Journal of Rare Cardiovascular Diseases 2024; 4(8): 157–162
www.jrcd.eu

Review Article

Atrial Fibrillation Management: The Combined Approach ofLeft Atrial Appendage Closure and Catheter Ablation

John Alex[1,*]
[1] University of Ljubljana.

Abstract

Atrial fibrillation (AF) is a prevalent cardiac arrhythmia associated with significant thromboembolic and bleeding risks. The combined procedure of left atrial appendage closure (LAAC) and catheter ablation has emerged as an innovative approach to address these dual challenges, particularly in high-risk patients. This review explores the evolution of LAAC, highlights clinical evidence supporting its integration with catheter ablation, and discusses technological advancements shaping its future. Studies demonstrate that the combined procedure significantly reduces stroke and bleeding risks, achieves high procedural success rates, and ensures effective arrhythmia control. Real-world data further validate its safety and efficacy, particularly in specialized centers. Despite its promise, challenges such as residual leaks, procedural complexity, and the need for standardized protocols persist. Emerging technologies, including personalized device designs and artificial intelligence, hold the potential to optimize outcomes and expand accessibility. The combined procedure represents a transformative strategy in AF management, offering a holistic solution for improving patient outcomes while minimizing risks. JRCD 2024; 4(8): 157–162

key words: atrial fibrillation, left atrial appendage closure, catheter ablation, stroke prevention, combined procedure, arrhythmia control, thromboembolic risk, bleeding risk, WATCHMAN device, Amulet device, pulmonary vein isolation, intracardiac echocardiography, 3D printing, personalized medicine, artificial intelligence, real-world evidence

Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, characterized by irregular and often rapid heartbeats, affecting millions worldwide. Its prevalence increases significantly with age, with one in four individuals at risk of developing AF during their lifetime. Despite advancements in management strategies, AF continues to be a major public health concern due to its association with severe complications, most notably ischemic stroke and systemic thromboembolism [1]. Strokes associated with AF are often catastrophic, accounting for 15–20% of all ischemic strokes. Effective stroke prevention in AF patients has been a cornerstone of management, traditionally achieved using oral anticoagulants (OACs), such as vitamin K antagonists (VKAs) or the more recent non-vitamin K antagonist oral anticoagulants (NOACs). However, OAC therapy has limitations, including bleeding risks and contraindications in certain patient populations, necessitating alternative treatment approaches [2].

The left atrial appendage (LAA) has been identified as a primary site for thrombus formation in patients with AF, contributing to over 90% of thromboembolic events. This insight has shifted focus toward mechanical interventions targeting the LAA for stroke prevention. Left atrial appendage closure (LAAC), a minimally invasive percutaneous procedure, was introduced as a non-pharmacological alternative for patients with contraindications to OACs [3]. The LAAC procedure aims to occlude the LAA, preventing thrombus formation and subsequent embolization. Early clinical trials, such as the PROTECT AF and PREVAIL studies, demonstrated the non-inferiority of LAAC compared to warfarin in preventing stroke, systemic embolism, and cardiovascular death. Furthermore, advancements in device technology and procedural techniques have significantly improved the safety and efficacy of LAAC over the past decade, paving the way for its inclusion in contemporary AF management guidelines [4].

While LAAC has established itself as a viable stan-

Please cite this article: John Alex. Atrial Fibrillation Management: The Combined Approach of Left Atrial Appendage Closure and Catheter Ablation. J Rare Cardiovasc Dis. 2024; 4(8): 157–162;
Conflict of interest: none declared. Submitted: January 12, 2024. Accepted: March 13, 2024.
* Corresponding author: john.alexwonder@gmail.com.

dalone intervention, the combined procedure of LAAC with catheter ablation has emerged as a novel therapeutic strategy to address both the thromboembolic and arrhythmic aspects of AF simultaneously. Catheter ablation, particularly pulmonary vein isolation (PVI), is a well-established treatment for rhythm control in symptomatic AF [5]. Combining it with LAAC offers a dual benefit—reducing stroke risk through mechanical LAA exclusion and addressing arrhythmia recurrence through electrical substrate modification. This combined approach is particularly appealing for patients with high stroke and bleeding risks, where rhythm control and anticoagulation therapy may not be sustainable options [6].

The concept of the combined procedure was first introduced in the early 2010s, with initial studies demonstrating its feasibility and safety. These early experiences, though limited in sample size, provided compelling evidence of the combined procedure's potential to achieve high procedural success rates with acceptable safety profiles. Subsequent studies and registries have expanded the evidence base, showcasing consistent improvements in long-term outcomes, including reduced stroke rates, lower bleeding complications, and a high rate of OAC discontinuation. The evolution of the combined procedure has been driven by advancements in both ablation technologies and LAAC device design, along with the development of specialized heart teams trained in these complex procedures.

Despite its promising results, the combined procedure remains a subject of ongoing investigation and debate. Procedural complexities, learning curve effects, and the need for multidisciplinary expertise limit its widespread adoption. Furthermore, the long-term efficacy and safety of the combined approach in diverse patient populations warrant further evaluation through large-scale, multicenter randomized trials [7]. Emerging technologies, such as intracardiac echocardiography (ICE) and 3D printing for patient-specific device customization, hold the potential to address some of these challenges, improving procedural precision and patient outcomes.

This review aims to provide a comprehensive overview of the past, present, and future perspectives of LAAC and the combined procedure in the management of AF [8]. It will explore the historical evolution of these interventions, highlight key clinical studies and outcomes, and discuss emerging trends and challenges in their implementation. By synthesizing current evidence and identifying areas for future research, this review seeks to contribute to the growing body of knowledge on integrated approaches to AF management, ultimately guiding clinical decision-making and advancing patient care [9].

As the burden of AF continues to rise globally, innovative treatment strategies like the combined procedure are poised to play a pivotal role in improving outcomes

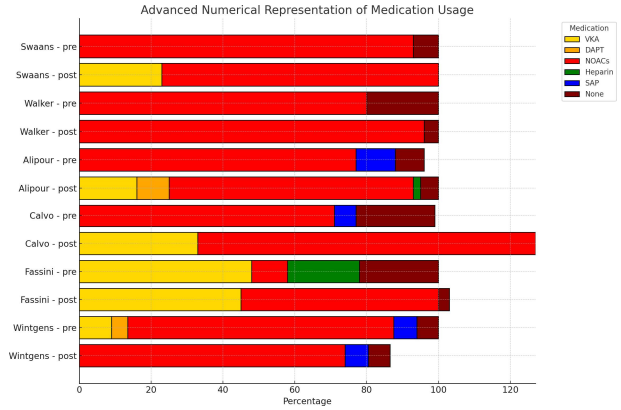

Figure 1: Anti-thrombontc regimen frequencies pre and post combined procedure in different studies. VKA: vitamin K antagonists; DAPT: dual anti platelet; NOACs: non vitamin K antagonist oral anti coagulants; SAP: single anti platelet

for high-risk patients. However, translating this promising approach into routine clinical practice requires addressing several critical gaps, including optimizing patient selection criteria, standardizing procedural protocols, and refining post-procedural care strategies. This review will delve into these aspects, emphasizing the importance of multidisciplinary collaboration and technological innovation in shaping the future of LAAC and the combined procedure [10].

Evolution of Left Atrial Appendage Closure (LAAC)

The evolution of left atrial appendage closure (LAAC) as a therapeutic intervention represents a significant milestone in the management of atrial fibrillation (AF) [11]. Recognizing the left atrial appendage (LAA) as the origin of over 90% of thrombi in AF patients led to a shift in focus from systemic anticoagulation to localized mechanical intervention. This section explores the historical development, key trials, and technological advancements that have shaped LAAC into a mainstream treatment option for stroke prevention.

The concept of mechanically occluding the LAA dates back to the 20th century, initially performed surgically during open-heart procedures. However, surgical LAA exclusion carried substantial risks, particularly in patients with comorbidities, making it unsuitable for widespread use. The advent of catheter-based, minimally invasive techniques revolutionized the field, offering a safer and more feasible alternative [12].

The landmark PROTECT AF trial in 2009 marked the beginning of the modern era of percutaneous LAAC. This randomized controlled trial compared the WATCHMAN device, the first FDA-approved LAA closure device, to warfarin therapy in patients with non-valvular AF. The study demonstrated the non-inferiority of

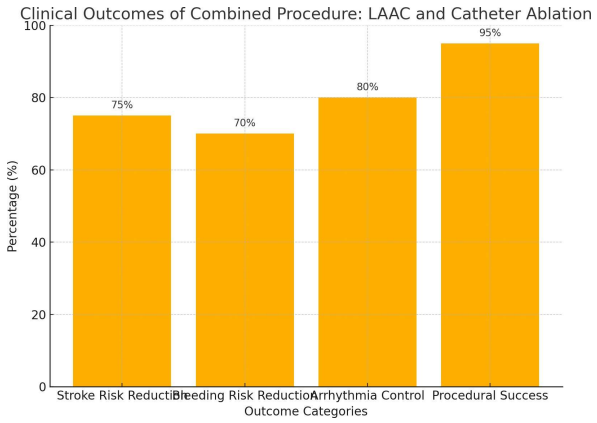

Figure 2: Clinical outcomes of the combined procedure (LAAC and catheter ablation) across key categories: stroke risk reduction, bleeding risk reduction, arrhythmia control, and procedural success

LAAC to warfarin in preventing stroke, systemic embolism, and cardiovascular death, albeit with initial concerns about peri-procedural complications such as pericardial effusion. Subsequent analyses revealed improvements in long-term outcomes, including significant reductions in hemorrhagic strokes and non-procedural bleeding [13].

Building on these findings, the PREVAIL trial in 2014 reassessed the safety and efficacy of LAAC with the WATCHMAN device, benefiting from advancements in procedural techniques and operator experience. This trial confirmed the safety improvements and reinforced the role of LAAC as a viable alternative for patients contraindicated for long-term anticoagulation therapy [12].

The success of the WATCHMAN device catalyzed the development of alternative devices, each designed to address specific challenges and improve procedural outcomes. Notable among these is the Amplatzer Cardiac Plug (ACP), later succeeded by the Amulet device, which introduced design features aimed at achieving better sealing and reducing the risk of residual leaks. Comparative studies between WATCHMAN and ACP devices have shown similar efficacy and safety profiles, though direct head-to-head trials remain limited [11].

Further innovations include devices tailored for diverse anatomical variations of the LAA, employing advanced imaging modalities such as transesophageal echocardiography (TEE) and intracardiac echocardiography (ICE) for precise implantation. These advancements have enhanced procedural success rates and minimized complications, establishing LAAC as a robust option for stroke prevention.

Beyond randomized controlled trials, large-scale registries have provided invaluable insights into the real-world performance of LAAC. The EWOLUTION registry, for instance, enrolled over 1,000 patients, reporting a high procedural success rate (98.5%) with low complication rates. Notably, the registry demonstrated significant reductions in predicted stroke and bleeding risks, validating the effectiveness of LAAC in diverse clinical settings.

Similarly, the WASP registry and subsequent meta-analyses have highlighted consistent improvements in peri-procedural safety and long-term outcomes, underscoring the importance of operator experience and technological refinement. These data have reinforced the utility of LAAC in routine clinical practice, especially for high-risk patient populations.

The incorporation of LAAC into major AF management guidelines has further legitimized its role in contemporary practice. Current recommendations advocate LAAC for patients with high thromboembolic risk who are unsuitable for OACs due to bleeding complications or contraindications. As the evidence base continues to grow, the adoption of LAAC is expected to expand, driven by ongoing refinements in technology and procedural techniques [7].

Despite its success, LAAC faces several challenges that warrant attention. Residual leaks, though typically minimal, remain a concern due to their potential association with thromboembolic events [6]. Additionally, the need for temporary post-procedural anticoagulation or antiplatelet therapy poses a challenge in high-bleeding-risk patients. Further research is needed to refine patient selection criteria, optimize post-procedural care protocols, and address anatomical variations that complicate device implantation.

Combined Procedure: Integration of LAAC with Catheter Ablation

The combination of left atrial appendage closure (LAAC) with catheter ablation represents a groundbreaking approach to managing atrial fibrillation (AF), particularly in patients with concurrent high stroke and bleeding risks. This synergistic technique addresses both thromboembolic risk and arrhythmia control in a single procedure, thereby offering a comprehensive solution for a challenging patient population. This section explores the rationale, clinical evidence, procedural advancements, and limitations associated with the combined procedure.

Rationale for the Combined Procedure

Catheter ablation, particularly pulmonary vein isolation (PVI), is a cornerstone treatment for rhythm control in patients with symptomatic paroxysmal and persistent AF. However, rhythm control alone does not mitigate the elevated risk of stroke in patients with structural heart abnormalities or prior thromboembolic events [2]. On the other hand, while LAAC effectively addresses stroke risk by mechanically isolating the thrombus-

prone left atrial appendage (LAA), it does not prevent arrhythmia recurrence.

The combined procedure leverages the strengths of both interventions, addressing the electrical substrate responsible for arrhythmia while simultaneously eliminating the anatomical reservoir for thrombus formation. This dual benefit is particularly advantageous for patients with high CHA_2DS_2-VASc and HAS-BLED scores, where neither catheter ablation nor LAAC alone is likely to provide comprehensive clinical benefits.

Early Experiences and Proof of Concept

The first case series on the combined procedure was published in 2012 by Swaans et al., involving 30 patients undergoing simultaneous LAAC and PVI. This study demonstrated high procedural success rates with acceptable safety profiles, setting the stage for further exploration. Notably, the procedure did not significantly prolong ablation times, and patients experienced reduced stroke risks without the need for long-term oral anticoagulants (OACs) [9]. These promising findings were replicated in subsequent small-scale studies, which confirmed the feasibility and safety of combining LAAC with ablation techniques such as phased radiofrequency and cryoablation.

Clinical Evidence from Larger Studies

Over time, larger observational studies and registries have strengthened the evidence base for the combined procedure. Key findings include:

Combined procedures have consistently demonstrated substantial reductions in stroke and bleeding risks compared to expected outcomes based on CHA_2DS_2-VASc and HAS-BLED scores. In long-term follow-ups, annualized stroke rates as low as 0.7% and bleeding rates of 1.1% have been reported.

Procedural success rates nearing 100% have been documented, with satisfactory LAA sealing achieved in the majority of patients. This success is attributed to advancements in device technology and operator experience.

A significant proportion of patients undergoing combined procedures can discontinue OACs long-term, addressing one of the key challenges in managing high-bleeding-risk populations.

The combined procedure achieves rhythm control outcomes comparable to catheter ablation alone, with freedom from arrhythmia rates exceeding 70% in many studies. This suggests that the addition of LAAC does not compromise the effectiveness of ablation.

Advancements in technology have played a pivotal role in the evolution of the combined procedure. Key innovations include:

The introduction of cryoablation for PVI has enhanced procedural safety by reducing the risk of thrombus formation and peri-procedural complications. Studies have shown comparable efficacy between cryoablation and radiofrequency energy in achieving durable PVI lesions.

High-resolution imaging techniques, such as intracardiac echocardiography (ICE) and 3D imaging, have improved procedural precision, enabling accurate device placement and minimizing complications.

New-generation LAAC devices, such as the WATCHMAN FLX and Amulet, offer enhanced conformability to varied LAA anatomies, ensuring better sealing and reducing the risk of residual leaks.

Clinical Outcomes and Real-World Evidence

The combined procedure of left atrial appendage closure (LAAC) and catheter ablation has gained traction in clinical practice, supported by a growing body of evidence from observational studies, registries, and meta-analyses. This section summarizes the clinical outcomes and real-world data, highlighting the efficacy, safety, and limitations of this innovative approach in managing atrial fibrillation (AF).

One of the primary goals of the combined procedure is to reduce the risk of ischemic stroke, a significant complication of AF. Studies consistently report favorable outcomes:

Long-term follow-up data from combined procedure studies demonstrate annualized stroke rates as low as 0.7% in high-risk populations. This represents a significant risk reduction compared to predicted rates based on CHA_2DS_2-VASc scores. The Wintgens et al. multicenter registry, encompassing 349 patients, highlighted a 75% reduction in stroke risk, underscoring the efficacy of the combined approach in mitigating thromboembolic events.

Although residual leaks (<5 mm) are observed in a minority of patients, their clinical significance remains debatable. Current evidence suggests these leaks do not substantially increase stroke risk when antithrombotic therapy is appropriately managed.

Bleeding Risk Reduction

Another critical benefit of the combined procedure is the potential to reduce bleeding complications associated with long-term anticoagulant therapy:

Several studies report a significant reduction in major bleeding events, with annualized bleeding rates ranging from 1.1% to 2.9%, depending on the population and follow-up duration. The EWOLUTION and WASP registries showed that high-risk patients undergoing LAAC experienced a 48% reduction in bleeding risk compared to HAS-BLED score predictions.

A major advantage of the combined procedure is the high rate of OAC discontinuation. Studies report freedom from OACs in 70–85% of patients, reducing long-term bleeding risks while maintaining stroke prevention.

The success of the combined procedure in addressing rhythm control mirrors that of standalone catheter ablation:

Freedom from atrial fibrillation recurrence after combined procedures is consistently reported in 60–80% of patients at 12-month follow-ups. This is comparable to outcomes observed with standalone catheter ablation, demonstrating that LAAC does not compromise ablation efficacy.

Patients undergoing combined procedures report significant improvements in symptoms and quality of life, attributed to the dual benefits of arrhythmia control and stroke risk reduction.

Procedural Success and Safety

Advances in technology and operator experience have resulted in high procedural success rates and reduced complications:

Combined procedures achieve procedural success rates nearing 100%, with acute LAAC device implantation success exceeding 95% in most studies. These outcomes reflect improved device design and imaging techniques.

The peri-procedural adverse event rate has decreased significantly over time, with serious complications such as pericardial effusion occurring in less than 2% of cases in experienced centers. Importantly, these rates are comparable to those observed in standalone catheter ablation or LAAC procedures.

The learning curve associated with the combined procedure has been a critical determinant of outcomes. Dedicated heart teams and specialized training programs have been instrumental in minimizing complications and improving efficiency.

Real-World Evidence from Registries

Large registries provide robust insights into the real-world application of the combined procedure:

This registry enrolled over 1,000 patients undergoing LAAC, with 139 cases involving combined procedures. The findings confirmed the safety and efficacy of the combined approach, with low complication rates and favorable long-term outcomes.

The largest study to date on the combined procedure, this registry demonstrated consistent reductions in stroke and bleeding risks across diverse populations, with a median follow-up of 34.5 months. It highlighted the feasibility of the procedure even in high-risk patients.

Despite the positive outcomes, several limitations and challenges persist:

Most evidence for the combined procedure comes from observational studies and registries. High-quality randomized controlled trials are needed to confirm its superiority over standalone interventions.

Differences in procedural protocols, device selection, and post-procedural care regimens across studies make it challenging to generalize findings.

While short- to mid-term outcomes are well-documented, longer-term data on stroke, bleeding, and arrhythmia recurrence are limited, necessitating ongoing follow-up.

1. Conclusion

The combined procedure of left atrial appendage closure (LAAC) and catheter ablation represents a paradigm shift in the management of atrial fibrillation (AF), particularly for high-risk patients. By addressing both thromboembolic and arrhythmic risks simultaneously, this innovative approach provides a comprehensive solution for patients who are often ineligible for long-term oral anticoagulant therapy. Over the past decade, advancements in device technology, procedural techniques, and operator expertise have significantly improved the safety, efficacy, and feasibility of the combined procedure.

Clinical evidence highlights the substantial benefits of the combined approach, including reduced stroke and bleeding risks, high procedural success rates, and favorable arrhythmia control outcomes. Real-world data from large registries further corroborate these findings, demonstrating the feasibility and safety of the procedure in diverse patient populations. Additionally, the integration of advanced imaging modalities, personalized device design, and emerging technologies like artificial intelligence continues to refine procedural workflows, enhance precision, and expand the scope of the combined procedure.

However, challenges remain. The procedure requires highly skilled operators and specialized centers, limiting its widespread availability. The lack of randomized controlled trials and long-term data also presents hurdles in establishing standardized protocols and broad acceptance. Addressing these gaps through ongoing research and innovation will be critical to the continued evolution of this therapy.

References

[1] Calvo N, Salterain N, Arguedas H, Macias A, Esteban A, García de Yébenes M, Gavira JJ, Barba J, García-Bolao I. Combined catheter ablation and left atrial appendage closure as a hybrid procedure for the treatment of atrial fibrillation. Ep Europace. 2015 Oct 1;17(10):1533-40.

[2] Chen M, Sun J, Wang QS, Zhang PP, Li W, Zhang R, Mo BF, Yu YC, Cai X, Yang M, Lian XM. Long-term outcome of combined catheter ablation and left atrial appendage closure in atrial fibrillation patients. International Journal of Cardiology. 2022 Dec 1;368:41-8.

[3] Alipour A, Swaans MJ, van Dijk VF, Balt JC, Post MC, Bosschaert MA, Rensing BJ, Reddy VY, Boersma LV. Ablation for atrial fibrillation combined with left atrial appendage closure. JACC: Clinical Electrophysiology. 2015 Dec;1(6):486-95.

[4] Chen M, Wang ZQ, Wang QS, Sun J, Zhang PP, Feng XF, Li W, Yu Y, Liu B, Mo BF, Zhang R. One-stop strategy for treatment of atrial fibrillation: feasibility and safety of combining catheter ablation and left atrial appendage closure in a single procedure. Chinese medical journal. 2020 Jun 20;133(12):1422-8.

[5] Du X, Chu H, Ye P, He B, Xu H, Jiang S, Lin M, Lin R, Liu J, Wang B, Feng M. Combination of left atrial appendage

closure and catheter ablation in a single procedure for patients with atrial fibrillation: multicenter experience. Journal of the Formosan Medical Association. 2019 May 1;118(5):891-7.

[6] SWAANS, Martin J., et al. Ablation for atrial fibrillation in combination with left atrial appendage closure: first results of a feasibility study. Journal of the American Heart Association, 2012, 1.5: e002212.

[7] WATS, Karan, et al. The convergent atrial fibrillation ablation procedure: evolution of a multidisciplinary approach to atrial fibrillation management. Arrhythmia & Electrophysiology Review, 2020, 9.2: 88.

[8] SWAANS, Martin J., et al. Catheter ablation in combination with left atrial appendage closure for atrial fibrillation. JoVE (Journal of Visualized Experiments), 2013, 72: e3818.

[9] HE, Ben, et al. Combination of ablation and left atrial appendage closure as "One-stop" procedure in the treatment of atrial fibrillation: Current status and future perspective. Pacing and Clinical Electrophysiology, 2021, 44.7: 1259-1266.

[10] PHILLIPS, Karen P.; WALKER, Daniel T.; HUMPHRIES, Julie A. Combined catheter ablation for atrial fibrillation and Watchman® left atrial appendage occlusion procedures: Five-year experience. Journal of arrhythmia, 2016, 32.2: 119-126.

[11] KAWAKAMI, Hiroshi, et al. Cost-effectiveness of combined catheter ablation and left atrial appendage closure for symptomatic atrial fibrillation in patients with high stroke and bleeding risk. American Heart Journal, 2021, 231: 110-120.

[12] WINTGENS, Lisette, et al. Combined atrial fibrillation ablation and left atrial appendage closure: long-term follow-up from a large multicentre registry. EP Europace, 2018, 20.11: 1783-1789.

[13] WANG, An, et al. Efficacy and safety of catheter ablation combined with left atrial appendage closure in the treatment of atrial fibrillation: a systematic review and meta-analysis. Anatolian Journal of Cardiology, 2022, 26.3: 154.