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Review

Contemporary Review of Left Atrial Appendage Occlusion in Atrial Fibrillation

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Abstract

Atrial fibrillation (AF) is the most common cardiac arrhythmia worldwide and a major contributor to ischemic stroke and cardioembolic events. Although oral anticoagulation remains the cornerstone of stroke prevention in AF, its use may be limited by bleeding risk, contraindications, intolerance, and adherence challenges. Because the left atrial appendage (LAA) is the predominant site of thrombus formation in nonvalvular AF, LAA closure has emerged as a mechanistically targeted, non-pharmacologic approach to reduce embolic risk in selected patients. This review critically appraises the evidence supporting surgical and percutaneous LAA occlusion, with emphasis on AF-related thromboembolism, the role of the LAA in thrombogenesis, procedural techniques, patient selection, peri-procedural multimodality imaging, clinical outcomes, and complications. Surgical LAA occlusion performed during concomitant cardiac surgery has been shown in randomized trials and meta-analyses to reduce ischemic stroke and systemic embolism and is endorsed by major society guidelines as an adjunct to continued anticoagulation in eligible patients. Percutaneous LAA closure with contemporary devices, including Watchman FLX and Amulet, offers an alternative to long-term anticoagulation for selected patients with nonvalvular AF and elevated bleeding risk, although randomized trial findings remain mixed. Evidence in special populations, including patients with prosthetic valves, advanced age, chronic kidney disease, congenital heart disease, and prior LAA occlusion, is also reviewed, highlighting unique procedural considerations and persistent knowledge gaps. Continued investigation is needed to refine patient selection across AF phenotypes, standardize post-closure antithrombotic and imaging follow-up strategies, and clarify the net benefit of prophylactic surgical LAA occlusion in patients without pre-existing AF. A multidisciplinary, individualized approach remains essential to balancing thromboembolic and bleeding risks and optimizing patient outcomes.

Keywords: atrial fibrillation; left atrial appendage; left atrial appendage occlusion; anticoagulation; stroke

1. Introduction

Atrial fibrillation (AF) is the most common persistent cardiac arrhythmia, with prevalence increasing significantly over the last ten years in parallel with an aging population and higher risk factor comorbidity burden [1]. AF constitutes a significant risk of causing ischemic stroke; thus stroke prevention is a key goal of long-term management in patients with AF, and therapeutic oral anticoagulation (OAC) based on CHA_2DS_2-VASc score remains the standard of care [2]. However, anticoagulation use may be practically challenging in some patients with high bleeding and/or falls risk, medication intolerance or poor adherence. This has sparked interest in non-pharmacological approaches for reducing stroke risk in patients who may not be able to take OAC long-term [2]. The left atrial appendage (LAA) is a cul-de-sac and trabeculated structure arising from the anterolateral aspect of the left atrium. It has limited function but is a major site of blood stasis and thrombus formation in AF [3,4]. As a result, LAA occlusion has evolved over the last two decades as an interventional target to lower cardio-embolic risk in AF, either as a substitute for long-term OAC in carefully chosen patients or as an addition to anticoagulation [2,5]. This review aims to discuss the contemporary strategies, peri-procedural planning, and evidence for efficacy and safety for surgical and percutaneous LAA occlusion (s-LAAO and p-LAAO).

2. Literature Review

2.1 Pathophysiology and Stroke Risk

The increased risk of stroke in AF arises from a mix of complex physiological changes, which can include alterations in the structure and function of the left atrium, abnormal blood flow kinetics due to irregularity in heart rate, thereby increasing the tendency of thrombus formation [6]. At the heart of this thrombogenesis tendency is the LAA [6]. The LAA is an embryonic remnant from the early stages of heart development and is quite different in both structure and function from the left atrial body. It features an

Table 1. Comparisons between valvular and non-valvular AF.

Feature	Valvular AF	Non-valvular AF
Associated pathology/etiology	Rheumatic mitral valve disease, prosthetic heart valves	Hypertension, coronary artery disease, diabetes, obesity, cardiomyopathy/heart failure
Location of thrombus formation	Left atrium and/or left atrial appendage due to high left atrial pressure causing increase risk of stasis risk	Left atrial appendage
Stroke risk		
Mechanism	Turbulent flow due to mitral stenosis or prosthetic mitral valve disease, atrial dilation	Atrial myopathy whereby there is loss of atrial contractility or adverse atrial remodeling. Endothelial dysfunction is also implicated
Anticoagulation of choice	VKA (warfarin)	VKA or DOAC
Left atrial appendage closure device recommended?	No VKA (warfarin) indicated	Can be considered

AF, atrial fibrillation; VKA, vitamin K antagonist; DOAC, direct oral anticoagulant.

ostium, which can vary in length, and has a highly trabeculated interior lined with pectinate muscles. These unique characteristics make the LAA prone to blood pooling, especially when the atrial contractions are reduced in function. The LAA can be heterogeneous in anatomy in terms of ostial size, length/deepness, number of lobes. In a healthy individual with normal sinus rhythm, the LAA is crucial for the atrial reservoir function, absorbing increases in left atrium (LA) pressure, but it must contract vigorously to ensure blood is actively ejected out of the LAA pouch. However, during AF, the lack of coordinated atrial contractions leads to a significant reduction in the emptying velocities of the LAA. This can result in blood pooling and clumping of red blood cells [7].

The location of thrombi formation differs between valvular AF and nonvalvular AF, with up to 90% of thrombi occurring within the LAA in patients with nonvalvular AF and up to 57% in patients with valvular AF [6]. Table 1 summarizes the different mechanistic qualities between these 2 AF entities [5,8]. Valvular AF is often linked to rheumatic mitral stenosis or mechanical heart valves, which intrinsically poses a notably higher risk for thrombus. Mechanical valves can heighten the risk of thrombogenesis due to abnormal blood flow and the activation of coagulation factors on their surfaces. Therefore, thrombi in valvular related AF can develop in any part of the left atrial cavity itself as well as the LAA. Randomized data support vitamin K antagonists (VKA) over direct oral anticoagulants (DOAC) in these settings. In RE-ALIGN, dabigatran was associated with higher thromboembolic and bleeding events compared with warfarin in patients with mechanical valves, leading to early termination [9]. Similarly, PROACT Xa demonstrated increased valve thrombosis and thromboembolism with apixaban versus warfarin in patients with On-X mechanical aortic valves [10]. In rheumatic heart disease–associated AF, predominantly driven by rheumatic mitral stenosis, the INVICTUS trial showed that rivaroxaban resulted in more cardiovascular events and deaths compared with vitamin K antagonist therapy without a bleeding advantage [11]. Thus, patients with valvular AF are treated with warfarin to prevent stroke. On the other hand, nonvalvular AF occurs without mitral stenosis or mechanical valves and is more frequently associated with comorbidities like high blood pressure, heart failure, diabetes, coronary artery disease, and increased age [12,13,14]. These comorbidities can promote LA dilatation, and even negative remodeling and fibrosis causing atrial myopathy [15].

For non-valvular AF, due to the LAA being such an important source of cardioembolic stroke, the advent of LAA occlusion devices have further enhanced treatment options for stroke prevention for AF. LAA occlusion can be performed surgically by cardiothoracic surgeons or percutaneously by cardiologists. Both surgical and percutaneous methods of LAA occlusion have undergone significant changes over the years with new devices, and modern practice is increasingly influenced by randomized and observational data [16,17].

2.2 Surgical LAA Occlusion (s-LAAO) Device

2.2.1 Surgical Techniques

s-LAAO was described by Cox et al. [18] as part of the Cox-Maze procedure, which conferred stroke reduction over 11.5 years follow up.

s-LAAO can be performed using several techniques, including direct surgical approaches during open cardiac surgery, minimally invasive thoracoscopic or minithoracotomy procedures, and device-based methods. These strategies allow exclusion of the LAA under direct visualization and are most employed in patients undergoing cardiac surgery or in those with contraindications to percutaneous LAA occlusion [19].

Direct surgical approaches involve either ligation or excision of the LAA during open-heart surgery and may be performed as standalone procedures or in conjunction

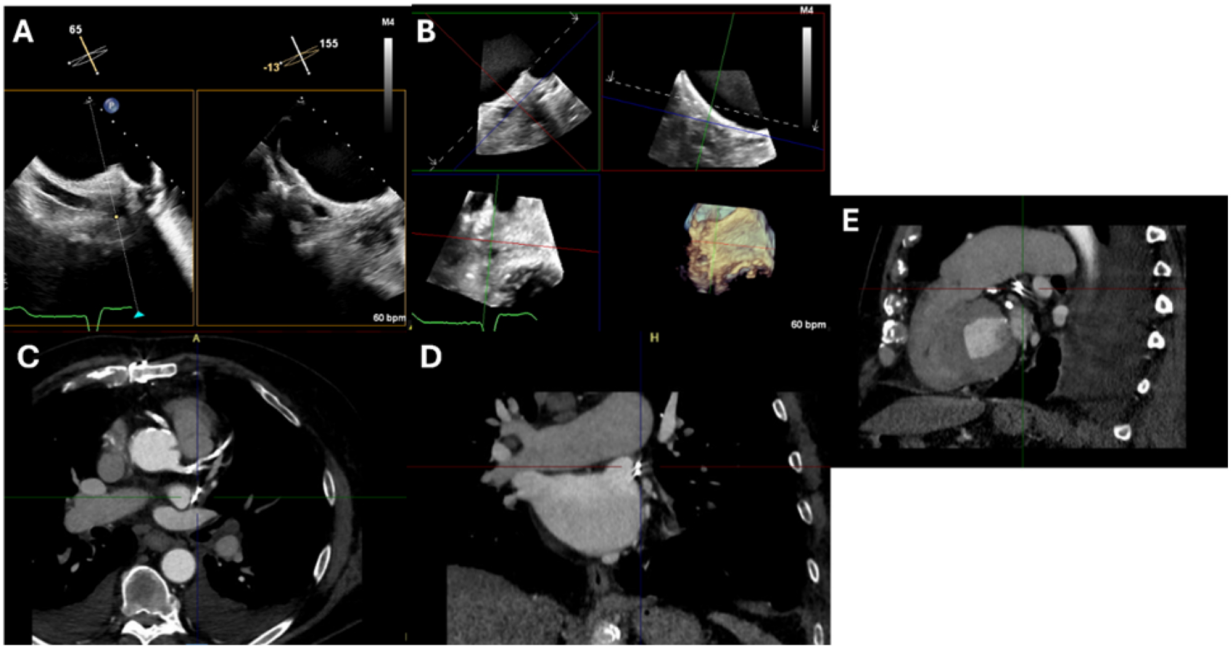

Fig. 1. Transesophageal echocardiography and Computed Tomography (CT)of patients who underwent left atrial appendage (LAA) ligation with a clip. (A) LAA at 65 and 155 degrees of transesophageal echocardiography (TEE) showing absence of LAA. (B) Multiplanar reconstruction at multiple angles including a 3D bottom right of figure showing successful LAA clip. (C) Axial image of LAA clip manifesting as brightly hyper-attenuated structure. Similar brightness to calcification seen in coronary arteries in same figure. (D) Coronal section illustrating LAA clip. (E) Sagittal cut showing LAA clip.

with other cardiac operations, such as coronary artery bypass grafting or valve surgery. Surgical ligation consists of closure of the LAA at its base using sutures or clips, thereby excluding it from the left atrium [20] (Fig. 1). Among clip-based methods, the AtriClip system has emerged as a widely used epicardial exclusion device. Applied externally at the base of the appendage, the AtriClip enables mechanical closure of the LAA under direct visualization and can be used during open surgery or through minimally invasive thoracoscopic approaches. Its design allows durable epicardial exclusion while avoiding entry into the appendage cavity itself. Alternatively, surgical excision entails complete removal of the appendage [21]. While excision provides definitive elimination of the LAA, it is technically more demanding and may be associated with increased procedural complexity. Importantly, the efficacy of surgical LAA occlusion is highly technique-dependent, and contemporary evidence suggests that not all surgical approaches achieve equivalent rates of complete appendage exclusion. In a recent systematic review, epicardial clip deployment and surgical excision/amputation were associated with the highest success rates of complete closure, whereas endocardial or epicardial suture ligation and stapling techniques showed substantially lower efficacy and higher rates of residual LAA patency [22]. This distinction is clinically relevant because incomplete closure may leave a residual stump or persistent flow, potentially diminishing thromboembolic protection and creating a substrate for thrombus formation. Accordingly, although traditional suture-based ligation remains widely used, current data increasingly favor techniques that provide reproducible anatomic exclusion under direct visualization, particularly epicardial clip devices such as AtriClip and surgical excision when technically feasible. Surgical techniques offer the advantage of direct visualization and detailed anatomical assessment of the LAA, allowing meticulous closure [23].

In addition to direct surgical techniques, s-LAAO may also be performed using epicardial devices applied under direct visualization through open or minimally invasive approaches. They can externally occlude the appendage at its base without entering the left atrial cavity and can be deployed during sternotomy or thoracoscopic and minithoracotomy procedures [19].

2.2.2 Evidence for Efficacy of s-LAAO

Evidence supporting s-LAAO has evolved over two decades. Early randomized data emerged from the Left Atrial Appendage Occlusion Study (LAAOS I)study, which demonstrated the technical feasibility and procedural safety of surgical LAA closure in patients with AF undergoing coronary artery bypass grafting, although it was not powered for clinical outcomes [20]. This was followed by LAAOS II [24], which further evaluated surgical techniques and perioperative safety while informing the design of a definitive outcomes trial.

Subsequently, the Left Atrial Appendage Closure by Surgery (LAACS) study randomized patients with AF undergoing open-heart surgery to LAA closure versus no closure and demonstrated a significant reduction in long-term ischemic stroke and thromboembolic events among patients receiving surgical LAA management [25].

The most definitive evidence comes from the landmark LAAOS III, which enrolled 4770 patients with AF undergoing concomitant cardiac surgery. Despite continued OAC in most participants, s-LAAO reduced the composite of ischemic stroke or systemic embolism (relative risk (RR) 0.67; 95% confidence interval (CI) 0.53–0.85), with the benefit primarily driven by a reduction in ischemic stroke. No significant reduction in all-cause mortality was observed, and secondary analyses confirmed that the protective effect was independent of anticoagulation use [17].

In contrast, the OPINION trial, which enrolled patients without pre-operative AF but with elevated CHA_2DS_2-VASc scores undergoing valve surgery, found that routine prophylactic s-LAAO did not significantly reduce stroke, transient ischemic attack (TIA), or cardiovascular death at 1 year, and therefore does not extend the randomized efficacy data for s-LAAO in AF itself [26].

Beyond individual randomized trials, a large meta-analysis, encompassing over 280,000 patients including more than 36,000 who underwent s-LAAO, demonstrated a 29% relative reduction in stroke or thromboembolism and a significant reduction in all-cause mortality at two years, reinforcing the consistency of benefit across diverse surgical populations [27]. Collectively, these data support s-LAAO as an effective adjunctive stroke prevention strategy in patients with AF undergoing cardiac surgery.

LAAO using an epicardial clip has been shown to be safe and effective, with reported complete occlusion rates approaching 95% based on cardiac computed tomography (CT) [28]. Several case series and larger observational studies have also examined isolated LAAO performed using a thoracoscopic approach, demonstrating acceptable short and long-term outcomes [29,30] (Table 2, Ref. [17,20,24,25,26,31,32]).

2.2.3 Periprocedural Anticoagulation Considerations

For patients with AF undergoing invasive procedures or surgery, peri-procedural anticoagulation management should be individualized based on thromboembolic risk, bleeding risk, and the anticoagulant used. In most patients receiving warfarin or DOACs, temporary interruption of OAC without bridging is recommended, except in those with mechanical heart valves or a recent stroke or TIA, in whom interruption strategies differ.

Postoperative anticoagulation strategies following s-LAAO vary according to the technique employed. In LAAOS III, patients routinely continued OAC after surgery. The rationale for maintaining OAC after surgery is supported by imaging data. Transesophageal echocardiography (TEE) and cardiac CT studies have shown that s-LAAO is frequently incomplete, with residual stumps or persistent peri-ostial flow that may permit thrombus formation [23,33]. Even small residual communications can sustain embolic risk. Consequently, in patients with high intrinsic thrombotic risk, particularly those with mechanical prosthetic valves or rheumatic (valvular) AF, systemic anticoagulation remains indicated irrespective of surgical LAA management.

In contrast, epicardial surgical approaches such as AtriClip generally do not require postprocedural anticoagulation. This strategy has been evaluated in patients with contraindications to anticoagulant or antiplatelet therapy; notably, Kanderian et al. [23] reported that thoracoscopic epicardial LAA closure using the AtriClip PRO2 device was a safe and effective option for stroke prevention in patients with nonvalvular AF unable to receive anticoagulant or antiplatelet therapy.

2.2.4 Complications

Complications related to s-LAAO are uncommon and most often arise from direct manipulation of the appendage. In the LAAOS pilot trial, appendage tears occurred in 9/77 patients (11.7%), all of which were repaired easily with sutures [20]. Suboptimal positioning/technique can also leave a residual LAA stump; in the TEE-based series by Kanderian et al. [23], successful closure occurred in 73% with excision vs 23% with suture exclusion vs 0% with stapler exclusion (i.e., stapling had a very high residual patency/stump rate), and among unsuccessful exclusions. LAA thrombus was seen in 28/68 patients (41%) with unsuccessful LAA exclusion versus none with excision [23]. Rarely, an epicardial clip can impinge the circumflex coronary artery [34].

2.2.5 Guidelines

Contemporary guidelines consistently support surgical management of the LAA in patients with AF undergoing cardiac surgery, but do not recommend routine s-LAAO in patients without history of AF during cardiac surgery. The Society of Thoracic Surgeons (STS) 2023 Clinical Practice Guidelines recommend LAAO during all first-time, non-emergent cardiac surgical procedures, whether concomitant surgical ablation is performed or not, to reduce morbidity related to thromboembolic complications (Class I, Level of Evidence A). The STS further notes that isolated s-LAAO may be considered in selected patients with longstanding persistent AF, high stroke risk, and contraindications to or failure of long-term OAC (Class IIb, Level of Evidence B-NR) [19]. Similarly, the 2023 American College of Cardiology (ACC)/the American Heart Association (AHA)/American College of Clinical Pharmacy (ACCP)/the Heart Rhythm Society (HRS) Guideline for the Diagnosis and Management of Atrial Fibrillation recommends s-LAAO in patients with AF undergoing cardiac su-

Table 2. Major trials, observational studies, and guideline recommendations for s-LAAO.

Study/ Guideline	Design	Population/Setting	Surgical LAA strategy (allowed techniques)	Comparator	Key findings (selected)
LAAOS I (2005) [20]	Randomized controlled pilot trial	Patients undergoing CABG with stroke risk factors (n = 77)	LAA occlusion using sutures or stapling device; completeness assessed by post-op TEE	No s-LAAO	No significant differences in bypass time or perioperative outcomes; appendage tears occurred but were repaired. Complete occlusion: 45% with sutures vs 72% with staples. Thromboembolism during ~13 ± 7 months: 2.6%.
LAAOS II (2013) [24]	Multicenter feasibility randomized controlled trial (plus cross-sectional screening cohort)	AF patients undergoing cardiac surgery with increased stroke risk (n = 51; 26 occlusion vs 25 control); feasibility cohort n = 1.88	LAA amputation/occlusion at surgery	No s-LAAO + OAC	No significant bleeding at LAA site. At 1 year, composite (death/MI/stroke/systemic emboli/major bleeding) RR 0.71 (95% CI 0.19–2.66); strokes: 1 vs 3.
LAACS (2018) [25]	Prospective, randomized, open-label trial	First-time open-heart surgery (CABG/valve/both), with/without prior AF (n = 187)	Protocol recommended double closure (purse-string + running suture), not mandatory; postoperative TEE offered to assess closure	No s-LAAO	Primary composite (ischemic stroke/TIA and/or silent cerebral ischemic lesions) reduced: 14 (16%) control vs 5 (5%), HR 0.3 (95% CI 0.1–0.8), $p = 0.02$ over mean follow-up 3.7 years; no mortality difference detected.
LAAOS III (2021) [17]	Randomized controlled trial	AF patients undergoing concomitant cardiac surgery (n = 4770)	Mixed surgical LAA approaches. Amputation and closure were the most used.	No s-LAAO	Reduced composite of ischemic stroke/systemic embolism (RR 0.67; 95% CI 0.53–0.85); no all-cause mortality benefit. Secondary analysis: Reduction in thromboembolic events reported as independent of OAC use.
LAACS II (2023) [31]	Long-term follow-up analysis of LAACS	Same randomized LAACS population reviewed, mean follow-up 6.2 years	Same LAACS surgical closure approach as randomized arm	No s-LAAO	Fewer cerebrovascular events with closure: ITT 11 vs 19 ($p = 0.033$); per-protocol 9 vs 17 ($p = 0.186$); interpreted as "safe" and possibly event-reducing but still limited by size/crossovers.
LAACS-2 (2023) [32]	Randomized, open-label, blinded outcome assessor protocol	Adults undergoing first-time elective open-heart surgery; includes patients with and without AF	Concomitant LAA closure (technique per protocol/site; adjudicated neurologist outcomes)	Standard care (open LAA)	No outcomes yet in the protocol publications. Designed to test whether concomitant LAA occlusion reduces stroke/TIA (and related endpoints) with blinded adjudication.
OPINION trial (2025) [26]	Multicenter, open-label, randomized superiority trial	No pre-op AF, CHA_2DS_2-VASc ≥2, undergoing mitral/aortic valve repair/replacement in China; ITT n = 2118 (1062 s-LAAO vs 1056 control)	Prophylactic s-LAAO during valve surgery	No s-LAAO	Primary composite (ischemic stroke/TIA/CV death at 1 year): 6.9% vs 8.2%, HR 0.83 (95% CI 0.61–1.14), $p = 0.25$. No significant benefit at 1 year.

LAAOS, Left Atrial Appendage Occlusion Study; LAACS, Left Atrial Appendage Closure by Surgery; CABG, coronary artery bypass grafting; LAA, left atrial appendage; TEE, transesophageal echocardiography; s-LAAO, surgical left atrial appendage occlusion; AF, atrial fibrillation; OAC, oral anticoagulation; MI, myocardial infarction; RR, relative risk; CI, confidence interval; HR, hazard ratio; ITT, intention to treat; TIA, transient ischemic attack; CV, cardiovascular.

Table 3. STS, AHA/ACC and ESC guidelines: Key findings and differences.

Guideline/Society	Population	Surgical strategy	Recommendation/Level of evidence
STS 2023 Surgical Treatment of AF [19]	First-time, non-emergent cardiac surgery (with or without surgical ablation)	Surgical ablation during eligible cardiac surgery	LAAO recommended to reduce thromboembolic morbidity (Class I, LOE A) Isolated s-LAAO in selected patients with longstanding persistent AF, high stroke risk, and contraindications to or failure of long-term OAC (Class IIb, Level of Evidence B-NR)
ACC/AHA/ACCP/HRS AF Guideline (2023) [35]	AF undergoing cardiac surgery with CHA_2DS_2-VASc ≥2 (or equivalent risk)	s-LAAO with no residual flow and stump <1 cmon intra-op TEE	s-LAAO in addition to continued anticoagulation (Class I, LOE A)
ESC Valvular Heart Disease Guidelines (2025) [36]	AF undergoing valve surgery	s-LAAO	s-LAAO as an adjunct to oral anticoagulation to reduce cardioembolic stroke/systemic thromboembolism (Class I, LOE B)

AF, atrial fibrillation; ESC, European Society of Cardiology; LAAO, left atrial appendage occlusion; LOE, level of evidence; OAC, oral anticoagulation; s-LAAO, surgical left atrial appendage occlusion; STS, Society of Thoracic Surgeons; TEE, transesophageal echocardiography; ACC, American College of Cardiology; AHA, American Heart Association; ACCP, American College of Clinical Pharmacy; HRS, Heart Rhythm Society. The class guidelines and level of evidence are reported according to the original issuing societies.

rgery who have a CHA_2DS_2-VASc score ≥2 or equivalent stroke risk, in addition to continued anticoagulation, to reduce the risk of stroke and systemic embolism (Class I, Level A). When LAA exclusion is performed, techniques achieving complete closure, defined by the absence of residual flow and a residual stump <1 cm on intraoperative TEE, are advised (Class I, Level A), while the benefit of LAA exclusion without ongoing anticoagulation remains uncertain (Class IIb, Level A) [35]. Consistent with these recommendations, the 2025 European Society of Cardiology (ESC) Guidelines for the Management of Valvular Heart Disease endorse s-LAAO as an adjunct to OAC in patients with AF undergoing valve surgery to reduce the risk of cardioembolic stroke and systemic thromboembolism (Class I, Level of Evidence B) [36] (Table 3, Ref. [19,35,36]).

2.3 Percutaneous LAA Occlusion (p-LAAO) Devices

p-LAAO is a non-pharmacological method of preventing stroke for individuals with non-valvular AF who are not candidates for long-term OAC [37,38]. The transcatheter procedure, including femoral venous access, transseptal puncture and device deployment, is usually performed under imaging guidance, traditionally with TEE, and more recently with intracardiac echocardiography (ICE) [37]. Many devices have been developed to facilitate this technique including Watchman Devices and Amulet devices. Table 4 (Ref. [39,40]) shows different p-LAAO devices currently available in clinical practice.

2.3.1 Watchman Device (Boston Scientific)

In major randomized controlled studies (PROTECT AF, PREVAIL), the first-generation Watchman device (Watchman 2.5) was assessed and found to be non-inferior to warfarin in preventing stroke, systemic embolism, and cardiovascular death in patients with AF who were at increased risk of stroke [35]. The newest model, the Watchman FLX, has better anchoring mechanisms, a closed distal end, a shorter device length, and full recapture/repositioning functionality. These changes are meant to make deployment easier, enhance conformability to various LAA anatomies, and reduce peridevice leak (PDL) and device-related thrombosis (DRT) [41,42,43].

Under fluoroscopic and TEE supervision, both generations are administered via transseptal access. After being deployed and moved into the LAA, the device's stability and seal are evaluated. Compared to the 2.5 device, the FLX device offers full recapture and repositioning, allowing for more accurate insertion and lowering the risk of embolization or inadequate sealing. With a high percentage of successful first-attempt implantation and no need for device size adjustments, the FLX's flexible design and closed distal end make it easier to navigate and adapt to complex LAA geometries [42,43]. In recent registries and research, both Watchman 2.5 and FLX have great procedural success rates, usually surpassing 96–99%. Specifically, the FLX device has demonstrated a procedural success rate of 98.8–99.5% [41,42,43].

2.3.2 Amulet Device (Abbott)

The Amulet device evolved from the original Amplatzer Cardiac Plug (ACP) to become a second-generation p-LAAO system. Compared to its predecessor, the Amulet has design changes meant to increase procedural efficiency, lower PDLs, and minimize Device Related Thrombus(DRTs) [44]. The Amulet has a longer waist, a wider

Table 4. Summary of the main p-LAAO devices [39,40].

	Watchman device	Amulet device	LARIAT
Company	Boston Scientific	Abbott	Atricure
Size	20 mm, 24 mm, 27 mm, 31 mm, 35 mm	16 mm, 18 mm, 20 mm, 22 mm, 25 mm, 28 mm, 31 mm, 34 mm	Can accommodate up to 50 mm LAA structure
Device design	Self-expanding nitinol frame with fixation anchors and permeable PET fabric cap (endocardial plug)	Dual-seal design: distal lobe + proximal disc (nitinol mesh with polyester patch)	Epicardial suture delivery system (no intracardiac implant); pre-tied suture loop ligation
Access	14 Fr Transseptal	14 Fr Transseptal	Require trans-septal and pericardial access, usually 12 Fr
Repositionable	Yes (fully recapturable before release; FLX allows full recapture/redeployment)	Yes (fully recapturable and repositionable)	Partially (snare can be repositioned before suture deployment)
Randomized trials	PROTECT AF, PREVAIL, PRAGUE-17	Amulet IDE	No large randomized stroke-outcome RCT; observational data only

p-LAAO, percutaneous left atrial appendage occlusion; PET, polyethylene terephthalate; IDE, Investigational Device Exemption.

lobe and disc, and a recessed screw to enable deeper and more stable implantation. These modifications have led to decreased fluoroscopy time, radiation exposure, and contrast use during deployment, as well as decreased rates of device resizing and recapture. Comparative research has shown that, in comparison to the ACP, the Amulet device is linked to better procedural metrics and less PDLs.

Using a 12–14 Fr delivery sheath and a device sized according to the architecture of the LAA, amulet deployment is carried out by transseptal access. In most cases, full closure is made possible by the dual-seal mechanism. If the first placement is not ideal, the gadget permits full or partial recapture and repositioning [44]. TEE is utilized to evaluate closure and identify problems after the procedure, and echocardiographic guidance is usual during implantation [45].

2.3.3 Additional Devices

o LARIAT (SentreHEART): This technique, which uses a combined endocardial and epicardial approach to ligate the LAA, is less frequently utilized because of its technical complexity and potential for partial closure. As a combined epicardial-endocardial approach, the LARIAT can accommodate challenging anatomic features, including large or posteriorly rotated LAA and pericardial adhesions resulting from prior cardiac surgery or pericarditis. The LARIAT procedure employs an epicardial snare-based device to ligate the LAA, achieving complete appendage exclusion without leaving any intracardiac implants. This epicardial ligation strategy has been associated with lower rates of residual PDL. An additional advantage of the epicardial approach is the ability to maintain direct control of the pericardial space in the event of cardiac perforation.

o Lambre (Lifetech): For varying LAA anatomies, it uses a disc-and-lobe design in several sizes. Long-term results are less reliable, although the technique is similar to other devices [46].

2.3.4 Imaging Considerations, Peri-Procedural Planning and Ongoing Surveillance

Multi-modality imaging is useful for p-LAAO purposes. Baseline pre-procedural imaging with TEE or CT is usually recommended prior to any p-LAAO procedure. p-LAAO requires a structured, multimodality imaging approach across preprocedural, intraprocedural, and postprocedural phases which will be further elaborated [47]. Utilities of imaging are further described as follow alongside Table 5 which demonstrates the strength and limitations of each modality.

2.3.4.1 Pre-Procedural and Intra-Procedural Evaluation.

TEE is one of the more widely used modalities of choice for assessing the LAA. Pre-LAAO imaging is done prior to the p-LAAO device being deployed. Fig. 2 shows the typical TEE angles. TEE offers the ability to evaluate LAA anatomy, including device dimension sizing, lobe complexity, relation to pulmonary vein/mitral valve and circumflex coronary artery (denoted by the orange arrow) and emptying velocity (Fig. 3). Another benefit of TEE is to evaluate the trajectory and location of the ideal transseptal puncture area as well as the fluoroscopic angle/implant angle that best optimize the visualization of the LAA. TEE also helps to ensure that there is no LAA thrombus, which is a contraindication for p-LAAO (Fig. 3). CT provides superior spatial resolution helpful for device sizing, by allowing the determination of the optimal C-arm position, and delineates adjacent structures, LAA thrombus, transseptal planning, and virtual device deployment, reducing procedural cancellation and improving device selection, but inferior temporal resolution and not for real-time procedural guidance [37,48,49,50].

2.3.4.2 Post-Procedural Imaging.

Post p-LAAO, surveillance is usually performed with TEE, but CT-scan can be utilized for surveillance. The benefit of TEE is that it can evaluate not just for peri-device or fabric leaks, but also for

Table 5. Multi-modality imaging evaluation of LAAO (surgical/transcatheter): strengths and limitations.

Imaging	LAA assessment	Strengths	Limitations
Transthoracic Echocardiography (TTE)	• Initial assessment of cardiac structure and function • Evaluation of left atrial size, ventricular function, and valvular disease • Screening tool prior to advanced imaging • Difficult to visualize LAA	• Widely available and non-invasive • No ionizing radiation • Useful for global cardiac assessment • Portable and cost-effective	• Limited visualization of LAA anatomy • Low sensitivity for LAA thrombus • Image quality dependent on acoustic windows • Not suitable for procedural guidance
Transesophageal Echocardiography (TEE)	• Gold standard for LAA thrombus detection • Detailed assessment of LAA anatomy, morphology, and flow velocities • Peri-procedural guidance for transcatheter LAA closure • Post-procedural assessment of device position and leaks	• High spatial and temporal resolution • Excellent sensitivity for thrombus and spontaneous echo contrast • Real-time imaging during interventions • Allows Doppler assessment of LAA flow	• Semi-invasive; requires sedation/anesthesia • Contraindicated in esophageal pathology • Limited field of view for surrounding structures • Operator-dependent
Cardiac Computed Tomography Angiography (CTA)	• Detailed anatomical characterization of LAA • Assessment of LAA morphology, ostial dimensions, and lobes • Pre-procedural planning for device sizing and selection • Evaluation of device position and peri-device leaks post-closure	• High spatial resolution and 3D reconstruction • Superior delineation of complex LAA anatomy • Useful when TEE is contraindicated • Facilitates procedural planning • Determination of the optimal C-arm position	• Exposure to ionizing radiation • Requires iodinated contrast (renal risk) • Limited functional and flow assessment • Less sensitive than TEE for small thrombi without delayed imaging
Fluoroscopy	• Intraprocedural guidance during p-LAAO • Visualization of device deployment and positioning • Assessment of device stability and compression	• Real-time imaging during intervention • Essential for device delivery and release • Widely available in catheterization laboratories	• No soft tissue or thrombus visualization • Inability to assess LAA anatomy independently • Ionizing radiation exposure • Requires adjunctive imaging (TEE or CTA)

LAA, left atrial appendage; p-LAAO, percutaneous left atrial appendage occlusion.

DRT. CT scan can offer good spatial resolution to evaluate for any uncovered lobes, and allows DRT evaluation [45,51].

2.3.5 Evidence for Efficacy of p-LAAO

The evidence for the efficacy of p-LAAO for stroke prevention in patients with nonvalvular AF has been established in several randomized clinical trials (RCTs) and ongoing studies. The majority of these RCTs compared the efficacy of p-LAAO versus OAC as a reference group. Table 6 (Ref. [16,52,53,54,55,56,57,58,59]) details the key studies.

The first significant RCT to compare p-LAAO (using the Watchman device) to warfarin in patients with nonvalvular AF who were at higher risk of stroke was the PROTECT-AF trial. In addition to lowering cardiovascular and all-cause mortality in the device group, PROTECT-AF showed that p-LAAO was not inferior to warfarin for the composite endpoint of stroke, systemic embolism, and cardiovascular/unexplained death. Nevertheless, the trial also revealed a greater incidence of periprocedural problems with p-LAAO, which decreased in later research as operator expertise increased [16,35]. Similar efficacy for stroke prevention and a decrease in severe bleeding with p-LAAO compared to warfarin over long-term follow-up was verified by a patient-level meta-analysis of PROTECT-AF and the ensuing PREVAIL study [35,52]. A 2025 systematic review and meta-analysis of randomized controlled trials, including PROTECT-AF and PREVAIL (≈1516 patients), found no significant difference in overall stroke or systemic embolism between p-LAAO and warfarin. However, p-LAAO was associated with significantly lower rates of hemorrhagic stroke, non-procedural major bleeding, cardiovascular death, and all-cause mortality, with no meaningful effect modification by age. These findings support p-LAAO as an effective alternative to warfarin.

The role of p-LAAO in patients receiving catheter ablation for AF was the focus of the OPTION study. For the composite endpoint of death, stroke, or systemic embolism at 36 months, p-LAAO was not inferior to OAC in this co-

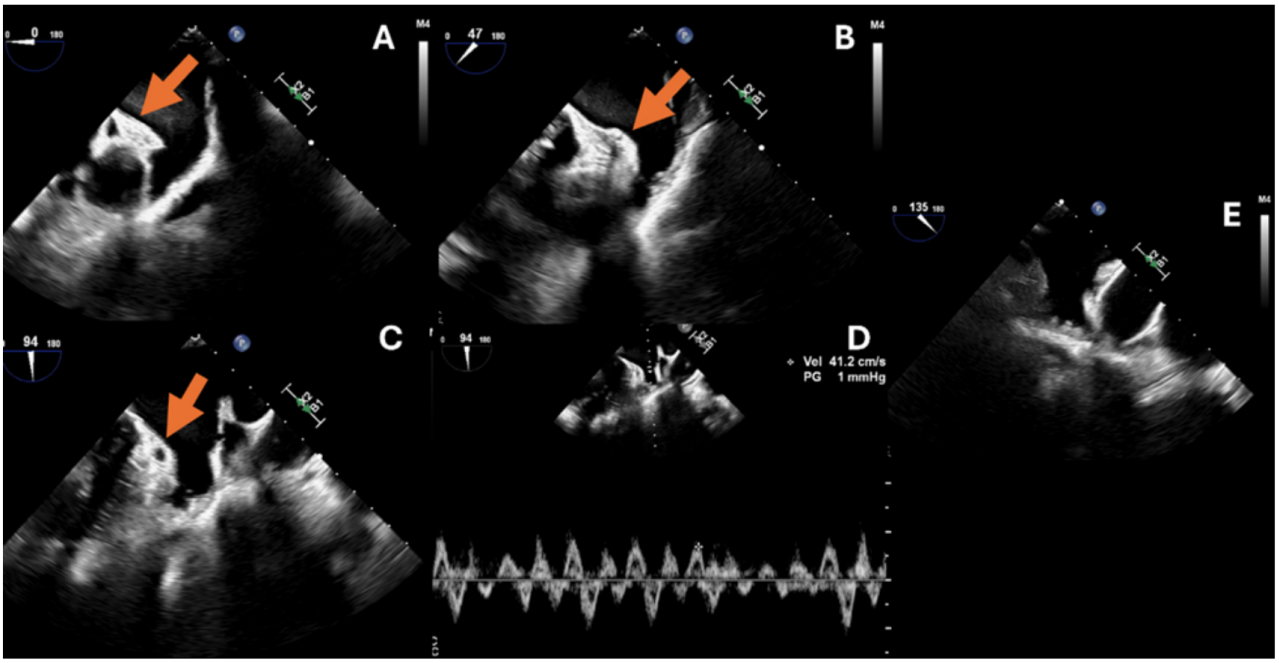

Fig. 2. Transesophageal echocardiography (TEE) acquisition of the left atrial appendage. Views taken on multiple angles to ensure there is no LAA thrombus. (A) LAA at 0 degrees. (B) LAA at 47 degrees. (C) LAA at 94 degrees. (D) Emptying velocity obtained by pulsed-wave Doppler. This emptying velocity is >40 cm/s suggestive of good emptying velocity. (E) LAA at 135 degrees (there are trabeculation at the apex seen which are pectinate muscles). The orange arrows point toward the LAA.

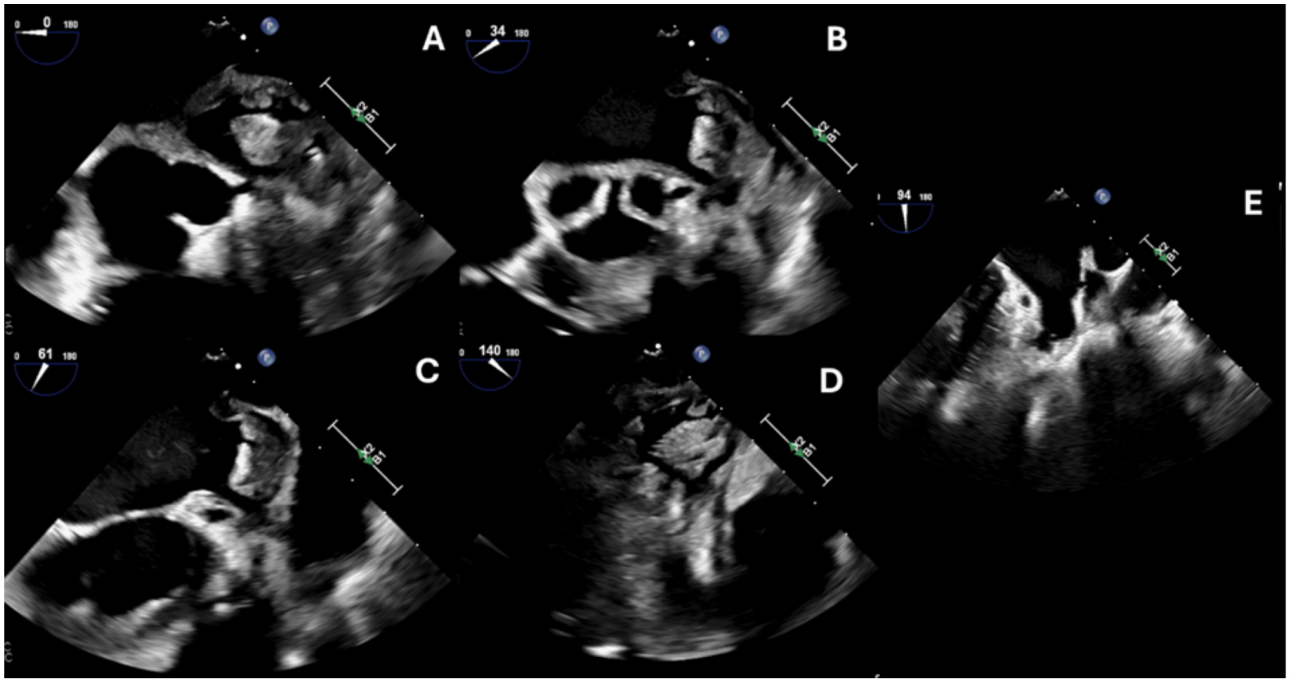

Fig. 3. LAA thrombus on trans-esophageal echocardiogram. (A) LAA and LAA thrombus at 0 degrees. (B) LAA and LAA thrombus at 34 degrees. (C) Similar findings at 61 degrees. (D) LAA thrombus at 140 degrees of TEE. (E) (A–D) shows LAA thrombus and this is in stark contrast to (E) which is a different patient with no LAA thrombus.

hort. It was also linked to a considerably decreased risk of major or clinically significant nonmajor bleeding that was not connected to the procedure. These findings are in favor of using p-LAAO instead of OAC in some post-ablation patients who have a higher risk of stroke [53].

Table 6. Summary of randomized trials for percutaneous LAA closure/exclusion.

Trial name and year	Design	Sample size	Comparison	Primary outcome	Key findings
PROTECT AF (2013) [16]	Noninferiority RCT	707 (463 device, 244 control)	Watchman vs warfarin	Stroke, SE, CV/unexplained death	Event rate 3.0 vs 4.9 per 100 patient-years (RR 0.62, 95% CI 0.35–1.25); higher safety events in device group (7.4 vs 4.4 per 100 patient-years)
PREVAIL (2014) [52]	Noninferiority RCT	407 (269 device, 138 control)	Watchman vs warfarin	Two coprimary endpoints: (1) stroke, SE, CV/unexplained death; (2) stroke or SE >7 days	First coprimary endpoint: RR 1.07 (95% CI 0.57–1.89); did not meet prespecified noninferiority criteria; adverse events lower than PROTECT AF (4.2% vs 8.7%)
ASAP-TOO (2017) [54]	RCT	~500 (stopped early)	p-LAAO vs standard care in OAC-ineligible patients	Not reported	Stopped prematurely due to slow enrollment
STROKECLOSE (2017) [55]	RCT	Ongoing	p-LAAO in OAC-ineligible patients	Not yet reported	Enrollment challenged by off-label LAAO use
Occlusion-AF (2022) [56]	Noninferiority RCT (PROBE design)	750 planned	p-LAAO (Amulet or Watchman FLX) vs DOAC in patients with recent stroke/TIA	Composite of stroke, SE, major bleeding (BARC ≥3), all-cause mortality at 2 years	Trial ongoing; designed for secondary stroke prevention in high-risk AF patients
OPTION (2025) [53]	Noninferiority RCT	1600 (803 Watchman FLX, 797 OAC)	p-LAAO vs DOAC	Composite of all-cause death, stroke, or systemic embolism at 3 years	p-LAAO noninferior to DOAC for death, stroke, or systemic embolism (HR 0.86; 95% CI 0.57–1.30). Significantly lower major or clinically relevant bleeding (HR 0.60; 95% CI 0.41–0.88)
CLOSURE-AF (2026) [57]	Noninferiority RCT	912 enrolled (completed April 2025)	p-LAAO vs best medical care (including DOAC if eligible) in high bleeding risk patients	Composite of stroke, SE, CV/unexplained death, or major bleeding (BARC 3–5)	Trial in progress
SimpLAAfy (2026) [58]	Prospective, randomized, open-label, multicenter, triple-arm RCT	Up to 1857	WATCHMAN FLX Pro with aspirin monotherapy vs reduced-dose NOAC monotherapy vs DAPT	Composite of all-cause death, all stroke, systemic embolism, and major bleeding at 6 months after randomization	Trial in progress
LAAOS-4 (2024) [59]	RCT	Ongoing	p-LAAO in AF patients at high stroke risk despite OAC	Ischemic stroke or systemic embolism	Trial in progress

RCT, randomized controlled trial; SE, systemic emboli; CV, cardiovascular; RR, relative risk; CI, confidence interval; p-LAAO, percutaneous left atrial appendage occlusion; OAC, oral anticoagulation; DOAC, direct oral anticoagulation; TIA, transient ischemic attack; AF, atrial fibrillation; HR, hazard ration; BARC, Bleeding Academic Research Consortium; NOAC, Non-vitamin K antagonist oral anticoagulants; DAPT, Dual antiplatelet therapy; ASAP-TOO, Assessment of the WATCHMAN™ Device in Patients Unsuitable for Oral Anticoagulation.

Differentiating between surgical and p-LAAO is crucial. Although the LAAOS III trial showed that s-LAAO during cardiac surgery lowers stroke and systemic embolism in AF patients already receiving OAC, it is unclear

whether these findings directly apply to percutaneous procedures due to differences in invasiveness and patient selection [60]. The noninferiority of p-LAAO to warfarin and direct OAC for stroke prevention in nonvalvular AF is supported by strong RCT data, and there may be a decrease in significant bleeding, especially in patients with high bleeding risk or those receiving AF ablation.

A 2023 systematic review of observational studies (≈3039 patients) reported comparable rates of ischemic stroke and systemic embolism between p-LAAO and DOAC therapy, with some analyses favoring p-LAAO for major bleeding and mortality, although they had wide confidence intervals [61]. More recently, a large 2025 mixed-design meta-analysis (≈18,507 patients) demonstrated lower all-cause and cardiovascular mortality with p-LAAO and a reduced composite of death, hemorrhagic stroke, or major bleeding, despite substantial heterogeneity and confounding by indication. Collectively, these data generate the hypothesis that p-LAAO may offer durable safety benefits in carefully selected, high-bleeding-risk patients, while underscoring the critical need for adequately powered randomized trials directly comparing p-LAAO with DOACs in contemporary populations.

2.3.6 Peri-Procedural Anticoagulation

2.3.6.1 Management of Preprocedural Anticoagulation.

For p-LAAO, routine preprocedural interruption of anticoagulation and heparin bridging are not recommended. OAC is generally continued through the procedure (with intraprocedural IV heparin), and bridging strategies are avoided due to increased bleeding risk without proven thromboembolic benefit [38].

2.3.6.2 Considerations for Intraprocedural Anticoagulation.

To reduce the danger of DRT formation during p-LAAO, intravenous unfractionated heparin is given to maintain an active clotting time (ACT) >250–300 seconds. For safe device deployment, intraprocedural imaging (TEE or ICE) and technical know-how are essential [38,62].

2.3.6.3 Postprocedural Antithrombotic Strategies.

Standard regimens include warfarin plus aspirin, DOAC plus aspirin, DOAC alone, or dual antiplatelet therapy (DAPT: aspirin + clopidogrel), tailored to bleeding risk and device type. Warfarin or DOAC alone may be associated with lower adverse event rates compared to warfarin plus aspirin. A 2025 meta-analysis comparing seven post-LAAO antithrombotic strategies found that DOAC monotherapy provided the most favorable balance between thromboembolic prevention and major bleeding, with lower rates of DRT than antiplatelet-based regimens. Although limited by indirect comparisons and heterogeneity, these data support a paradigm favoring short-term, often reduced-dose DOAC after LAAO as a key determinant of optimizing long-term safety [63]. Typically, anticoagulation is continued for 45 days post-implant, followed by DAPT for 3–6 months, then aspirin monotherapy [37,64]. Anticoagulation is used to avoid DRT until the device has endothelized, which usually happens six weeks after implant [37,38]. Patient comorbidities, device type, and bleeding risk must all be considered when customizing antithrombotic medication. Although there is less solid evidence, DAPT may be utilized for patients who have a significant risk of bleeding or who are completely contraindicated for OAC [35,38]. Shared decision-making is essential.

2.3.7 Complications

p-LAAO is associated with PDL, device-related DRT, and device embolization, which may influence long-term outcomes and stroke risk [33]. PDL is common, occurring in 10–25% of cases (>3 mm) and 1–3% (>5 mm) on TEE [19,38,65]. Leak rates are lower with newer devices, including Watchman FLX and Amulet, and TEE-detected leaks, particularly >5 mm, are associated with increased bleeding, mortality, and thromboembolism, whereas the clinical significance of CT-detected leaks is less clear [41,42,43,45,65,66].

Although DRT has historically been reported in approximately 3–7% of patients, rates with newer-generation devices appear lower, generally around 2–4%, with WATCHMAN FLX reporting 2.4% in the FLXibility study [67]. It is linked to a three to four-fold increased stroke risk; rates are lower with Watchman FLX and Amulet devices. Risk factors include prior stroke/TIA, persistent AF, reduced Left Ventricular Ejection Fraction (LVEF), vascular disease, and early anticoagulation cessation, and surveillance imaging at 45–90 days is recommended [68].

Device embolization is rare (0.2–0.6%) but may require urgent retrieval; its incidence has declined with improved device design and operator experience [38]. Other uncommon complications include pericardial effusion/tamponade (~1%), vascular access complications, procedural stroke, major bleeding, infection, device erosion, allergic reactions, and iatrogenic atrial septal defects, with overall major adverse event rates being low and comparable across contemporary devices [38,54,55,56,69].

2.3.8 Guidelines

p-LAAO is recommended for some patients with nonvalvular AF who have a moderate to high risk of stroke (CHA_2DS_2-VASc score ≥2) and are contraindicated for long-term OAC due to irreversible causes; LAAO is considered reasonable in these patients (Class IIa, Level of Evidence B-NR). For patients with AF who have a moderate to high risk of stroke and a high risk of major bleeding on OAC, LAAO may be considered as an alternative to OAC with careful consideration of procedural risks and the knowledge that the evidence base for OAC is more extensive (Class IIb, Level of Evidence B-R) [35].

According to the Society for Cardiovascular Angiography & Interventions (SCAI)/HRS expert consensus and clinical practice guidelines, p-LAAO is appropriate for patients with nonvalvular AF, high thromboembolic risk, and who are not suitable for long-term OAC, provided that they have a life expectancy and quality of life sufficient to benefit from the procedure [37,38]. Shared decision-making is stressed, and operators and programs must possess procedural competence [38].

It is advised to use intraprocedural imaging guidance and preprocedural imaging using cardiac CT or TEE. Both OAC and DAPT are recommended for postprocedural antithrombotic therapy, with DAPT being preferred in patients with major contraindications to OAC. Postprocedural antithrombotic medication should be customized to the individual's bleeding risk and device usage guidelines. To check for PDL and DRT, surveillance imaging (TEE or CT) is advised 45–90 days after implant [37,38]. Iatrogenic atrial septal defects should not be routinely closed, and anticoagulation and repeated imaging should be used to treat DRT. Although the complete clinical impact of PDL is unknown, attempts should be made to reduce leaks after implantation [37,38].

According to findings from a recent randomized trial (OPTION trial), p-LAAO is associated with a decreased risk of non-procedure-related major or clinically meaningful nonmajor bleeding, and it is noninferior to OAC for preventing death, stroke, or systemic embolism at 36 months in patients receiving AF ablation [53]. Combined catheter ablation and percutaneous left atrial appendage occlusion are now increasingly used in contemporary U.S. practice; a U.S. nationwide analysis demonstrated approximately 63% annual growth in combined procedures from 2016 to 2019 [70].

In conclusion, with careful patient selection, procedural expertise, and postprocedural management as previously mentioned, guideline recommendations support p-LAAO mainly for patients with AF and contraindications to long-term OAC, as well as a reasonable alternative in those at high bleeding risk [35,37,38,53].

2.4 Special Populations

2.4.1 Mechanical and Bioprosthetic Heart Valves

The role of LAAO in patients with prosthetic heart valves depends on the underlying thromboembolic source. A multicenter Italian pilot study showed that p-LAAO is technically feasible in patients with mechanical mitral valves, with a 100% procedural success rate and long-term outcomes similar to those seen in nonvalvular AF, most commonly indicated for LAA thrombus despite therapeutic anticoagulation [71]. However, evidence supporting routine s-LAAO at the time of mechanical valve replacement is limited; a retrospective study showed increased operative times without reduction in thromboembolism or mortality [72]. The STS acknowledges potential benefit in select patients on mandatory anticoagulation, though larger studies are needed [19].

In contrast, prophylactic LAAO during bioprosthetic valve surgery in patients without AF did not reduce stroke or cardiovascular mortality in the OPINION trial, arguing against routine use in this setting [26].

2.4.2 Elderly and Very Elderly Populations

Elderly patients with AF pose management challenges due to high competing risks of stroke, bleeding, frailty, and comorbidities, making LAAO an attractive alternative to long-term anticoagulation. In the Left-Atrium-Appendage Occluder Register - GErmany (LAARGE) registry, patients ≥75 years had similar procedural success and periprocedural event rates compared with younger patients, with higher 1-year mortality driven by non-cardiovascular causes and no differences in stroke or major bleeding [73].

National registry data show improving outcomes in octogenarians, with declining stroke, bleeding, and readmission rates and hospital mortality <0.5%, although age ≥75 years, particularly in women, remains a risk factor for perforation and tamponade [74,75]. Consistently, the French National Registry found comparable thromboembolic outcomes in patients ≥80 years despite higher risk profiles, with excess mortality attributable to non-cardiovascular causes [76]. Overall, these data support considering LAAO in selected elderly patients with AF, high stroke risk, and contraindications to oral anticoagulation [73,77].

2.4.3 Chronic Kidney Disease (CKD) and End-Stage Renal Disease (ESRD)

Patients with CKD undergoing LAAO have higher procedural risk but similar stroke prevention efficacy compared with non-CKD patients [78,79,80]. A meta-analysis of over 61,000 patients showed increased in-hospital mortality, acute kidney injury, major bleeding, and pericardial effusion, particularly in ESRD, while procedural success and long-term stroke rates were comparable across groups [78,80,81].

In patients with kidney failure on dialysis, LAAO may be safer than OAC, with lower bleeding and mortality and a reduced stroke risk in observational data [79].

Studies in advanced CKD similarly demonstrate comparable stroke outcomes after LAAO, despite higher bleeding and mortality driven largely by comorbidity burden rather than the procedure itself, underscoring the importance of careful patient selection and close follow-up [80,81,82,83].

2.4.4 Prior Left Atrial Appendage Occlusion

Management after prior LAAO is challenging when complications or suboptimal results occur. DRT affects ~3–5% of patients and is linked to thromboembolism, while PDL (2–22%), particularly >5 mm, may require long-term

anticoagulation or, less commonly, repeat LAAO with another device [84].

Patients undergoing LAAO after OAC failure remain at high risk. Registry data show only modest stroke reduction compared with patients treated for OAC contraindications, despite elimination of major bleeding, supporting consideration of continued OAC or prolonged DAPT in selected patients without major bleeding risk [85].

Emerging strategies combining LAA isolation and closure show technical feasibility with acceptable long-term arrhythmia and event rates, and real-world data suggest that early antithrombotic discontinuation after LAAO may be safe in carefully selected patients [86,87].

2.4.5 Congenital Heart Disease (CHD)

Evidence for transcatheter LAAO in patients with CHD and AF is extremely limited, with no dedicated studies in this population. While general LAAO principles apply, CHD-related anatomic complexity from prior surgeries, shunts, and variable appendage morphology may complicate procedures [60]. OAC remains first-line therapy, and LAAO should be considered selectively based on bleeding risk, anatomic suitability, and contraindications to anticoagulation, ideally at experienced centers with detailed preprocedural imaging [62,88]. The growing adult CHD population highlights a major evidence gap, underscoring the need for dedicated studies to define the safety and efficacy of LAAO across CHD subtypes [89].

2.4.6 CABG Without Pre-existing Atrial Fibrillation

The benefit of prophylactic LAAO during CABG in patients without pre-existing AF remains uncertain. Current guidelines note that evidence supporting s-LAAO is limited to patients with established AF, with prior meta-analyses showing no clear benefit in those without AF [35]. More recent meta-analyses suggest a possible long-term reduction in stroke and modest survival benefit, but these findings are largely driven by observational data [90,91]. Conversely, propensity-matched and registry studies report increased postoperative AF, longer operative times, higher resource use, and greater costs with prophylactic LAAO, without consistent reductions in stroke or mortality [19,92,93]. As a result, routine prophylactic LAAO during CABG in patients without AF is not currently supported, and results from ongoing randomized trials are awaited to clarify its role.

2.5 Research Gaps and Future Directions

The American College of Cardiology/American Heart Association/ACCP/Heart Rhythm Society guidelines highlight several research gaps and future directions regarding LAAO for stroke prevention in patients undergoing cardiac surgery. The guidelines recommend s-LAAO for patients with AF undergoing CABG or valve surgery, based on robust evidence from the LAAOS III trial showing a 33% reduction in stroke and systemic embolism when s-LAAO is added to OAC [35]. Guidelines emphasize that the benefit of s-LAAO in patients without preoperative AF remains uncertain, as existing meta-analyses and observational studies show inconsistent stroke reduction; ongoing randomized trials are needed to clarify its role in patients without AF or with transient postoperative AF. They also highlight unresolved questions regarding whether OAC can be safely discontinued after successful LAAO, as LAAOS III did not address this and available data are heterogeneous. Finally, complete and durable LAAO is critical for efficacy, and although modern techniques achieve high success rates, further study is required to optimize long-term outcomes [35].

Building on these gaps, ongoing research highlights several unresolved issues in LAAO for cardiac surgery patients. Although LAAOS III confirmed the benefit of s-LAAO in patients with AF, it did not determine whether LAAO can replace OAC, directly compare surgical with percutaneous approaches, or fully address closure durability, technique-specific efficacy, or long-term effects on heart failure and other clinical outcomes [17]. Observational studies and meta-analyses suggest LAAO may reduce stroke and mortality in patients with AF, but benefit in those without AF is uncertain and may be offset by higher rates of postoperative AF or related hospitalizations [19,90,94]. Heterogeneity in populations, techniques, and outcome definitions limits interpretation and generalizability [19]. To address these gaps, large randomized trials such as the Left Atrial Appendage Closure by Surgery-2 (LAACS-2) and the Left Atrial Appendage Exclusion for Prophylactic Stroke Reduction (LeAAPS) are underway to evaluate whether prophylactic LAAO during cardiac surgery reduces stroke in patients without preoperative AF and to better define safety, long-term outcomes, and subgroups most likely to benefit [32,90,95]. Further research is also needed to define optimal post–LAAO antithrombotic strategies, particularly in high bleeding–risk patients, and to compare surgical and percutaneous approaches for efficacy, safety, and cost-effectiveness [17,62]. Ongoing advances in devices and imaging require validation in prospective studies [62].

Overall, future work should clarify the role of LAAO in non-AF populations, postprocedural anticoagulation needs, and comparative effectiveness of closure techniques, with ongoing RCTs expected to guide practice [32,62,90,95].

3. Conclusion

AF-related thromboembolism is predominantly driven by thrombus formation within the LAA, making LAAO a mechanistically targeted strategy for stroke prevention. Surgical and percutaneous approaches have both evolved substantially, with randomized and observational data supporting their efficacy in appropriately selected patients. s-LAAO is now guideline-endorsed for patients with AF un-

dergoing cardiac surgery, primarily as an adjunct to OAC, while p-LAAO offers a validated alternative for patients with nonvalvular AF who are unsuitable for long-term anticoagulation. Despite these advances, important uncertainties remain regarding optimal patient selection given the diverse AF phenotypes especially in special populations, post-procedural antithrombotic strategies, imaging surveillance, and the role of prophylactic LAAO in patients without pre-existing AF. Ongoing randomized trials and advances in device technology and imaging are expected to refine indications and improve outcomes. Until these gaps are addressed, LAAO should be implemented through a multidisciplinary, individualized approach that balances thromboembolic and bleeding risks while adhering to contemporary guideline recommendations.

Author Contributions

TKMW and KH conceived the study. KH, EH, AA, and ADA performed the literature review, extracted relevant data, and contributed to drafting the manuscript. KH, CT and YWBL contributed to the creation and design of the tables and figures. All authors provided critical revisions, and helped structure the final version of the manuscript. All authors critically reviewed and approved the final version. TKMW is the guarantor of this work and accepts full responsibility for the conduct of the study. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

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The authors declare no conflicts of interest.

Declaration of AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work the authors used ChatGpt-5.2 in order to check spell and grammar. After using this tool, the authors reviewed and edited the content as needed and takes full responsibility for the content of the publication.

References

[1] Chugh SS, Havmoeller R, Narayanan K, Singh D, Rienstra M, Benjamin EJ, et al. Worldwide epidemiology of atrial fibrillation: a Global Burden of Disease 2010 Study. Circulation. 2014; 129: 837–847. https://doi.org/10.1161/CIRCULATIONAHA.113.005119

[2] Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. European Heart Journal. 2021; 42: 373–498. https://doi.org/10.1093/eurheartj/ehaa612

[3] Blackshear JL, Odell JA. Appendage obliteration to reduce stroke in cardiac surgical patients with atrial fibrillation. The Annals of Thoracic Surgery. 1996; 61: 755–759. https://doi.org/10.1016/0003-4975(95)00887-X.

[4] Watson T, Shantsila E, Lip GYH. Mechanisms of thrombogenesis in atrial fibrillation: Virchow's triad revisited. Lancet (London, England). 2009; 373: 155–166. https://doi.org/10.1016/S0140-6736(09)60040-4

[5] Glikson M, Wolff R, Hindricks G, Mandrola J, Camm AJ, Lip GYH, et al. EHRA/EAPCI expert consensus statement on catheter-based left atrial appendage occlusion - an update. Europace: European Pacing, Arrhythmias, and Cardiac Electrophysiology: Journal of the Working Groups on Cardiac Pacing, Arrhythmias, and Cardiac Cellular Electrophysiology of the European Society of Cardiology. 2020; 22: 184. https://doi.org/10.1093/europace/euz258

[6] Beigel R, Wunderlich NC, Ho SY, Arsanjani R, Siegel RJ. The left atrial appendage: anatomy, function, and noninvasive evaluation. JACC. Cardiovascular Imaging. 2014; 7: 1251–1265. https://doi.org/10.1016/j.jcmg.2014.08.009

[7] Anwar AM. Morphological and functional assessment of the left atrial appendage in daily practice: a comprehensive approach using basic and advanced echocardiography with practical tips. Journal of Cardiovascular Imaging. 2024; 32: 12. https://doi.org/10.1186/s44348-024-00017-2

[8] Collado FMS, Lama von Buchwald CM, Anderson CK, Madan N, Suradi HS, Huang HD, et al. Left Atrial Appendage Occlusion for Stroke Prevention in Nonvalvular Atrial Fibrillation. Journal of the American Heart Association. 2021; 10: e022274. https://doi.org/10.1161/jaha.121.022274

[9] Eikelboom JW, Connolly SJ, Brueckmann M, Granger CB, Kappetein AP, Mack MJ, et al. Dabigatran versus Warfarin in Patients with Mechanical Heart Valves. New England Journal of Medicine. 2013; 369: 1206–1214. https://doi.org/10.1056/NEJMoa1300615

[10] Wang TY, Svensson LG, Wen J, Vekstein A, Gerdisch M, Rao VU, et al. Apixaban or Warfarin in Patients with an On-X Mechanical Aortic Valve. NEJM Evidence. 2023; 2: EVIDoa2300067. https://doi.org/10.1056/EVIDoa2300067

[11] Connolly SJ, Karthikeyan G, Ntsekhe M, Haileamlak A, El Sayed A, El Ghamrawy A, et al. Rivaroxaban in Rheumatic Heart Disease-Associated Atrial Fibrillation. The New England Journal of Medicine. 2022; 387: 978–988. https://doi.org/10.1056/NEJMoa2209051

[12] Khurram IM, Dewire J, Mager M, Maqbool F, Zimmerman SL, Zipunnikov V, et al. Relationship between left atrial appendage morphology and stroke in patients with atrial fibrillation. Heart Rhythm. 2013; 10: 1843–1849. https://doi.org/10.1016/j.hrthm.2013.09.065

[13] Mendez K, Kennedy DG, Wang DD, O'Neill B, Roche ET. Left Atrial Appendage Occlusion: Current Stroke Prevention Strategies and a Shift Toward Data-Driven, Patient-Specific Approaches. Journal of the Society for Cardiovascular Angiography & Interventions. 2022; 1: 100405. https://doi.org/10.1016/j.jscai.2022.100405

[14] Ueno H, Imamura T, Tanaka S, Fukuda N, Kinugawa K. Left atrial appendage closure for stroke prevention in nonvalvular atrial fibrillation: A current overview. Journal of Cardiology. 2023; 81: 420–428. https://doi.org/10.1016/j.jjcc.2022.11.006

[15] Iwama M, Kawasaki M, Tanaka R, Ono K, Watanabe T, Hirose T, et al. Left atrial appendage emptying fraction assessed by a feature-tracking echocardiographic method is a determinant of thrombus in patients with nonvalvular atrial fibrillation. Journal of Cardiology. 2012; 59: 329–336. https://doi.org/10.1016/j.jjcc.2012.01.002

[16] Reddy VY, Doshi SK, Sievert H, Buchbinder M, Neuzil P, Huber K, et al. Percutaneous Left Atrial Appendage Closure for Stroke Prophylaxis in Patients With Atrial Fibrillation. Circulation. 2013; 127: 720–729. https://doi.org/10.1161/CIRCULATIONAHA.112.114389

[17] Whitlock RP, Belley-Cote EP, Paparella D, Healey JS, Brady K, Sharma M, et al. Left Atrial Appendage Occlusion during Cardiac Surgery to Prevent Stroke. New England Journal of Medicine. 2021; 384: 2081–2091. https://doi.org/10.1056/NEJMoa2101897

[18] Cox JL, Ad N, Palazzo T. Impact of the maze procedure on the stroke rate in patients with atrial fibrillation. The Journal of Thoracic and Cardiovascular Surgery. 1999; 118: 833–840. https://doi.org/10.1016/s0022-5223(99)70052-8

[19] Wyler von Ballmoos MC, Hui DS, Mehaffey JH, Malaisrie SC, Vardas PN, Gillinov AM, et al. The Society of Thoracic Surgeons 2023 Clinical Practice Guidelines for the Surgical Treatment of Atrial Fibrillation. The Annals of Thoracic Surgery. 2024; 118: 291–310. https://doi.org/10.1016/j.athoracsur.2024.01.007

[20] Healey JS, Crystal E, Lamy A, Teoh K, Semelhago L, Hohnloser SH, et al. Left Atrial Appendage Occlusion Study (LAAOS): results of a randomized controlled pilot study of left atrial appendage occlusion during coronary bypass surgery in patients at risk for stroke. American Heart Journal. 2005; 150: 288–293. https://doi.org/10.1016/j.ahj.2004.09.054

[21] Ailawadi G, Gerdisch MW, Harvey RL, Hooker RL, Damiano RJJ, Salamon T, et al. Exclusion of the left atrial appendage with a novel device: early results of a multicenter trial. The Journal of Thoracic and Cardiovascular Surgery. 2011; 142: 1002–1009, 1009.e1. https://doi.org/10.1016/j.jtcvs.2011.07.052

[22] D'Abramo M, Romiti S, Saltarocchi S, Saade W, Spunticchia F, Bruno N, et al. Different Techniques of Surgical Left Atrial Appendage Closure and Their Efficacy: A Systematic Review. Reviews in Cardiovascular Medicine. 2023; 24: 184. https://doi.org/10.31083/j.rcm2406184

[23] Kanderian AS, Gillinov AM, Pettersson GB, Blackstone E, Klein AL. Success of surgical left atrial appendage closure: assessment by transesophageal echocardiography. Journal of the American College of Cardiology. 2008; 52: 924–929. https://doi.org/10.1016/j.jacc.2008.03.067

[24] Whitlock RP, Vincent J, Blackall MH, Hirsh J, Fremes S, Novick R, et al. Left Atrial Appendage Occlusion Study II (LAAOS II). The Canadian Journal of Cardiology. 2013; 29: 1443–1447. https://doi.org/10.1016/j.cjca.2013.06.015

[25] Park-Hansen J, Holme SJ V, Irmukhamedov A, Carranza CL, Greve AM, Al-Farra G, et al. Adding left atrial appendage closure to open heart surgery provides protection from ischemic brain injury six years after surgery independently of atrial fibrillation history: the LAACS randomized study. Journal of Cardiothoracic Surgery. 2018; 13: 53. https://doi.org/10.1186/s13019-018-0740-7

[26] Yuan X, Ju F, Wu H, Zhao Y, Wang X, Liu S, et al. Surgical left atrial appendage occlusion in valvular heart disease without atrial fibrillation: the OPINION trial. European Heart Journal. 2025; ehaf674. https://doi.org/10.1093/eurheartj/ehaf674 (Online ahead of print)

[27] Martín Gutiérrez E, Castaño M, Gualis J, Martínez-Comendador JM, Maiorano P, Castillo L, et al. Beneficial effect of left atrial appendage closure during cardiac surgery: a meta-analysis of 280 585 patients. European Journal of Cardio-thoracic Surgery: Official Journal of the European Association for Cardio-thoracic Surgery. 2020; 57: 252–262. https://doi.org/10.1093/ejcts/ezz289

[28] Emmert MY, Puippe G, Baumüller S, Alkadhi H, Landmesser U, Plass A, et al. Safe, effective and durable epicardial left atrial appendage clip occlusion in patients with atrial fibrillation undergoing cardiac surgery: first long-term results from a prospective device trial. European Journal of Cardio-thoracic Surgery: Official Journal of the European Association for Cardio-thoracic Surgery. 2014; 45: 126–131. https://doi.org/10.1093/ejcts/ezt204

[29] van Laar C, Verberkmoes NJ, van Es HW, Lewalter T, Dunnington G, Stark S, et al. Thoracoscopic Left Atrial Appendage Clipping: A Multicenter Cohort Analysis. JACC. Clinical Electrophysiology. 2018; 4: 893–901. https://doi.org/10.1016/j.jacep.2018.03.009

[30] Kim JY, Jeong DS, Park SJ, Park KM, Kim JS, On YK. Long-Term Efficacy and Anticoagulation Strategy of Left Atrial Appendage Occlusion During Total Thoracoscopic Ablation of Atrial Fibrillation to Prevent Ischemic Stroke. Frontiers in Cardiovascular Medicine. 2022; 9: 853299. https://doi.org/10.3389/fcvm.2022.853299

[31] Madsen CV, Park-Hansen J, Holme SJV, Irmukhamedov A, Carranza CL, Greve AM, et al. Randomized Trial of Surgical Left Atrial Appendage Closure: Protection Against Cerebrovascular Events. Seminars in Thoracic and Cardiovascular Surgery. 2023; 35: 664–672. https://doi.org/10.1053/j.semtcvs.2022.06.012

[32] Madsen CL, Park-Hansen J, Irmukhamedov A, Carranza CL, Rafiq S, Rodriguez-Lecoq R, et al. The left atrial appendage closure by surgery-2 (LAACS-2) trial protocol rationale and design of a randomized multicenter trial investigating if left atrial appendage closure prevents stroke in patients undergoing open-heart surgery irrespective of preoperative atrial fibrillation status and stroke risk. American Heart Journal. 2023; 264: 133–142. https://doi.org/10.1016/j.ahj.2023.06.003

[33] Aryana A, Singh SK, Singh SM, O'Neill PG, Bowers MR, Allen SL, et al. Association between incomplete surgical ligation of left atrial appendage and stroke and systemic embolization. Heart Rhythm. 2015; 12: 1431–1437. https://doi.org/10.1016/j.hrthm.2015.03.028

[34] Kuzmin B, Staack T, Wippermann J, Wacker M. Left atrial appendage occlusion device causing coronary obstruction: A word of caution. Journal of Cardiac Surgery. 2021; 36: 723–725. https://doi.org/10.1111/jocs.15222

[35] Joglar JA, Chung MK, Armbruster AL, Benjamin EJ, Chyou JY, Cronin EM, et al. 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2024; 149: e1–e156. https://doi.org/10.1161/CIR.0000000000001193

[36] Praz F, Borger MA, Lanz J, Marin-Cuartas M, Abreu A, Adamo M, et al. 2025 ESC/EACTS Guidelines for the management of valvular heart disease: Developed by the task force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). European Heart Journal. 2025; 46: 4635–4736. https://doi.org/10.1093/eurheartj/ehaf194

[37] Goldsweig AM, Glikson M, Joza J, Kavinsky CJ, Khalique O, Lakkireddy D, et al. 2025 SCAI/HRS clinical practice guidelines

on transcatheter left atrial appendage occlusion. Heart Rhythm. 2025; 22: e1048–e1063. https://doi.org/10.1016/j.hrthm.2025.05.048

[38] Saw J, Holmes DR, Cavalcante JL, Freeman JV, Goldsweig AM, Kavinsky CJ, et al. SCAI/HRS expert consensus statement on transcatheter left atrial appendage closure. Heart Rhythm. 2023; 20: e1–e16. https://doi.org/10.1016/j.hrthm.2023.01.007

[39] AtriCure. Atrial Fibrillation Treatment. Pain Management. 2023. Available at: https://www.atricure.com/ (Accessed: 26 January 2026).

[40] SentreHEART Receives CE Mark for LARIAT-RS™ 50mm and Expanded Indication for Left Atrial Appendage Exclusion. BioSpace. 2019. Available at: https://www.biospace.com/sentreheart-receives-ce-mark-for-lariat-rs-50mm-and-expanded-indication-for-left-atrial-appendage-exclusion (Accessed: 26 January 2026)

[41] Price MJ, Tan Z, Zimmerman S, Curtis JP, Freeman JV. Clinical Effectiveness of Transcatheter Left Atrial Appendage Occlusion With Watchman FLX Compared With First-Generation Watchman. JACC. Cardiovascular Interventions. 2025; 18: 1318–1326. https://doi.org/10.1016/j.jcin.2025.03.025

[42] Cruz-González I, Korsholm K, Trejo-Velasco B, Thambo JB, Mazzone P, Rioufol G, et al. Procedural and Short-Term Results With the New Watchman FLX Left Atrial Appendage Occlusion Device. JACC. Cardiovascular Interventions. 2020; 13: 2732–2741. https://doi.org/10.1016/j.jcin.2020.06.056

[43] Vizzari G, Grasso C, Sardone A, Mazzone P, Laterra G, Frazzetto M, et al. Real-world experience with the new Watchman FLX device: Data from two high-volume Sicilian centers. The FLX-iEST registry. Catheterization and Cardiovascular Interventions: Official Journal of the Society for Cardiac Angiography & Interventions. 2022; 100: 154–160. https://doi.org/10.1002/ccd.30237

[44] Lam SCC, Bertog S, Gafoor S, Vaskelyte L, Boehm P, Ho RWJ, et al. Left atrial appendage closure using the Amulet device: an initial experience with the second generation amplatzer cardiac plug. Catheterization and Cardiovascular Interventions: Official Journal of the Society for Cardiac Angiography & Interventions. 2015; 85: 297–303. https://doi.org/10.1002/ccd.25644

[45] Hildick-Smith D, Landmesser U, Camm AJ, Diener HC, Paul V, Schmidt B, et al. Left atrial appendage occlusion with the Amplatzer™ Amulet™ device: full results of the prospective global observational study. European Heart Journal. 2020; 41: 2894–2901. https://doi.org/10.1093/eurheartj/ehaa169

[46] Gianni C, Anannab A, Sahore Salwan A, Della Rocca DG, Natale A, Horton RP. Closure of the left atrial appendage using percutaneous transcatheter occlusion devices. Journal of Cardiovascular Electrophysiology. 2020; 31: 2179–2186. https://doi.org/10.1111/jce.14471

[47] Arockiam AD, Hoyek K, Haroun E, Mendpara V, Gurram A, Okushi Y, et al. Contemporary Multimodality Imaging Evaluation in Native Aortic Stenosis. Cardiovascular Science. 2025; 2: 10014. https://doi.org/10.70322/cvs.2025.10014

[48] Jain R, Wessly P, Saric M, Richardson K, Garcia-Sayan E, Addetia K, et al. Multimodality Imaging in Evaluating and Guiding Percutaneous Left Atrial Appendage Occlusion. Journal of the American Society of Echocardiography: Official Publication of the American Society of Echocardiography. 2025; 38: 1198–1218. https://doi.org/10.1016/j.echo.2025.07.009

[49] Stankowski K, Volpi B, Balata F, Buonamici L, Biroli M, Figliozzi S, et al. Multimodality imaging assessment of the left atrial appendage for percutaneous closure. Progress in Cardiovascular Diseases. 2025; 92: 80–96. https://doi.org/10.1016/j.pcad.2025.09.003

[50] Rajiah P, Alkhouli M, Thaden J, Foley T, Williamson E, Ranganath P. Pre- and Postprocedural CT of Transcatheter Left Atrial Appendage Closure Devices. Radiographics: a Review Publication of the Radiological Society of North America, Inc. 2021; 41: 680–698. https://doi.org/10.1148/rg.2021200136

[51] Singh G, Bamba H, Saravanan CR, Dinesh A, Chandrasekaran SH, John J, et al. Left atrial appendage closure versus anticoagulation in the management of atrial fibrillation: a systematic review, meta-analysis, and meta-regression analysis. Annals of Medicine and Surgery (2012). 2025; 87: 6684–6693. https://doi.org/10.1097/MS9.0000000000003703

[52] Holmes DR, Jr, Kar S, Price MJ, Whisenant B, Sievert H, Doshi SK, et al. Prospective randomized evaluation of the Watchman Left Atrial Appendage Closure device in patients with atrial fibrillation versus long-term warfarin therapy: the PREVAIL trial. Journal of the American College of Cardiology. 2014; 64: 1–12. https://doi.org/10.1016/j.jacc.2014.04.029

[53] Wazni OM, Saliba WI, Nair DG, Marijon E, Schmidt B, Hounshell T, et al. Left Atrial Appendage Closure after Ablation for Atrial Fibrillation. The New England Journal of Medicine. 2025; 392: 1277–1287. https://doi.org/10.1056/NEJMoa2408308

[54] Holmes DR, Reddy VY, Buchbinder M, Stein K, Elletson M, Bergmann MW, et al. The Assessment of the Watchman Device in Patients Unsuitable for Oral Anticoagulation (ASAP-TOO) trial. American Heart Journal. 2017; 189: 68–74. https://doi.org/10.1016/j.ahj.2017.03.007

[55] Tzikas A. Left Atrial Appendage Occlusion with Amplatzer Cardiac Plug and Amplatzer Amulet: a Clinical Trials Update. Journal of Atrial Fibrillation. 2017; 10: 1651. https://doi.org/10.4022/jafib.1651

[56] Korsholm K, Damgaard D, Valentin JB, Packer EJS, Odenstedt J, Sinisalo J, et al. Left atrial appendage occlusion vs novel oral anticoagulation for stroke prevention in atrial fibrillation: rationale and design of the multicenter randomized occlusion-AF trial. American Heart Journal. 2022; 243: 28–38. https://doi.org/10.1016/j.ahj.2021.08.020

[57] Landmesser U, Skurk C, Kirchhof P, Lewalter T, Hartung J, Rroku A, et al. Catheter-based left atrial appendage CLOSURE in patients with atrial fibrillation at high risk of stroke and bleeding as compared to best medical therapy: Rationale and design of the prospective randomized CLOSURE-AF trial. American Heart Journal. 2026; 292: 107273. https://doi.org/10.1016/j.ahj.2025.09.005

[58] Study Details|NCT06521463|SIMPLAAFY Clinical Trial. ClinicalTrials.gov. 2026. Available at: https://clinicaltrials.gov/study/NCT06521463 (Accessed: 24 March 2026).

[59] Reed GW, Nakhla S, Miyasaka R, Harb S, Kanj M, Wazni O, et al. Left Atrial Appendage Occlusion: Expanding Indications and New Developments. Structural Heart: the Journal of the Heart Team. 2024; 9: 100354. https://doi.org/10.1016/j.shj.2024.100354

[60] Seiffge DJ, Cancelloni V, Räber L, Paciaroni M, Metzner A, Kirchhof P, et al. Secondary stroke prevention in people with atrial fibrillation: treatments and trials. The Lancet. Neurology. 2024; 23: 404–417. https://doi.org/10.1016/S1474-4422(24)00037-1.

[61] Razzack AA, Lak HM, Erasani G, Rahman S, Hussain N, Ali BF, et al. Long-Term Efficacy and Safety of Left Atrial Appendage Occlusion (LAAO) vs Direct Oral Anticoagulation (DOAC) in Patients with Atrial Fibrillation: A Systematic Review and Meta-Analysis. Reviews in Cardiovascular Medicine. 2023; 24: 44. https://doi.org/10.31083/j.rcm2402044

[62] Landmesser U, Skurk C, Tzikas A, Falk V, Reddy VY, Windecker S. Left atrial appendage closure for stroke prevention in atrial fibrillation: current status and perspectives. European Heart Journal. 2024; 45: 2914–2932. https://doi.org/10.1093/eurheartj/ehae398

[63] Samaras A, Karakasis P, Feidakis A, Giannakoulas G, Fra-

gakis N, Nielsen-Kudsk JE, et al. Antithrombotic strategies and DOAC dosing following left atrial appendage occlusion: a network meta-analysis. European Heart Journal. Cardiovascular Pharmacotherapy. 2026; 12: 38–51. https://doi.org/10.1093/ehjcvp/pvaf078

[64] Freeman JV, Higgins AY, Wang Y, Du C, Friedman DJ, Daimee UA, et al. Antithrombotic Therapy After Left Atrial Appendage Occlusion in Patients With Atrial Fibrillation. Journal of the American College of Cardiology. 2022; 79: 1785–1798. https://doi.org/10.1016/j.jacc.2022.02.047

[65] Samaras A, Papazoglou AS, Balomenakis C, Bekiaridou A, Moysidis DV, Patsiou V, et al. Residual leaks following percutaneous left atrial appendage occlusion and outcomes: a meta-analysis. European Heart Journal. 2024; 45: 214–229. https://doi.org/10.1093/eurheartj/ehad828

[66] Mostafa MR, Eid MM, Abuelazm M, Al-Abdouh A, Najim M, Hassan AR, et al. Meta-Analysis of the Outcomes of Peri-Device Leak After Left Atrial Appendage Closure. The American Journal of Cardiology. 2023; 204: 325–332. https://doi.org/10.1016/j.amjcard.2023.07.102

[67] [67] Betts TR, Grygier M, Kudsk JEN, Schmitz T, Sandri M, Casu G, et al. Real-world clinical outcomes with a next-generation left atrial appendage closure device: the FLXibility Post-Approval Study. Europace. 2023; 25: 914–21. https://doi.org/10.1093/europace/euac270

[68] Nielsen JC, Lin YJ, de Oliveira Figueiredo MJ, Sepehri Shamloo A, Alfie A, Boveda S, et al. European Heart Rhythm Association (EHRA)/Heart Rhythm Society (HRS)/Asia Pacific Heart Rhythm Society (APHRS)/Latin American Heart Rhythm Society (LAHRS) expert consensus on risk assessment in cardiac arrhythmias: use the right tool for the right outcome, in the right population. Heart Rhythm. 2020; 17: e269–e316. https://doi.org/10.1016/j.hrthm.2020.05.004

[69] Osmancik P, Herman D, Neuzil P, Hala P, Taborsky M, Kala P, et al. 4-Year Outcomes After Left Atrial Appendage Closure Versus Nonwarfarin Oral Anticoagulation for Atrial Fibrillation. Journal of the American College of Cardiology. 2022; 79: 1–14. https://doi.org/10.1016/j.jacc.2021.10.023

[70] Pasupula DK, Siddappa Malleshappa SK, Munir MB, Bhat AG, Anandaraj A, Jakkoju A, et al. Combined atrial fibrillation ablation and left atrial appendage occlusion procedure in the United States: a propensity score matched analysis from 2016-2019 national readmission database. Europace: European Pacing, Arrhythmias, and Cardiac Electrophysiology: Journal of the Working Groups on Cardiac Pacing, Arrhythmias, and Cardiac Cellular Electrophysiology of the European Society of Cardiology. 2023; 25: 390–399. https://doi.org/10.1093/europace/euac181

[71] Preda A, Margonato D, Gaspardone C, Rizza V, Vella C, Rampa L, et al. Left Atrial Appendage Closure in Patients With a Mechanical Mitral Valve Prosthesis: A Multicentre Italian Pilot Study. The Canadian Journal of Cardiology. 2024; 40: 1635–1642. https://doi.org/10.1016/j.cjca.2024.01.039

[72] Zheng Y, Rao CF, Chen SP, He L, Hou JF, Zheng Z. Surgical left atrial appendage occlusion in patients with atrial fibrillation undergoing mechanical heart valve replacement. Chinese Medical Journal. 2020; 133: 1891–1899. https://doi.org/10.1097/CM9.0000000000000967

[73] Nasasra AE, Brachmann J, Lewalter T, Akin I, Sievert H, Nienaber CA, et al. Comparison in Patients 75 Years on One-year-Events With Atrial Fibrillation and Left Atrial Appendage Occluder (From the Prospective Multicenter German LAARGE Registry). The American Journal of Cardiology. 2020; 136: 81–86. https://doi.org/10.1016/j.amjcard.2020.09.017

[74] Ashraf M, Allaqaband SQ, Bajwa T, Mortada ME, Sra J, Jan MF. Age-Based Trends in the Outcomes of Percutaneous Left Atrial Appendage Occlusion: Insights from a Real-World Database. The American Journal of Cardiology. 2023; 207: 322–327. https://doi.org/10.1016/j.amjcard.2023.08.177

[75] Shatla I, El-Zein RS, Kennedy K, Elkaryoni A, Ubaid A, Wimmer AP. Comparison of the Safety of Left Atrial Appendage Occlusion in Patients Aged <75 Versus Those Aged ≥75 Years (from a Nationwide Cohort Sample). The American Journal of Cardiology. 2022; 172: 35–39. https://doi.org/10.1016/j.amjcard.2022.02.036

[76] Teiger E, Eschalier R, Amabile N, Rioufol G, Ducrocq G, Garot P, et al. Left atrial appendage closure in very elderly patients in the French National Registry. Heart (British Cardiac Society). 2024; 110: 245–253. https://doi.org/10.1136/heartjnl-2023-322871

[77] Volgman AS, Nair G, Lyubarova R, Merchant FM, Mason P, Curtis AB, et al. Management of Atrial Fibrillation in Patients 75 Years and Older: JACC State-of-the-Art Review. Journal of the American College of Cardiology. 2022; 79: 166–179. https://doi.org/10.1016/j.jacc.2021.10.037

[78] Liu C, Han S, Cui K, Wang F. Efficacy and safety of patients with chronic kidney disease undergoing left atrial appendage closure for atrial fibrillation. PloS One. 2023; 18: e0287928. https://doi.org/10.1371/journal.pone.0287928

[79] Dhar G, Phadnis MA, Hunt SL, Du HE, Ong V, Khandekar N, et al. Left Atrial Appendage Occlusion vs Anticoagulants in Dialysis With Atrial Fibrillation. JAMA Network Open. 2025; 8: e2530990. https://doi.org/10.1001/jamanetworkopen.2025.30990

[80] Flores-Umanzor E, Asghar A, Cepas-Guillén PL, Farrell A, Keshvara R, Alvarez-Rodriguez L, et al. Transcatheter left atrial appendage occlusion in patients with chronic kidney disease: a systematic review and meta-analysis. Clinical Research in Cardiology: Official Journal of the German Cardiac Society. 2024; 113: 1485–1500. https://doi.org/10.1007/s00392-023-02359-1

[81] Lee WC, Chang WT, Shih JY, Wu PJ, Fang CY, Chen HC, et al. Impact of chronic kidney disease on left atrial appendage occlusion: A meta-analysis of procedural outcomes and complications. Medicine. 2024; 103: e38935. https://doi.org/10.1097/MD.0000000000038935

[82] López-Tejero S, Antúnez-Muiños P, Fraile-Gómez P, Sousa GBD, Rodríguez-Collado J, Herrero-Garibi J, et al. Left atrial appendage occlusion in patients suffering from advanced chronic kidney disease (stage 4 and 5). Long-term follow-up. Catheterization and Cardiovascular Interventions: Official Journal of the Society for Cardiac Angiography & Interventions. 2024; 103: 499–510. https://doi.org/10.1002/ccd.30946

[83] Faroux L, Cruz-González I, Arzamendi D, Freixa X, Nombela-Franco L, Peral V, et al. Effect of Glomerular Filtration Rates on Outcomes Following Percutaneous Left Atrial Appendage Closure. The American Journal of Cardiology. 2021; 145: 77–84. https://doi.org/10.1016/j.amjcard.2020.12.081

[84] Saw J, Lempereur M. Percutaneous left atrial appendage closure: procedural techniques and outcomes. JACC. Cardiovascular Interventions. 2014; 7: 1205–1220. https://doi.org/10.1016/j.jcin.2014.05.026

[85] Pracoń R, Zieliński K, Bangalore S, Konka M, Kruk M, Kępka C, et al. Residual stroke risk after left atrial appendage closure in patients with prior oral anticoagulation failure. International Journal of Cardiology. 2022; 354: 17–21. https://doi.org/10.1016/j.ijcard.2022.02.030

[86] Efe TH, Ebrahimi R, Schaack D, Urbanek L, Bordignon S, Schmidt B, et al. Empirical cryoballoon-based left atrial appendage isolation followed by closure, including cases with LAA thrombosis, in patients with persistent atrial fibrillation and durable pulmonary vein isolation: Feasibility and long-term outcomes (CB LAAI + LAAC after durable PVI in persistent AF). Heart Rhythm. 2026; 23: 1120- 1130. https://doi.org/10.1016/j.

hrthm.2025.12.004

[87] Briosa E Gala A, Pope MTB, Monteiro C, Leo M, Dawkins S, Newton JD, et al. Long-term outcomes and periprocedural safety and efficacy of percutaneous left atrial appendage closure in a United Kingdom tertiary center: An 11-year experience. Heart Rhythm. 2021; 18: 1724–1732. https://doi.org/10.1016/j.hrthm.2021.06.1170

[88] Piccini JP, Sievert H, Patel MR. Left atrial appendage occlusion: rationale, evidence, devices, and patient selection. European Heart Journal. 2017; 38: 869–876. https://doi.org/10.1093/eurheartj/ehw330

[89] Turagam MK, Velagapudi P, Kar S, Holmes D, Reddy VY, Refaat MM, et al. Cardiovascular Therapies Targeting Left Atrial Appendage. Journal of the American College of Cardiology. 2018; 72: 448–463. https://doi.org/10.1016/j.jacc.2018.05.048

[90] Baudo M, Sicouri S, Yamashita Y, Senzai M, McCarthy PM, Gerdisch MW, et al. Stroke Prevention With Prophylactic Left Atrial Appendage Occlusion in Cardiac Surgery Patients Without Atrial Fibrillation: A Meta-Analysis of Randomized and Propensity-Score Studies. Circulation: Cardiovascular Interventions. 2024; 17: e014296. https://doi.org/10.1161/CIRCINTERVENTIONS.124.014296

[91] Dong A, Lee G, Krishna V, Whitlock R, Kiankhooy A, Bowdish M, et al. Reconstructed Patient-Level Meta-analysis of Prophylactic Left Atrial Appendage Closure During Cardiac Surgery. The Canadian Journal of Cardiology. 2025; S0828–282X(25)01568–5. https://doi.org/10.1016/j.cjca.2025.12.008 (Online ahead of print)

[92] Melduni RM, Schaff HV, Lee HC, Gersh BJ, Noseworthy PA, Bailey KR, et al. Impact of Left Atrial Appendage Closure During Cardiac Surgery on the Occurrence of Early Postoperative Atrial Fibrillation, Stroke, and Mortality: A Propensity Score-Matched Analysis of 10 633 Patients. Circulation. 2017; 135: 366–378. https://doi.org/10.1161/CIRCULATIONAHA.116.021952

[93] Noona SWW, Young SD, Weber MP, El Moheb M, Norman AV, Wisniewski AM, et al. Prophylactic left atrial appendage ligation during coronary artery bypass grafting: A propensity score-matched analysis. The Journal of Thoracic and Cardiovascular Surgery. 2025; 170: 207–215. https://doi.org/10.1016/j.jtcvs.2024.08.004

[94] Yao X, Gersh BJ, Holmes DR, Jr, Melduni RM, Johnsrud DO, Sangaralingham LR, et al. Association of Surgical Left Atrial Appendage Occlusion With Subsequent Stroke and Mortality Among Patients Undergoing Cardiac Surgery. JAMA. 2018; 319: 2116–2126. https://doi.org/10.1001/jama.2018.6024

[95] Whitlock RP, McCarthy PM, Gerdisch MW, Ramlawi B, Alexander JH, Sultan I, et al. The left atrial appendage exclusion for prophylactic stroke reduction (LEAAPS) trial: Rationale and design. American Heart Journal. 2025; 284: 94–102. https://doi.org/10.1016/j.ahj.2024.10.006