Surgical management of the left atrial appendage: a must or a myth?

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Summary

Surgical treatment of the left atrial appendage (LAA) has increased over the past few years. The most serious complication of atrial fibrillation is a cerebral cardioembolic stroke. In most patients with atrial fibrillation, the LAA is the anatomical source of the embolism. Several surgical techniques for occluding the LAA using different devices have been developed with different prospects of success. It is still not clear which of these techniques represents the optimum treatment for reducing the incidence of stroke in patients with atrial fibrillation. This text focuses on the surgical closure of LAA and critically considers the results with respect to closure success and the associated complications.

Keywords: Left atrial appendage • Pathophysiology • Surgical occlusion techniques

Surgical treatment of the left atrial appendage (LAA), either from the endocardium or the epicardium, to exclude a potential source of emboli in patients with atrial fibrillation (AF) has increased over the past decades. The most serious complication of AF is a cerebral stroke. Generally, this disease occurs with a frequency of 8% in the Western population; in patients over 65 years old, it is as high as 20%. Approximately 20% of these strokes are caused by AF. If a stroke occurs during atrial arrhythmia, the subsequent cerebral ischaemia is much more serious than ischaemia caused by non-cardioembolic events. Stroke is currently the third leading cause of death in Western countries. Thus, AF with its associated complication of embolic cerebral infarction is responsible for a significant proportion of morbidity and mortality in the general population [1]. In most cases, the LAA is the anatomical source of the embolism, because the 3 characteristics of Virchow's triad are fulfilled [2–4]. Multiple surgical LAA occlusion techniques with different devices have been developed with different prospects of success, but it is still not clear whether these treatment strategies represent the optimum treatment when it comes to reduction of strokes in patients with AF. This article focuses on the surgical closure of the LAA and critically considers the results with respect to successful closure and associated complications.

ANATOMY/PHYSIOLOGY/PATOPHYSIOLOGY

The LAA is an anatomical region of the left atrium with different possible anatomical shapes [5]. In a computed tomography and magnetic resonance imaging study, the different shapes of the LAA were classified into 4 categories: chicken wing (48%), cactus (30%), windsock (19%) and cauliflower (3%) [6]. Since then, some authors have questioned the classification system because the different anatomical shapes can be applied to the same LAA, depending on the angle of the viewer [7]. Although the LAA has long been described as a non-functioning anatomical structure of the left atrium, its physiological capacity, e.g. transportation and hormone secretion of the atrial natriuretic peptide (ANP), is now well-established. Distension of the LAA leads to elevated plasma levels of ANP, which, at the level of the kidneys, leads to elevated secretion of potassium and chloride; at the arteriolar level, it leads to vasodilation due to the direct antagonism of renin; at the cerebral level, to inhibition of thirst at the hypothalamus, and in the pituitary gland, to decreased release of antidiuretic hormone. All these effects result in a significant reduction in body fluids [8]. This effect was observed in patients after a full Cox-Maze III operation during the initial successful surgical treatment of AF. 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 [9]. Abandoning the excision of the right atrial appendage tip thereafter reduced the risk of fluid overload, because ANP was still produced within the muscles of the right atrial appendage.

In patients with sinus rhythm, the LAA serves as a reservoir during diastole and contracts actively during systole, thereby washing out the body of the LAA. In AF, this active role of the LAA seems to be severely reduced. Virchow's triad, which comprises alterations in blood flow (e.g. stasis), vascular endothelial injury and alterations in the constitution of the blood, is most likely evident in patients with AF, because stasis may occur in the fibrillating left atrium as well as within the LAA due to the lack of regular atrial wall muscle contraction cycles to pump the blood.
Alterations in the left atrial surface may develop due to overstretching of the muscle fibres of the atrial wall with fibroblastic infiltration and the subsequent onset of inflammation. Last but not least, alterations in the blood such as haemostasis, platelet activation, inflammation and changes in the growth factor can occur [3, 10]. Overstretching of the atrial wall even occurs in patients with sinus rhythm but with severely reduced LV function or severe diastolic dysfunction with elevated LV pressure and filling [11]. Thus, in patients with AF, up to 91% of thrombi form within the LAA. Thrombi may also exist in other anatomical regions such as the left atrial pouch, although to a much lesser extent [12]. All of these thrombi incorporate the risk of thrombus migration and the development of cerebral ischaemia.

SURGICAL TREATMENT OPTIONS FOR THE LEFT ATRIAL APPENDAGE

Pharmacological anticoagulative treatment either with a vitamin K antagonist, e.g. warfarin, phenprocoumon or acenocoumarol, or with the more modern direct-acting oral anticoagulants, which directly inhibit factor Xa (dabigatran also inhibits thrombin), is still considered the first line of treatment to reduce thrombus formation within the LAA [13]. It has been shown in multiple registries that treatment with either of these anticoagulants is capable of significantly reducing the risk of stroke [14–16]. In a meta-analysis by Blackshear and Odell [17], the risk of stroke was reduced by up to 65% in patients with AF compared to placebo. The risk of stroke can be assessed with special risk scores, of which the CHA₂DS₂-VASc score is considered the most applicable and is recommended in the current European Society of Cardiology guidelines for the treatment of AF (Class IA) [13]. The administration of any anticoagulant therapy with all its benefits, though, has to be weighed against the risk of minor or major bleeding. Therefore, several bleeding risk scores have been introduced, such as the HAS-BLED score. It is recommended that one thoroughly weigh all the scores of all of the parameters listed before administering any anticoagulant therapy [13]. However, anticoagulant therapy still leads to a high risk of bleeding in some patients, especially in elderly patients or patients with symptoms of liver or kidney dysfunction. Furthermore, the risk for cerebral haemorrhage in these patients is a major concern [18, 19].

Hence, a non-pharmacological approach to reduce the risk of thrombus migration originating from the LAA would be of benefit. The first surgical excision of the LAA was described in 1949 by Madden [20], who resected the LAA during surgery for mitral valve stenosis as a prophylactic procedure because LAA thrombi were present in their patients. In the years following this event, the cardiothoracic community paid little attention to this concept until the late 1980s and early 1990s, when Cox et al. [21] developed a definitive surgical procedure to treat AF. This procedure, known as the Cox-Maze III procedure, in addition to a specific pattern of surgical incisions within both atria, also required complete excision of the LAA. The authors postulated in a long-term follow-up study that the low rate of cerebral embolisms was not only due to successful sinus rhythm restoration, but also due to the elimination of the left atrial auricle of the heart [22]. These results were supported by Prasad et al. [23], who reported low rates of cerebral embolisms in their cohort of Cox-Maze III patients. These results were all the more remarkable because the majority of the patients in the observed groups were not taking anticoagulation medications. In a recent meta-analysis and in a smaller German study, the authors documented a significant survival benefit in a group of patients without antirhythmic surgery but a surgically eliminated LAA compared to patients with AF and a non-resected LAA [24, 25].

Surgical exclusion of the LAA can be achieved either endo- or epicardially by over-sewing or excision or epicardially only by resection, ligation, stapling with or without amputation of the LAA or application of a clip system (AtriClip LAA exclusion system, AtriCure, Mason, OH, USA) at the bottom of the LAA [4, 26] (Figs 1A and B, 2, 3). The Tiger Paw System (Maquet Medical Systems, Getinge, Sweden), which enabled epicardial closure at the bottom of the LAA with a soft silicone clamp, was withdrawn from the market by the U.S. Food and Drug Administration [27] due to possible safety issues. Most of these procedures are performed concomitantly during open chest cardiac surgery but can also be performed epicardially during thoracoscopic AF ablation or as a pure stand-alone procedure, either minimally invasive (minithoracotomy) or thoracoscopically [28–31].

Because the majority of surgical LAA closure studies are retrospective in design and are performed mostly at single centres, conclusions about success rates and complication rates must be drawn with caution. Randomized controlled trials (RCTs) are rare and mostly scientifically underpowered [25, 31–33]. In the previously
mentioned meta-analysis by Tsai et al., the authors concluded that LAA exclusion results in a reduction of neurological events [24]. In a press briefing from the American College of Cardiology during their meeting in March 2017, a large retrospective analysis from the Society of Thoracic Surgeons database with more than 10,000 patients was presented. This study showed a 38% reduction in thromboembolisms and a 15% lower risk of all-cause mortality at 1 year compared to non-atrial appendage closure. However, due to the inconsistencies of the surgical LAA closure techniques and follow-up strategies, a definite recommendation of a safe, easy-to-perform procedure could not be drawn from this publication. In fact, in the face of the different techniques with different outcomes, the early postoperative complication rate, even including in-hospital deaths, was significantly higher than in the non-treatment group [34]. These data support the surgical concomitant LAA exclusion procedure, but further clarification from the results of RCTs needs to be performed by the cardiothoracic society to put the surgical treatment of LAA on a robust scientific base.

A large prospective multicentre RCT that solely examines the results of LAA closure during cardiac surgery with respect to neurological outcomes (LAOOS III) with 4500 patients is still recruiting patients and will not provide initial results before 2020 [35, 36]. Given that the LAA closure technique and the postsurgical medical regimen will not be standardized, conclusions may be inconsistent.

Another recent RCT, The ATLAS study (AtriClip® Left Atrial Appendage Exclusion Concomitant to Structural Heart Procedures), is a prospective multicentre randomized trial that compares the impact of postoperative AF on patients with no preoperative history of AF in 2 randomized treatment arms: patients with postoperative AF and surgical LAA closure (using AtriClip LAA Exclusion Systems, Mason, OH, USA) versus patients with postoperative AF and no surgical LAA closure with an estimated group size of 2000 patients started in 2016 and will not be completed before 2020 [37]. Since LAA occlusion will be standardized in this trial, results might have a more profound impact than those from LAOOS III. However, because this is the first trial in patients with sinus rhythm and no documented AF prior to surgery, routine surgical closure of the LAA in patients without a history of AF cannot be recommended. This ‘protective’ treatment strategy might only be indicated in light of the results of the ATLAS trial, when they become available.

For all surgical LAA procedures, it is of the utmost importance to choose the right technique with the right device in order to avoid incomplete LAA closure, which might be devastating with respect to neurological complications [38]. Kanderian et al. [39], in a very important workup of surgical LAA procedures, reported that, in total, complete closure of the LAA was achieved in only 55 (40%) of 137 patients. The techniques with the highest failure rates included endocardial oversewing (77%!) (Fig. 4) and non-

Figure 2: Endoscopic removal of the left atrial appendage by means of a cutting stapling device. (A) Device application, (B) resected left atrial appendage with staple suture line. From Hanke et al. [4]. Reproduced with permission from Springer.

Figure 3: (A) Suture attachment and removal of the left atrial appendage (suture line I ‘Blalock’); (B) completion of the suture line (suture line I and suture line II overcast stitch); (C) intraoperative picture. From Hanke et al. [4]. Reproduced with permission from Springer. Picture on the right owned by the author.
cutting stapler devices (100%), because with both treatments, a recanalized LAA was still detectable postoperatively with transoesophageal echocardiography. In patients being treated with excision only, no recanalization was observed, but a stump was detectable, with occurrence of a remaining thrombus in these stumps in about 25% [39]. To truly excise the LAA, it should be taken down to the very bottom; suture reinforcement with either felt or a pericardial strip is recommended [40] (Fig. 2). When performing epicardial stapling, either during thoracoscopic AF ablation or during stand-alone procedures, a modern cutting stapler with a 6-fold clip series (Echelon Flex, Ethicon, Johnson & Johnson, New Brunswick, NJ, USA) is recommended, because this excision therapy yields optimal results [39, 40] (Fig. 2).

Epicardial heart-beating closure of the LAA is now increasingly being performed in a stand-alone fashion, mostly either using a minimally invasive procedure with a small left-sided thoracotomy or thoracoscopically. The AtriCure LAA Exclusion system, a nitinol-based clip surrounded by a cotton scarf, was invented to securely close the LAA at the base with equal force distribution over the complete length of the clip. This device was introduced for use with concomitant cardiac surgery in 2007 with very good results in the short term as well as in the long-term follow-up period [41–45]. Suwalski et al. [46], in a subsequent transoesophageal echocardiography study, showed that successful closure of the LAA during off-pump heart surgery with the AtriClip LAA exclusion system was possible in all patients studied, irrespective of the anatomy of the LAA. This device was also recently applied successfully during minimally invasive stand-alone procedures, of which thoracoscopy represents the most minimalized surgical approach [31, 47]. The Stroke Feasibility Study, a multicentre prospective trial of minimally invasive surgery that examined the performance of the AtriClip LAA exclusion system in patients with AF, was completed in 2015. In this trial, successful placement of the device was possible in 80% of patients; no neurological events occurred in any of the studied patients [48].

In addition, because AF recurrence after AF ablation often originates from the LAA orifice, this clipping device isolates the LAA electrically, thus eliminating a potential source of AF recurrence after ablation therapy [31, 49, 50]. By introducing the second-generation LAA exclusion clip device (AtriClip Pro2), the thoracoscopic surgical procedure has been facilitated due to the reduced width of the delivery stent.

Despite all these promising results of modern surgical LAA occlusion therapy, acceptance of this procedure among cardiac surgeons and interventional cardiologists is low. In 2013, in view of the positive effects of surgical LAA closure, Cox supported the idea of a more ‘aggressive’ lone concomitant additional LAA closure in patients with AF undergoing heart surgery without performing surgical ablation, because the LAA has been described as the ‘most lethal attachment’ to the heart [51, 52]. Some surgeons are reluctant to use LAA closure, since the LAA is fragile, and complications within this anatomical region are difficult to manage. However, with the new surgical devices on the market, complication rates are low if not negligible. So far, more than 100 000 AtriClip LAA occlusion devices have been implanted worldwide with no major cardiac adverse events being reported so far. During open-heart surgery, direct visualization of the treated LAA (e.g. resection, ligation) is possible, and complications, e.g. bleeding from a suture line, can be treated right away. In minimally invasive procedures, conversion to full sternotomy or implantation of extracorporeal circulation via the groin might be necessary, but since these surgical procedures are performed in an operating theatre, these complications can be handled instantly.

GUIDELINES/RECOMMENDATIONS

To date, because only a few scientifically robust trials of the effect and clinical outcome of LAA occlusion can be found in the cardiothoracic literature, the recommendations do not reach high grade levels. In the most recent 2016 European Society of Cardiology (ESC)/European Society for Cardio-Thoracic Surgery (EACTS) guidelines, treatment of the LAA concomitantly with cardiac surgery may be considered (Class IIb, level of evidence B), and in the 2017 Society of Thoracic Surgeons guidelines, treatment of the LAA concomitantly with cardiac surgery is considered reasonable (Class IIa, C limited data) [13, 53]. Stand-alone surgical treatment of the LAA is not listed in either of these new guidelines. On the other hand, regarding the interventional approach of LAA closure, the stand-alone procedure is listed in the ESC 2016 guidelines but
recommended only in patients with AF with contraindications for anticoagulation therapy and a high risk of stroke (Class IIb, level of evidence B). Furthermore, despite successful surgical LAA exclusion, life-long anticoagulation is recommended in the 2016 ESC/EACTS (Class I, level of evidence B). This recommendation seems to be based on the fact that 2 studies from the last decade were used for classification assessment [54, 55]. In one of these pilot studies, after 1500 patients were screened, 77 patients were eligible for randomization into 2 groups: surgical closure of the LAA (n = 52) with 2 therapeutic options: staples or suture, and a control group (n = 25). The primary end point of the study was ‘feasibility and safety of surgical occlusion of the LAA’; only 44 patients were assessed postoperatively with transoesophageal echocardiography. Because of LAA recanalization in the suture line group in the first 16 patients, the surgeons switched to the stapler device. Failure occurred when the line of the staples was too high, leaving a stump of more than 1 cm, i.e. too much space for further thrombus formation. The LAA occlusion rate ranged from 41% to 81% [32]. The stroke rate was 2.6%. The neurological events occurred in 1 patient perioperatively and in the other patient during the early postoperative phase (day 3), with 1 patient having a patent foramen ovale and carotid stenosis. During the long-term follow-up period, none of the patients had a stroke [54]. As stated by the authors, the main limitation of the study was its small number of patients and ‘the fact, that stapler use was not randomized’. Because of these shortcomings, the scientific impact of this study with respect to determining the impact of surgical LAA closure on neurological events is questionable. Figure 5: Algorithm of stroke protection in atrial fibrillation. LAA: left atrial appendage; NOAC: novel (non-vitamin K antagonist) oral anticoagulant; OAC: oral anticoagulant. Reprinted from Meier et al [55] Author(s), with permission from Europa Digital & Publishing.

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**REFERENCES**


