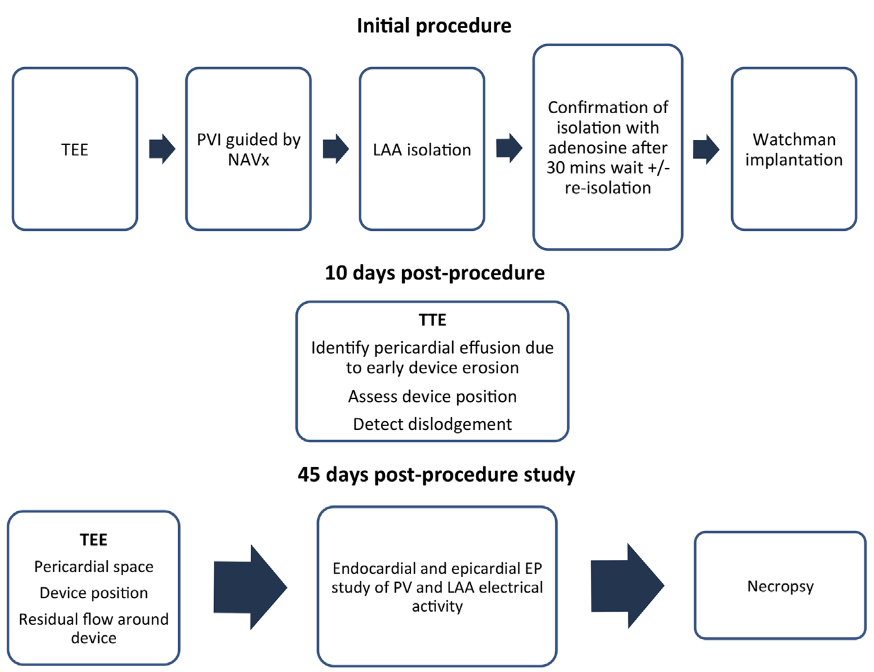

Figure 1 Study design flow chart. EP = electrophysiology; LAA = left atrial appendage; NavX = 3-dimensional electroanatomic mapping system; PVI = pulmonary vein isolation; TEE = transesophageal echocardiogram; TTE = transthoracic echocardiogram.