

International Journal of Health Science

Acceptance date: 08/04/2025

MANAGEMENT OF ATRIAL FIBRILLATION: THERAPEUTIC APPROACHES AND STRATEGIES TO PREVENT THROMBOEMBOLIC EVENTS

Matheus de Castro Fernandes Andrade

Medical student at the Universidade de Vassouras -RJ

<http://lattes.cnpq.br/2458146658534249>

Debora Lucy de Souza Bastos Antonio

Medical student at the Universidade de Vassouras -RJ

<http://lattes.cnpq.br/5092083425548421>

Maisa Cristina Ramos Batista

Medical student at the Universidade de Vassouras -RJ

<http://lattes.cnpq.br/0837775919724069>

Carolina Pimentel Fogaça de Souza

Medical student at the Universidade de Vassouras -RJ

<http://lattes.cnpq.br/5262047207999808>

Juliana Tavares de Araújo

Medical student at the Universidade de Vassouras -RJ

<http://lattes.cnpq.br/7727215381519105>

Matheus de Souza Joaquim

Medical student at the Universidade de Vassouras -RJ

<http://lattes.cnpq.br/0637959946887498>

All content in this magazine is licensed under a Creative Commons Attribution License. Attribution-Non-Commercial-Non-Derivatives 4.0 International (CC BY-NC-ND 4.0).



Beatriz Almeida Assed Kiki

Medical student at the Universidade de Vassouras -RJ
<http://lattes.cnpq.br/8075456891369731>

Filipe de Oliveira Lopes Rego

Lecturer at the Universidade de Vassouras-RJ
<http://lattes.cnpq.br/3525428346216377>

Abstract: Atrial fibrillation (AF) is a common arrhythmia linked to thromboembolic complications, such stroke. This study reviewed its epidemiology, pathophysiology, and therapeutic strategies, emphasizing the use of anticoagulants and thrombolysis. DOACs were shown to be effective for preventing thromboembolic events, while thrombolysis proved useful but limited in acute scenarios. The study concludes that technological advances and personalized approaches are crucial for improving AF management.

Keywords: Atrial fibrillation; thrombolysis; treatment.

INTRODUCTION

Atrial fibrillation (AF) is one of the most common cardiac arrhythmias, characterized by disorganized electrical activity in the atria, which results in ineffective atrial contractions. This condition is associated with a significantly increased risk of thromboembolic complications, such as stroke, as well as other cardiovascular morbidities (KUMAR et al., 2020). Understanding the pathophysiological and clinical aspects of AF, as well as developing effective therapies, is essential to reducing the mortality and morbidity associated with the disease.

From an epidemiological point of view, AF affects around 33 million people worldwide, with increasing prevalence due to population aging. Studies indicate that approximately 1 to 2% of the global population is affected, with the highest incidence in individuals over the age of 65 (CHUGH et al., 2014). This prevalence varies according to factors such as gender, ethnicity and the presence of comorbidities such as hypertension, diabetes and heart failure. The growing burden of AF represents a substantial challenge for health systems in terms of early diagnosis, management and prevention of complications (HINDRICKS et al., 2021).

One of the most worrying aspects of AF is its association with thromboembolic risk. Arrhythmia contributes to blood stasis in the atria, particularly in the left atrium, creating ideal conditions for the formation of thrombi. These thrombi can detach and cause embolization in distant organs, such as the brain, leading to events such as ischemic stroke (WATSON et al., 2022). Patients with AF have a five times higher risk of stroke compared to individuals without the arrhythmia, which reinforces the importance of an effective prevention strategy (LIP et al., 2018).

The prevention of thromboembolic events in AF patients is a fundamental pillar in the management of this condition. The CHA₂DS₂-VASc score is widely used to stratify the risk of thromboembolism in AF patients, guiding the decision on the need for antithrombotic therapies. Studies show that the introduction of oral anticoagulants, such as vitamin K antagonists (warfarin) and direct oral anticoagulants (DOACs), significantly reduces the incidence of thromboembolic events, such as stroke and systemic embolism (GIUGLIANO et al., 2013). In addition, advances in the perioperative management of anticoagulants have allowed for safer control in patients undergoing invasive procedures (STEFFEL et al., 2021).

The pathophysiological mechanisms underlying thrombosis in AF patients are complex and involve the interaction of three main components: blood stasis, endothelial dysfunction and hypercoagulability, as described in Virchow's triad. Atrial stasis, particularly in the left atrium, is the main contributor to thrombus formation. Histopathological studies suggest that alterations in the atrial endothelium and the rheological properties of the blood also play critical roles in this process (THRUSTON et al., 2019). These findings underline the importance of therapeutic interventions targeting each of these mechanisms.

Antithrombotic therapies are the main approach in the management of patients with AF. In addition to oral anticoagulants, antiplatelet therapies, such as the use of acetylsalicylic acid, have been investigated, although their efficacy in preventing thromboembolic events in AF is inferior to anticoagulants. Recently, left atrial occlusion devices have emerged as an option for patients with contraindication to the use of anticoagulants (HOLMES et al., 2019). These advances highlight the evolution of management strategies to address the limitations of conventional therapies. Thrombolysis, or thrombolytic therapy, is a potentially life-saving intervention in emergency situations such as acute ischemic stroke, especially in patients with AF. However, its indication is surrounded by controversy, since the presence AF increases the risk of complications, such as intracranial hemorrhages (SAVER et al., 2015). Strict patient selection criteria and careful management during and after the procedure are essential to minimize the risks and maximize the benefits of thrombolysis (EMMERSON et al., 2020).

The efficacy of thrombolysis in preventing thromboembolic complications in patients with AF has been widely studied. Clinical data show that early administration of thrombolytic agents, such as alteplase, can significantly improve outcomes in cases of ischemic stroke associated with AF. However, the restricted therapeutic window and the risks associated with the therapy limit its use in some patients (NINOMIYA et al., 2018). These factors highlight the need to carefully balance the risks and benefits of thrombolysis in each clinical situation.

The clinical challenges in managing patients with AF and thrombosis are numerous and range from early diagnosis to the selection of appropriate therapeutic interventions. The presence of comorbidities, such

as chronic kidney disease and heart failure, can complicate management and increase the risk of complications. In addition, adherence to antithrombotic treatment is often compromised due to factors such as the associated costs and side effects of medications (ROSE et al., 2021).

The relevance of new studies to improve AF and thrombosis management strategies cannot be underestimated. Research areas such as genetics, biomarkers and new pharmacological therapies has the potential to transform the care of these patients. In addition, the use of digital technologies, such as monitoring apps and wearable devices, can improve the early detection and management of AF (VARMA et al., 2019). These advances offer new opportunities to improve clinical outcomes and reduce the burden of disease at a population level.

The aim of this study was to review epidemiological, pathophysiological and therapeutic aspects of atrial fibrillation (AF), with a focus on preventing thromboembolic complications. The study explored the efficacy of anticoagulants and thrombolysis, as well as the limitations of these approaches, analyzing the role of alternative devices and technological advances in the personalized management of AF patients.

METHODS

The search for scientific articles was carried out using the National Library of Medicine (PubMed) database. The descriptors were “*H Pylori*”; “*infection*”; “*treatment*”, using the Boolean operator “AND” between the respective words. The categories were: clinical trial and randomized clinical trial. The studies were selected from publications between 2014 and 2024, using articles in English and Portuguese as inclusion criteria. The exclusion criteria were articles that added other pathologies to the central theme,

disconnected from the proposed subject. The academic papers were reviewed using the following steps, in the following order: defining the topic; establishing the study categories; proposing inclusion and exclusion criteria; checking and then analyzing the publications; organizing the information; and presenting the data.

RESULTS

By combining the descriptors used, a total of 1,353 papers were obtained from the PubMed database. Using the inclusion criterion: articles published in the last 10 years (2014-2024), resulted in a total of 1007 articles. Next, clinical trials, randomized controlled trials or journal articles were added as inclusion criteria, giving a total of 95 articles. Articles in Portuguese or English were selected, resulting in 95 articles and then the free full text option was added, totaling 39 articles. After reading the abstracts, those that did not fit the topic or were duplicated were excluded, totaling 24 articles, as shown in Figure 1.

DISCUSSION

Atrial fibrillation (AF) is the most common arrhythmia in adult patients and is associated with a significantly increased risk of ischemic stroke. Studies such as that by Carnicelli et al. (2022) evaluate the efficacy of direct oral anticoagulants compared to warfarin, highlighting benefits in the prevention of embolic events in specific populations, including the elderly and women. This approach is crucial, as individualizing treatment can mitigate hemorrhagic risks, especially in patients with comorbidities or concomitant use of antithrombotic drugs. Analysis of large databases reinforces that factors such as age and gender influence the response to treatment, outlining the need for personalized criteria (CARNICELLI et al., 2022).

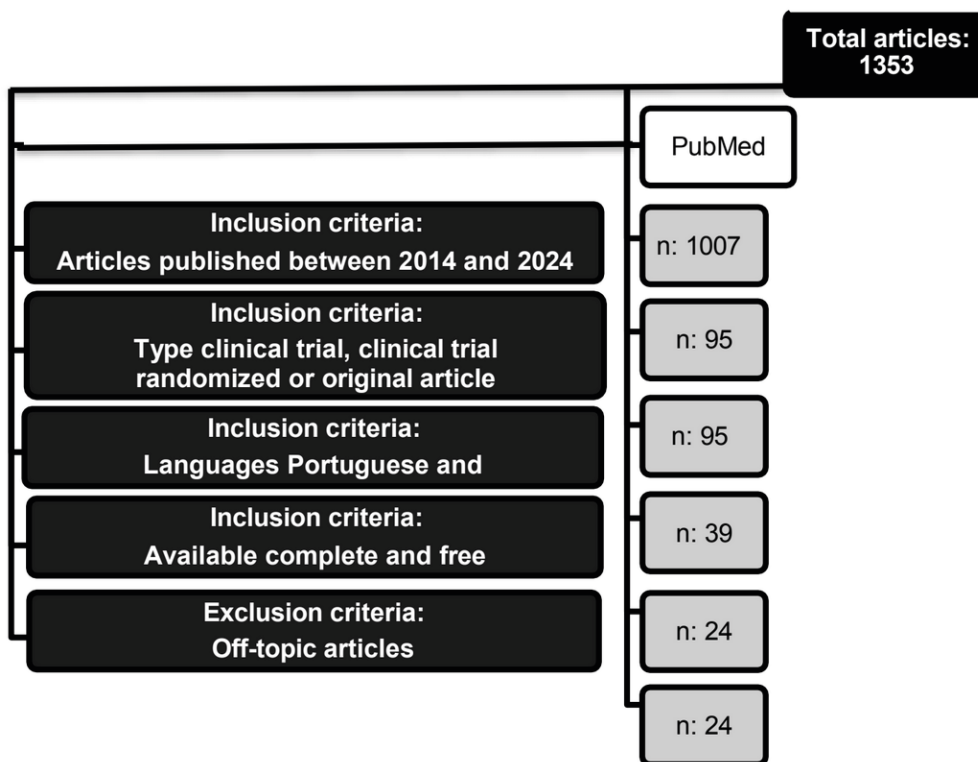


FIGURE 1: Flowchart for identifying articles in PubMed.

Source: Authors (2024)

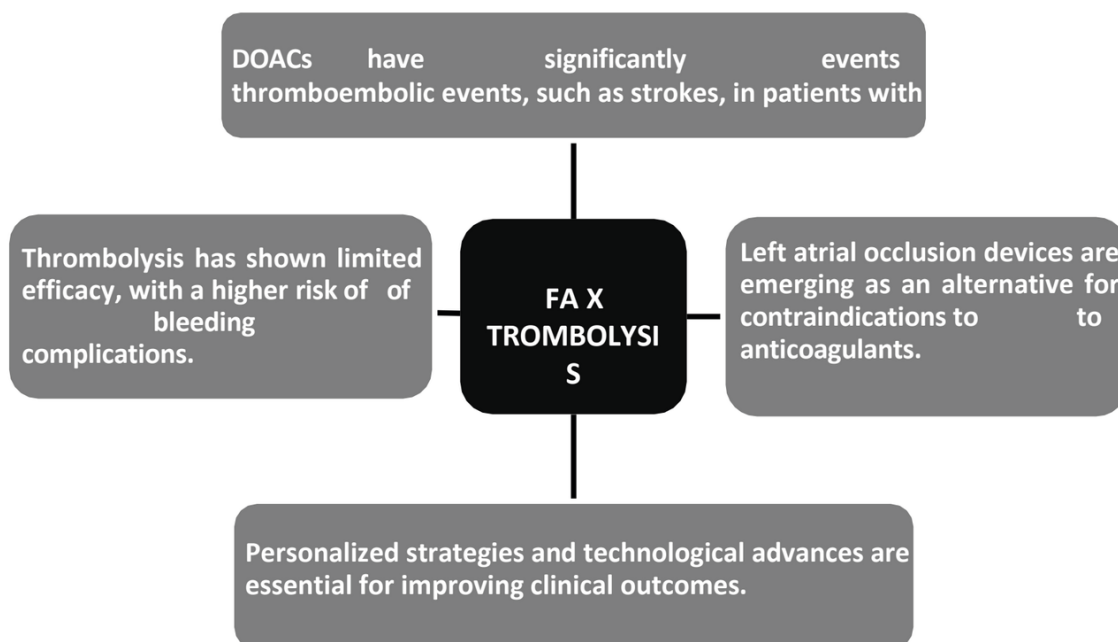


FIGURE 2: Summary of the most frequently found results according to the articles analyzed.

Source: Authors (2024)

The relationship between AF and the occurrence of bleeding in patients undergoing percutaneous coronary intervention (PCI) is addressed in the study by Gibson et al. (2016). This highlights the importance of combined anticoagulation and antithrombotic strategies in reducing bleeding complications, especially in high-risk patients. Results indicate that dose adjustments of drugs such as edoxaban, a factor Xa inhibitor, can offer sufficient protection against thromboembolic events without excessively increasing the risk of bleeding. This reinforces the need for continuous monitoring to optimize the risk-benefit ratio (GIBSON et al., 2016).

Patients with AF often have thromboembolic complications, even when treated with anticoagulants. Benz et al. (2023) examined ischemic stroke patients who were previously on anticoagulation, revealing that therapeutic failures can occur due to factors such as poor adherence to treatment or pharmacodynamic changes. Thus, the study suggests that monitoring methods, such as continuous arrhythmia detection devices, can be integrated into clinical management to improve therapeutic efficacy. In addition, subgroup analysis can help to identify patients with a higher risk of recurrent events (BENZ et al., 2023).

Regarding the early diagnosis of AF, studies such as that by Bernstein et al. (2021) demonstrate the effectiveness of continuous cardiac monitoring, especially in patients with cryptogenic stroke. The STROKE-AF study revealed that the detection of previously undiagnosed AF in patients with small- or large-vessel disease directly impacts stroke recurrence rates, highlighting the importance of implantable devices and remote monitoring in clinical practice. This personalized approach can prevent future events, reinforcing the role of technology in AF management (BERNSTEIN et al., 2021). Com-

parisons between direct oral anticoagulants, such as edoxaban, and warfarin in specific subgroups, such as patients with a history of falls, are discussed in ENGAGE AF-TIMI 48. Steffel et al. (2021) show that adjusted doses of edoxaban can be a safe and effective alternative in these patients, reducing serious bleeding events. This highlights the importance of considering individual characteristics, such as frailty and a history of falls, when choosing anticoagulant treatment, especially in elderly populations (STEFFEL et al., 2021).

In addition, Wilkinson et al. (2020) address the impact of frailty on clinical outcomes in AF patients, emphasizing that frail patients have higher rates of mortality and complications. This reinforces the need for specific protocols for this population, with rigorous monitoring and interventions that consider frailty as an independent risk factor. Including frailty in risk algorithms can significantly improve clinical decision-making (WILKINSON et al., 2020).

Thrombolysis also plays an essential role in the treatment of AF in stroke patients. Studies such as that by Lau et al. (2016) explore the effects of direct oral anticoagulants on clot formation and thrombolysis, highlighting that these agents not only prevent thrombus formation, but also facilitate its dissolution. This is particularly relevant in acute stroke contexts, where the speed of thrombus resolution can significantly influence clinical outcomes. The choice of anticoagulant agent must consider these additional effects in order to maximize therapeutic benefits (LAU et al., 2016).

The interaction between AF and other conditions, such as liver disease, is analyzed by Qamar et al. (2019), who investigated the safety and efficacy of edoxaban in patients with a history of liver dysfunction. This study reinforces that direct oral anticoagulants can be used safely in complex

subgroups, provided there is adequate monitoring of liver and kidney function. These findings expand the therapeutic options for patients previously considered unsuitable for anticoagulation (QAMAR et al., 2019). Studies focused on risk scoring strategies, such as the ABC score, were analyzed by Berg et al. (2019), who emphasize their applicability in stratifying the risk of stroke and bleeding in AF patients. These tools help personalize treatment, allowing decisions based on risk-benefit. In addition, the incorporation biomarkers in these algorithms can improve the accuracy of predictions, promoting a more effective and safer approach to clinical management (BERG et al., 2019).

The role of AF in postoperative conditions, such as after cardiac interventions, is analyzed in the EXCEL study, which examines new-onset atrial fibrillation after coronary artery bypass grafting. Kosmidou et al. (2018) conclude that these patients have a higher risk of long-term adverse events, suggesting that preventive strategies and targeted treatments should be implemented to improve clinical outcomes. Early detection of AF in these cases is essential to initiate anticoagulation in a timely manner (KOSMIDOU et al., 2018).

Finally, Giugliano et al. (2016) discuss the mortality associated with AF in patients treated with edoxaban or warfarin, pointing out that although both are effective in reducing

thromboembolic events, edoxaban has a superior safety profile in terms of major bleeding. This analysis is particularly relevant for patients with multiple risk factors, in whom the safety of the treatment is as important as its efficacy (GIUGLIANO et al., 2016).

CONCLUSION

Atrial fibrillation (AF) represents one of the greatest challenges in modern cardiology due to its high prevalence, high risk of thromboembolic complications and complex clinical management. This study highlighted the importance of preventing thromboembolic events in AF patients by understanding the pathophysiological mechanisms and applying antithrombotic therapies. The use of oral anticoagulants, particularly DOACs, has been shown to be fundamental in reducing the incidence of events such as stroke. However, thrombolysis, although effective in emergency situations, has significant limitations due to the risk of complications, especially in patients with AF. Technological advances and new therapeutic approaches, such as left atrial occlusion devices, show potential to address gaps in the care of these patients. In short, the research reinforces the need to individualize clinical management, taking into account the characteristics of each patient, and to continue investigating innovative approaches to improve clinical outcomes.

REFERENCES

- CARNICELLI AP et al. **Direct Oral Anticoagulants Versus Warfarin in Patients With Atrial Fibrillation: Patient-Level Network Meta-Analyses of Randomized Clinical Trials With Interaction Testing by Age and Sex.** *Circulation*, v. 145, n. 4, p. 242-255, 2022. doi: 10.1161/CIRCULATIONAHA.121.056355.
- GIBSON CM et al. **Prevention of Bleeding in Patients with Atrial Fibrillation Undergoing PCI.** *N Engl J Med*, v. 375, n. 25, p. 2423-2434, 2016. doi: 10.1056/NEJMoa1611594.
- BENZ AP et al. **Outcomes of patients with atrial fibrillation and ischemic stroke while on oral anticoagulation.** *Eur Heart J*, v. 44, n. 20, p. 1807-1814, 2023. doi: 10.1093/eurheartj/ehad200.

LEE PH et al. **Cryptogenic Stroke and High-Risk Patent Foramen Ovale: The DEFENSE- PFO Trial.** J Am Coll Cardiol, v. 71, n. 20, p. 2335-2342, 2018. doi: 10.1016/j.jacc.2018.02.046.

BERNSTEIN RA et al. **Effect of Long-term Continuous Cardiac Monitoring vs Usual Care on Detection of Atrial Fibrillation in Patients With Stroke Attributed to Large- or Small- Vessel Disease: The STROKE-AF Randomized Clinical Trial.** JAMA, v. 325, n. 21, p. 2169- 2177, 2021. doi: 10.1001/jama.2021.6470.

STEFFEL J et al. **Randomized, Double-Blind Comparison of Half-Dose Versus Full-Dose Edoxaban in 14,014 Patients With Atrial Fibrillation.** J Am Coll Cardiol, v. 77, n. 9, p. 1197- 1207, 2021. doi: 10.1016/j.jacc.2020.12.053.

WILKINSON C et al. **Clinical outcomes in patients with atrial fibrillation and frailty: insights from the ENGAGE AF-TIMI 48 trial.** BMC Med, v. 18, n. 1, p. 401, 2020. doi: 10.1186/s12916-020-01870-w.

STEFFEL J et al. **Edoxaban Versus Warfarin in Atrial Fibrillation Patients at Risk of Falling: ENGAGE AF-TIMI 48 Analysis.** J Am Coll Cardiol, v. 68, n. 11, p. 1169-1178, 2016. doi: 10.1016/j.jacc.2016.06.034.

KOSMIDOU I et al. **New-Onset Atrial Fibrillation After PCI or CABG for Left Main Disease: The EXCEL Trial.** J Am Coll Cardiol, v. 71, n. 7, p. 739-748, 2018. doi: 10.1016/j.jacc.2017.12.012.

LAU YC et al. **Effects of non-vitamin K antagonist oral anticoagulants on fibrin clot and whole blood clot formation, integrity and thrombolysis in patients with atrial fibrillation .** J Thromb Thrombolysis, v. 42, n. 4, p. 535-544, 2016. doi: 10.1007/s11239-016-1399-3.

DING WY et al. **Relationship between temporal rhythm-based classification of atrial fibrillation and stroke: real-world vs. clinical trial.** J Thromb Thrombolysis, v. 54, n. 1, p. 1- 6, 2022. doi: 10.1007/s11239-022-02638-0.

QAMAR A et al. **Edoxaban Versus Warfarin in Patients With Atrial Fibrillation and History of Liver Disease.** J Am Coll Cardiol, v. 74, n. 2, p. 179-189, 2019. doi: 10.1016/j.jacc.2019.04.061.

CORBALÁN R et al. **Edoxaban Versus Warfarin in Latin American Patients With Atrial Fibrillation: The ENGAGE AF-TIMI 48 Trial.** J Am Coll Cardiol, v. 72, n. 13, p. 1466-1475, 2018. doi: 10.1016/j.jacc.2018.07.037.

BERG DD et al. **Performance of the ABC Scores for Assessing the Risk of Stroke or Systemic Embolism and Bleeding in Patients With Atrial Fibrillation in ENGAGE AF-TIMI 48.** Circulation, v. 139, n. 6, p. 760-771, 2019. doi: 10.1161/CIRCULATIONAHA.118.038312.

GIUGLIANO RP et al. **Mortality in Patients with Atrial Fibrillation Randomized to Edoxaban or Warfarin: Insights from the ENGAGE AF-TIMI 48 Trial.** Am J Med, v. 129, n. 8, p. 850-857.e2, 2016. doi: 10.1016/j.amjmed.2016.02.028.

EISEN A et al. **Digoxin Use and Subsequent Clinical Outcomes in Patients With Atrial Fibrillation With or Without Heart Failure in the ENGAGE AF-TIMI 48 Trial.** J Am Heart Assoc, v. 6, n. 7, p. e006035, 2017. doi: 10.1161/JAHA.117.006035.

HOSHI T et al. **Short-duration triple antithrombotic therapy for atrial fibrillation patients who require coronary stenting: results of the SAFE-A study.** EuroIntervention, v. 16, n. 2, p. e164-e172, 2020. doi: 10.4244/EIJ-D-19-00920.

CHALOS V et al. **Endovascular Treatment With or Without Prior Intravenous Alteplase for Acute Ischemic Stroke.** J Am Heart Assoc, v. 8, n. 11, p. e011592, 2019. doi: 10.1161/JAHA.118.011592.

WANG K et al. **Impact of Spontaneous Extracranial Bleeding Events on Health State Utility in Patients with Atrial Fibrillation: Results from the ENGAGE AF-TIMI 48 Trial.** J Am Heart Assoc, v. 6, n. 8, p. e006703, 2017. doi: 10.1161/JAHA.117.006703.

ZHANG L et al. **Associations between model-predicted rivaroxaban exposure and patient characteristics and efficacy and safety outcomes in patients with non-valvular atrial fibrillation.** J Thromb Thrombolysis, 2020.

HU C et al. **Vasodilator-stimulated phosphoprotein-guided Clopidogrel maintenance therapy reduces cardiovascular events in atrial fibrillation patients requiring anticoagulation therapy and scheduled for percutaneous coronary intervention: a prospective cohort study.** BMC Cardiovasc Disord. 2018 Jun 18;18(1):120. doi: 10.1186/s12872-018-0853-x. PMID: 29914380; PMCID: PMC6006722.

CHUGH, S. S. et al. **Worldwide epidemiology of atrial fibrillation: A Global Burden of Disease 2010 Study.** Circulation, v. 129, n. 8, p. 837-847, 2014.

EMMERSON, C. J. et al. **Safety and efficacy of thrombolysis in patients with atrial fibrillation and acute ischemic stroke: A systematic review.** Journal of Stroke and Cerebrovascular Diseases, v. 29, n. 6, p. 104-112, 2020.

GIUGLIANO, R. P. et al. **Edoxaban versus warfarin in patients with atrial fibrillation.** New England Journal of Medicine, v. 369, n. 22, p. 2093-2104, 2013.

HINDRICKS, G. et al. **2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio- Thoracic Surgery (EACTS).** European Heart Journal, v. 42, n. 5, p. 373-498, 2021.

HOLMES, D. R. et al. **Left atrial appendage occlusion in atrial fibrillation: An updated review.** Journal of the American College of Cardiology, v. 74, n. 23, p. 2962-2975, 2019.

KUMAR, S. et al. **Pathophysiological insights into atrial fibrillation: Mechanisms and therapeutic targets.** Cardiology Clinics, v. 38, n. 2, p. 179-196, 2020.

LIP, G. Y. H. et al. **Antithrombotic therapy for atrial fibrillation: CHEST guideline and expert panel report.** Chest, v. 154, n. 5, p. 1121-1201, 2018.

NINOMIYA, T. et al. **Alteplase in the treatment of acute ischemic stroke with atrial fibrillation: A review of clinical trials and current practice.** Stroke Research and Treatment, v. 2018, p. 1-8, 2018.

ROSE, A. J. et al. **Barriers to anticoagulation in atrial fibrillation: Perspectives from patients and providers.** Journal of the American Heart Association, v. 10, n. 2, p. 1-12, 2021.

SAVER, J. L. et al. **Thrombolysis for acute ischemic stroke in patients with atrial fibrillation.** Stroke, v. 46, n. 4, p. 1013-1019, 2015.

THRUSTON, C. et al. **Endothelial dysfunction and thrombosis in atrial fibrillation: Mechanisms and implications.** Journal of Thrombosis and Haemostasis, v. 17, n. 1, p. 1-11, 2019.

VARMA, N. et al. **Use of wearable devices in atrial fibrillation management: A new frontier.** Journal of the American College of Cardiology, v. 74, n. 24, p. 2995-3005, 2019.

WATSON, T. et al. **Pathophysiology of thromboembolism in atrial fibrillation: The role of the left atrial appendage.** Journal of the American College of Cardiology, v. 74, n. 4, p. 404- 416, 2019.