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REVIEW

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Current methods of left atrial appendage closure: the non-pharmacological approach for stroke prevention in atrial fibrillation patients

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Abstract

Background Atrial fibrillation (AF) is a significant contributor to cardioembolic stroke, with the left atrial appendage (LAA) often being the principal source of thrombus. Given the substantial impact of stroke on patient quality of life, and its potential life-threatening nature, stroke prevention is paramount in the management of AF. Nonvitamin K oral anticoagulants (NOACs) or vitamin K antagonists are typically the first line of treatment to prevent strokes caused by AF. However, for patients unable to tolerate oral anticoagulants, alternatives such as percutaneous LAA closure (LAAC) or surgical LAAC might be considered.

Main body The most widely used percutaneous LAAC methods are the AMPLATZER Amulet and WATCHMAN devices. Registry studies have shown promising results for both devices, with low ischemic stroke rates in patients undergoing LAAC (Reddy in J Am Coll Cardiol 70(24):2964–75, 2017, Holmes in J Am Coll Cardiol 64(1):1–12, 2014). However, catheter-based LAAC has some limitations, such as a risk of device-related thrombus and the need for antithrombotic medication to facilitate device endothelialization Mesnier (Circ Cardiovasc Interv 16(5):e012812, 2023.). Surgical LAAC is being considered as a method that can complement the shortcomings of percutaneous LAAC. In the past, surgical LAAC was performed either by LAA resection or internal obliteration during open-heart surgery, but it was not widely used as a standalone treatment due to its high invasiveness. More recently, the development of a new clip device allows for LAAC via thoracoscopy, eliminating the need for cardiopulmonary bypass. Moreover, its safety and efficacy profiles surpass those of previous LAAC.

Conclusion The recent surgical LAAC devices have not only demonstrated high success rates but also shown low invasiveness. It becomes a feasible treatment alternative for non-valvular AF patients who experience NOAC failure or have a high bleeding risk with oral anticoagulants.

Keywords Ischemic stroke, Atrial fibrillation, Left atrial appendage closure

Introduction

Atrial fibrillation (AF) is the most common arrhythmia encountered in clinical practice [1–4]. Its prevalence is steadily increasing, in line with population aging [5]. AF-related strokes mostly occur due to stasis of blood flow, leading to thrombi formation in the left atrium—most of which are typically found within the left atrial appendage [6]. Oral anticoagulants, including vitamin K antagonists

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(VKAs) or novel oral anticoagulants (NOACs), are used to prevent strokes in AF patients with a high risk of thromboembolism, based on the CHA_2DS_2-VASc score [7, 8]. Oral anticoagulants have shown their effectiveness in stroke prevention, but they also have an increased risk of major bleeding complications. Other drawbacks of anticoagulation include a narrow therapeutic range, potential interactions with food and medications, and the need for regular monitoring and dosage adjustments. Left atrial appendage closure (LAAC) could be a therapeutic alternative for such patients. Two approaches are available for LAAC: percutaneous endocardial closure and surgical closure. Among the percutaneous LAAC methods, the AMPLATZER Amulet (Abbott, Plymouth, Minnesota, USA) and WATCHMAN (Boston Scientific, Marlborough, Massachusetts, USA) devices are most widely used. Several prospective registry studies have investigated the clinical outcomes of two devices. In the EWOLUTION registry, which included patients ineligible for oral anticoagulants (61.8%), the rate of ischemic stroke in patients undergoing LAAC with WATCHMAN was found to be 1.1%. This rate was significantly lower than the expected rate based on the CHA2DS2-VASc score [9]. Additionally, the global Amulet observational registry, which involved patients contraindicated to oral anticoagulants (82.8%), reported promising one-year follow-up results. The study showed that patients who received LAAC with Amulet had a low annual ischemic stroke rate of 2.9% [10]. While both devices have been studied, WATCHMAN is the only one that has been evaluated in two pivotal randomized controlled trials, namely PREVENT-AF and PREVAIL. Current guidelines suggest that percutaneous LAAC might be considered for patients with a high risk of stroke and contraindications for long-term oral anticoagulants, with a Class IIB recommendation [11–13]. However, catheter-based LAAC does not demonstrate significant benefits compared to medical therapy and has its limitations, such as a risk of device-related thrombus and the need for antiplatelet therapy post-procedure. On the other hand, surgical left atrial appendage (LAA) resection is considered a potential method to offset the shortcomings of percutaneous LAAC. Surgical LAAC can be performed through either the endocardium or the epicardium.

Indications for surgical LAAC

The AHA/ACC/ESC guidelines for the treatment of valvular heart disease recommend the exclusion of the LAA during concomitant procedures as a prophylactic measure to eliminate a primary source of thrombus, with a Class I indication [11–13]. The LAAOS III prospective randomized trial demonstrates that surgical epicardial exclusion of the LAA reduces the risk of ischemic stroke or systemic embolism [14]. Although there is no explicit guideline for surgical LAAC as a standalone option for stroke prevention in patients with AF, it is reasonable to consider its use based on the guidelines established for the catheter-based LAAC. The 2020 EHRA/EAPCI expert consensus statement addresses three important aspects related to percutaneous LAAC in their guidelines [15]. The first indication is for patients who are eligible for anticoagulations but refuse medication. The second indication is for individuals who are absolutely contraindicated for anticoagulations due to major bleeding or adverse effects. The third indication is for patients who have a poor adherence to prescription. According to experts, in cases where catheter-based endovascular LAAC is indicated, but antiplatelet therapy is contraindicated, the preference may be for epicardial clip devices [15]. This is because endovascular devices like the WATCHMAN device require the use of antiplatelet agents during the neo-endothelialization process following the procedure [4].

Endocardial surgical LAAC

Endocardial surgical closure is performed by opening the left atrium, using cardiopulmonary bypass, and suturing the interior of the left atrial appendage. Due to its invasiveness, endocardial surgical closure is mostly performed as a part of Cox-Maze procedure or concomitant other open-heart surgery, and it is rarely done as a standalone approach for the treatment of non-valvular AF. The Cox-Maze procedure was initially developed with the primary goal of creating atrial conduction barriers to control AF, and LAAC was not included in the early versions. However, starting in the mid-1990s, LAA was routinely amputated in the Cox-Maze procedure to reduce the risk associated with atrial thrombus formation. The inclusion of LAAC in the Cox-Maze procedure has demonstrated significant effectiveness not only in achieving rhythm control but also in providing a high efficacy for stroke prevention [16].

Epicardial surgical LAAC

Epicardial surgical LAAC involves the exclusion of the LAA through various methods from outside the heart without opening the heart (Fig. 1). Epicardial techniques include the use of suture closure, stapler closure, and clip closure devices. Compared suture or stapler, the clip devices are a relatively recent development for LAAC. Epicardial surgical LAAC can also be performed during open-heart surgery and Cox-Maze procedure, but it is not essential to open the heart, making it possible to perform through thoracoscopy or robotic surgery. Among these approaches, the traditional surgical LAAC methods (suture, stapler) have shown lower success rates

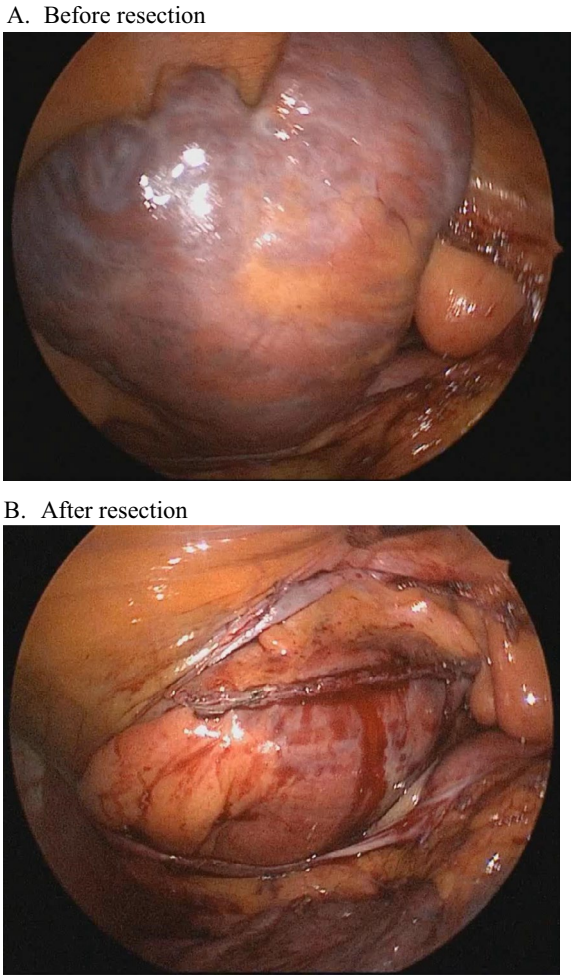

Fig. 1 Left atrial appendage resection using stapler device

than expected. In the LAAOS study, suture ($n=52$) and stapler ($n=25$) procedures were performed on 77 coronary artery bypass surgery patients at high risk for stroke. After 8 weeks,

transesophageal echocardiography was conducted to assess the outcomes. The success rate of suture exclusion was 45% when defined as the presence of residual flow to the appendage or a residual neck of 1 cm or more [17]. Similarly, the success rate of stapler exclusion reached only 72%. In a retrospective study involving 137 patients, an overall success rate of 40% was observed. Surgical excision (73%) had the highest success rate, while suture exclusion (23%) and stapler exclusion (0%) showed lower success rates. These results are believed to be attributed to the gradual reopening of the entrance through the appendage wall when using suture or stapler exclusion without excision [18]. Due to these factors, achieving complete exclusion of the LAA has proven challenging with suture or stapler closure methods. Furthermore, incomplete closure or amputation of the LAA has been demonstrated to elevate the risk of thromboembolism. Nevertheless, recent findings from the LAAOS III trial have shown a clear role of LAAC for stroke prevention. In this trial, LAAC was performed on patients undergoing cardiac surgery, and the results revealed a 33% reduction in stroke risk during the 3.8-year follow-up period. These findings strongly support the effectiveness of LAAC as a preventive treatment for stroke in surgical patients [14].

Recent advanced in epicardial LAAC devices

Epicardial LAAC devices are designed to mechanically close off the LAA from the outside of the heart. They are placed over the LAA and provide immediate closure. Examples of epicardial LAAC devices include surgical device, AtriClip (AtriCure, OH, USA) and catheter-based device, LARIAT (SentreHEART, CA, USA). In the early stages, LATIAT posed challenges in ensuring a safe procedure due to complications such as pericardial bleeding observed in over.

10% of cases. Additionally, pericarditis commonly occurred after the procedure [19, 20]. However, the utilization of microneedles and the introduction of a colchicine regimen to prevent pericarditis have significantly improved the procedural safety [19, 21].

The AtriClip, the first approved device for surgical exclusion of the LAA, has been successfully deployed in over 300,000 patients worldwide. The AtriClip is designed as a self-closing implantable clip, composed of two parallel titanium bars connected by nitinol hinges, and covered with a braided polyester lining. The clip is attached to a disposable applicator and can be repositioned if the initial placement is suboptimal. Once closed, the AtriClip exerts a consistent compression pressure, ensuring complete exclusion of the LAA. The shape and size of the LAA can vary among individuals [22]. AtriClip devices are available in sizes ranging from 35 to 50 mm with 5 mm increments (Fig. 2). Preliminary animal studies have demonstrated that the clip achieves a smooth and linear occlusion without causing laceration, migration, or damage to adjacent structures [23–25]. The AtriClip is currently available not only for use in open-heart surgery but also for procedures performed through totally thoracoscopic surgery. The use of AtriClip is gradually increasing, supported by recent studies demonstrating its clinical safety and efficacy [26–29].

Long-term outcomes of the AtriClip

There is currently a lack of sufficient research on the long-term outcomes of this device. Although there is a lack of large-scale randomized studies comparing it to traditional LAAC methods, current literature reports suggest a reasonably high success rate for AtriClip. In a

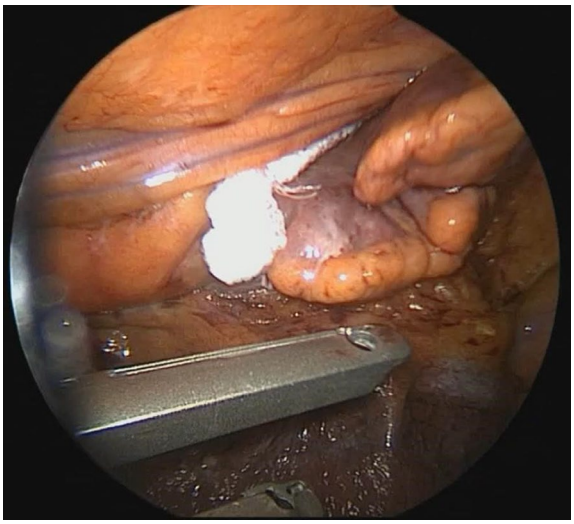

Fig. 2 Left atrial appendage exclusion using clip device

prospective study, the analysis involved 97 patients with a mean CHA2DS2-VASc score of 2.4 ± 1.4. AtriClips were inserted using video-assisted thoracic surgery ($n=74$) and through sternotomy or thoracotomy ($n=23$). The study observed a successful closure rate of 96% (93 out of 97) at the one-year follow-up assessment using TEE [30]. In another study, 65 patients who underwent totally thoracoscopic LAAC with AtriClip were evaluated. After 90 days of AtriClip placement, the success of the procedure was assessed using CT angiography, revealing that 93.9% of the patients had successful closure [31]. A recent meta-analysis evaluating the safety and effectiveness of the AtriClip device, whether placed thoracoscopically or during open concomitant surgery, included 922 patients. The analysis revealed an acute closure rate of 97.8%, and no device-related adverse events were reported during the peri-procedural period. Stroke rates during follow-up ranged from 0.2 to 1.5 per 100 patient-years, with 59% of patients being able to discontinue anticoagulation therapy [32].

Adjunctive anticoagulation

There is currently no definitive conclusion regarding post-AtriClip anticoagulant therapy. Although studies have demonstrated that the WATCHMAN device is non-inferior to nonvitamin K antagonist oral anticoagulants (NOACs), there is a lack of clear comparative research between AtriClip and anticoagulant therapy, as well as between AtriClip and other percutaneous endocardial LAAC devices. Therefore, according to current guidelines, the decision to initiate anticoagulant therapy should be based on the assessment of CHA2DS2VASc risk factors, regardless of LAAC. However, given that AtriClip is frequently utilized in patients who are unable to tolerate anticoagulants or exhibit poor adherence, cautiously considering discontinuation of anticoagulant therapy in such patients may be a reasonable option. In certain scenarios, it may be advisable to consider adjunctive anticoagulation therapy even after LAAC, especially when there are other risk factors for thromboembolism or if the closure of the LAA is incomplete.

Considerations before LAAC

Prior to performing the LAAC, it is essential to confirm the presence or absence of thrombus in the LAA. Transesophageal echocardiography, cardiac magnetic resonance imaging, and cardiac computed tomography can provide useful information for examining LAA morphology and evaluating the presence of thrombus within the LAA [22, 33–35]. These examinations can also help identify any underlying congenital heart abnormalities that need to be considered during the procedure. If there is no thrombus present in the LAA and no contraindications due to underlying congenital abnormalities, an epicardial LAAC or percutaneous endocardial LAAC can be considered.

Concerns about cardiac hormone reduction

There is a concern that LAAC may lead to a decrease in the secretion of atrial natriuretic peptide (ANP) from the LAA [36–38]. ANP is a hormone known to assist in sodium excretion and diuresis in response to volume overload, and it is also involved in the renin–angiotensin–aldosterone pathway [39, 40]. However, studies have revealed that epicardial LAAC does not have a negative hemodynamic impact. [41, 42]. In these studies, when epicardial LAAC was performed, a rapid increase in ANP within 24 h was observed, but it significantly decreased in the long term after 7 days. Additionally, it was noted that the levels of norepinephrine, including epinephrine, also decreased in the long term as the sympathetic and parasympathetic nerves distributed in the LAA were damaged due to necrosis after LAAC. Based on these findings, it was hypothesized that the sharp increase in ANP levels during the initial stages of the procedure may explain the decrease in blood pressure, and the long-term decrease in blood pressure, despite the decrease in ANP levels, may be attributed to the LAA necrosis after LAAC, which reduces the levels of epinephrine, norepinephrine, and the activity of the renin–angiotensin–aldosterone system. Therefore, it was concluded that epicardial LAAC in AF patients is associated with persistent neurohormonal changes favoring blood pressure reduction [43].

Concern about residual LAA function

The LAA is a trabecular pouch that extends from the LA. The unique shape of this structure enables it to function as a volume reservoir, particularly when there is volume overload, accounting for more than 10% of the LA volume [44]. Although LAAC eliminates the LAA's role in thrombus formation, it is important to consider the potential impact on overall cardiac function. The LAA plays a role in cardiac performance, such as LAA kick motion. The LAA kick, also known as LAA contraction or LAA systole, refers to the mechanical contraction or squeezing motion of the LAA during the cardiac cycle. During the diastolic phase of the cardiac cycle, when the left atrium is in systolic phase, the LAA contracts, contributing to the active emptying of blood from the LAA into the left ventricle. This contraction provides an additional boost or kick to the blood flow, aiding in the efficiency of overall cardiac function. Therefore, the closure of LAA may affect atrial contraction and cardiac output, leading to the belief that a decrease in reservoir function and reduced atrial contractility would be inevitable following LAAC. However, according to a meta-analysis, LAA exclusion is associated with improvement of left atrial reservoir function and its contractile function did not differ significantly after LAA exclusion [20].

Summary

AF requires alternative stroke prevention strategies to oral anticoagulants due to their associated risks. LAAC is emerging as a viable alternative, with surgical and percutaneous methods. Although traditional surgical methods showed mixed results, newer epicardial LAAC devices such as the AtriClip have demonstrated higher success rates. However, potential impacts on cardiac hormones and function necessitate further investigation. Post-LAAC anticoagulation remains debatable and requires personalization based on individual risk factors. Future research should continue to refine these strategies.

Abbreviations

AF	Atrial fibrillation
LAA	Left atrial appendage
LAAC	Left atrial appendage closure
NOAC	Nonvitamin K oral anticoagulant
VKA	Vitamin K antagonists
ANP	Atrial natriuretic peptide

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Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

I agree.

Competing interests

The authors declare that they have no conflict of interest.

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