Left atrial appendage occlusion: Percutaneous and surgical approaches in everyday practice

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ABSTRACT

Prophylactic left atrial appendage occlusion has been suggested as a means of reducing cardioembolism risk in patients with atrial fibrillation. Its clinical benefits have been discussed together with potential endocrine or hemodynamic adverse effects, with conflicting conclusions. We aimed to provide a thorough overview of the current literature and a recommendation for daily clinical decision-making. A comprehensive Medline search through PubMed was conducted to search for relevant articles, which were further filtered using the title and abstract. Sixty-five articles were selected as relevant to the topic. Concomitant left atrial appendage occlusion during cardiac surgery for other reasons is effective in terms of thromboembolism risk reduction in patients with a history of atrial fibrillation and higher CHA_2DS_2-VASc scores. Surgical occlusion is safe, and epicardial closure techniques are preferred. Thoracoscopic and transcatheter techniques are also feasible, and the individual treatment choice must be tailored to the patient. The concerns about endocrine imbalance or risk of heart failure after occlusion are not supported by evidence. Current evidence is conflicting with regard to hemodynamic consequences of appendage occlusion.

Key words: atrial fibrillation, hemodynamic response, left atrial appendage occlusion, surgical resection, transcatheter closure

INTRODUCTION

Atrial fibrillation (AF) is the most frequent cardiac arrhythmia worldwide with an estimated prevalence of 0.5% of the world population [1]. Chaotic and ineffective activity of the atrial muscle leads to a loss of atrial pump function, impairment of the left ventricular diastolic filling, intraatrial stagnation of blood, and potential thrombus formation with risk of cardioembolism [2]. Individual risk of thromboembolism in AF depends on many factors, most of which are included in the CHA_2DS_2-VASc score [3]. The left atrial appendage (LAA) is indisputably the most vulnerable area as up to 91% of thrombi are formed here in non-rheumatic AF [4]. All three pillars of the Virchow triad contribute to the thrombogenesis in LAA in AF: blood stasis, endothelial injury (due to the blood stasis, appendage dilation, and fibroelastic degeneration), hypercoagulable state (consequence of platelet activation secondary to growth factor imbalance) [5].

From a pragmatic point of view, LAA occlusion seems to be a logical solution for reducing the long-term risk of cardioembolism [6]. Simultaneously, one must weigh carefully benefits against harms before organ resection. In severing the LAA, a tiny trabecular *cul-de-sac*, do we get the pure benefit of eliminating the thrombogenic site, or should we regret the loss of some indispensable LAA features?

METHODS

A comprehensive Medline search through PubMed was conducted to search for relevant articles using the keywords: “left atrial appendage occlusion”, “surgical”, “thoracoscopic”, “transcatheter”, “natriuretic peptides”, “hemodynamics”, and “safety”. The results were further filtered using the title and abstract. Similar articles offered by the PubMed algorithm were also scanned. Sixty-five articles were selected as adequate for this topic. The gathered information is provided in a structured manner below.

Left atrial appendage as a legitimate target for thromboembolism risk reduction

The LAA with its variant and rather peculiar morphology (Figure 1) [7] has long been recognized for its predisposition to thrombus formation [6]. LAA occlusion (LAAO) was historically carried out by many surgeons to reduce the thromboembolism risk in AF patients despite the absence of clear evidence [6]. A meta-analysis of several smaller studies by Tsai et al. favored LAAO in terms of long-term stroke risk reduction (odds ratio [OR] = 0.48; P = 0.04) [8]. The study included 3653 patients, with half of them having the LAA occluded. However, of the seven trials included, only two were prospective randomized, and these were small in size.

Recently the outcomes of the LAAOS III study were published [9]. It was a randomized, multicenter prospective study focused on concomitant surgical LAAO in patients with a history of AF undergoing cardiac surgery for other reasons. LAAOS III brought to the table a strong reason for a change of paradigm. The study included 4811 patients from more than 100 centers. All had a CHA_2DS_2-VASc score of at least 2 and a history of AF. The study was double-blind, i.e. nobody, except the surgical team, knew if the patient had the LAA occluded or not. Patients continued to receive oral anticoagulation after surgery. The most important study outcome was a 33% reduction in the risk of stroke or systemic embolism over the period of 3.8 years postoperatively in patients with their appendage occluded (hazard ratio [HR] = 0.67, 95% confidence interval [CI], 0.53–0.85; P = 0.001). Subgroup analyses showed that the reduction in stroke risk was independent of sex, comorbidities, AF type, or even the addition of AF surgical ablation. LAA occlusion was not associated with increased blood loss, risk of postoperative tamponade, or higher risk of readmission for heart failure. Moreover, the benefit of surgical LAAO was additive to oral anticoagulant treatment. Based on these conclusions, concomitant surgical LAAO was shifted from class recommendation IIB to IIA (level of evidence B) in the 2021 European guidelines for the treatment of heart valve disease [10]. Very recently, American guidelines for the management of atrial fibrillation have given a class I recommendation (level of evidence A) for surgical

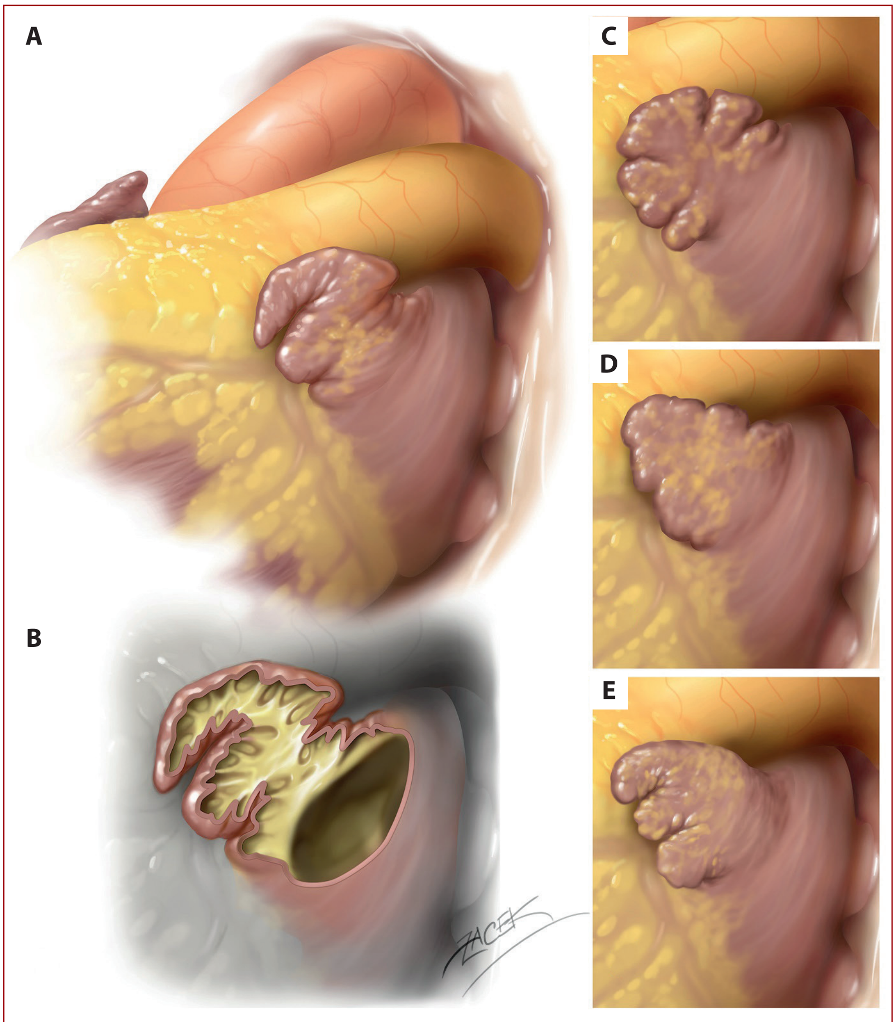

Figure 1. Left atrial appendage morphology variations. **A.** Chicken wing. **B.** Cactus. **C.** Cauliflower; **D.** Windsock. **E.** Internal complexity of the appendage structure

concomitant LAAO in patients with CHA_2DS_2-VASc score of at least 2 [11].

The LAAOS III-driven enthusiasm has naturally raised the question of offering concomitant LAAO to cardiac surgery patients without a history of AF. AF is the most frequent arrhythmia in the post-cardiotomy period, with an incidence of 10%–65% of patients [12]. LAAO could provide a cardioembolism reduction in short and long term post-operatively in patients with higher CHA_2DS_2-VASc scores despite the absence of AF before the surgery [13]. A smaller prospective randomized study, ATLAS, observed an insignificant drop in the incidence of thromboembolism after LAAO (3.4 vs. 5.6%; $P = 0.4$) [14]. Based on the presented data, another multicenter prospective study called LeAAPS was commenced. It aims to ultimately answer the question of concomitant surgical LAAO in patients with no AF [15].

An isolated LAAO procedure represents a separate topic of discussion. It may function as a nonpharmacological way to reduce stroke risk in AF patients where oral anticoagulation is undesired [11]. The 2020 European guidelines were restrained with regard to LAAO as a surrogate to oral anticoagulation due to potential undertreatment of overall stroke risk related to atrial cardiomyopathy (class IIB, level of evidence B) [16]. The current American guidelines (2023) are more liberal and recommend transcatheter appendage occlusion in patients with a bleeding of nonreversible cause, mostly intracerebral or visceral (class IIA, level of evidence B) [11]. Patients who wish to avoid anticoagulation and/or reversible bleeding causes may give preference to LAAO over drug treatment although, in this context, there is less robust evidence (class IIB, level of evidence B). Specific clinical scenarios, such as end-stage renal disease with a need for hemodialysis [17] or hereditary bleeding disorders (e.g. hemophilia) [18], also represent suitable indications for nonpharmacological stroke risk prevention. Transcatheter percutaneous LAAO techniques are recommended in these scenarios. Surgical thoracoscopic occlusion could perform at least equally well, but solid evidence is lacking [19].

Closure technique

Over the years, several surgical LAAO techniques have been used (see Figure 2). A simple resection of the body of the LAA followed by suturing the atrial cavity opening is a straightforward and reproducible technique [6]. Although a length of "stump" of less than 1 centimeter was achieved in 70% of procedures (according to ultrasound) [20], a long-term protective effect was observed and thrombus or

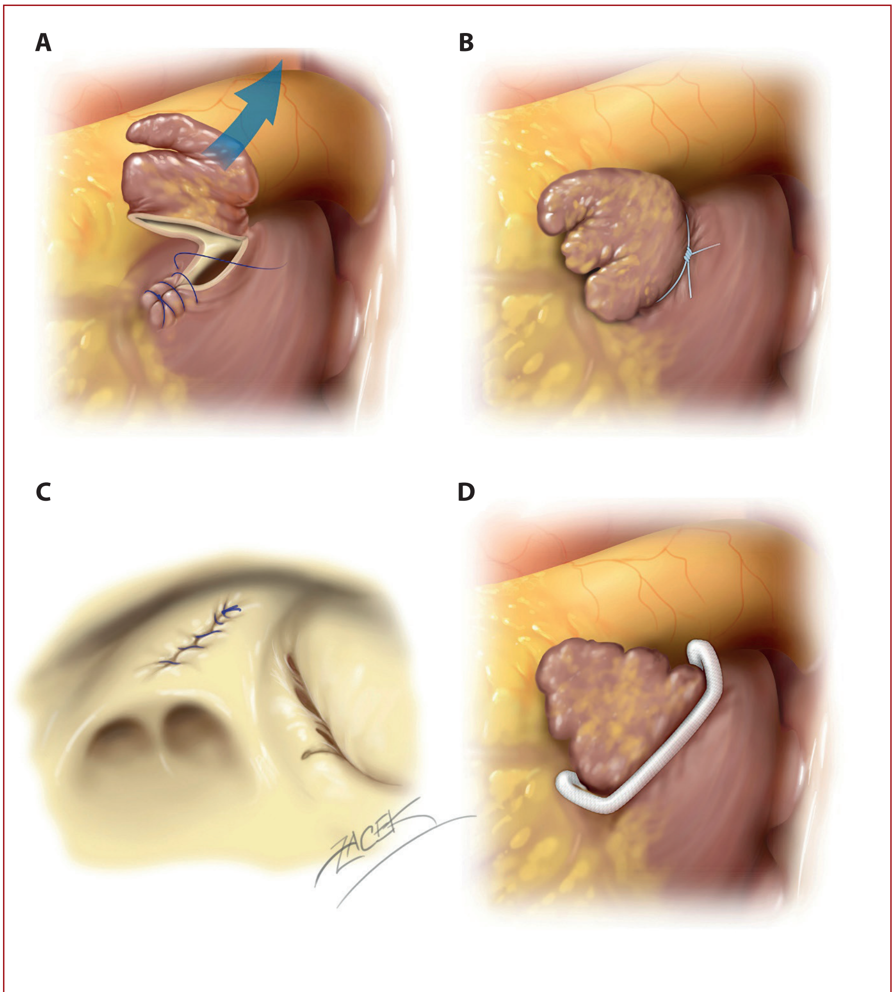

Figure 2. Surgical techniques of left atrial appendage occlusion**.** **A.** Resection. **B.** Ligation. **C.** Endocardial closure. **D.** Clipping

spontaneous echo-contrast in the appendage stump was never seen. Complete excision of the trabecular part of LAA tissue seems to be a logical prerequisite for effective long-term stroke risk reduction. The presence of a shallow bulge above 1 centimeter may result from concerns of circumflex artery injury and should not carry thrombogenic risk. In the LAAOS III study, most of the occlusions were performed with this technique [9].

A straightforward ligature of the appendage is another option that offers a 33%–95% success rate. Consistent long-term outcomes have not been published [21, 22].

LAAO with a stapler device, with or without excision of appendage tissue, is another simple epicardial technique [23]. Considering the criterion of less than 1 cm stump, 40%–72% of procedures were deemed successful [6, 9, 20].

During mitral valve surgery, endocardial closure of the appendage ostium by a suture from inside the atrial cavity is a readily practicable option [24]. Preservation of the appendage tissue and its endocrine activity could be of potential benefit. Nonetheless, a high recanalization rate was observed in the long term postoperatively. Successful closure was seen in 23%–89% of procedures [20, 23, 24]. Residual communication between the atrium and the LAA may provoke thrombogenesis and paradoxically lead to a higher cardioembolism risk than leaving the appendage open [24, 25].

A novel technique of epicardial LAA closure with a clip was developed (Atriclip®, AtriCure Inc, Winchester, Ohio) [26]. The device consists of a nitinol clip covered with polyester mesh. It is deployed surgically at the base of the LAA, in either an open or thoracoscopic manner. According to the meta-analysis of more than 900 implants, LAAO has an occlusion success rate of >95% [27]. It is fast, safe, and offers good protection against cardioembolism [28]. There are no studies directly comparing Atriclip® with other surgical LAAO techniques; however, at least equivalent outcomes are anticipated. A higher cost is its only drawback against the conventional techniques [29].

Percutaneous transcatheter LAAO techniques have been developed in the last two decades (see Figure 3). Large registry data suggested promising periprocedural and long-term outcomes in terms of stroke risk reduction [30, 31]. The Watchman® device (Boston Scientific, St Paul, Minnesota) comprises a nitinol basket with fixation hooks covered by a polyethylene membrane. It occludes the LAA ostium as a plug. Its protective effect against cardioembolism was compared with vitamin K antagonists (VKA) in two prospective trials, PROTECT-AF [32] and PREVAIL [33]. Five-year joint analysis of both trials showed a trend toward a higher incidence of ischemic events in the device group (HR = 1.71 [95% CI, 0.94–3.11]; $P = 0.08$) but a significantly lower risk of major bleeding when compared with VKA (HR = 0.48 [95% CI, 0.32–0.71]; $P < 0.001$) [34]. All-cause mortality was also significantly lower in the device arm (HR = 0.73 [95% CI, 0.54–0.98]; $P = 0.035$). However, a relatively high risk of periprocedural complications (cardiac tamponade, device embolization, arteriovenous fistula, major bleeding) was reported in the transcatheter arm (4.5%–8.7%).

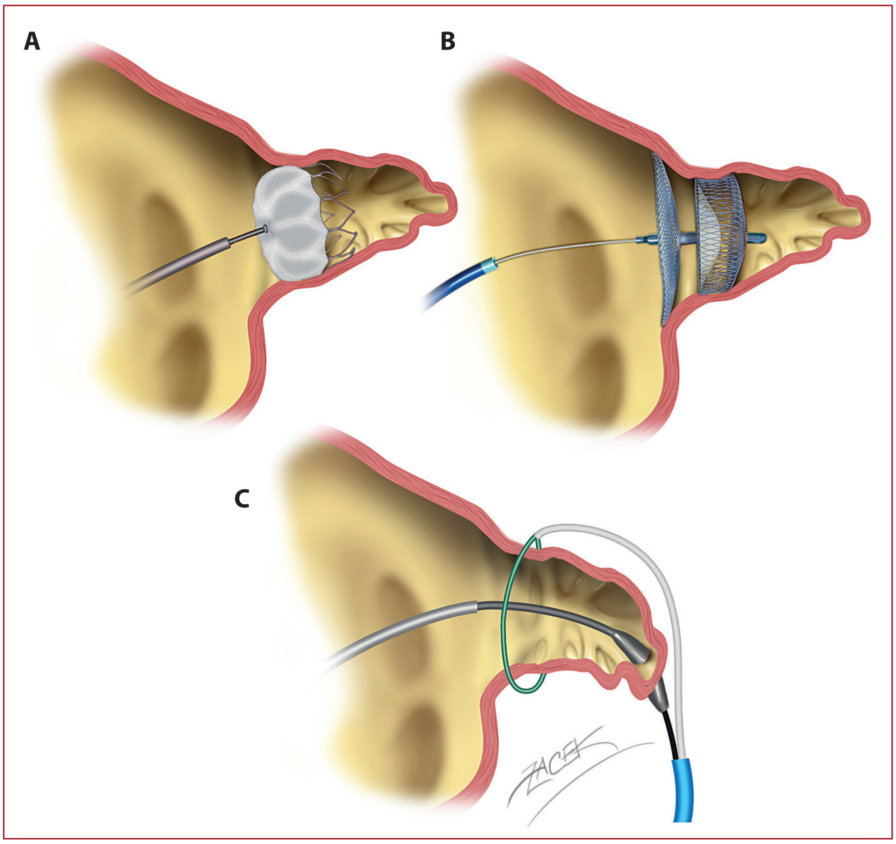

Figure 3. Transcatheter techniques of left atrial appendage occlusion. **A.** Watchman®. **B.** Amulet®. **C.** Lariat®

The Amulet® is another device based on the principle of Amplatz occluder (Abbott Inc., St Paul, Minnesota). The occluder consists of two conjoint parts: a device body with fixation hooks (implanted into the appendage cavity) and a disc (which covers the LAA orifice), forming a two-layer closure. A prospective randomized comparison of Amulet® and Watchman® showed a higher success rate and lower incidence of peri-device leak in the Amulet® group at a cost of higher periprocedural complication risk [35]. The long-term stroke incidence was similar in both groups.

With regard to the growing use of direct oral anticoagulants, the PRAGUE-17 study was performed to compare transcatheter LAAO (both Watchman and Amulet) with anticoagulants [36]. The study randomized patients with AF and increased stroke risk to the device (Amulet® or Watchman® based on center preference) or the drug (rivaroxaban, apixaban, or dabigatran based on physician decision) treatment arm. Similar to previous studies, the transcatheter treatment was non-inferior to pharmacotherapy in terms of stroke risk reduction (HR = 0.84 [95% CI, 0.53–1.31]; $P = 0.4$). However, the study was not sufficiently powered to confirm the observed outcomes. The risk of periprocedural complications was 4.5%, similar to previous reports.

After transcatheter LAAO, anticoagulation with VKA is necessary for the first 45 days to cover the endothelization period (applies for Watchman®). If the follow-up echocardiogram shows no or small peri-device leakage, VKA is withdrawn, and dual antiplatelet treatment continues for up to 6 months after implantation. After this period, the patient is left on a long-term single antiplatelet treatment. Alternatively, dual-antiplatelet treatment may be considered for the first 3-6 months after implantation. However, data to support such strategies are limited and stem from the study protocols of the abovementioned trials (PREVAIL, PROTECT-AF, and PRAGUE-17).

Another option is a combined transcatheter and epicardial closure using the Lariat® (Sentreheart, Redwood City, California) [37]. Lariat® is a lasso-like closure device that is deployed at the base of LAA with the help of epi- and endocardial magnetic leads. The risk of periprocedural complications is 4%–5%. Long-term outcomes have not been reported. Similar to surgical techniques, the Lariat® device does not require any antithrombotic treatment since it is not in direct contact with blood.

There is an ongoing debate on LAAO feasibility in the presence of a thrombus or spontaneous echo contrast in the appendage [38]. Natural concerns about periprocedural thrombus release support the use of various technical precautions, such as cerebral protection devices or "touchless techniques" [39]. Pre-procedural intensification of antithrombotic therapy may be also reasonable, at the cost of higher bleeding risk [40]. Large retrospective data did not suggest increased periprocedural thromboembolism risk when thrombus/echo contrast was present [40–42]. Further studies are warranted to better evaluate LAAO safety and to recommend eventual precautions in this tricky scenario.

In general, a variety of surgical and transcatheter LAAO techniques can currently be chosen. Basically, any concomitant cardiac surgery is a pathway to surgical LAAO. If no other cardiac surgery is necessary, the patient's capability to undergo thoracoscopic occlusion must be weighed against the risk of periprocedural complications and anticoagulation needed after transcatheter closure.

Collateral impact of LAA loss

Clinical research has provided enough evidence that LAAO leads to a significant reduction in cardioembolism in AF patients. But is the procedure safe from adverse long-term consequences, particularly due to endocrine [43] or hemodynamic response [44]?

James Cox, the father of the MAZE procedure, has observed a slightly higher risk of pulmonary edema after bilateral appendage resection (in the earlier versions of MAZE) [45]. The tissue of atrial appendages exhibits higher production of natriuretic peptides compared to the rest of the atrial musculature. However, the maximum production is localized in the right appendage, and not left [46]. The evolution of surgical techniques toward preserving the right atrial appendage has led to a reduction in the incidence of postoperative pulmonary edema [45]. Two small studies indicated a slight rise in brain natriuretic peptide levels after transcatheter LAAO (32 patients together) [47, 48]. On the other hand, there are several studies demonstrating that LAAO does not lead to any significant changes in natriuretic peptide levels at all [43, 49–52]. For instance, the abovementioned prospective randomized study PRAGUE-17 (400 patients) did not observe a difference in levels of natriuretic peptides between the LAAO and anticoagulated groups [53]. Similar outcomes have been observed after concomitant and standalone surgical LAAO [49, 52]. A detailed endocrinological analysis of LAAO was performed by Lakkireddy et al. who observed a drop in natriuretic peptide levels only immediately after occlusion [43]. Twenty-four hours after occlusion, the levels were overcompensated to twofold preoperative values. Three months after the procedure, the values returned to preoperative levels. Based on a review of pertinent literature, there is a lack of evidence to claim that LAAO leads to an endocrine imbalance or homeostasis impairment.

Hemodynamically, the left atrium (including its appendage) represents a reservoir of blood flowing from the pulmonary veins (systole), a conduit for passive blood flow to the ventricle (early diastole), and a pump (active contraction of the atrial wall leading to additional ventricular filling in late diastole, i.e. "atrial kick" or "booster pump") [54].

A phenomenon of impaired left atrial compliance (i.e. loss of reservoir function) after LAAO was described in a canine experiment [55]. Another experimental work reported an increase in pulmonary vein and transmitral flow in early diastole, both interpreted as an improvement in atrial conduit function to compensate for the reduction of reservoir function [56].

Table 1. Review of articles on cardiac hemodynamics after LAAO

First Author	Year of Publication	Occlusion technique	Number of patients	Study design	Observed changes	Overall interpretation of LAAO influence on hemodynamics by study authors
Coisne A. [62]	2017	Transcatheter — Watchman	33	Prospective	↑ LA volume, ↑ PALS, ↑ PACS, ↑ LA ejection fraction	Positive
De Maat G.E. [60]	2015	Thoracoscopic — stapler excision	16 vs. 16	Retrospective — manually matched	↓ PALS (but the same in the non-LAAO group)	No influence
Hanna I.R. [58]	2004	Transcatheter — not specified	12	Prospective	No change	No influence
Heuts S. [61]	2021	Thoracoscopic — Atriclip	7	Prospective	No change (in invasive measurements, too)	No influence
Ijuin S. [63]	2020	Transcatheter — Watchman	95	Retrospective	↑ PALS, ↑ PACS, ↑ LA ejection fraction	Positive
Luani B. [51]	2017	Transcatheter — Watchman	58	Prospective	↑ LA volume	Negative
Madeira M. [59]	2018	Transcatheter — Amplatzer	16	Retrospective	No change	No influence
Phan Q.T. [57]	2019	Transcatheter — Amplatzer	47 vs. 141	Retrospective — propensity-matched	↑ LA volume index, ↑ E, ↑ E/E' ratio	Negative
Pommier T. [50]	2021	Transcatheter — Amplatzer or Watchman	43	Prospective	No change	No influence
Sabanoglu C. [47]	2021	Transcatheter — Watchman	12	Prospective	↑ Systolic pulmonary vein flow, ↑ E/Vp ratio	Negative
Sharma E. [64]	2022	Transcatheter — Watchman	67	Retrospective	↑ PALS, ↑ E, ↑ E/E' ratio, ↑ LVEF	Positive
Tabata T. [44]	1998	Open surgical — clamp	15	Prospective	↑ LA pressure, ↑ LA size, ↓ systolic pulmonary vein flow	Negative
Yang J. [65]	2022	Transcatheter — Watchman	62 vs. 62	Retrospective — manually matched	↑ PALS, ↑ PACS, ↑ LA volume, ↑ LA ejection fraction — the same in both groups	No influence
Zhang Z. [49]	2021	Thoracoscopic — stapler excision	46	Prospective	Temporary ↓ LA volume and LA ejection fraction then restored	No influence

Abbreviations: E, early diastolic mitral flow velocity; E', early diastolic mitral annulus velocity; LA, left atrial; LVEF, left ventricular ejection fraction; PACS, peak atrial contractile strain; PALS, peak atrial longitudinal strain; Vp, color M-mode flow propagation velocity in early diastolic transmitral flow

Many recent clinical studies elaborated on the impact of LAAO on cardiac hemodynamics after either surgical or transcatheter occlusion. However, the results vary considerably, and any consistent conclusions are difficult to draw due to the diversity of findings (see Table 1):

- **Impairment of cardiac hemodynamics** in terms of left atrial enlargement and increase/drop in pulmonary vein systolic blood flow, all of those being interpreted as indirect signs of diastolic left ventricular dysfunction [44, 47, 51, 57].
- **No change in cardiac hemodynamics** [49, 50, 58–61].
- **Improvement in cardiac hemodynamics** in terms of improvement in contractile and reservoir function of the left atrium (deduced from higher left atrial ejection fraction, peak atrial longitudinal, and contractile strain) [62–65].

To provoke even more controversy, the same observation could have been differently interpreted by different authors. For instance, the enlargement of the left atrium or the rise of the E/E' ratio in transmitral blood flow were appraised positively by some authors [62, 64, 65], while others considered these changes a functional impairment [51, 57].

Heuts et al. performed extended invasive hemodynamic measurements during thoracoscopic LAAO, including a pulmonary artery catheter and transseptally inserted left atrial catheter [61]. They did not observe any objective change in measured parameters. The largest study to evaluate the hemodynamics after LAAO was performed by Ijuin et al. [63] who performed transesophageal echocardiography 45 and 180 days after LAAO and observed an improvement in left atrial hemodynamics (rise of left atrial ejection fraction, rise of longitudinal and contractile strain). No work has observed the influence of LAAO on atrial booster pump function. We have not found a study that utilized preoperative appendage blood flow velocity as a variable in decision-making algorithms, and its preoperative values did not have an impact on postoperative hemodynamics. In the LAAOS III study (and other abovementioned studies), no increase in readmissions for heart failure was observed after LAAO [9].

CONCLUSION

It is the nature of surgery that, at the end of the day, the surgeon has to make a binary decision to do or not to do. To answer the question of whether to occlude or not to occlude the LAA in AF patients, we have substantial data, together with a common clinical sense. Stroke is a serious adverse event affecting the lives of patients and their relatives. Every effort to reduce that risk is worth making. The concerns about potential endocrine imbalance or risk of heart failure have not been supported by evidence and hemodynamic consequences of LAAO remain unclear.

Concomitant surgical left atrial appendage occlusion is recommended to reduce the long-term risk of thromboembolism in patients with a history of atrial fibrillation and a CHA_2DS_2-VASc score of 2 or higher. Surgical occlusion is safe, and epicardial closure techniques are preferred. A question of concomitant surgical LAAO in patients without a history of prior AF remains to be elucidated by ongoing studies. Thoracoscopic and transcatheter occlusion techniques are also feasible as a means of nonpharmacological stroke risk reduction. The treatment strategy must be tailored to individual patient needs.

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