

Review Article

The Comparative Effectiveness of Left Atrial Appendage Closure for the Prevention of Cardioembolic Strokes in Atrial Fibrillation

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Abstract

Oral Anticoagulation (OAC) therapy is an effective medical therapy to reduce the risk of cardioembolic strokes related to atrial fibrillation. However, OAC therapy has limitations that include poor follow-up and pharmacotherapy monitoring, bleeding complications, or a reluctance to continue with therapy because of concerns with the potential risk of bleeding. The majority of strokes in atrial fibrillation are believed to arise from thrombi originating within the Left Atrial Appendage (LAA). Therefore, devices that occlude or ligate the LAA is one potential strategy to offer patients an alternative to chronic OAC therapy. The focus of this review is on surgical techniques and percutaneous methods for closing the LAA. Particular emphasis is the evidence of efficacy of these procedures compared to dose-adjusted warfarin. The limitations of the available evidence are critically reviewed.

ABBREVIATIONS

LAA: Left Atrial Appendage; AF: Atrial Fibrillation; OAC: Oral Anticoagulation; FDA: Food and Drug Administration; TEE: Transesophageal Echocardiogram

INTRODUCTION

Atrial Fibrillation (AF) is the most common arrhythmia and currently affects about 6 million people in the United States. The prevalence of AF rises sharply with age increasing from under 1% in those between ages 55-59 years to over 10% among those greater than 80 years [1]. Overall, the lifetime risk of developing AF is about 25% for men and women 40 years of age or older [2]. Other risk factors such as hypertension, diabetes, sleep apnea, and left ventricular dysfunction can increase the odds of developing AF.

The most devastating complication of AF is cardioembolic stroke. The risk of stroke is increased 5-fold in patients with nonvalvular AF and 17-fold in those with valvular AF [3]. Of the estimated 800,000 strokes each year in the United States, the percentage attributable to AF ranges from 1.5% in those under the age of 59 years to 23% in those over the age of 80 years [4]. Cardioembolic strokes are generally more severe than other types of ischemic strokes and are associated with higher 30 day and 1

year mortality [5,6]. Overall, stroke is the third leading cause of death and the number one cause of major disability in the United States and related healthcare costs are about 30 billion dollars each year.

The majorities of AF-related strokes are embolic and are believed to originate from thrombus formation within in the Left Atrium Appendage (LAA) [7]. The LAA is a remnant of the embryonic left atrium and forms a finger-like multi-lobulated blind pouch. The surface of the LAA is irregular due to trabeculations and the wall is paper-thin [8]. The LAA is separated from the main body of the left atrium by an oval shaped orifice that averages about 1.1 cm in diameter. In the setting of atrial fibrillation there is progressive stretching and dilation of the appendage resulting in increased tendency for blood to stagnant and form clots around small crevices and trabeculations. In surgical pathology studies, appendages removed from patients who underwent the surgical MAZE procedure for AF ablation were larger and showed evidence of inflammation and remodeling [9]. In addition, there is growing evidence that AF can activate inflammatory processes and produce a prothrombotic state [10].

Traditionally, Oral Anticoagulation Therapy (OAC) with vitamin K antagonists has been the mainstay of reducing the risk of cardioembolic stroke. In multiple clinical trials and meta-analysis

dose adjusted warfarin has been shown to reduce AF-related stroke by 65% [11]. More recently, several novel agents have been shown to be superior or non-inferior to warfarin therapy, are associated with fewer bleeding related events, and have the advantage of not requiring INR monitoring [12-14]. Although OAC is highly effective long-term therapy is not without risks; the most important of which is bleeding. It is estimated that within the first year of starting warfarin about 28% of patients will stop because of bleeding or the perception of bleeding risk [15]. By 2 years nearly 50% of eligible patients will stop taking warfarin because of bleeding, risk of bleeding, failure to control the INR, or life-style issue related to the need for frequent monitoring of the INR [16]. Another limitation is the narrow therapeutic window of warfarin and the effect of other drugs on warfarin metabolism. As a result patients who are treated with warfarin spend about half the time outside the therapeutic range [17]. Lastly, the likelihood of being prescribed OAC therapy or maintained on OAC therapy decreases as the risk of stroke increases, primarily because of the perception of higher risk for bleeding complications in this group of patients [18].

Not all patients with AF have the same long-term risk of stroke. As a result a number of algorithms have been developed to help inform the decision-making regarding the benefits of chronic OAC therapy. The best validated and most commonly used is the CHADS2 score which assigns 1 point each for heart failure (EF<35%), hypertension, age >75 years, diabetes, and 2 points for prior stroke/TIA [19]. A more recent scoring system is the CHA2DS2-vasc which refines the stroke risk for patients at the low end of the CHADS2 score who otherwise might not receive chronic OAC therapy by adding points for age between 64-74 years and a history of vascular disease [20]. The most up to date guideline recommends chronic OAC therapy for patients with a CHADS2 score or CHA2DS2-vasc score of at least 2. Many patients with a CHADS2 of 1 will have a CHA2DS2-vasc score of 2 and qualify for chronic OAC therapy. Patients with a score of 1 can be offered either aspirin or chronic OAC therapy, while patients with a score 0 should be offered aspirin only [21].

Because of these concerns there has been interest in developing alternative methods of reducing the long-term risk of thromboembolic events and exposure to chronic OAC therapy in patients with AF and high CHADS2 scores. Since it is believed that the vast majority of emboli originate in the LAA one potential strategy for accomplishing this is mechanical closure of the LAA. A variety of methods have been developed, including surgical closure at the time of open-heart surgery and percutaneous methods that plug the LAA with a filter-type device or ligate the LAA orifice using a percutaneous pericardial snare and loop. Before these devices can routinely be recommended, several questions need to be addressed. First, is LAA closure noninferior to chronic OAC therapy? Specifically, is LAA closure an acceptable alternative to OAC therapy for reducing the risk of ischemic strokes? If not what are the trade-offs between efficacy and bleeding? Second, can mechanical closure of the LAA be predictable, reproducible, and safe? Third, will the procedure be cost effective and result in improved health status?

Open-Chest Surgical Ligation of the Left Atrial Appendage

In 1949, Madden described resection of the LAA in 2 patients with recurrent arterial emboli [22]. Left atrial appendage obliteration was then performed sporadically in high-risk patients primarily at the time of mitral valve surgery. However, a review article published in 1970 concluded that LAA obliteration was not effective in reducing embolic events and as a result the procedure was largely abandoned [23]. However, since the early 1990s there has been growing interest in developing surgical and percutaneous techniques for excising or closing the LAA. A variety of surgical techniques have been developed. This includes suturing the LAA orifice from the from the endocardial surface, over-sewing the orifice from the epicardial surface, mechanically stapling across the orifice, or excision of the LAA followed by stapling, and more recently an atraumatic clipping technique for sealing the LAA orifice.

The results of surgical excision of the LAA have been previously reviewed [24]. The majority of surgical studies are nonrandomized case series. The selection of patients, methods of closure, assessment of closure success, and follow-up varied between all the studies. Because of this variation it is not possible to systematically analyze the data in any statistically meaningful way. However, the data can be summarized as follows. First, suturing or stapling methods frequently do not achieve high closure rates. Second, tears and lacerations requiring additional repair are not uncommon. Third efficacy with respect to preventing thromboembolic risk cannot be determined. Indeed, in several of the reports the risk of embolic events was actually higher because of incomplete LAA closure.

There have been two randomized trials of surgical LAA closure. The LAAOS I trial randomized 77 patients in a 2:1 ratio to LAA occlusion or no occlusion [25]. Initially, a suturing method was used but because of persistent leaks a stapling method was subsequently adopted. Mechanisms of failure included persistent flow across suture lines, or residual stump length >1 mm when staples were used. Complete closure was achieved in only 66% of the patients. Intraoperative tears of the LAA or the atrium were not uncommon and in all cases additional suturing was necessary. In the 30-day post-operative period there were 2 thromboembolic events in the closure group, corresponding to an event rate of 3.8% at 30 days, and none in the control group. After hospital discharge, randomized patients were followed for an average of 13 months during which time no additional patients experienced a thromboembolic event. No information regarding chronic OAC therapy or the prevalence of atrial fibrillation in either the closure or the control group is available, so it is not possible to reach a conclusion about the efficacy of LAA closure.

The LAAOS II trial randomized 52 patients with AF and at least one additional risk factor for stroke to LAA closure or to no closure [26]. Closure success determined by intraoperative Transesophageal Echocardiography (TEE) was 100%. There was nonsignificant trend toward higher reoperation for bleeding in the closure group compared to the control group (8% vs. 3.9%, NS). At 1 year there was no difference in the primary composite

efficacy outcome of death, MI, stroke, non-CNS embolism, or major bleeding. Importantly, between 50-60% of the patients were being treated with dose adjusted warfarin therapy.

More recently specially designed clips have been developed specifically for the purpose of LAA closure under direct surgical visualization. The AtriClip system (AtriCure-USA, West Chester, Ohio), and the Tigerpaw system (Maquet, Rastatt, Germany) have FDA 510K clearance for marketing in the United States [27,28]. The AtriClip was evaluated in the EXCLUDE registry in which the LAA was closed under direct visualization in 70 patients at the time of open-heart surgery [28]. Successful exclusion of the LAA was accomplished in 96% of the patients. The reason for device failure was the presence of a residual stump in 3 patients. During the follow-up period CT scanning showed the device to be stable and there were no late leaks or complications related to the device. At 1 year 3.1% of the patients had a stroke or TIA and 30% were on dose adjusted warfarin therapy. Thus while the device appears safe its efficacy with respect to reducing the risk of thromboembolic events cannot be determined.

The broad application of surgical LAA closure is limited because the majority of patients with atrial fibrillation do not require open-heart surgery. In addition the results of surgical closure are highly variable primarily because of failure to completely exclude the LAA. Stapling and suturing methods are clearly inadequate and should be abandoned. Clipping devices offer an advantage because they can be deployed when the heart is beating, and real-time TEE guidance can be used to check the position of the clip before final deployment. While LAA clipping is technically feasible and appears safe very limited conclusions can be drawn about efficacy because there are no randomized controlled trials. Until such time routine surgical closure of the LAA is probably not recommended, except in patients who have contraindications to chronic oral anticoagulation therapy.

Percutaneous Methods of LAA Closure

Percutaneous techniques for LAA closure have the potential to be less invasive and more broadly applicable. Development and demonstration of clinical efficacy and safety of these devices could offer patients a choice between OAC, and device based treatment that is not currently available. Several devices and techniques have been developed. This includes filter like devices that sit in the orifice of the LAA and prevents clots from moving from the LAA into the atrium. These devices use a percutaneous transeptal delivery system. A second technique uses a pericardial approach to slip a pre-tied polyester suture incorporated into a nitinol loop catheter-based delivery system over the LAA and down around the neck of the orifice. In both methods, real time TEE guidance is used to exclude any pre-existing clots in the left atrium or the LAA and to confirm complete closure of the LAA before final deployment.

One of the first such devices was the PLAATO (percutaneous left atrial appendage transcatheter occlusion) system which, consisted of a self-expanding, retrievable nitinol cage covered with an expanded polytetrafluoroethylene (ePTFE) membrane laminated directly to its outer frame so that it is in direct contact with the wall of the LAA [29]. The PLAATO device is no longer in development or production but experience with the device has

been insightful because it showed that a filter type device could be safely implanted in patients. The most frequent complication was procedural related pericardial effusion. Importantly, late device complications, such as embolization or pericardial effusion were not common. Moreover, the device appeared to be effective in reducing the risk of stroke compared to historical controls. However, certain design features of the PLAATO device such as its rigid nature and the need for significant oversizing of the device to achieve stability limited its use.

The Watchman LAA occlusion device (Boston Scientific, Natick Massachusetts) also consists of a self-expanding nitinol frame with fixation barbs and a permeable polyester fabric that covers the atrial facing surface of the device. This device is more flexible and has a flatter profile, which reduces the need for oversizing. As a result the device can be used in a wider range of LAA sizes and shapes. One potential limitation of the Watchman system is the need for oral anticoagulation for a minimum of 45 days to allow for endothelialization and sealing of any residual leaks.

Initial worldwide experience with the Watchman device was reported in 2007 [30]. In this study, 75 patients at 3 centers in Europe and 4 centers in the United States underwent device implantation. Successful device deployment was achieved in 88% of the patients. The majority of device related failures were due to unsuitable LAA anatomy. Of the patients who had follow-up 93% were considered to satisfy the primary efficacy endpoint of complete closure of the LAA without significant flow around the device. However, there were a significant number of adverse events: device embolization (n=2), significant pericardial effusions requiring intervention (n=2), and minor pericardial effusions not requiring treatment (n=4). There were no device related mortalities. During the follow-up period thrombus formation was noted on the surface of several of the devices that required continuation of dose-adjusted warfarin. There have been 3 major clinical trials using the Watchman device. The Protect AF study was a randomized controlled multicenter trial comparing the Watchman LAA closure device with chronic dose adjusted warfarin therapy in patients with AF and risk factors for stroke [31]. The Continue Access Protocol registry (CAP) was a nonrandomized registry that began at the conclusion of Protect AF study [32]. Under this protocol the US Food and Drug Administration (FDA) allowed continued access to the Watchman device for a subset of the Protect AF investigators to gain further safety data. The Prevail study is a randomized controlled trial requested by the FDA and sponsored by the device manufacturer to address concerns regarding the safety and efficacy of the device [33].

The Protect AF study was designed as a non-inferiority trial in which 707 patients were randomized 2:1 to closure of the LAA or warfarin therapy [31]. The non-inferiority margin was set at 2, meaning that events in the Watchman group could be twice the events in the control group and still satisfy non-inferiority. Patients were required to have paroxysmal, persistent, or permanent AF with a CHADS2 score of at least 1. Those in the device group were treated with warfarin for 45 days. TEE imaging was done at 45 days and if there complete closure or a residual leak of ≤ 5 mm in width warfarin was discontinued. Patients

were then treated with aspirin and clopidogrel for 6 months after which aspirin was continued indefinitely. Patients assigned to the control group received warfarin to maintain the INR between 2-3. The primary efficacy composite end-point consisted of any stroke, any death, or systemic embolism. The composite safety endpoint consisted of excessive bleeding or procedural-related complications (serious pericardial effusion, device embolization, or procedure-related stroke).

The primary efficacy event rate was 3 per 100 patient-years in the intervention group and 4.9 per 100 patient-years in the control group. The rate ratio was 0.62 with an upper limit of 1.25 satisfying the non-inferiority margin of 2. At a mean of 3.8 years of follow-up (2621 pt-yrs) the primary event rate in the Watchman group was 2.3% and 3.8% in the control group [34]. The rate ratio is 0.60 and the probability of non-inferiority is 0.999. While all-cause strokes were lower in the Watchman group, the rate of ischemic strokes favored the control group. There were 15 ischemic strokes in the device group: one before the scheduled procedure, 5 related to the procedure, and 9 during the follow-up period. There were 6 ischemic strokes in the control group (rate ratio of 1.34, CI: 0.6-4.29, likelihood of non-inferiority of 71%). At the end of 3.8 years of follow-up the rate of ischemic strokes in the intervention still exceeded that in the control group.

Besides the issue of ischemic stroke there were other concerns about the safety of the device, in particular the high rate of cardiac perforation (1.7%) and pericardial effusion with tamponade (3%). To address these safety concerns the FDA allowed continued access to the device in certain select centers. Data from the CAP registry demonstrated the importance of operator experience for decreasing the likelihood of complications, in particular pericardial effusion and procedural strokes [32].

One concern with the Protect AF study was that the patient population was not representative of a warfarin eligible population. Between 27-34% of the patients enrolled in Protect AF had a CHADS2 score of 1 and could have been treated with aspirin. Another issue was the ongoing use of warfarin therapy in the device group and the discretionary use of antiplatelet agents like aspirin and clopidogrel. These confounding factors make it difficult to interpret the clinical significance of non-inferiority and the added value of the Watchman device in low risk patients being treated with aspirin or clopidogrel.

The Prevail trial was designed to address these and other concerns. For example, in Prevail patients were required to have a CHADS2 of at least 2 or a CHADS2 score of 1 plus an additional risk factor. To address the issue of antiplatelet therapy, post implant patients received 45 days of adjusted-dose warfarin plus 81 mg of aspirin. If the TEE at 45 days showed complete closure the warfarin was discontinued and patients were changed over to 325 mg of aspirin plus 75 mg of clopidogrel. The clopidogrel was stopped at six months and aspirin was continued indefinitely. Patients who had another indication for chronic clopidogrel were excluded from the trial. In addition a secondary primary composite endpoint, which excluded device related strokes in the first 7 days after implantation, was specifically developed to evaluate the mechanism of action of LAA closure.

The results of the Prevail trial have not published but are available through the FDA website [33]. The Prevail trial was

designed as a non-inferiority trial using Bayesian statistics. By using a Bayesian design investigators are able to include the data from prior studies (prior probability) in the analysis of the new data to reach a posterior probability of non-inferiority. For the Prevail trial the FDA approved this approach but the Protect AF data was discounted by 50%. A total of 138 patients were randomized to dose-adjusted warfarin and 269 patients to Watchman plus short-term warfarin. The mean CHADS2 score was 2.6. For the 265 patients in which Watchman implant was attempted the success rate was 95.1%. At 45 days post-implantation 92.3% of the patients were able to discontinue warfarin.

For the first primary endpoint the margin of non-inferiority was not met. Using the prior discounted data, the 18-month posterior event rate in the Watchman group was 0.064 versus 0.063 for the control group. The upper bound of the rate ratio was 1.88, which exceeded the noninferiority margin of 1.75. When only the Prevail data are used the 18-month rate ratio is 2.01 (95% confidence interval: 0.56-6.02). Events rates for the first primary endpoint all favored the control group. The rate of ischemic stroke in the Watchman group was 1.94 versus 0.71 in the control group. For the second primary endpoint (ischemic events after the 7th post-procedural day) non-inferiority was not met, using the rate ratio but was satisfied when noninferiority was tested on the basis of the 18-month rate difference. Event rates including ischemic stroke favored the control group. The third primary endpoint evaluating safety of Watchman was achieved. However, major bleeding occurred more frequently in the Watchman group than in the control group.

When viewed critically the Prevail trial is largely a negative trial because it did not meet the most important goal of non-inferiority compared to dose adjusted warfarin. Not only did the Watchman device fail to reduce ischemic strokes there were fewer bleeding complications in the control group. The failure to reduce ischemic strokes is especially troublesome given the proposed mechanism of action of the Watchman device by excluding thrombus formation in the LAA. Based on the available data it would be difficult to justify Watchman implantation over warfarin in AF-patients who are otherwise good candidates for chronic OAC therapy. The requirement for warfarin therapy after device implantation is also a limitation because it increases the risk of post procedural bleeding and it excludes patients who can't tolerate warfarin therapy from alternative therapy.

To address some of these concerns a nonrandomized multicenter prospective study was done to determine the feasibility of substituting 6 months of theinopyridine therapy (ticlopidine or clopidogrel) and life-long aspirin for warfarin in patients with contraindications to OAC therapy [35]. 150 patients were enrolled in this study. Procedural or device related complications occurred in 13 (8.7%) patients. At 177 patient-years of follow-up (about 1 year) the ischemic stroke rate was 1.7% compared to an expected ischemic stroke rate of 7.3% for similar patients treated only with aspirin. The data suggest that warfarin can be safely eliminated from the Watchman implant protocol perhaps reducing bleeding complications and opening an alternative therapy for high risk patients who cannot tolerate chronic OAC therapy.

The Lariat device (SentreHeart, Inc., Redwood City, California) received 510(K) clearance for soft tissue approximation and/or ligation with a pretied polyester suture. Early pre-clinical work demonstrated the feasibility of using the Lariat device to close the orifice of the LAA [36]. Initial clinical experience was reported in 2011 when 13 patients underwent LAA ligation using this device [37]. 11 of these patients underwent percutaneous LAA ligation following atrial fibrillation ablation and 2 had open chested ligation following mitral valve repair.

In 2012, results of a single center nonrandomized study (PLACE II) were reported in abstract form at the Heart Rhythm Society and subsequently published in 2013 [38]. Patients aged 35 to 81 years were identified and enrolled between December 2009 and December 2010. Inclusion criteria included 1) age >18 years, 2) nonvalvular atrial fibrillation, 3) at least one risk factor for embolic stroke (CHADS₂ >1), 4) a poor candidate or ineligible for warfarin therapy, and 5) life expectancy greater than 1 year. Patients were excluded for the following reasons: 1) history of pericarditis, 2) history of cardiac surgery, 3) pectus excavatum, 4) recent myocardial infarction, 5) embolic stroke within the previous 30 days, 6) history of chest radiation, 7) New York Heart Association class IV, and 8) left ventricular function <30%, 9) presence of a clot in the LA or LAA.

Overall, 119 patients satisfied the clinical inclusion criteria. Of these 16 were excluded after CT scanning showed the left atrial appendage was too large to be snared by the Lariat device. An additional 11 patients were excluded due to presence of a thrombus on the pre-procedure TEE. Therefore, 92 patients went on to LAA ligation. Technical success, defined as complete closure or the presence of a ≤ 1 mm jet by color Doppler was achieved in 85 cases (92.3%). Technical failure was due to persistent jet on color Doppler, inability to perform transeptal puncture, and pericardial access complications related to puncture or laceration of the right ventricle. Transesophageal Echocardiography (TEE) done at 1-year showed persistent closure, and no new or increasing jet leaks in the LAA. In fact several of the procedures that were deemed to be technical failures because of jets greater than 1 mm demonstrated subsequent closure 1 year later. There is no long-term efficacy data and no control group.

As with any procedure there is always the potential for complications. The most common complications are related to pericardial access including right ventricular perforation, pericarditis, and pericardial effusion. More recently, there have been several reports of LAA laceration occurring immediately after successful closure or during removal of the Lariat device [39]. The mechanism of this is not understood but might be due to traction placed on friable left atrial tissue, or entrapment of a small portion of a small nonligated lobe during knot tightening. This appears to be a relatively uncommon complication but can be life threatening when it does occur.

Currently, the Lariat suture delivery system is the only commercially available device in the United States that is used to exclude the LAA through a percutaneous closed chest approach. There is no efficacy data and the Lariat device is used off-label primarily to close the LAA in patients with AF who are at very high risk for embolic events and have contraindications to chronic OAC therapy. These patients would otherwise be left

unprotected. Over the past 3 years experience with this device has increased and now there are many centers offering this procedure to high-risk patients.

It is helpful to place all this data in context. First, there are no prospective randomized surgical studies demonstrating efficacy of LAA closure at the time of open-heart surgery. While the AtriClip and Tigerpaw devices do have FDA clearance for LAA closure the efficacy of these devices compared to oral anticoagulation therapy is unknown. The Lariat pericardial device does not have FDA clearance for LAA ligation and there is no efficacy data.

Second, the Protect AF is the only published randomized control trial demonstrating non-inferiority of LAA closure compared to dose adjusted warfarin. However, the device did not receive FDA approval because of concerns about efficacy and safety. Unfortunately, the Prevail and Protect AF trials realized divergent results making it very hard to reach any strong conclusions. In the both studies the rates of ischemic strokes favored the control group. This raises serious questions about the mechanism of action of LAA closure and whether the procedure really is non-inferior to warfarin.

Third, since the Protect AF and Prevail studies were carried out, new oral anticoagulation agents with greater efficacy and safety profiles have been introduced. These newer agents do not require dose adjustments and are less likely to result in hemorrhagic cerebral bleeding. To address this issue, the recently launched ACP (Amplatzer Cardiac Plug Clinical Trial) using the Amplatzer occluder (St. Jude Medical, St. Paul, Minnesota) will include control patients on newer oral agents.

A final issue is whether patients with AF are still at risk for clot formation even after the LAA is closed. In the original Watchman studies the rate of thrombus formation on the device is between 4-6%. In the Prevail study 5% of patients with successful device implantation had layered thrombus on the device, although none of them experienced an ischemic event. Recently, thrombus formation after Lariat LAA closure has also been reported [40]. These data suggest that clot formation outside of the LAA may still present a risk to patients with AF.

As of yet no LAA closure device has received FDA approval for stroke prevention. Only a single randomized trial has demonstrated non-inferiority to warfarin. One problem is the interpretation of non-inferiority trials since the device can be non-inferior and inferior to chronic OAC therapy. This can happen if the margin of non-inferiority is satisfied but the event rate is higher in the device group. For example, in the Prevail study the rate difference for the secondary primary end-point favored the control group but the noninferiority margin was still satisfied. This suggests that there might be a trade-off between lower risks of bleeding for less protection against ischemic strokes. Certainly, device based therapy would give patients an option that is not currently available. In particular patients with high CHADS₂ scores and contraindications to OAC therapy would likely benefit from LAA closure. Whether, all patients with AF would fare better with device based therapy is unknown and further clinical trials will need to be completed to answer this question.

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