Percutaneous Left Atrial Appendage Closure Using the Lariat
To Close, or Not to Close, That Is the Question*

Srinivas R. Dukkipati, MD, Marc A. Miller, MD

It has been almost 10 years since the Lariat device (SentreHeart, Inc., Redwood City, California) received U.S. Food and Drug Administration 510(k) intermediate risk clearance for use in “surgical applications where soft tissue is being approximated,” and 5 years since the first publications on the feasibility of its use for left atrial appendage (LAA) exclusion (1). As an alternative to systemic anticoagulation for at-risk patients with atrial fibrillation, the initial published data in 89 patients from Poland was encouraging (2). Acute complete LAA closure was achieved in 92% with an overall complication rate of only 3.3%. Accordingly, the use of Lariat technology for LAA closure began to rapidly expand. However, like many new interventional technologies, additional real-world experience demonstrated more sobering results. In our own multicenter retrospective series, the rate of acute LAA closure was high (93%) but nearly one-quarter of patients developed reconstitution of LAA flow (“LAA leak”) at 3 months. Furthermore, 20% of patients developed pericardial effusions requiring drainage and 9% of patients experienced LAA perforation (of which 2 required urgent cardiac surgery) (3). More recently, a systematic review of published reports confirmed the relative effectiveness of the Lariat for achieving acute LAA closure (90%), but it also reiterated the concerning safety profile (4). Most notable was the need for urgent cardiac surgery in 2.3% of patients. It should also be noted that in the most of the previously published series, a majority of patients (>60%) were receiving oral anticoagulation prior to the procedure, and a significant number of patients remained on oral anticoagulation after the procedure, making interpretation of the impact of the Lariat device on the rate of stroke and system embolism rates difficult, if not impossible, to assess (3,5). Common to all of these studies is the retrospective design and lack of pre-specified safety and efficacy endpoints that thereby further obscure assessment of the risk-to-benefit ratio.

It is in this context that Sievert et al. (6), in this issue of JACC: Clinical Electrophysiology, report their results from a prospective, multicenter observational study on the clinical outcomes of the Lariat system in patients with nonvalvular atrial fibrillation (AF) who were ineligible for oral anticoagulation therapy. The pre-specified safety endpoint was 30-day peri-procedural adverse events. The 2 pre-specified composite efficacy endpoints were as follows: 1) stroke and systemic embolism; and 2) stroke, systemic embolism, and death of any cause. In total, 139 patients with a mean CHA2DS2-VASc (Congestive Heart Failure, Hypertension, Age ≥75 Years, Diabetes Mellitus, Prior Stroke or Transient Ischemic Attack or Thromboembolism, Vascular Disease, Age 65 to 75 Years, Sex Category) of 3.6 ± 1.8 (CHADS2 [Congestive Heart Failure History, Hypertension History, Age ≥75 Years, Diabetes Mellitus History, Stroke or Transient Ischemic Attack Symptoms Previously]; 2.4 ± 1.2) underwent LAA ligation. Follow-up consisted of transesophageal echocardiograms performed at 30 to 45 days post-procedure, routine office visits, and telephone calls. As patients were ineligible for oral anticoagulation, the post-procedural antithrombotic
regimen consisted of either antiplatelet therapy (single therapy: 62%, dual therapy: 6%) or nothing (32%). Although acute LAA closure was achieved in 99% of patients, the rate of leaks was 10% in those that underwent follow-up transesophageal echocardiograms; all of which were 2 to 4 mm. From a safety perspective, periprocedural adverse events occurred in 11.5% of patients, including 2 patients who required cardiac surgery for right ventricular perforation, and 1 patient who developed a fatal pulmonary embolism 1 day after the procedure. With respect to efficacy, the stroke and systemic embolism rate was 1.0% per year (mean follow-up of 2.9 years), whereas the composite event rate for stroke, systemic embolism, and death of any cause was 2.8% per year. When comparing the observed stroke rate to the expected rate from the National Registry of AF based on the CHADS2 score, there was an 84% reduction, a rate that is comparable to patients treated with the Watchman LAA occlusion device (Boston Scientific Corp., Marlborough, Massachusetts) and antiplatelet therapy as part of the ASAP (ASA Plavix Feasibility Study With Watchman Left Atrial Appendage Closure Technology) study (7). This is the first study of the Lariat device using a multicenter prospective design and pre-specified safety and efficacy endpoints; thus, this study represents the strongest quality data to date. However, due to the lack of randomization and an active comparator cohort, the study fails to provide direct evidence that Lariat is responsible for the low stroke and systemic embolization rate observed (i.e., it does not prove that successful closure of the LAA with the Lariat device prevents AF-related embolic events).

With respect to establishment of safety of the Lariat device, this study falls short of appeasing concerns. The 11.5% complication rate is attributable to pericarditis persisting >2 days in 5.9% of patients, requirement for emergency surgery in 1.4%, and death in 1.8%. Although some of these rates are slightly lower than reported in other studies, the findings should be interpreted in the context that safety events were adjudicated by investigators rather than by an independent clinical events committee, thereby introducing the potential for interpretation bias. For example, all safety events were attributed to the procedure rather than the device, which is conceivable but inconsistent with real-world experience (3-5). Eliminated in this study is major bleeding, which has been reported in up to 9% of procedures (5), a finding that may partly be attributable to elimination of post-procedure anticoagulation. Whereas the present study demonstrates the most favorable safety profile of Lariat to date, it is hard to ignore the real-world experience, which has been concerning as indicated by the recent U.S. Food and Drug Administration Safety Communication, based on information obtained from the MAUDE (Manufacturer and User Facility Device Experience) database (8). There were 45 adverse events reported, 34 of which (75%) required emergent cardiac surgery. Serious complications included laceration or perforation of the heart, complete LAA detachment, and death. It would seem that several factors, as identified by the investigators, may lead to more favorable safety outcomes, including: 1) increased operator training; 2) use of a micropuncture needle for pericardial access; 3) leaving a pericardial drain in place for 24 h post-procedure; 4) elimination of post-procedure anticoagulation; and 5) use of periprocedure colchicine and nonsteroidal anti-inflammatory agents. However, the effect of these factors on safety events has not been systematically evaluated.

Despite a high rate of acute closure, 10% of all cases in this study demonstrated reconstitution of LAA flow (all ≤4 mm) at surveillance imaging. Based on the surgical experience with LAA ligation, incomplete closure may result in blood stasis and increased risk of thrombus formation and hence stroke (9). Furthermore, despite the absence of any intracardiac foreign material, thrombus at the site of ligation was diagnosed in 1.4% of patients. The rates of LAA leak and thrombus have been reported to be as high as 24% and 2.8%, respectively, with the Lariat device (3,5). However, it should be noted, that even these higher estimates are comparable with the Watchman device with leaks seen in 32% (albeit in a peridevice location as opposed to a central location) and thrombus in 4.2% of patients (10,11). Due to the potential risk of stroke, 2 of the 4 patients with 4-mm leaks in the present study underwent closure with an Amplatzer Vascular Plug (St. Jude Medical, St. Paul, Minnesota) to mitigate risk. Based on these observations, it is clear that more data is required regarding the prognostic implications of LAA leaks and closure of these using percutaneous devices. The 2 patients with thrombus in the present study underwent treatment with oral anticoagulation despite being deemed ineligible for long-term anticoagulation. This raises the point that many patients who are ineligible for long-term anticoagulation may have lower and acceptable risk with short-term therapy (i.e., 45 days). It is our practice to recommend the Watchman device in these patients rather than the Lariat, a decision that is backed by the robust randomized clinical data (12).

In our minds, the 2 most important questions have not yet been answered—whether successful LAA closure with the Lariat system actually prevents...
stroke and whether the potential benefits outweigh the risk profile. Although annualized stroke rates appear to be lower than expected stroke rates (based on the CHADS, score), there is no randomized data to demonstrate that the Lariat system is effective for stroke prevention in nonvalvular AF patients. When considered together with the concerning safety profile, the Lariat device should probably be reserved only for those patients who are truly ineligible for short-term anticoagulation, who are at high risk for stroke, and who are otherwise not deemed candidates for a Watchman device. As always, a candid discussion with the patient about efficacy and safety data is warranted. Patients who can take anticoagulation drugs, even in the short-term, are arguably better served with the Watchman device, which is U.S. Food and Drug Administration approved and has robust randomized clinical trial data to support its use. It should be noted that outside the United States, the Watchman device is now routinely implanted with the use of antiplatelet therapy alone post-procedure. It may be just a matter of time before this translates to clinical practice in the United States, shrinking the potential candidates for the Lariat device even further. A robust multicenter randomized trial is badly needed to establish efficacy in stroke reduction and a more favorable safety profile before the Lariat device can be routinely recommended for the prevention of stroke in patients with AF.

**REPRINT REQUESTS AND CORRESPONDENCE:** Dr. Srinivas R. Dukkipati, Helmsley Electrophysiology Center, Icahn School of Medicine at Mount Sinai, One Gustave L. Levy Place, Box 1030, New York, New York 10029. E-mail: srinivas.dukkipati@mountsinai.org.

**KEY WORDS** atrial fibrillation, cardioembolic stroke, Lariat device, left atrial appendage, suture ligation