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Left atrial appendage occlusion in patients with Nonvalvular Atrial Fibrillation

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RESUMO

OBJECTIVE

To review the scientific literature on left atrial appendage occlusion (LAAO) in patients with non-valvular atrial fibrillation (NVAF), by investigating its benefits in the prevention of thromboembolic events, particularly stroke, in patients with or without prior use of oral anticoagulants (OA).

METHODS

This is a descriptive review, with a literature search conducted in the PubMed, Scielo and Lilacs databases between January 2015 and July 2024. Studies with prospective or retrospective designs, in Portuguese or English, involving human subjects and addressing NVAF and LAAO were included.

RESULTS

LAAO has shown similar efficacy to new OA in preventing ischemic stroke, with a lower incidence of major bleeding. Double occlusion devices exhibited a lower rate of peri-device leakage and complications, although new models of single occlusion devices showed similar and even superior results. Imaging techniques, such as 3D computed tomography angiography, were crucial in selecting the device. Transseptal puncture assisted by guidewire was more efficient and safer. LAAO combined with procedures such as transcatheter aortic valve implantation or percutaneous coronary intervention proved to be feasible. The high cost of the LAAO procedure still limits its widespread application.

CONCLUSIONS

LAAO is an effective and safe alternative for the prevention of thromboembolic complications in patients with NVAF, especially for those with contraindications to chronic use of OA. Technical advancements and new devices have the potential to expand its clinical use and improve patients' quality of life.

KEYWORDS

Left atrial appendage occlusion; Stroke; Atrial fibrillation.

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INTRODUCTION

Arrhythmias are changes in the heart rhythm caused by dysfunctions in the heart's electrical system. In this context, atrial fibrillation (AF) is the most common sustained arrhythmia in adults.,[1-3] and it is frequently more common in men than in women.[4,5]

It occurs due to the formation of ectopic foci and the presence of micro-reentry circuits, which are disorganized pathways of electrical conduction in the atrial tissue. These circuits prevent the orderly propagation of the electrical impulse, resulting in rapid, irregular, and ineffective atrial contractions.[6,7]

AF can be classified as valvular, when associated with mitral stenosis or valve prostheses, or non-valvular (NVAF), when there is no mitral stenosis or artificial valves present.[8]

AF is a condition with a multifactorial origin, triggered by a variety of clinical factors such as arterial hypertension (AH), coronary artery disease, cardiomyopathies, valvular heart diseases (such as mitral stenosis and mitral regurgitation), obstructive sleep apnea, chronic obstructive pulmonary disease, myocarditis, pericarditis, obesity, family history, genetic factors, and advanced age. [8] Diagnosis is made through a detailed collection of the patient's medical history, complemented by tests such as resting electrocardiogram and 24-hour Holter monitoring. Once confirmed, it is essential to initiate therapeutic treatment as soon as possible to prevent potential serious complications.[9]

AF can be asymptomatic in many patients, while in others it presents with symptoms such as palpitations, fatigue, dyspnea, irregular pulse, dizziness, and chest discomfort. In some cases, the diagnosis is made only after the occurrence of more severe complications, such as stroke.[11] The increased risk of clot formation in the heart, due to electrical dysfunction, is strongly associated with the occurrence of embolisms, ischemic stroke (IS), hemorrhagic stroke (HS), cognitive impairments, heart failure (HF), and even mortality. These outcomes can be irreversible, highlighting the importance of early diagnosis of AF.[8] To estimate the risk of stroke in patients with AF, the CHA_2D-S_2-VASc score is used to help assess the need for oral anticoagulation (OAC). This score takes into account risk factors such as heart failure (HF), arterial hypertension, age, diabetes mellitus, previous stroke, prior transient ischemic attack, arterial thromboembolism, and vascular disease. Patients with higher scores have an increased risk of thromboembolic complications, and OAC is recommended to reduce the risk of stroke. For example, patients with a score of 2 or higher generally require anticoagulants.[12]

Patients with AF have a threefold increased risk of developing HF and a fivefold increased risk of experiencing a stroke.[9] For this reason, once AF is identified, it is essential to initiate treatments such as anticoagulant therapy and heart rate control using beta-blockers. [11] In specific cases, catheter ablation may be indicated, which has a low complication rate and, in patients with early AF, can even be considered a first-line treatment option. [13]

Studies indicate that in 90% of cases, clot formation with potential embolization, leading to IS, occurs predominantly in the left atrial appendage (LAA). Due to the absence of effective contraction of the left atrium (LA) during AF, emptying of the LAA is reduced, promoting blood stasis and subsequent thrombus formation. This thrombus can detach and migrate into the systemic circulation, particularly to the brain, causing IS.[14] It is estimated that approximately 87% of ischemic strokes associated with AF are of thromboembolic origin, reinforcing its clinical significance.[15]

With increasing life expectancy and the rising prevalence of AF, new approaches have emerged to prevent serious complications. One such innovation is the left atrial appendage occlusion (LAAO) technique, an alternative to OAC, with the primary goal of preventing stroke in patients with AF.[8] The procedure aims to mechanically isolate the LAA from the atrial cavity, eliminating the main site of thrombus formation and consequently reducing the risk of thromboembolic events, particularly stroke.[16]

The procedure is performed via venous access, followed by a transseptal puncture, usually guided by transesophageal (TEE) and/or intracardiac echocardiography. There are different types of devices for LAAO, including single- or double-seal occluders, which prevent blood stasis in the LAA. This approach is particularly relevant in patients with AF, in whom reduced ejection fraction and decreased blood flow velocity increase the risk of thrombus formation.[15]

Although OAC remains the main strategy to prevent embolisms in patients with AF, the increased risk of HS and gastrointestinal bleeding, particularly in elderly patients, makes LAAO a promising alternative.[17]

In this context, the present study aims to investigate the potential benefits of LAAO, using single- or double-seal occluders, in patients with NVAF, regardless of prior stroke history or current use of OAC.

METHODS

This is a descriptive review.

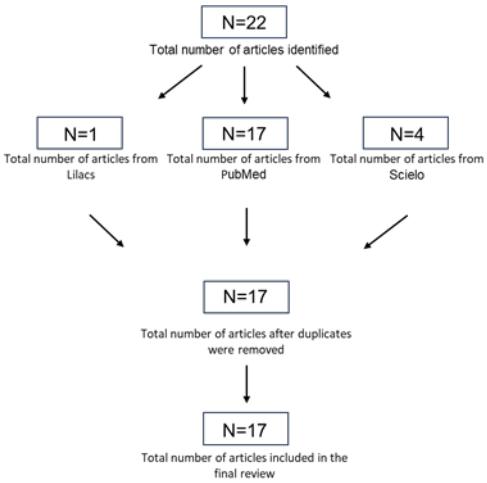
Search Strategy

The search for studies was conducted in the PubMed, SciELO, and Lilacs databases, covering the period from January 2015 to July 2, 2024. The selection of 2015 as the starting year was based on the approval of the LAAO technique in the United States, marking a turning point in the clinical adoption of the procedure.

A broad search strategy was used, employing the following keywords: "oclusão do apêndice atrial esquerdo" OR "OAAE" OR 'left atrial appendage oclusion" OR "LAAO" OR "fibrilação atrial" OR "atrial fibrilation" OR "acidente vascular encefálico" OR "stroke".

Studies with retrospective or prospective designs, available in Portuguese or English, and involving only human subjects were included. Duplicated articles, narrative reviews, letters to the editor, and animal studies were excluded. The complete search strategy is presented in Tables 1 and 2 in the Results section. Below is attached Figure 1, illustrating the article inclusion flowchart.

Figure 1. Article Inclusion Flowchart



Source: Authors (2025)

RESULTS

The initial literature search yielded 22 articles selected for preliminary screening. After applying the inclusion and exclusion criteria, 17 studies were included in the final analysis, with 14 from the PubMed database and 3 from SciELO. The search results, as well as the study design, objectives, sample characteristics, and main findings, are detailed in Tables 1 and 2.

The results presented demonstrated that patients with NVAF can be treated with warfarin, dual antiplatelet therapy (DAPT)[18] or novel oral anticoagulants (NOACs), such as rivaroxaban, apixaban, and edoxaban. NOACs have shown a lower incidence of major bleeding, including gastrointestinal bleeding, and similar or superior efficacy to warfarin in preventing thromboembolic events, such as ischemic stroke.[19]

furthermore, NOACs demonstrated efficacy comparable to LAAO, offering a less invasive alternative with a favorable safety profile.[20,21] In the studies analyzed, LAA occluder devices varied in shape and size, making it essential to assess the LAA ostium measurements to select the appropriate occluder. The most commonly used techniques were transesophageal echocardiography (TEE) and 3D computed tomography (3D-CT), with the latter providing a more precise visualization of LAA anatomy, allowing better evaluation of the septum, implantation site, and a higher first-attempt success rate.[22,23]

After the LAAO procedure, patients generally receive OAC for the first three months to prevent clot formation while the device heals and integrates with the cardiac tissue. In one study, two groups were compared: apixaban and dual antiplatelet therapy (DAPT). Apixaban showed a lower incidence of device thrombosis and thromboembolic events, including stroke, as well as a reduction in major bleeding, such as gastrointestinal and intracranial hemorrhages, compared to DAPT.[18] Furthermore, the procedure proved to be effective and safe, with a low incidence of long-term complications, including peri-device leak (PDL) and device thrombosis in 8 patients, with no occurrence of stroke.[24]

Several studies[25-28] compared the efficacy between two types of occluders. It was observed that peri-device leak (PDL) was more frequent with the single-seal occluder, which was associated with a higher incidence of thromboembolic and cardiovascular events. The measurement techniques were similar, but the double-seal occluder used the landing zone diameter, whereas the single-seal occluder considered the LAA ostium diameter. [25,28]

Regarding adverse effects, they were more common in women (4.4%) than in men (1.9%), including bleeding and pericardial effusions. The incidence of PDL, ischemic stroke (IS), hemorrhagic stroke (HS), systemic embolism, and device thrombosis was similar between groups. Some cases of stroke occurred only with the single-seal occluder. Overall, the double-seal occluder showed a lower rate of severe PDL.[27,28] They also demonstrated high efficacy and safety, with a reduction in stroke and thromboembolic events, a low complication rate, and improved long-term quality of life.[29-31]

Conventional transseptal puncture (CTP) is the standard technique for accessing the LA and LAA. Studies comparing CTP with angioplasty wire-assisted transseptal puncture (AW-TP) demonstrated a higher success rate and shorter procedure time with AW-TP, while maintaining a similar safety profile.[32]

Furthermore, studies evaluated LAAO performed concomitantly with other procedures. The combination with transcatheter aortic valve implantation (TAVI) showed a reduction in thromboembolic risk and symptom improvement in patients with NVAF and aortic stenosis. Combining LAAO with percutaneous coronary intervention (PCI) was also found to be feasible and safe, with complication rates similar to those of isolated procedures.[33,34]

Table 1: PubMed Articles

ARTICLE	STUDY DESIGN	OBJECTIVES	SAMPLE	MAIN FINDINGS
TURAGAM ET AL. [19]	Prospective, observational	To evaluate the risk of bleeding and stroke (warfarin vs. NOACs) in patients with AF.	n=263	NOACs further reduced the risk of stroke and bleeding.
ENG ET AL. [22]	Prospective, randomized	To investigate two approaches for guiding LAAO: 3D-CT and TEE.	n=24	3D-CT ≥ TEE in accuracy and safety.
STAUBACH ET AL. [24]	Propective,non randomized	To evaluate complications associated with LAAO 12 months after the procedure guided by TEE.	n=63	Effective and safe, with a low incidence of long-term complications.
FLORES ET AL. [18]	Clincial trial, randomized, multicenter	To compare the efficacy and safety of DAPT versus apixaban over 9 months.	n=44 (apixaban) n=46 (TAD)	Apixaban: fewer hemorrhagic and thromboembolic complications.
MANSOUR ET AL. [25]	Prospective, multicenter, observational	To evaluate PDL and its clinical impact 12 months after LAAO.	n=60	PDL slightly increases the risk of stroke.
KORSHOLM ET AL. [20]	Prospective, multicenter, randomized	To compare LAAO versus NOACs regarding stroke, embolic events, and bleeding in patients with AF.	n=375 (LAAO) n=375 (NAOs)	Both are effective in preventing stroke.
HUIJBOOM ET AL. [21]	Multicenter, randomized	To compare the efficacy and safety of LAAO versus standard treatment in patients ineligible for OAC.	n=406 (LAAO) n=203 (OAC)	LAAO is effective in preventing stroke in patients with AF who cannot use OAC.
ALKHOULI ET AL. [26]	Prospective, observational, randomized	To evaluate sex differences in the safety and efficacy of LAAO.	n=537 (male) n=380 (female)	More adverse events occurred in women (4.4%) than in men (1.9%).
SCHMIDT ET AL. 27	Prospective, observational	To evaluate the incidence, predictors, and clinical outcomes of LAAO device-related thrombi.	n=903 (double) n=885 (single)	Early thrombi are observed with the double-seal occluder, while late thrombi occur with the single-seal occluder.

LOSIK ET AL. 34	Prospective, randomized	To evaluate the feasibility of combining LAAO with PCI.	n=50	No complications were observed, with no difference in hospital stay duration.
WANG ET AL. 23	Clinical trial, randomized	To evaluate the impact of pre-procedural planning with 3D-CT for LAAO.	n=96	3D-CT can reduce the need for occluder replacement and shorten the procedure time.
LAKKIREDDY ET AL. 35	Prospective,randomized	To investigate predictors of PDL between double-seal and single--seal occluders.	n=1.878	3D-CT can reduce the need for occluder replacement and shorten the procedure time.
KAPADIA ET AL. 36	Observatinal, multicenter, randomized	To evaluate the safety and feasibility of LAAO combined with TAVI.	n=363	LAAO + TAVI is not inferior to TAVI + OAC.
HU ET AL. 37	Prospective, multicenter, randomized	To compare AW-TP with CTP.	n=131 (AW-TP) n=132 (PTC)	AW-TP achieved higher success in LAAO.

NOACs: NEW ORAL ANTICOAGULANTS; **AF:** ATRIAL FIBRILLATION; **LAAE;** LEFT ATRIAL APPENDAGE OCCLUSION; **3D-CT:** COMPUTED ANGIOTOMOGRAPHY; **TEE:** TRANSESOPHAGEAL ECOCARDIOGRAPHY; **DAPT:** DUAL ANTIPLATELET THERAPY; **PDL;** PERI-DEVICE LEAK; **PCI:** PERCURTANEOUS CORONARY INTERVENTION; **LAA:** LEFT ATRIAL APPENDAGE; **TAVI:** TRANSCATHETER AORTIC VALVE IMPLANTATION; **CTP:** CONVENTIONAL TRANSSEPTAL PUNCTURE; **AW-TP:** ANGIOPLASTY GUIDEWIRE-ASSISTED TRANSSEPTAL PUNCTURE.

Source: Authors

Table 2: Scielo Articles

ARTICLE	STUDY DESIGN	OBJECTIVES	SAMPLE	MAIN FINDINGS
GUÉRIOS ET AL.	Prospective	To present the immediate results and long-term follow-up of patients undergoing LAAO.	n=91	LAAO was effective in preventing stroke and bleeding.
MONTENEGRO ET AL. 39	Retrospective, observational	To evaluate the safety of LAAO with a double-seal occluder in preventing major cardiovascular events during long-term follow-up.	n=15	LAAO proved to be safe, with a high procedural success rate and favorable patient outcomes at 12 months.
CHAMIÉ ET AL.[40]	Prospective	To describe the initial results of a multicenter early experience in Brazil with a double-seal device for LAAO.	n=51	Left atrial appendage occlusion with the double-seal device showed a 100% success rate, with no deaths, strokes, or major complications after 18 months.

LAAE; LEFT ATRIAL APPENDAGE OCCLUSION; **AF:** ATRIAL FIBRILLATION; **OAC:** ORAL ANTICOAGULANT; **LAA:** LEFT ATRIAL APPENDAGE.

DISCUSSION

Although effective, NOACs and DAPT are associated with gastrointestinal and intracranial bleeding, which complicates clinical management.[18] The choice of the most appropriate therapeutic approach should take into account individual factors such as tolerance to OAC, bleeding risk, and patient preferences. In this context, LAAO emerges as a promising alternative, as it eliminates the need for continuous anticoagulation but requires careful assessment of procedural risks. However, since it is an invasive procedure, LAAO carries potential risks, while pharmacological therapy requires continuous use and close monitoring, which may affect adherence and outcomes.[41]

Apixaban demonstrated a safe profile as adjuvant therapy after LAAO, especially in patients with NVAF and a high risk of thrombosis or bleeding, reinforcing the importance of an individualized approach.[42]

The choice of occluder device is crucial for the success of LAAO, and the analyzed data highlight the need for individualized anatomical assessment. The variety of occluder shapes and sizes requires careful evaluation of the LAA ostium, making the use of precise imaging techniques essential. This approach contributes to a higher first-attempt success rate, reflecting technological advances and technical improvements in performing the procedure. Therefore, accurate imaging methods should be increasingly valued in the planning and execution of LAAO.[43,44]

The findings suggest that isolated complications are more frequent with single-seal occluders. However, recent analyses indicate that new single-seal occluder devices show more favorable results, with lower rates of perioperative complications compared to earlier double-seal models.[45] The incidence of PDL (0.01% vs. 0.34%) and the success rate (99.9% vs. 99.4%) were higher with the new single-seal occluder, reflecting better sealing and greater prevention of thromboembolism. These data suggest that the new model offers greater anatomical adaptability, establishing itself as a safer and more effective option.

AW-TP appears to be a preferred approach for LAAO, as it increases procedural efficiency, reduces duration, and improves success rates while minimizing complications associated with the conventional technique. Its adoption represents a significant advancement in clinical practice and a promising strategy for future LAAO therapeutic protocols. In addition, combining

LAAO with TAVI has proven to be a safe and effective strategy, showing promising clinical benefits.[33,34] However, further studies are needed to assess long-term safety and outcomes in order to confirm its efficacy and expand its applicability.

Although LAAO is an effective therapeutic option for preventing thromboembolic events in patients with NVAF, its high cost still limits access for many patients, especially in resource-limited settings. Despite the initial investment, studies indicate that, in the long term, LAAO may become a cost-effective alternative compared to continuous anticoagulation, considering the expenses associated with thromboembolic events and hemorrhagic complications. Expanding access to the procedure would not only diversify therapeutic options but also improve long-term clinical outcomes, offering a more definitive and safer solution for the management of NVAF.[47,48]

CONCLUSION

LAAO appears to be an effective and permanent strategy for preventing thromboembolic events in patients with NVAF, offering an alternative to continuous OAC. The new single-seal occluder devices demonstrate improved safety, efficacy, and anatomical adaptability, while double-seal occluders maintain a low rate of serious complications. Combined procedures with TAVI or PCI are feasible and safe, and techniques such as AW-TP increase the procedural success rate.

In summary, LAAO represents a definitive and safe solution, capable of reducing the risk of major bleeding, preventing stroke, and improving the quality of life in patients with NVAF, establishing itself as a promising therapeutic alternative in high-risk clinical scenarios.

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