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Review

Prophylactic Left Atrial Appendage Exclusion During Open Heart Surgery: Focus on Marfan Patients

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Abstract

The left atrial appendage (LAA) is a dynamic atrial structure with both physiological and thromboembolic significance. While the endocrine and reservoir functions of the LAA support cardiovascular homeostasis, the LAA becomes the predominant source of thrombus formation in atrial fibrillation (AF). Approximately 90% of left atrial thrombi in patients with nonvalvular atrial fibrillation are located within the left atrial appendage (LAA), making it the predominant anatomical site of thrombus formation in this population. Systemic anticoagulation remains the cornerstone of stroke prevention; however, limitations such as bleeding risk, contraindications, and suboptimal long-term adherence have prompted the development of mechanical LAA exclusion strategies. LAA exclusion can be achieved through different approaches, including surgical epicardial exclusion using external clipping devices, such as the AtriClip (AtriCure), or percutaneous transcatheter occlusion using endocardial devices, such as the WATCHMAN and Amulet systems. These techniques aim to eliminate the LAA as a potential source of thrombus formation and subsequent thromboembolism. Transcatheter LAA occlusion (LAAO) has demonstrated efficacy in stroke prevention for patients with AF who cannot tolerate anticoagulation, achieving high procedural success and favorable long-term outcomes. However, the role of prophylactic surgical LAA exclusion during open-heart surgery in patients with sinus rhythm remains debated in the general population. Indeed, while some advocate a selective, patient-centered approach, routine exclusion is not universally recommended due to uncertain long-term benefits in patients without pre-existing AF. In younger populations, such as those with Marfan syndrome, prophylactic LAA exclusion is a compelling adjunctive strategy to consider. These patients often undergo early mitral valve repair or aortic valve-sparing procedures, thereby avoiding long-term anticoagulation. Nonetheless, these patients remain at increased lifetime risk for AF due to intrinsic connective tissue abnormalities, profound atrial remodeling driven by mitral annular disjunction (MAD), and residual or recurrent valvular regurgitation. Concomitant surgical LAA exclusion adds minimal operative time, ensures durable closure, and avoids the risks of transcatheter approaches in fragile, complex tissues. Nevertheless, while highly promising for reducing future thromboembolic risk, prospective studies are required before routine adoption. This review aims to examine the potential rationale, available clinical evidence, surgical considerations, and limitations of prophylactic surgical LAA exclusion in patients with Marfan syndrome undergoing open-heart surgery while in sinus rhythm, with particular attention to their lifetime risk of atrial fibrillation and thromboembolism.

Keywords: left atrial appendage; prophylactic exclusion; Marfan syndrome; atrial fibrillation; stroke prevention; transcatheter LAAO; mitral valve repair; mitral annular disjunction

1. Introduction

Prophylactic surgical exclusion of the left atrial appendage (LAA) during open heart surgery has attracted growing attention as a potential strategy to reduce future thromboembolic risk in selected patients who are predisposed to atrial arrhythmias [1,2]. While current evidence and clinical practice have largely focused on patients with established atrial fibrillation (AF), the role of LAA exclusion in individuals in sinus rhythm (SR) at the time of surgery remains less clearly defined [3]. This question is especially relevant in subgroups with unique clinical trajectories, such as patients with Marfan syndrome. Patients with Marfan syndrome constitute a unique subgroup within contemporary cardiac surgical practice. Because of the progressive cardiovascular manifestations of their connective tissue disorder, many patients undergo elective surgery at a relatively young age, most commonly for aortic root aneurysm and degenerative myxomatous mitral valve disease [4]. Contemporary management increasingly favors valve-preserving strategies, including aortic valve-sparing root replacement and mitral valve repair [5,6,7]. Preservation of the native valves avoids prosthesis-related complications and usually eliminates the need for lifelong anticoagulation required after mechanical valve replacement.

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Although this strategy minimizes bleeding risk and improves quality of life, it also leaves patients without continuous pharmacological protection should atrial fibrillation develop later in life. Patients with Marfan syndrome undergoing valve-sparing or reparative procedures are typically managed without chronic antithrombotic therapy, making the potential development of AF clinically significant due to the absence of baseline protection. Recent observational cohort studies have demonstrated that atrial arrhythmias occur in approximately 16% of individuals with Marfan syndrome, with atrial fibrillation accounting for approximately 94% of these cases [8,9]. A similar, and possibly greater, predisposition has been reported in related heritable thoracic aortopathies (HTAD) such as Loeys-Dietz syndrome (LDS), where recent cohort data identify an alarming 31.9% prevalence of atrial arrhythmias (with 28.7% presenting explicitly with AF) [10]. These studies suggest that Marfan syndrome is associated with a clinical lifetime susceptibility to atrial arrhythmias rather than representing an incidental finding confined to advanced valvular disease. The increased arrhythmic burden has been linked to progressive atrial remodeling, mitral annular disjunction, and underlying connective tissue abnormalities, supporting the concept that Marfan syndrome represents a lifelong arrhythmogenic substrate. Among the structural abnormalities implicated in this process, mitral annular disjunction (MAD) has attracted particular attention. Initially described in association with mitral valve prolapse, MAD is increasingly recognized as a marker of myocardial remodeling and electrical instability that may facilitate the development of atrial fibrillation. This clinical profile differs from that of the general mitral valve surgical population, in whom preexisting atrial fibrillation is present in approximately 30–50% of patients at the time of surgery, reflecting advanced atrial remodeling secondary to longstanding mitral regurgitation [8,11,12]. By contrast, patients with Marfan syndrome frequently undergo valve repair at a substantially younger age, often before permanent atrial fibrillation has developed. Structural atrial remodeling, including dilation and altered tissue properties related to the underlying connective tissue disorder, may predispose to arrhythmogenesis, further influenced by prior surgical interventions [13]. Emerging evidence indicates that atrial remodeling in Marfan syndrome is not solely a consequence of chronic mitral regurgitation or atrial dilatation. Abnormal fibrillin-1 architecture, dysregulated transforming growth factor-β signaling, and progressive myocardial fibrosis contribute to an intrinsic arrhythmogenic substrate that increases susceptibility to atrial fibrillation independently of mechanical valvular disease. These disease-specific alterations may be further influenced by prior surgical interventions and progressive atrial remodeling over time. Given their long life expectancy after successful repair, the cumulative lifetime risk of AF remains non-negligible, even in patients not classified as high risk at the time of surgery. This raises the question of whether prophylactic LAA exclusion at the time of index surgery could provide additional long-term protection against thromboembolic events in patients with Marfan syndrome in SR. Although the intraoperative setting allows LAA management with minimal added burden, the balance between potential benefit, the physiological role of the LAA, and the durability of exclusion techniques must be carefully considered. This decision is further influenced by the young age of patients with Marfan syndrome and the predominance of reparative strategies, and the absence of routine anticoagulation, and lifestyle, which increases the relative importance of mechanical stroke prevention should AF develop later [14,15,16,17]. Despite these considerations, robust data specifically addressing prophylactic LAA exclusion in patients with Marfan syndrome in SR are lacking. Most evidence derives from broader surgical populations or patients with established AF, limiting definitive conclusions [3]. At present, clinical decision-making largely depends on individual surgeon preference because, evidence remains limited. In this context, a focused evaluation of prophylactic surgical LAA exclusion in patients with Marfan syndrome undergoing open heart surgery is warranted, with attention to patient age, valve repair strategy, absence of anticoagulation, long-term outcomes, and AF risk to support individualized decision-making [18]. Taken together, these considerations provide the rationale for evaluating prophylactic surgical LAA exclusion as a selective adjunct during open heart surgery in carefully chosen patients with Marfan syndrome.

2. The Left Atrial Appendage: Functional Role, Anatomical Complexity, and Implications for Thromboembolic Risk and Anticoagulation

The LAA represents a structurally and functionally distinct component of the left atrium, with biological and clinical functions that extend well beyond its relatively small anatomical size [15]. Although often regarded as a target for exclusion in thromboembolic prevention, the LAA embodies a complex interplay between physiology, anatomy, and pathophysiology essential to understanding both its benefits and risks. The LAA contributes to left atrial dynamics under hemodynamic stress, helping to accommodate changes in left atrial pressure and thereby supporting ventricular filling [19]. Beyond its mechanical function, the LAA serves as an endocrine organ, containing a high density of atrial natriuretic peptide (ANP)–secreting cells. Surgical LAA exclusion is associated with a transient postoperative reduction in circulating ANP levels; endocrine compensation by the remaining atrial myocardium generally restores hormone concentrations within a few months, and persistent clinically relevant neurohormonal impairment has not been demonstrated [17,20]. Despite these physiological roles, the LAA is uniquely predisposed to thrombus formation, largely due to its anatomical charac-

teristics. Unlike the smooth-walled left atrium, the LAA wall consists of pectinate muscles that create a highly trabeculated surface. This increases surface area and generates recesses where blood flow may become sluggish [21]. The geometry of the appendage, including orifice size, length, curvature, and number of lobes, further influences local hemodynamics. Morphological variability is considerable and correlates with thromboembolic risk. Complex multilobed or short, irregular configurations are associated with reduced flow velocities and increased stasis, whereas more streamlined morphologies support more efficient emptying [21,22]. These differences have direct clinical implications, influencing both thrombus formation and feasibility of transcatheter mechanical exclusion. At the interface between structure and function lies LAA flow dynamics. Under normal conditions, coordinated atrial contraction maintains effective blood flow and appendage washout. Reduced emptying velocities, spontaneous echo contrast, and localized stasis represent key steps in thrombogenesis and may occur not only in overt atrial fibrillation but also in subclinical dysfunction [23]. The propensity of the LAA to act as a nidus for thrombus formation must be considered within patient-specific risk factors [24]. Thromboembolism is multifactorial, involving stasis, endothelial dysfunction, and hypercoagulability. Conditions such as hypertension, diabetes, heart failure, and vascular disease contribute to this milieu, while age remains a major determinant of risk. Risk stratification tools such as CHA_2DS_2-VASc score integrate clinical variables to estimate thromboembolic risk but do not incorporate anatomical or functional LAA characteristics [24,25]. This creates a disconnect between structural thrombogenic substrate and routine clinical assessment, highlighting the need for a more comprehensive approach, especially in the young population. This limitation may be particularly relevant in Marfan syndrome, where inherited structural remodeling and lifelong arrhythmogenic susceptibility are not adequately captured by conventional clinical risk scores. In Marfan syndrome, these considerations are further influenced by the underlying connective tissue disorder. Pathogenic variants affecting fibrillin-1 and dysregulated transforming growth factor-β signaling promote progressive extracellular matrix remodeling, myocardial fibrosis, atrial dilatation, and impaired atrial mechanical function. Together with mitral valve prolapse, mitral annular disjunction (MAD), and chronic mitral regurgitation, these abnormalities create a disease-specific arrhythmogenic substrate characterized by progressive fibrosis, electrical heterogeneity, and atrial remodeling that may precede clinically overt atrial fibrillation. Consequently, the thromboembolic significance of the LAA in patients with Marfan syndrome may extend beyond conventional clinical risk factors, supporting consideration of individualized preventive strategies during cardiac surgery. Systemic anticoagulation remains the primary strategy for risk reduction by targeting the coagulation cascade. Direct oral anticoagulants have improved safety profiles compared with vitamin K antagonists [26,27]. However, anticoagulation is limited by bleeding risk, patient-specific factors, and the need for long-term adherence. Drug interactions and variability in response further contribute to suboptimal protection, particularly in real-world settings [28,29]. It does not modify appendage anatomy and may be limited by bleeding risk, adherence, and long-term treatment burden. These considerations may be particularly relevant in younger patients with long projected treatment duration.

3. Open Heart Surgery in Marfan Syndrome: Aortic and Mitral Valve Interventions

Marfan syndrome is a heritable connective tissue disorder characterized by progressive cardiovascular involvement, most notably affecting the aortic root and cardiac valves [30,31]. Compared with the general population, patients with Marfan syndrome undergo complex cardiovascular procedures at a younger age, because of the natural history rather than age-related degenerative pathology. A defining feature of Marfan syndrome (MFS) is progressive dilation of the aortic root due to structural weakness of the medial aortic wall, predisposing patients to aneurysm formation, dissection, and rupture [32]. Prophylactic aortic root replacement is standard once diameter thresholds or growth rates are reached. In contemporary practice, patients with Marfan syndrome typically undergo elective aortic or mitral valve surgery in their mid-20s to mid-30s, decades earlier than individuals with degenerative aortic or mitral disease [5,13]. Early elective intervention is associated with excellent long-term survival and reduced incidence of acute aortic syndromes. Aortic root replacement is the most common procedure, with two principal strategies: composite graft replacement with a prosthetic valve and valve-sparing root replacement [5,11]. Valve-sparing techniques, such as reimplantation or remodeling, are attractive in younger patients as they preserve the native valve and avoid lifelong anticoagulation. Valvular disease beyond the aortic valve is also common. Mitral valve prolapse, often associated with leaflet redundancy and chordal elongation, may progress to severe regurgitation. Mitral surgery, repair or replacement, can be performed concomitantly with aortic procedures or separately. Repair is preferred to preserve valve function and avoid prosthesis-related complications, but structural features in patients with Marfan syndrome may make repair technically challenging [6,13]. Surgical planning often considers not only immediate pathology but also potential future disease progression. Younger age at surgery contributes to favorable recovery and long-term survival, although it implies a longer period of follow-up and exposure to late complications. Valve-sparing aortic root replacement and mitral valve repair have become key components of contemporary management, optimizing outcomes over a prolonged lifespan. However, recurrence of

valve regurgitation might occur particularly in complex repairs, with increased risks to developing AF.

4. Postoperative Atrial Fibrillation: Immediate and Long-Term Incidence

Postoperative atrial fibrillation (POAF) is the most frequent arrhythmic complication following cardiac surgery, representing a spectrum of atrial electrical instability ranging from brief, self-limiting episodes to persistent arrhythmias with significant clinical implications [33]. Understanding its timing, mechanisms, and long-term consequences is essential for optimizing perioperative management and informing prophylactic strategies such as LAA exclusion. POAF typically occurs within the first four postoperative days. Observational studies report that 20–50% of patients without prior AF develop new-onset POAF, with incidence varying by procedure: approximately 20–25% after isolated coronary artery bypass grafting (CABG) and up to 30–50% following valve or combined procedures [34]. The pathophysiology of early POAF is multifactorial. Cardiopulmonary bypass induces systemic inflammation, cytokine release, and oxidative stress, altering atrial electrophysiology [35]. In parallel, atrial stretch due to fluid shifts and transient pressure overload promotes electrical heterogeneity. Autonomic imbalance and perioperative electrolyte disturbances further contribute to triggered activity and re-entry mechanisms. Although often self-limiting, POAF is not benign. Even transient episodes may lead to hemodynamic instability, thromboembolic events, and prolonged hospitalization. Pharmacologic prophylaxis, most commonly beta-blockers, amiodarone, or magnesium, can reduce incidence, particularly in high-risk patients, although tolerability and side effects must be considered. Several factors influence POAF development. Advanced age remains the strongest predictor. Structural atrial abnormalities, including enlargement, impaired function, and fibrosis, increase susceptibility, as do more complex procedures such as valve surgery [35]. Elevated inflammatory markers and genetic predisposition may further contribute. Additional modifiers include obesity, chronic lung disease, and prolonged cardiopulmonary bypass time. Despite recognition of these factors, preventive strategies remain only partially effective. POAF has important short- and long-term consequences. Acute episodes may compromise hemodynamics and increase thromboembolic risk, while also prolonging intensive care and hospital stay [33,36]. POAF strongly predicts the subsequent development of recurrent or permanent atrial fibrillation. Long-term studies indicate that 20–30% of patients with early POAF develop recurrent or persistent AF years after surgery [36]. This progression reflects ongoing atrial remodeling, fibrosis, and scarring. Residual or recurrent valvular dysfunction may further increase atrial pressure and wall stress, while aging and comorbidities such as hypertension, diabetes, and heart failure contribute to continued structural and electrical remodeling. MAD is increasingly recognized as an important contributor to structural remodeling and arrhythmogenesis in Marfan syndrome, which carries a documented prevalence of 34% in MFS cohorts [37]. Extensive MAD is independently associated with severe arrhythmic events and an increased requirement for mitral surgery. Similarly, in LDS cohorts, MAD (11.7%) and mitral valve prolapse (35.1%) demonstrate a multi-fold positive association with advanced arrhythmias ($p < 0.001$). This confirms that a genetically driven atrial cardiomyopathy frequently precedes overt clinical AF, beginning as early as childhood, where MAD has been strongly linked to heightened ventricular arrhythmic burdens, suggesting a potential pathomechanistic rationale for early mechanical intervention [10]. Mitral annular disjunction (MAD) has been increasingly recognized as a structural abnormality associated with ventricular arrhythmias, particularly in patients with Marfan syndrome [35,38]. In Marfan syndrome cohorts, MAD has been reported in 34%–62% of patients [35]. Similarly, in Loeys-Dietz syndrome (LDS), MAD (11.7%) and mitral valve prolapse (35.1%) have been associated with an increased burden of ventricular arrhythmias [9]. However, current evidence does not establish a direct association between MAD and atrial arrhythmias or atrial fibrillation (AF). Although mitral valve and annular abnormalities may warrant further investigation in the context of cardiac remodeling, a direct mechanistic link between MAD, atrial fibrosis, atrial remodeling, and AF remains unproven. Therefore, the established association between MAD and ventricular arrhythmias should be distinguished from any potential relationship with AF, which remains speculative. Beyond these macro-structural parameters, this anatomy introduces a powerful mechanical driver of arrhythmogenesis. MAD alters the physiological, systolic D-shaped dynamics of the mitral apparatus, causing an abnormal atrial displacement of the posterior leaflet hinge point away from the basal ventricular myocardium [39,40]. This systolic separation induces chronic, paradoxical hypermobility of the annulus, subjecting both the valvular leaflets and the adjacent left atrial wall to excessive mechanical stress. Over time, this localized stretch acts as a trigger for both profound tissue fibrosis and severe electrical disorganization directly correlating with clinical ectopy and sustained tachyarrhythmias in Marfan cohorts [41]. Recent clinical evidence demonstrates that even after a successful surgical procedure (mitral valve repair or replacement) that effectively achieves complete anatomical correction of the disjunction, a high burden of tachyarrhythmias persists postoperatively. This indicates that the chronic mechanical stress inflicts permanent, irreversible fibrotic remodeling within the tissue substrate that continues to function as an active electrical nidus long after the structural mechanism of MAD has been eliminated. Consequently, long-term AF

carries a thromboembolic risk comparable to non-surgical AF. It must be emphasized that current evidence does not definitively demonstrate that an elevated arrhythmic risk profile alone mandates prophylactic LAA exclusion in sinus rhythm; rather, these observations support hypothesis generation and argue for a highly individualized, patient-centered surgical strategy. In younger populations, such as patients with Marfan syndrome, AF may manifest years after surgery, underscoring the importance of early risk stratification and preventive strategies.

The association between POAF and future AF raises the hypothesis that selected patients may benefit from preventive strategies, although direct evidence supporting prophylactic LAA exclusion remains limited. This is particularly relevant in patients with Marfan syndrome undergoing valve-sparing or reparative procedures, where long life expectancy, absence of routine anticoagulation, and progressive atrial remodeling increase lifetime thromboembolic risk [11]. Surgical exclusion of the LAA may represent a one-time intervention deserving further prospective evaluation in carefully selected populations [17].

5. Transcatheter Left Atrial Appendage Occlusion: Benefits and Limitations

Transcatheter LAA occlusion (LAAO) has emerged as an established alternative for stroke prevention in carefully selected patients with AF who are unsuitable for long-term oral anticoagulation [42,43]. Advances in device technology and imaging have improved procedural success and expanded anatomical applicability. LAAO provides mechanical exclusion of the appendage, reducing thromboembolic risk without the need for lifelong systemic anticoagulation. Clinical studies demonstrate stroke prevention comparable to vitamin K antagonists, with lower rates of hemorrhagic stroke, particularly among patients at increased bleeding risk [44,45]. Despite these advances, several important limitations remain. Early procedural complications include pericardial effusion and, rarely, device embolization. Late complications such as device-related thrombus, in particular if complete device endothelialization has not occurred, and peri-device leaks may necessitate ongoing antithrombotic therapy and continued surveillance. Current guidelines therefore recommend LAAO primarily in AF patients with high thromboembolic risk and contraindications to anticoagulation [27]. Its role in patients without AF, including those undergoing cardiac surgery, has not yet been established. Recent randomized trials have further clarified the role of transcatheter LAAO. The CHAMPION-AF trial reported noninferiority of percutaneous LAAO compared with non-vitamin K antagonist oral anticoagulant (NOAC) therapy for a composite endpoint of cardiovascular death, stroke, or systemic embolism and superiority to the NOACs group at 3 years follow-up, after exclusion of procedure-related complications [43]. However, ischemic events were numerically higher in the device group, and the overall reduction in bleeding became less pronounced when early procedural complications were included in the analysis. In contrast, the CLOSURE-AF trial did not demonstrate noninferiority compared with medical therapy, suggesting that the clinical benefit of transcatheter LAAO depends heavily on patient selection and procedural risk [46]. Additional concerns, including device-related thrombosis, residual leaks, the need for ongoing antiplatelet therapy, and potential long-term effects on cardiac function, continue to limit broad adoption. In younger populations such as patients with Marfan syndrome, the long-term applicability of transcatheter LAAO remains insufficiently studied and should not be directly extrapolated from older AF cohorts. In the CHAMPION-AF trial, which enrolled 3000 patients with non-valvular atrial fibrillation who were eligible for anticoagulation (mean age 71.7 ± 7.5 years; mean CHA_2DS_2-VASc score 3.5 ± 1.3), LAAO demonstrated noninferiority to NOAC therapy for the primary efficacy endpoint, comprising cardiovascular death, stroke, or systemic embolism [43]. Importantly, LAAO demonstrated superiority for the primary safety endpoint of non-procedure-related bleeding, with a significantly lower incidence compared with NOAC therapy. These findings support LAAO as an alternative to long-term anticoagulation in appropriately selected patients, but do not establish its superiority for thromboembolic protection. By contrast, the CLOSURE-AF trial enrolled an older population at particularly high thromboembolic and bleeding risk (mean age 77.9 ± 7.1 years; mean CHA_2DS_2-VASc score 5.2 ± 1.5; mean HAS-BLED score 3.0 ± 0.9). In this population, LAAO failed to demonstrate noninferiority to physician-directed best medical therapy for the primary composite endpoint of stroke, systemic embolism, major bleeding, or cardiovascular or unexplained death. The numerical difference in primary endpoint events favored medical therapy (16.8 versus 13.3 events per 100 patient-years). These findings should be interpreted in the context of the substantial baseline risk and clinical complexity of the enrolled population, while recognizing that they do not invalidate the findings of other randomized trials conducted in different patient populations and against different comparators. Although transcatheter LAAO is designed to mechanically exclude the left atrial appendage, the primary source of thrombus formation in atrial fibrillation, this strategy does not eliminate all thromboembolic risk. Approximately 90% of thrombi in patients with non-valvular atrial fibrillation are attributed to the LAA; however, a non-negligible proportion of thromboembolic events originates from other cardiac or vascular sources. In the CLOSURE-AF trial, the observed increase in ischemic events in the device group should therefore be interpreted in the context of the high baseline thromboembolic risk of the enrolled population, as reflected by elevated CHA_2DS_2-VASc scores [46]. In such patients, residual risk related to systemic atherosclerosis, atrial cardiomyopathy, or non-LAA thrombus forma-

tion may contribute to embolic events despite successful appendage exclusion [47]. These findings highlight that residual thromboembolic risk may persist despite successful appendage exclusion.

In this context, the role of LAA exclusion differs in surgical patients. When performed concomitantly during open heart surgery, LAA exclusion can be achieved with minimal incremental surgical risk and without device-related limitations, potentially providing durable protection without the long-term limitations associated with transcatheter devices [3].

6. Surgical Techniques for Left Atrial Appendage Exclusion

Over the past two decades, surgical techniques for LAA exclusion have evolved considerably, resulting in several operative approaches that differ in technical complexity, reproducibility, and long-term durability [48,49]. Selection of the most appropriate technique depends on appendage anatomy, surgical exposure, and surgeon experience rather than on a universally accepted standard. Although all techniques aim at elimination of the LAA cavity, they differ substantially in completeness, reproducibility, and durability. Complete surgical excision remains the reference technique for LAA exclusion [50]. The appendage is completely resected, and the atrial wall is closed with a double-layer polypropylene suture, thereby removing rather than simply isolating the trabeculated appendage [2]. Successful excision requires meticulous dissection at the base of the appendage, with attention to adjacent structures such as the circumflex coronary artery and pulmonary veins. When performed correctly, excision achieves a high rate of complete closure and avoids residual stump formation. However, it is more technically demanding than other techniques and may increase operative time. In minimally invasive settings, excision can be challenging due to limited exposure, which has contributed to the growing use of alternative methods. External ligation involves encircling the base of the LAA from the epicardial surface using a purse-string or running suture. The simplicity and speed of this technique make it attractive, particularly in cases where cardiopulmonary bypass is not employed or where atriotomy is avoided. It must be emphasized that procedural success relies strictly on precise placement and adequate tightening of the suture line. Over time, tissue remodeling or suture loosening may lead to recanalization [51]. As a result, external ligation has been associated with significant variability in outcomes and a relatively high incidence of incomplete exclusion. An alternative suture-based approach is internal closure of the LAA orifice. This technique is performed from within the left atrium, typically during procedures that already require atriotomy. Direct visualization of the LAA ostium allows for precise placement of sutures, which may be applied in a running or interrupted fashion to obliterate the LAA orifice [52]. While this method avoids manipulation of the epicardial surface, it does not remove the appendage itself. Residual cavities may therefore persist if the closure is incomplete or if late suture dehiscence occurs. The effectiveness of internal suturing depends on achieving a watertight seal across a frequently irregular orifice. In larger appendages, multiple layers of sutures or reinforcement may be required. Although technically straightforward in open procedures, especially when performed in minithoracotomy, this method shares the limitation of potential residual spaces and variable long-term durability. Stapled exclusion combines appendage resection and closure in a single maneuver using a surgical stapling device [53]. This technique offers the advantage of speed and consistent mechanical application, reducing reliance on manual suturing. It can be particularly useful in minimally invasive or thoracoscopic approaches. However, the success of stapler exclusion depends on proper alignment of the device and complete capture of the appendage base. Irregular anatomy or thick tissue may prevent uniform compression, leading to incomplete sealing or the formation of a residual stump. Additionally, staple line bleeding or leaks may occur, particularly if tissue thickness exceeds the optimal range for the device. While staplers provide a reproducible option, their effectiveness may be limited in anatomically complex cases. Epicardial clip systems have become one of the most widely adopted methods of surgical LAA exclusion [53]. These devices are applied externally at the base of the appendage, using a preformed clip that exerts uniform pressure to occlude the lumen. The procedure is typically performed under direct visualization and may be guided by intraoperative imaging to confirm positioning. Clip application does not require atriotomy and can be integrated into both open and minimally invasive procedures. The design of the clip allows it to conform to the base of the LAA, accommodating variations in size and shape. Once released, the clip remains in place, providing continuous mechanical closure without reliance on tissue healing or fibrosis. Because manipulation of the atrial wall is limited, bleeding risk may also be reduced. Clinical series consistently report high rates of complete exclusion with minimal residual stump formation when the device is correctly positioned. Despite excellent procedural results, several limitations deserve consideration. Successful deployment requires adequate exposure of the appendage, which may be difficult in patients with dense adhesions or during selected minimally invasive procedures. Improper positioning can result in incomplete closure, particularly if the clip is placed too distally, leaving a residual stump. Device cost is also a consideration, especially in resource-limited settings. Furthermore, while short- and mid-term outcomes are favorable, long-term durability continues to be evaluated. Regardless of the selected technique, anatomical variability remains the principal determinant of procedural success. The appendage can differ markedly in size, orientation, and number of lobes, resulting in substan-

tial heterogeneity in closure feasibility and effectiveness across techniques. Given the significant variability in LAA anatomy, including size, orientation, and number of lobes, ensuring complete and durable closure is paramount [54]. To achieve this, intraoperative imaging modalities such as transesophageal echocardiography or intracardiac echocardiography should be routinely employed to confirm complete exclusion before completing the procedure. Postoperative imaging follow-up with transesophageal echocardiography or computed tomography (CT) scans is also recommended to detect residual leaks or recanalization, particularly in high-risk populations. Techniques that depend heavily on precise anatomical closure, such as suturing or stapling, may be more susceptible to incomplete exclusion in complex morphologies. Conversely, approaches that involve resection of the entire appendage or application of external clips tend to provide more consistent and reliable results across diverse anatomical presentations. The clinical reality behind the historical 'lack of good procedures' stems primarily from the high prevalence of incomplete surgical closure, which ranges from 23% to 80% depending on the chosen modality [55,56,57]. Standard endocardial suturing and external purse-string ligation frequently led to late recanalization or residual stump formation. Modern imaging studies have demonstrated that even a small residual communication allows persistent blood flow into the remaining pouch, creating a stagnant environment with substantial thrombogenic potential. Incomplete closure has been associated with an approximately 1.8-fold increase in thromboembolic events compared with complete exclusion [58]. Therefore, modern surgical exclusion can no longer rely on simple blind techniques; it must prioritize highly reproducible mechanical approaches, such as complete anatomical excision or the deployment of specialized epicardial clip devices, which have demonstrated high rates of durable complete closure with minimal residual flow [59]. In summary, surgical techniques for LAA exclusion range from traditional suture-based methods to modern device-assisted approaches. Excision remains the most definitive technique, providing complete removal of the appendage but requiring advanced surgical skill. Suture ligation and internal closure offer simplicity but are limited by variability in completeness and durability. Stapler devices provide a rapid and standardized option, though their effectiveness may be influenced by anatomical factors. Epicardial clips represent a contemporary solution that combines high efficacy with technical ease and are increasingly favored in a variety of surgical settings. The choice of technique ultimately depends on anatomical considerations, surgical access, and operator experience, with no single method universally applicable to all cases. Whenever feasible, intraoperative imaging confirmation should be considered an integral component of the procedure, as technical success depends not only on the chosen technique but also on verification of complete appendage exclusion.

7. Prophylactic Surgical Left Atrial Appendage Exclusion in Patients in Sinus Rhythm

The role of prophylactic surgical exclusion of the LAA during open heart surgery in patients who are in sinus rhythm (SR) remains an area of ongoing debate [1,2,52]. While the LAA is widely recognized as a key anatomical structure implicated in thromboembolism under conditions of atrial dysfunction, its management in patients without documented atrial arrhythmias is less clearly defined. Increasingly, however, the concept of preventive LAA exclusion during cardiac surgery has gained attention, driven by the recognition that postoperative and late atrial fibrillation are common, and that stroke risk may evolve over time even in patients initially in SR [52,60]. LAA exclusion during open heart procedures is technically feasible and typically associated with minimal incremental operative time, particularly when performed with epicardial clipping devices or direct excision. Because the chest is already open and the appendage accessible, the threshold for intervention is lower than in standalone procedures. This has led some surgeons to adopt a more proactive approach, incorporating LAA exclusion as a routine adjunct even in the absence of preoperative atrial fibrillation. One of the principal arguments supporting prophylactic LAA exclusion in SR patients relates to the high incidence of postoperative atrial fibrillation following cardiac surgery [35,36,38]. Transient atrial arrhythmias occur frequently in the early postoperative period, and while they may resolve, they are associated with an increased risk of thromboembolic events. Moreover, a significant proportion of patients who are in SR at the time of surgery will develop atrial fibrillation later in life, particularly in the context of structural heart disease, advancing age, or atrial remodeling. Prophylactic exclusion of the LAA may be viewed as a preemptive strategy that mitigates future embolic risk without requiring additional anticoagulation therapy or interventions. Another consideration is the difficulty in consistently maintaining long-term anticoagulation in all patients who may later develop atrial fibrillation. Bleeding complications, treatment adherence, drug interactions, and evolving comorbidities frequently limit the long-term effectiveness of pharmacological stroke prevention [29,61,62,63]. Complete surgical exclusion of the LAA offers a mechanical solution that is independent of patient compliance and may provide durable protection against appendage-related thrombus formation. This concept has contributed to growing interest in performing LAA exclusion at the time of index surgery, when the opportunity is readily available. However, the rationale for prophylactic LAA exclusion in SR patients is not without important counterarguments. First, the LAA is not merely a passive structure but has physiological roles, including contributing to atrial compliance and acting as a reservoir during left atrial filling [2]. It is also a source of atrial natriuretic peptides, which play a role in volume

and pressure regulation. While the clinical significance of these functions is not fully established, their theoretical importance raises questions about the long-term consequences of routine removal or occlusion in patients without a clear indication. Although the LAA contributes to atrial compliance and endocrine regulation, current clinical evidence has not demonstrated clinically significant long-term impairment of cardiac performance or neurohormonal homeostasis following complete surgical LAA exclusion. Nevertheless, these physiological considerations should be balanced against the potential lifelong reduction in thromboembolic risk, particularly in carefully selected young patients. Second, the actual risk of thromboembolism in patients who remain in SR after surgery is relatively low, and the absolute benefit of prophylactic LAA exclusion in this population remains uncertain. Unlike patients with established atrial fibrillation, in whom the LAA is a well-documented source of thrombus formation, the contribution of the appendage to stroke risk in SR is less clearly defined. As a result, the balance between potential benefit and procedural intervention becomes less straightforward. The success of prophylactic LAA exclusion also depends on achieving complete and durable closure. Multiple surgical series have demonstrated that incomplete exclusion remains relatively common with conventional suture-based techniques [50,51]. Residual stumps or incomplete exclusion may paradoxically increase the risk of thrombus formation by creating areas of flow stagnation. Therefore, if prophylactic exclusion is to be performed, it is critical that the chosen technique achieves a high rate of complete and durable closure. In this regard, methods such as excision or the use of epicardial clip devices are generally preferred over simpler ligation techniques. Another key limitation is the lack of robust randomized data evaluating prophylactic LAA exclusion specifically in patients in sinus rhythm. Much of the existing evidence regarding the benefits of surgical LAA management derives from populations with atrial fibrillation, where the indication is clearer. Observational studies have suggested a potential reduction in stroke risk with concomitant LAA exclusion during cardiac surgery, but these analyses are often limited by selection bias and heterogeneity in surgical technique and patient populations. Furthermore, the long-term durability of LAA exclusion is a critical factor in determining its prophylactic value. Even in technically successful procedures, late recanalization may occur, potentially diminishing the protective effect over time. This underscores the importance of technique selection and intraoperative verification of closure, as well as the need for standardized postoperative imaging protocols in research settings. Despite these limitations, there is a growing trend toward more liberal use of prophylactic LAA exclusion during cardiac surgery and in experienced hands, the incremental morbidity associated with LAA exclusion is low, making it an attractive adjunct in selected patients. However, the evolving landscape of transcatheter LAA occlusion provides an alternative pathway for patients who later develop indications for appendage management [33,64]. This raises the question of whether it is preferable to defer intervention until it is clearly indicated, rather than performing prophylactic exclusion in all patients. Rather than supporting either routine or selective exclusion for all patients, the available evidence favors an individualized strategy based on patient-specific characteristics [1,2,3,18,65]. To optimize clinical decision-making in the setting of heritable thoracic aortopathies and connective tissue disorders, a nuanced risk-benefit assessment must account for the specific underlying genetic mutation and its associated mechanical tissue properties. While mechanical exclusion of the left atrial appendage provides robust protection against future thromboembolism, the feasibility, technical approach, and procedural safety profile vary significantly across different syndromes. Table 1 (Ref. [4,5,8,10,11,18,30,31,37,48,49,50,53,60,65]) outlines the comparative primary tissue characteristics, arrhythmic phenotypes, MAD, and surgical feasibility profiles for patients with Marfan syndrome, Loeys-Dietz syndrome, and Vascular Ehlers-Danlos syndrome, highlighting the necessity of a tailored, patient-centered strategy. Patients with Marfan syndrome may represent one of the clinical scenarios in which the balance between long-term benefit and procedural risk is particularly favorable. Unlike the general cardiac surgical population, these patients undergo surgery decades earlier and frequently receive valve-preserving or reparative procedures that avoid lifelong anticoagulation. Although this strategy reduces bleeding risk and improves quality of life, it also leaves patients without continuous pharmacological protection should atrial fibrillation develop later in life. Structural abnormalities inherent to connective tissue disorders, combined with progressive atrial dilation and long-term surgical effects, may create a substrate for arrhythmogenesis. Even mild residual valvular dysfunction can contribute to atrial remodeling and increase AF risk over time. Long-term studies show markedly lower mortality after mitral repair compared with replacement, although moderate or severe regurgitation develops in a substantial proportion of patients, potentially contributing to progressive atrial remodeling [13]. Given their extended life expectancy, the cumulative lifetime risk of atrial fibrillation becomes a central determinant of outcomes. Furthermore, the feasibility and effectiveness of transcatheter LAA occlusion in this population remain uncertain. Surgical exclusion under direct visualization may therefore provide a potentially more durable strategy for selected patients. Emerging randomized evidence on percutaneous LAAO has reinforced the pathophysiological rationale that most thromboembolic events in atrial fibrillation originate from the appendage, making it an attractive therapeutic target. While current guidelines restrict its use to selected high-risk patients with contraindications to long-term anticoagulation, recent trials have ex-

plored its broader applicability [27]. The conflicting results from studies such as CLOSURE-AF and CHAMPION-AF highlight the importance of careful patient selection and appropriate exclusion criteria for standalone LAAO, including clinical profile, comorbidities, and appendage anatomy, which may ultimately limit its applicability in many patients at risk of stroke or bleeding. In this context, the role of LAA exclusion may differ in patients undergoing open heart surgery [43,46,66]. For patients already undergoing open heart surgery, the clinical context is fundamentally different. Deferring appendage management may limit future therapeutic options because complex LAA anatomy can preclude transcatheter device implantation, and previous cardiac surgery may make subsequent thoracoscopic epicardial approaches technically challenging owing to pericardial adhesions [67]. Thoracoscopic surgical clipping represents an alternative approach to transcatheter LAAO in selected patients; however, evidence supporting its use as a rescue strategy following failed percutaneous implantation remains limited, and it should not be considered an established or routinely required intervention [68]. However, previous cardiac surgery may result in pericardial adhesions that complicate or even preclude subsequent minimally invasive thoracoscopic approaches. Consequently, in carefully selected patients already undergoing open heart surgery, concomitant LAA exclusion may avoid the need for future interventions while preserving the opportunity for durable appendage closure, particularly when subsequent minimally invasive approaches could be technically limited by postoperative adhesions [69].

Patients with Marfan syndrome represent a unique subgroup in whom prophylactic surgical LAA exclusion may be considered during index cardiac surgery. Their young age at operation, long life expectancy, progressive atrial remodeling, and the frequent use of valve-preserving procedures that avoid lifelong anticoagulation create a clinical scenario distinct from that of the general cardiac surgical population. Unlike percutaneous approaches, surgical exclusion can be achieved with minimal incremental risk when performed concomitantly, potentially providing lifelong protection without device-related complications or long-term pharmacological therapy [48,49,50]. Nevertheless, important questions remain, including effects on atrial function, risk of incomplete exclusion, and the absence of randomized data in patients in sinus rhythm. Thus, while transcatheter LAAO data support biological plausibility, they are insufficient to justify routine prophylactic exclusion, and prospective studies in surgical populations are needed. The incremental burden of adding LAA exclusion is generally minimal, with limited operative time and no need for costly devices, while achieving high rates of complete closure and minimizing residual flow associated with thromboembolic risk. Concerns regarding increased POAF warrant consideration. Although some studies report higher rates of early postoperative arrhythmias, these are typically transient. POAF occurs in 25–35% of cardiac surgery patients even without LAA intervention and often resolves without long-term consequences. Prophylactic LAA closure may potentially reduce long-term thromboembolic risk in selected patients, although its clinical benefit in patients without established AF remains to be determined [18,60]. In Marfan syndrome, left atrial enlargement and progressive atrial remodeling may reflect an underlying structural atrial substrate that could contribute to arrhythmogenesis and potentially increase thromboembolic susceptibility [5,6,21,33,35]. However, direct evidence linking left atrial enlargement to cerebrovascular events in Marfan patients without AF is currently lacking. Accordingly, left atrial enlargement may warrant further investigation as a potential marker of atrial disease, but its role in identifying patients who may benefit from prophylactic LAA exclusion remains unestablished. In high-risk populations such as Marfan syndrome, the high incidence of POAF and evidence of ongoing atrial remodeling suggest that prophylactic LAA exclusion may confer additional long-term protection against thromboembolism, even if preoperative sinus rhythm is preserved [18,60]. Anatomical variability of the LAA remains critical. Complex morphologies can limit percutaneous approaches, whereas surgical exclusion allows tailored techniques ensuring complete closure, particularly relevant in connective tissue disorders with tissue fragility. The 2019 AHA/ACC/HRS guideline assigned concomitant surgical left atrial appendage (LAA) exclusion in patients with AF undergoing cardiac surgery a Class IIb, Level B-NR recommendation [70], reflecting uncertainty regarding its clinical benefit at that time. Subsequently, the LAAOS III randomized trial demonstrated a significant reduction in ischemic stroke or systemic embolism with concomitant surgical LAA occlusion in patients with established AF undergoing cardiac surgery [69]. Accordingly, the 2023 ACC/AHA/ACCP/HRS guideline assigned surgical LAA exclusion a Class I, Level A recommendation as an adjunct to continued oral anticoagulation in eligible patients with AF undergoing cardiac surgery. Importantly, these recommendations apply to patients with pre-existing AF and should not be extrapolated to patients in sinus rhythm, for whom the benefit of prophylactic surgical LAA exclusion remains to be established. Following publication of randomized trials, particularly left Atrial Appendage Occlusion Study III (LAAOS III), contemporary guidelines (2023–2024) upgraded concomitant surgical LAA exclusion in patients with AF to Class I or IIa recommendations supported by higher-quality evidence [27,71]. These recommendations, however, apply exclusively to patients with established atrial fibrillation and should not be extrapolated to patients in sinus rhythm. In parallel, it is reasonable to speculate that, with further evidence, future guidelines may expand recommendations to include selected patients in sinus rhythm undergoing cardiac surgery, particularly those with a high lifetime risk of atrial fibrillation

Table 1. Comparative tissue characteristics, arrhythmic phenotypes, and surgical feasibility of LAA exclusion in heritable thoracic aortopathies (HTAD)*.

Clinical parameter	Marfan syndrome (MFS)	Loeys-Dietz syndrome (LDS)	Vascular Ehlers-Danlos syndrome (vEDS)
Genetic mutation [10,30]	*FBN1* (Fibrillin-1)	*TGFBR1*, *TGFBR2*, *SMAD3*, *TGFB2*, *TGFB3*	*COL3A1* (Type III Collagen)
Tissue fragility [4,30]	Moderate; tissue is holding sutures well but prone to late stretch	High; extreme arterial and tissue friability	Extreme; profound tissue and vascular fragility
Mitral/Aortic surgery [4,5,10,31]	High frequency of early valve repair/valve-sparing root replacement	High frequency of early root replacement	Rare elective surgery; high risk of intraoperative dissection
Baseline AF/Arrhythmia prevalence [8,10,11]	Moderate-High Ψ(~16% lifetime prevalence)	Very High (~31.9% lifetime prevalence)	Low-Moderate
Mitral annular disjunction (MAD) [37]	High prevalence (34%)	Present (~11.7%)	Rare
Concomitant LAA exclusion feasibility [48,49,50,53]	Highly Feasible: Excellent candidate for epicardial clipping or excision	Feasible with Caution: Prefer epicardial clipping over aggressive suture-based resection	High Risk/Contraindicated: Extreme risk of tissue tearing, bleeding, and rupture
Clinical recommendation [18,60,65]	Consider prophylactic exclusion during index valve/root surgery	Consider prophylactic exclusion	Avoid prophylactic LAA manipulation unless strictly indicated

*References: [4,5,8,10,11,18,30,31,37,48,49,50,53,60,65].

Abbreviations: AF, atrial fibrillation; HTAD, heritable thoracic aortopathies; LAA, left atrial appendage; LDS, Loeys-Dietz syndrome; MAD, mitral annular disjunction; MFS, Marfan syndrome; vEDS, vascular Ehlers-Danlos syndrome.

ΨReported prevalence estimates reflect individual study cohorts and should not be interpreted as directly comparable or as estimates of lifetime arrhythmia risk.

or thromboembolism. Prophylactic LAA exclusion in this setting could offer a one-time mechanical strategy to mitigate future embolic risk, especially in younger patients or those unlikely to tolerate long-term anticoagulation. However, such an approach must be balanced against potential risks, including incomplete closure with residual stump formation, procedure-related complications, and the loss of the physiological functions of the LAA [16,17,18,19,50,51]. In the absence of robust randomized data in this population, any extension of recommendations will require careful patient selection and confirmation of safety and long-term efficacy.

Despite the rationale, limitations of the current evidence must be acknowledged. Most data supporting LAA exclusion derive from populations with established AF or heterogeneous cardiac surgical cohorts [27]. Randomized data specific to young patients or those with connective tissue disorders are lacking. Therefore, caution and individualized assessment are paramount, pending further targeted research.

8. Conclusions

Prophylactic surgical LAA exclusion during open heart surgery should not be applied indiscriminately to all patients in sinus rhythm, but should be selectively considered in carefully chosen populations with an elevated lifetime risk of atrial fibrillation and thromboembolism. Marfan and Loeys-Dietz patients represent particularly suitable candidates because of their young age at index surgery, the predominance of valve-preserving strategies, and an intrinsic genetically mediated arrhythmogenic substrate characterized by progressive atrial remodeling, myocardial fibrosis, and the frequent presence of mitral annular disjunction, all of which may predispose to late-onset atrial fibrillation. Concomitant LAA exclusion using highly reproducible techniques, such as complete anatomical excision or epicardial clip occlusion, is a low-risk adjunct that may provide durable mechanical stroke protection while avoiding the bleeding risks and adherence challenges associated with lifelong anticoagulation. Although the pathophysiological rationale is compelling, current evidence remains insufficient to recommend routine prophylactic LAA exclusion in all patients with heritable connective tissue disorders. Future prospective studies and multicenter registries are needed to determine its long-term clinical efficacy, physiological safety, and the patient subgroups most likely to benefit. Until such evidence is available, decisions should remain individualized, balancing the uncertain long-term endocrine and hemodynamic consequences of LAA

exclusion against the cumulative lifetime risk of atrial fibrillation and thromboembolism.

Abbreviations

AF, atrial fibrillation; CABG, coronary artery bypass grafting; HTAD, heritable thoracic aortopathies; LAA, left atrial appendage; LAAO, left atrial appendage occlusion; LDS, Loeys-Dietz syndrome; MAD, mitral annular disjunction; MFS, Marfan syndrome; POAF, postoperative atrial fibrillation; SR, sinus rhythm; vEDS, vascular Ehlers-Danlos syndrome.

Author Contributions

Conceptualization: AI, EL, KS, JZ. Data acquisition: AI, JZ, MG. Writing original draft: AI, EL, JZ, HS. Writing review and editing: EL, JZ, MG, HS, KS. Table preparation: MG. Interpretation of data for the work: HS, JZ, KS. All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work.

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