LEFT ATRIAL APPENDAGE MANAGEMENT: A SURGICAL PERSPECTIVE

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Abstract

Atrial fibrillation (AF) is the most common atrial arrhythmia but it is not a benign disease. AF is an important risk factor for thromboembolic events, causing significant morbidity and mortality. The left atrial appendage (LAA) plays an important role in thrombus formation but the ideal way to manage the LAA is still debated. The increasing popularity of surgical epicardial ablation and hybrid endo-epicardial ablation approaches, especially in patients with a more advanced diseased substrate, has raised the interest in epicardial LAA management. Minimally invasive treatment options for the LAA offer a unique opportunity to close the LAA with a clip device. This review highlights morphologic, electrophysiologic and surgical aspects of the left atrial appendage with regard to atrial fibrillation surgery, and aims to illustrate the different surgical management strategies.

Key Words: Atrial fibrillation, Ablation, Left Atrial Appendage, Arrhythmia Surgery, Stroke.

Introduction.

Atrial fibrillation (AF) is the most common atrial arrhythmia and it should not be considered a benign disease. Besides symptomatology, loss of atrial and eventually ventricular function, AF is an important risk factor for cerebral stoke. This causes significant morbidity and mortality, especially in the aging population of Western countries. The left atrial appendage (LAA) plays an important role in thrombus formation. Data suggests that approximately 90% of atrial thrombi in non-rheumatic AF are found within the LAA[1]. Although oral anticoagulants offer an important stroke risk reduction, it also increases risk for bleeding. Benefits of rhythm control for more persistent forms of AF are becoming clearer, but results of catheter ablation remain far from ideal[2]. This caused a growing interest for minimally invasive AF surgery[3-6], especially in patients who are refractory to medical and transcatheter therapy[4, 7, 8].

To date, transcatheter closure of the LAA shows no significant benefit compared to OAC. During thoracoscopic AF ablation, the surgeon has the unique opportunity to manage the LAA. Previously, complete LAA exclusion has proven challenging, whilst incomplete closure or amputation may increase thrombo-embolic risk[9, 10]. However, clip occlusion devices have simplified the surgical LAA management with consistent exclusion and, also important, electrical isolation of the LAA[11, 12]. Since the introduction of epicardial LAA management, over 250.000 clip occlusions have been performed in patients worldwide. This review highlights morphologic, electrophysiological and surgical aspects of the left atrial appendage with regard to atrial fibrillation surgery, and aims to illustrate the practical implications for surgical rhythm management.

LAA management and effect on LA and LV mechanical function.

Historically considered a useless left atrium embryonic remnant[13], the LAA turned its definition, being the most common source of cardiac emboli in AF patients, from "the most lethal human attachment"[14] to an important structure with crucial interaction for both LA and LV functions. The LAA can act as a complementary reservoir that refills during left ventricular early systole when the mitral valve is closed and the LA is passively receiving preload from the pulmonary veins. The LAA has demonstrated to have a higher compliance compared to the LA, especially with diseases causing volume overload. Therefore, the LAA is supposed to play an important role in cardiac pressure-volume regulation[1]. However, decreased LA reservoir function is noted after LAA exclusion without affecting intrinsic LA contractility[15]. During early diastole, the LAA should be considered as a compliance chamber that passively fills the LA and LV once the mitral valve is open, while during late diastole, the LAA acts as booster pump due to its intrinsic contractile activity thus contributing to stroke volume[16, 17]. The LAA is calculated to contribute to the total LA volume up to 10%[18]. However, contemporary series seem to exclude significant echocardiography variations in LV stroke volume or LVEF in patients in sinus rhythm undergoing LAA occlusion[15]. These data are also confirmed in patients with reduced LVEF (<35%) despite a global increase in LA reservoir, conduit and booster pump is moderately improved following Frank-Starling mechanism[19-21]. It has to be noted that these findings were from endocardial LAA occlusion. Little is known about hemodynamics effects after epicardial LAA occlusion, which that remains an important field of investigation.

LAA management and humoral effects.

The endocrine role of the LAA is related to the presence of intrinsic stretch-sensitive receptors able to release ANP. Experimental analysis showed presence of so-called “ANP densely granulated cells” with the highest concentration in the LAA[22-24]. Fluid infusion at the level of the LAA increases blood ANP levels, leading to increased heart rate, natriuresis and diuresis determining reduction in volume load, vasodilatation and blood pressure reduction[25]. Percutaneous endocardial approaches do not seem to impact ANP levels and blood pressure but several studies demonstrated significant down-regulation and inhibition of the natriuresis pathway when the LAA is excluded surgically. Also, noradrenaline, adrenaline, renin and aldosterone showed a significant down-regulation in patients treated with epicardial LAA exclusion[26-28]. The appendage is richly innervated by sympathetic and parasympathetic nerves in strict relation to stretch receptors, actively interconnected with angiotensin system activated by ANP release. Turagam et al. demonstrated a significant reduction of systolic and diastolic blood pressure in hypertensive AF patients undergoing epicardial ablation and LAA exclusion, underlining the necessity to reduce antihypertensive medications[29]. Because the original Cox-Maze III operation incorporated excision of the LAA down to its base as well as excision of the right atrial appendage tip, patients developed severe postoperative fluid overload due to the decrease of ANP levels in the blood[30]. As a counter measure, spironolactone should be administered to prevent this fluid overload. The period of spironolactone administration is at least >1 month in our clinical practice.

Left Atrial Appendage Morphology.

Increased interest in ablation techniques and management of the LAA combined with improved imaging modalities have led to classification of LAA morphology. Most commonly the Wang classification is used to assign the LAAs into either; “Cactus”, “Chicken wing”, “Windsock” or “Cauliflower” [Figure 1][31]. It is supposed that classification can aid both planning interventions and identification of “dangerous” appendages who require intervention[32]. Large LAAs and LAAs with single lobe morphology are more frequently present in patients who suffer from stroke. However, AF induced elevated pressure and subsequently increased LAA volume may alter LAA morphology. The number of LAA lobes is reduced due to the remarkably thin (+/- 1mm) wall, combined with the lack of supporting tissue around the appendage. Also, due to dilatation, bending of the LAA can occur, creating turbulence and eventually increasing thrombo-embolic risk.

This knowledge might help decision making on which patients require LAA management[33] although more studies on this topic need to be conducted. For procedural planning, other imaging modalities such as contrast enhanced cardiac CT can be utilized, although CT study is static and the images are captured a few seconds after arrival of contrast to the left side of the heart (LA/LAA), it can be difficult to differentiate thrombus from sluggish flow. A promising imaging modality is cardiac magnetic resonance imaging which can reliably assess LAA shape and dimensions. At times, CCT and CMR can be challenging since irregular heart rate and tachycardia significantly reduce image quality (with an ideal heart rate <65 beats per minute). Trans-esophageal echocardiography (TEE) is used to assess the pre-procedural presence of thrombus in the LAA.

The role of LAA clip occlusion in thrombo-embolic stroke risk reduction.

In general, the LAA is the most common site for cardiac thrombi in patients, both in AF or in SR[34]. LA enlargement promotes stasis and therefore thrombo-embolic risk[35]. This is hypothesized to be most pronounced in the LAA. Additional stroke risk is the presence of a heavily trabeculated LAA endocardium[32]. Although there is a strong relationship between AF and stroke, evidence for the causal relationship between stroke and thrombus formation within the LAA is not undisputed. It has been demonstrated that in a AF patient population, 91% of all thrombi were formed within the LAA[36]. In another prospective study, TEE examination show that of 230 patients with AF >2 days, 33 out of 34 cardiac thrombi were located in the LAA[37]. As a part of the original Cox-Maze procedure, the atrial appendices were routinely amputated and his group has published extensively on rhythm outcome but also stroke reduction benefit after Maze surgery[38]. Besides stroke risk reduction interventions, it is possible that patients present with a thrombus present within the LAA. Recently a small case series has demonstrated that V-shaped clip with minimal manipulation can safely exclude partially thrombosed left atrial appendages[39, 40].

The role of LAA clip occlusion in rhythm control.

Remodeling of the LAA may also concur in the pathogenesis of atrial arrhythmias[41]. Electrical exclusion of the LAA therefore provides an anti-arrhythmogenic benefit. Di Biase et al. reported that 27% of their AF ablation patient population referred had firing from the LAA, and also that in 8.7% the LAA was the only mapped trigger[42]. Following transcatheter LAA isolation in addition to pulmonary vein isolation, studies show a higher arrhythmia-free survival in patients who undergo additional LAA isolation. Heeger et al. show 49% arrhythmia free survival compared to 37% in the control group ($p=0.02$)[43]. Similar results were achieved in the BELIEF Trial[44]. Nevertheless, there is concern of a potential excess stroke risk after electrical isolation of the LAA via catheter ablation since such procedure creates an akinetic cul-de-sac in communication with the left atrium which has proven to be very thrombogenic. To this regards the distinctive features of epicardial LAA clip exclusion are particularly intriguing. Using the clip to occlude the LAA, complete electrical isolation of the LAA has been demonstrated, excluding potential AF onset triggers[45]. At long term the LAA will completely dissolve following clip placement. To date, no clear data is available demonstrating the additional benefit of LAA clip closure as an addition to thoracoscopic PVI and more studies are warranted. In such rare cases of LAA driven automatic arrhythmias, stand-alone epicardial clip LAA closure is quite consistently an effective rhythm control strategy and, not infrequently, the best chance to get rid of the arrhythmia[12].

Indications for epicardial LAA clip closure.

The first line treatment to prevent thromboembolism is of course anticoagulation. In recent years direct acting oral anticoagulants have proven to be safe and give pharmacological advantages over vitamin K antagonists due to more predictable pharmacokinetics and less need for regular bloodwork and monitoring[46]. Current guidelines for AF management suggest to consider LAA occlusion as a stroke prevention strategy in patients who experienced cerebral hemorrhage or bleeding related to long-term anticoagulation therapy and/or patients with AF undergoing cardiac surgery (Class IIb, Level of evidence B)[47]. These indications are based on randomized clinical trials demonstrating non-inferiority of percutaneous devices versus anticoagulation therapy in stroke reduction for patients with AF, creating a basis for LAA closure as an alternative to oral anticoagulation[48-50]. However, there is a lack of data providing specific comparisons between percutaneous versus surgical occlusion devices and/or epicardial LAA closure versus DOAC for stroke prevention. The ongoing LAAOS III trial, randomizing 4700 open cardiac surgery patients to either LAA occlusion or not, will hopefully shed some light on this issue[51]. Accurate detection of underlying cardiomyopathies should be pursued and the benefits of LAA occlusion (thromboembolic prophylaxis and rhythm control), should be balanced against the potential for hemodynamic impairment, especially in patients without persistent arrhythmias. Patients with AF and end-stage renal failure (clearance < 15 mL/min) have a contraindication for NOAC but also high risk for bleeding; epicardial LAA occlusion in this specific subset of patients is still undefined but might offer a clinical benefit. Whether or not to exclude the LAA should be discussed in a multidisciplinary approach by the AF-Heart Team[52]: a case by case analysis of clinical indications, anatomical and morphological considerations. Risk scores analysis is warranted in order to provide a patient-tailored approach (guided by CHA2DS2-VASc and HASBLED score).

Beside previously reported indications, the 2020 EHRA/EAPCI expert consensus statement on catheter based LAA appendage occlusion resumes indications for LAA occlusion[53]: 1) AF patients eligible for long-term OAC/NOAC who refuse the medical treatment despite thorough explanation. 2) AF patients with absolute contraindication for long-term OAC/NOAC (hemorrage or side-effects due to VKA/NOAC) 3) AF patients not compliant to medical therapy.

According to the experts, in case of contraindication to antiplatelet therapy, patients may not be eligible for endovascular LAA exclusion and rather have epicardial clip occlusion[53].

Contraindication for epicardial LAA clip closure

A relative contraindication of LAA clip exclusion derives from the possible negative repercussion on LV filling properties in patients with severely impaired diastolic dysfunction. In such patients, an increased LA compliance through an increased volume is key to keeping a higher reservoir function and hence a lower postcapillary pressure. Acute amputation of the LAA, which is the most distensible part of the LA and accounts for 10-20% of the left atrial volume[54], might cause increased pulmonary pressure and congestion symptoms. Theoretically, such drawback would apply also in the case of endovascular LAA occlusion devices. Nevertheless, we believe that, due to the acute watertight feature of clip exclusion, epicardial LAA clip occlusion might unveil a higher potential for diastolic impairment in selected high-risk patients, when compared to transcatheter LAA occlusion devices. The latter work more like filters, and endothelialize gradually, leaving a residual distinct endoleak in up to 2/3 of the treated appendages [55].

Anticoagulation strategy following LAA occlusion.

An important issue is how to proceed with anticoagulation therapy following LAA occlusion. As is, AF anticoagulation guidelines do not correct for the absence of the LAA. Hence, patients have a class 1 indication for lifelong therapeutic anticoagulation guided by the CHA_2DS_2-VASc risk factors. Since there are no studies comparing epicardial LAA closure to OAC, it cannot be considered a replacement therapy. For now, contra-indication to anticoagulation seems to be the only indication.

Remembering that (D)OAC is the recommended therapy for stroke prevention in AF patients, if LAA exclusion is recommended because of high-risk of bleeding or contraindication for anticoagulation therapy, careful considerations have to be done about whether or not to restart (D)OAC after epicardial LAA occlusion. In patients with a history of previous uncontrolled life-threatening bleeding, discontinuation of OAC/NOAC seems to be reasonable but should be discussed on an individual patient level, tailored to patient characteristics.

Surgical techniques.

Initially, surgical closure by means of stapling, amputation, ligation and/or direct sewing provided a high rate of incomplete exclusion therefore paradoxically increasing the risk of stroke because of the presence of a residual "pouch" with a thrombogenic effect[9, 10]. In the last decade, surgical epicardial LAA occlusion by means of a preloaded nitinol clip (Gillinov-Cosgrove LAA clip a.k.a. Atriclip®, AtriCure, Inc., Mason, OH, USA) placed epicardially at the base of the LAA, showed to be a valuable tool with excellent results in terms of safe and durable LAA occlusion[56]. Durability and efficacy results were confirmed at 3-years follow-up, in terms of complete occlusion and reduced incidence of stroke and cerebrovascular events in AF patients undergoing concomitant LAA occlusion[57, 58]. The AtriClip is the only FDA-approved device for epicardial LAA management. In recent years, several modifications have been made to the original Atriclip to facilitate minimally invasive use. (Figure 2)

Ideally, the work up for surgical LAA management includes cardiac CT. This is important to rule out congenital anomalies such as persistent left superior vena cava, understanding of LAA morphology and it also provides a non-invasive screening for possible LAA thrombus. As described above, TEE remains the gold standard to allow a safe planning of the procedure and to check for appropriate accomplishment of LAA Clip deployment. TEE should be performed as close as possible to the LAA exclusion procedure, especially when a cardiac CT is not available or feasible (poor renal function, contrast allergy, impaired transportability). During the procedure TEE allows for confirmation of freedom from thrombosis – important, since many patients will not be appropriately anticoagulated, if at all, at such stage – right before deployment, to provide an endoluminal feedback on a possible residual LAA stump and to rule out possible residual leaks to the LAA. This last feature, is probably less compelling, since no such finding has been reported since the introduction of the LAA clip.

After general anesthesia and using with selective lung ventilation, the TEE probe is inserted, and defibrillation patches are applied. The patient is prepped on a dorsal decubitus, with a slight lifting of the left side (we use inflatable balloons), just as one would prepare the right chest for minimally invasive mitral surgery, with the left arm left down.

Three ports are utilized: a camera port, aligned with the midsternum (not considering the xyfoid), and 2 more anterior operating ports, a 5 mm port one intercostal space above and a 10-12mm port circa 2 intercostal spaces below. (Figure 3) We use a 0° camera through a 10-12 mm view port. After excluding the right lung from ventilation, and aided by CO_2 insufflation at 8-10 cm H_2O, the pericardial sac is opened with endo-scissors, cautery or harmonic forceps, parallel to and far from the phrenic pedicle. With normal mediastinal anatomy, retrophrenic pericardial access is preferred, though antephrenic pericardial incision can also provide a good exposure, especially when the phrenic pedicle is located posteriorly. A single stay suture on the anterior side of the pericardiotomy might occasionally be used to enhance exposure. The base of the LAA is measured with the AtriClip sizer. A device of appropriate size is then selected and deployed through the inferior 12mm port. Clip delivery is completely blunt and atraumatic. (Figure 4)

Before releasing the device from the deployment tool, ECG might help rule out exceptionally rare instances of inadvertent coronary compression of the circumflex artery, which might be easily corrected by reopening and repositioning. Following clip placement, TEE is used to confirm complete exclusion, by informing on possible residual stump which might guide a more proximal repositioning of the device. Although unreported so far with this technology, TEE control can confirm real time absence of residual leaks across the LAA clip. Time of such safety controls is key since, being LAA clip positioning most of the times performed in total absence of anticoagulation, adjustments entailing reopening of the device can only be executed within one minute, since reopening of a LAA clip after longer periods of time might restore flow to appendage containing thrombus. After LAA clip exclusion, the ports are closed leaving a pleural drainage in the lower port. The procedure lasts around 20 minutes in experienced hands and the patient is extubated directly post procedure and transferred to a stepdown ward.

Special considerations.

Due to the complete extracardiac nature of the procedure, no anticoagulation regimen is required. Therefore, LAA clip occlusion is very suitable for those patients with relative and absolute contraindication to anticoagulant drugs, like those with ongoing bleeding complications.

Since the standard device (Figure 2) has a closed structure, positioning requires it to slide around the LAA from its distal end, passing the body, to reach the very base of the structure, where it is closed and released. During such process, fresh thrombus within the LAA might be dislodged and embolize. Therefore, LAA thrombosis is a contraindication to LAA epicardial exclusion. Nevertheless, latest generation devices with a

V shaped closing mechanism (Figure 2) might provide potential for LAA closure in those patients with refractory LAA thrombosis that is limited to the distal end of the appendage[39].

In general, thoracoscopic LAA epicardial exclusion with an Atriclip device is a very safe and swift procedure[59]. In order to keep this procedure to a very low threshold of risk, we strongly recommend to cautiously assess patients by means of imaging techniques as previously described (TEE, CT scan or MRI). From a surgical stand-point we suggest to remain >1cm from the phrenic nerve, to avoid permanent or transient palsy of the hemidiaphragm. It is very important to manage the LAA cautiously avoiding to grabbing the LAA since this tissue is thin and can be damaged easily. The device can be set in place very easily by pushing it open on top of the LAA while a-traumatically "caressing" the LAA into the device frame with a peanut device.

Finally, it is very important to understand how this procedure, in experienced hands can be also performed in patients with different degree of cardio-vascular abnormalities. Our experience shows how a complete LAA exclusion was obtained without additional risks in patients with persistent left superior vena cava (Figure 5) and also in patients with situs inversus complete dextrocardia (Figure 6).

Conclusions.

There are several important clinical and theoretical advantages of epicardial LAA clip occlusion, including stroke risk reduction and improved rhythm outcome. Epicardial clip occlusion is reported to be feasible, safe and very effective, however its role as a stand-alone procedure remains to be established. Currently, isolated epicardial LAA clip closure remains reserved for patients with a relative or strict contra-indication for anticoagulation and/or to antiplatelet therapy and to those rare case of refractory automatic arrhythmias originating in the LAA. Understanding of LAA morphology and pathology may help planning epicardial LAA management.

Having the epicardial LAA clip occlusion within the technical armamentarium and openly discussing individual cases within an AF Heart Team is pivotal to develop a personalized approach and find the most appropriate LAA treatment in every single patient.

Figure Legend

Figure 1 - Wang's classification for LAA morphologies. LAA length was measured from the orifice area (dashed orange line) to the farthest point of the LAA via the center of the main lobe. The bend angle was measured with an imaginary vertical line (red dashed line) and a line between the main lobe and the farthest point of the LAA. Cactus has a dominant central lobe, one or more secondary lobes, and total length less than 4 cm. ChickenWing has only one lobe, total length more than 4 cm, and a bend angle less than 100°. WindSock has one dominant lobe with several secondary, or even tertiary lobes, total length more than 4 cm, and a bend angle of over 100°. CauliFlower has a total length less than 4 cm and complex internal structures. (*with permission:* https://journals.plos.org/plosone/s/licenses-and-copyright)

Figure 2 – Different available LAA clip occlusion devices (Atriclip Flex, Flex V, Pro2, ProV) *Copyright reserved to Atricure*

Figure 3 – Patient and ports positioning.

Figure 4 – LAA occlusion with device positioning and release. Left: device positioning. Right: device release.

Figure 5 – LAA occlusion in a patient with persistent superior vena cava (white arrow). Left: device positioning. Central: device closure. Right: device release.

Figure 6 – LAA occlusion in a patient with complete situs inversus dextrocardia. Left: device sizing. Central: device positioning. Right: device release.

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