Safety and Procedural Success of Left Atrial Appendage Exclusion With the Lariat Device
A Systematic Review of Published Reports and Analytic Review of the FDA MAUDE Database

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IMPORTANCE The Lariat device has received US Food and Drug Administration (FDA) 510(k) clearance for soft-tissue approximation and is being widely used off-label for left atrial appendage (LAA) exclusion. A comprehensive analysis of safety and effectiveness has not been reported.

OBJECTIVES To perform a systematic review of published literature to assess safety and procedural success, defined as successful closure of the LAA during the index procedure, of the Lariat device. We performed a formal analytic review of the FDA MAUDE (Manufacturer and User Facility Device Experience) database to compile adverse event reports from real-world practice with the Lariat.

DATA SOURCES For the systematic review, PubMed, EMBASE, CINAHL, and the Cochrane Library were searched from January 2007 through August 2014 to identify all studies reporting use of the Lariat device in 3 or more patients. The FDA MAUDE database was queried for adverse events reports related to Lariat use.

DATA EXTRACTIONS AND SYNTHESIS Data were abstracted in duplicate by 2 physician reviewers. Events from published literature were pooled using a generic inverse variance weighting with a random effects model. Cumulative and individual adverse events were also reported using the FDA MAUDE data set.

MAIN OUTCOMES AND MEASURES Procedural adverse events and procedural success.

RESULTS In the systematic review, 5 reports of Lariat device use in 309 participants were identified. Specific complications weighted for inverse of variance of individual studies were urgent need for cardiac surgery (2.3%; 7 of 309 procedures) and death (0.3%; 1 of 309 procedures). Procedural success was 90.3% (279 of 309 procedures). In the FDA MAUDE database, there were 35 unique reports of adverse events with use of the Lariat device. Among these, we identified 5 adverse event reports that noted pericardial effusion and death and an additional 23 reported urgent cardiac surgery without mention of death.

CONCLUSIONS AND RELEVANCE This review of published reports and case reports identified risks of adverse events with off-label use of the Lariat device for LAA exclusion. Formal, controlled investigations into the safety and efficacy of the device for this indication are warranted.
trial fibrillation (AF) has an estimated prevalence of 2.7 to 6.1 million people in the United States. Patients with AF have a 5-fold increased incidence of embolic stroke, the risk of which has traditionally been managed with warfarin therapy. However, warfarin elevates the risk of bleeding, has a narrow therapeutic range requiring regular monitoring of coagulation levels, and has high discontinuation rates. Novel oral anticoagulants circumvent some of these issues but have led to new concerns including persistently elevated bleeding risk, higher expense, and a current lack of readily available direct-acting antidotes.

Ninety percent of thrombi causing AF-related strokes arise from the left atrial appendage (LAA). Many of the limitations of oral anticoagulant use could theoretically be overcome with minimally invasive closure of the LAA, a strategy reportedly associated with risk reduction for strokes compared to warfarin, without the concomitant increase in risk of bleeds. In March 2015, the US Food and Drug Administration (FDA) approved the Watchman device (Boston Scientific Corp) for minimally invasive LAA closure after completion of two pivotal randomized clinical trials designed to demonstrate safety and efficacy of the device in comparison to warfarin therapy. US trials are being planned for other devices that are mechanismi

Methods
Systematic Review of Published Literature
Safety and efficacy data from published reports evaluating the Lariat device were compiled by 2 physician reviewers (S.C. and J.G.). The primary efficacy end point was defined as successful closure of the LAA during the index procedure with the Lariat device. Safety end points were initially defined as cardiac perforation, pericardial effusion, pericardial effusion requiring intervention, tamponade-hemodynamic instability, hypotension, emergent resuscitation, urgent pericardiocentesis, urgent cardiothoracic surgery, urgent need for cardiopulmonary bypass, left atrial laceration, stroke, and death. Published reports on safety were found by performing a keyword search without language restrictions in PubMed, EMBASE, CINAHL, and the Cochrane Library by using the keywords “Lariat,” “FindrWIRZ,” “EndoCATH,” “SoFTIP,” “TenSURE,” and “SureCUT” with, and without the phrases “suture,” “snare,” “left atrial appendage occlusion,” “left atrial appendage exclusion,” and “left atrial appendage closure,” for the period January 2007 through August 2014, to identify all published literature reporting outcomes associated with the use of the Lariat device. “FindrWIRZ,” “EndoCATH,” “SoFTIP,” “TenSURE,” and “SureCUT” are proprietary names for various devices needed to perform LAA exclusion with the Lariat snare. To include formal peer-reviewed research endeavors and avoid isolated case reports, we excluded reports of less than 3 cases and unpublished abstracts. We carefully evaluated studies for partial or complete patient overlap and included only studies with completely unique, nonoverlapping data sets.

Given the lack of formal evaluations of the Lariat with specified end points, it was noted that reporting of many of the above end points was unreliable and nonstandardized between studies. Therefore, adverse events were grouped into 2 categories representing the most severe and reliably ascertainable complications of the procedure: in-hospital death and need for urgent cardiac surgery.

Rates of adverse events reported in each study were pooled by weighing each study by the inverse of the variance (1/standard error [SE]) and were combined with a generic variance approach using a random-effects model, as recommended in the Cochrane Handbook of Systematic Reviews, and the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) statement. Study quality was appraised with the validated Newcastle-Ottawa scale for observational studies.

Query of the MAUDE Database
The MAUDE database is a searchable online database of medical device reports received by the FDA. Medical device reports are submitted by both mandatory (eg, manufacturers) and voluntary (eg, physicians) reporters. These MDRs serve as a passive surveillance tool to monitor device performance and potentially detect adverse events associated with device use. The information submitted by reporters has limitations, including the possibility of inaccurate or incomplete data. In addition, most reports are not verified through objective, independent assessment mechanisms. The prevalence and incidence of adverse events cannot be determined through the MAUDE database because events may be underreported and total number of devices used is not known.

We performed a review of complications associated with the Lariat device using the MAUDE database. In the online MAUDE database query form, the keywords “Lariat,” “FindrWIRZ,” “EndoCATH,” “SoFTIP,” “TenSURE,” and “SureCUT” were entered in the device field, and the keyword “SentreHeart” was entered into the manufacturer field. The date range of January 2007 through July 2014 was specified, and the search was last performed on August 12, 2014. This period was expected to include all Lariat device adverse events. All other query fields were left blank. When multiple complications were listed in the same report, each complication was tabulated separately in a standardized data collection spreadsheet.
Complications were initially separated into the aforementioned 11 prespecified categories but were then grouped into 2 categories matching those in the systematic review: in-hospital death and need for urgent cardiac surgery. We additionally classified each reported complication based on if it was attributable to the “FindrWIRZ,” “Lariat,” or “TenSURE” devices by the submitter of the MAUDE report. “FindrWIRZ” refers to the magnetic-tipped guidewires that are placed in the LAA and pericardial space serving as the rail for the Lariat snare device. The “TenSure” device is a mechanical suture tightener used to tighten the Lariat snare. Finally, we also determined whether the LAA was eventually closed successfully during the index procedure.

**Statistical Analysis**

Complications were identified as discrete events and were reported as absolute numbers. Procedural success was reported as the proportion of total reported procedures that resulted in successful LAA closure during the index procedure. Finally, rates of complications attributable to FindrWIRZ and the Lariat device/suture tightener were expressed as proportions of total reported adverse events and compared using the \( \chi^2 \) test. Per convention, \( P < .05 \) was deemed to be statistically significant.

**Results**

All reported instances of Lariat use in the medical literature were for the indication of LAA exclusion (Figure). We identified 5 reports of Lariat device use in human participants (\( n = 309 \)) in the published literature\(^{18-22} \) that included more than 3 patients, did not have any patient overlap, and reported safety and efficacy outcomes (Table 1). Procedural success, defined as successful closure of the LAA during the index procedure, was 90.3% (279 of 309 procedures). Specific complications weighted for inverse of variance of individual studies were need for urgent cardiac surgery (2.3%) (7 of 309 procedures) and in-hospital death (0.3%) (1 of 309 procedures). Formal statistical tests of heterogeneity, effect estimates, and statistical tests of significance were not performed noting the single-arm nature of the published reports. Assessment of quality identified the studies to be of good quality, apart from the absence of controls (Table 2).

A search of the MAUDE database returned 35 unique reports of adverse events with use of the Lariat device. We identified 1 adverse event report in 2009, 8 in 2012, 19 in 2013, and 7 from January through July 2014. Five adverse event reports noted pericardial effusion and in-hospital death, 22 reported pericardial effusion with the need for urgent cardiac surgery, and 1 reported the need for urgent cardiac surgery without mention of pericardial effusion. Seven additional reports noted urgent placement of a pericardial drain to address a pericardial effusion. Procedural success during these cases was noted to be 35.5% (11 of 31 procedures), with 4 cases unable to be characterized based on the report.

The majority of complications noted were similarly attributable to the FindrWIRZ magnetic wires used for device deployment and the Lariat device/suture tightener (40.0% vs 54.3%; \( P = .32 \)), while the remainder (5.7%) could not be clearly attributed to either or the reason for the complication was unknown.
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Discussion

In our systematic review of the reported literature and analysis of the FDA MAUDE database regarding Lariat device use, we found no reports of the Lariat being used for any purpose other than LAA closure. Our systematic review revealed a procedural success rate of 90.3% but a potentially concerning safety profile with 1 in-hospital death and 7 cases requiring emergent cardiac surgery among the 309 uniquely reported cases. Our review of the FDA MAUDE database identified a total of 5 reported deaths and 23 additional instances of urgent cardiac surgery associated with the procedure.

The FDA classifies medical devices into 3 categories. Class III devices are those deemed to pose the greatest potential harm to patients, and full premarket approval is required prior to commercial marketing. Class I and II devices (low and intermediate risk, respectively) are cleared by the FDA under the 510(k) pathway, which requires demonstration of substantial equivalence with a legally marketed device. The 510(k) pathway does not necessarily require rigorous assessments of device safety and efficacy with evaluations by expert panels, as is the case for class III device premarket approval.

In June 2006, the Lariat device was granted FDA 510(k) class II clearance owing to stated substantial equivalence with the Ethicon Endosuturing System (Ethicon US LLC), the Genzyme Saph-Loop Ligating Loop (Genzyme Corp), and the HystereX Liga-Loop Suture Applicator (Hysterx Inc). These devices are preformed sutures used during laparoscopic surgery and vein harvesting. Importantly, the Lariat device appears to have never been used for these indications, and US and global patient applications filed in 2008 specifically sought intellectual property rights for closing the LAA,24-25 Because the Lariat device was classified based on different indications than what it is used for in clinical practice, it may carry an inappropriate class II designation of “intermediate risk” to patients, when its actual risk to patients based on its current utilization patterns may be greater.

One indication that the Lariat device may have had greater difficulty being approved by the FDA for its current use is that other minimally invasive LAA closure technologies with intracardiac approaches have faced substantial scrutiny from the FDA,26-29 most notably the Watchman device (Boston Scientific Corp). Although the Watchman and Lariat devices accomplish closure of the LAA through different methods (the former is purely and intracardiac device, whereas the latter is a snare that cinches the LAA from the outside of the heart in the pericardial space), they share similar degrees of procedural complexity. Both are technically demanding procedures that involve general anesthesia, dual imaging modalities of transesophageal echocardiography and fluoroscopy; and atrial septal puncture. The initial premarket approval application for the Watchman in 2010 was based largely on results of the 800-patient PROTECT AF (Watchman Left Atrial Appendage System for Embolic PROTECTion in Patients With Atrial Fibrillation) trial,9 which demonstrated noninferiority against warfarin
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Acquisition, analysis, or interpretation of data: Chatterjee, Herrmann, Armstrong, Giri.

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Conflict of Interest Disclosures: Dr Yeh is on the advisory board for Abbott Vascular; is a consultant for Gilead Sciences; and receives research support from Harvard Clinical Research Institute. Dr Armstrong is on the advisory board for Abbott Vascular and is a consultant for Angiosteel. Dr Kumbhani is a consultant for the American College of Cardiology. Dr Herrmann has received research funding for the University of Pennsylvania from Edwards Lifesciences Inc, Medtronic Inc, and St Jude Medical Inc; is a consultant for and has received research funding from Siemens Medical Inc; and has equity in Microinterventional Devices Inc. Dr Wilensky reports that he is a member of the scientific advisor boards of Cardiostem, GenWay, Soteria, and Vascular Magnetics and has equity interest in Johnson & Johnson. Dr McCormick has received research grants from Abbott Vascular Corp, W L Gore, and Boston Scientific Corp. Dr Hirshfeld has served as a member of the FDA Circulatory Systems Device Advisory Panel. No other disclosures are reported.

REFERENCES


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