Multimodality evaluation of LAA Leaks arising after incomplete LAAC: Insights from the LAA-Leak Registry

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1. Background

Left Atrial Appendage (LAA) Closure (LAAC) is a potent technique of LAA isolation and exclusion for stroke prevention in patients with atrial fibrillation, with evidence from the PROTECT-AF and PREVAIL-AF trials, including their 5-year follow-up assessments, solidifying LAAC as a viable option in these patients with comparable stroke reduction in comparison to oral anticoagulation (OAC) as well as a reduction in bleeding risk, hemorrhagic CVA, and mortality [1-3]. However, the surge in the multiple methods of LAA exclusion has also brought to attention postprocedural complications specific to LAAC, namely, peri-device leaks (PDL) [4]. The stroke implication and classification of PDL itself still lacks consensus, with an increased thromboembolic (TE) potential due to PDL seen in patients with LARIAT and surgical ligation procedures, yet no statistically significant relationship seen in percutaneous and endocardial LAA closure approaches [5-9]. PDL > 5mm has been widely accepted as clinically significant, although there remains limited data with no current established guidelines. [5, 6, 10]. Placement of a septal occluder device such as Amplatzer Vascular Plug, Detachable embolization coils, Gore Cardioform Septal Occluder (CSO; W.L. Gore and Associates, Newark DE), and radiofrequency ablation (RFA) have all emerged as options to resolve residual PDL and post-surgical/ligation leaks [5, 10-12]. However, there exists no head-to-head comparison between these modalities. Given their emergence, we proposed a multi-center observational study to further assess and evaluate these three treatment modalities for their efficacy for leak closure, assessment of pre-, peri- and post-procedural characteristics after leak closure, TE events, and bleeding risk, and complication rates.

2. Objectives:

Primary Objective:

Our main objective is to collect data from multiple different centers that use different modalities to currently treat either central or peri-device leaks that occur after incomplete LAA closure, and compare each modality in their efficacy and safety outcomes.

Primary Outcome: To compare the efficacy of the three current methods of PDL closure modalities in patients with prior incomplete LAAC.

Secondary Outcome: To compare the rates or reduction of rates of thromboembolic events and procedure-related complications in patients after successful PDL closure with any of the three closure modalities.

3. Research Methods and Statistical Considerations:

Research Methods:

This will be a multi- center retrospective observational comparison study.

Study Population:

All patients at risk for stroke or thromboembolism that demonstrated any degree of the significant leak on follow up TEE imaging at least 4-6 weeks following either epicardial, endocardial, or surgical LAAC were included in this study population. All patients were evaluated and followed with imaging, and per investigators' respective clinical judgement, then proceeded to have an intervention for leak closure with either detachable embolization coils, vascular plugs/CSO, or RFA.

Inclusion Criteria:

- patients at risk for stroke or thromboembolism that demonstrated any degree of the significant leak on follow up TEE imaging at least 4-6 weeks following either epicardial, endocardial, or surgical LAAC
- Patients undergoing any form of eccentric or centric/central leak closure with available modalities (detachable embolization coils, vascular plug/septal/ASD occluders, or RF Ablation). Criteria for this was made based on the judgement of the operator, with no specific cutoffs for leak size, follow-up time from LAAC to leak closure, etc)
- Age greater than 18 years

Exclusion Criteria:

- Patients not undergoing leak closure after incomplete LAAC
- Patients unable to complete 45-day follow-up imaging for reevaluation of LAA leak
- Patients unable to consent

Primary Endpoints:

1. To compare the efficacy of the three PDL closure modalities in patients with prior LAAC

Secondary Endpoints:

1. To compare the reduction/rates of TE events and procedure-related complications (DRT, pericardial effusion/cardiac tamponade, or CVA/TIA) in patients after successful PDL closure with any of the three closure modalities
    a. Periprocedural complications occurring from Postoperative day #0 – day 7
    b. Delayed procedure-related complications and adverse events within 90 days of procedure

Informed Consent:

Given that this study was observational and retrospective in design, no informed consent was obtained or required. Patients who met inclusion/exclusion criteria were de-identified and added to word documents/excel spreadsheets.

Data storage/Confidentiality:

Data will be collected in word documents, PDFs, and excel sheets. Data recorded on the worksheets will be entered into a secure password protected computer database by the research staff at corresponding heart institutes/cardiac centers. Only investigators involved in the study will have access to the data. All data will be reported in aggregate form and no names will be used for any publications resulting from the research. De identification of data will be done at the earliest.

Sample Size:

We will plan to aim for a total size of 160 patients in total among all three modalities.

Statistical Analysis:

Continuous variables will be summarized using mean and standard deviation, while categorical variables will be summarized as counts and percent of the total. Comparison analysis between groups will be made using Kruskal-Wallis tests for nonparametric data sets as appropriate. Leak sizes were measured initially and then via postprocedural follow-up, with overall rates of closure, minimal-mild leaks, and clinically significant leaks listed with associated p-values. All tests were two-tailed, and a *P* value less than 0.05 was considered statistically significant. All analyses were performed using SPSS Statistics version 28.0.0.0 (IBM).

<u>Data/Variable Points for Collection:</u>

- Age
- Sex
- Height
- Weight
- BMI
- Diabetes (y/n)
- Smoking (y/n)
- Dyslipidemia (y/n)
- Prior stroke/TIA (y/n)

- Prior deep venous thrombosis/pulmonary embolism (y/n)
- Ejection Fraction
- History of CAD (y/n)
- Congestive heart failure (y/n)
- Chronic Kidney Disease (y/n)
- Type of Atrial Fibrillation (paroxysmal, persistent, permanent)
- Baseline antithrombotic regimen (aspirin, clopidogrel/prasugrel/ticagrelor, warfarin, direct oral anticoagulant, heparin)
- TIA/stroke after Watchman
- History of major bleeding
- High Fall risk (y/n)
- Previous major bleeding (y/n)
- Previous minor bleeding (y/n)
- Thromboembolism while on oral anticoagulant
- CHA2DS2-VASc Score
- HAS-BLED Score
- Time passed since LAA closure (months)
- Type of LAA Closure (watchman/watchman FLX, amulet, lariat, surgical ligation, atriclip)
- Device Size (if applicable)
- Thrombus on device (y/n)
- Peri-device/central leak size in mm
- Acute success (end of procedure closure) (y/n)
- Procedure duration (minutes)
- Flouroscopy time (minutes)
- Contrast usage (mL)
- Hospital length of stay
- Type of procedural anesthesia (general vs light sedation vs local)
- Procedural imaging (TEE, ICE, or both)
- Devices attempted
- Devices deployed
- Combination procedures (combined AF ablation, or LAA occlusion + AF ablation)
- Size/number of devices (plugs/coils)
- Major procedural complications from postoperative day 0-7: stroke, TIA, air embolism, myocardial infarction, cardiac tamponade, device embolization, ventricular tachycardia
- Minor procedural complications from postoperative day 0-7: pericardial effusion
- Complications seen within 90 days of the procedure: cardiovascular death, non-cardiovascular death, stroke/TIA, pericarditis
- Follow-up transesophageal echocardiogram time (months)
- Size of leak at follow up (in mm)
- Follow-up time
- Follow up antithrombotic regimen

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