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Prevalence, Management, and Outcomes of Atrial Fibrillation in Paediatric Patients: Insights from a Tertiary Cardiology Centre

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Abstract: Background: Atrial fibrillation (AF) is increasingly recognised in paediatric patients and presents unique management challenges. We aimed to investigate the prevalence, management strategies, and outcomes of AF in this population. **Methods:** This retrospective analysis was conducted at a tertiary paediatric cardiology centre, including patients aged ≤18 years who were diagnosed with AF between January 2015 and December 2023. Demographic details, clinical manifestations, treatments, and outcomes were also analysed. Patients with documented AF episodes were included. Descriptive statistics were used to assess the treatment efficacy, recurrence, and complications. **Results:** The study included 36 patients (mean age, 15 years; 58% male). Of these, 52.8% had acquired heart disease, 16.7% had congenital anomalies, and 16.7% had lone AF. The initial treatment involved electrical cardioversion (53.3%) and pharmacological conversion with amiodarone (46.7%). Over 80% of the patients received rhythm control therapy, and 63.9% were placed on oral anticoagulation, primarily for rheumatic and congenital heart diseases. The success rate of rhythm control was 50% with an AF recurrence rate of 3.8%. Ischaemic stroke was the most common complication (n=3) occurring in patients with underlying heart disease. **Conclusion:** AF in paediatric patients is predominantly associated with rheumatic and congenital heart diseases, although a notable proportion of patients present with lone AF. Despite the high intervention and antiarrhythmic therapy rates, neurological complications, particularly in those with underlying heart disease, remain a significant concern. These findings highlight the need for further comprehensive studies to understand better the aetiology, risk factors, and management of paediatric AF.

Keywords: atrial fibrillation; paediatric arrhythmias; paediatric cardiology; congenital heart disease; rheumatic heart disease

1. Introduction

Atrial fibrillation (AF) is a well-established and prevalent cardiac arrhythmia in the adult population characterised by disorganised atrial electrical activity that leads to irregular and often rapid atrial contractions. This condition has significant global health implications and is associated with increased morbidity, mortality, and healthcare burden. The mechanisms of AF in adults are multifactorial, encompassing structural, electrophysiological, and autonomic factors, with common risk factors including hypertension, coronary artery disease, and valvular heart disease. However, in

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the paediatric population, AF presents distinct challenges regarding its rarity and unique aetiological profile[1].

Historically, AF in children has been considered extremely rare and often dismissed as an anomaly or associated solely with secondary causes, such as congenital heart defects. However, recent studies have revealed that paediatric AF is more prevalent than previously recognised. Current estimates suggest a prevalence of less than 0.05% in individuals under 30 years of age, with a notable concentration in those with pre-existing cardiac conditions [2]. The largest published series on paediatric AF remains limited in scope, highlighting the need for more extensive research to understand the full spectrum of the disease in this population.

Children with congenital heart disease (CHD) represent a significant proportion of the paediatric AF population. Surgical interventions, especially those involving atrial incisions, are known to predispose patients to AF later in life, making postoperative monitoring critical [3]. Beyond CHD, other risk factors include cardiomyopathies and inherited arrhythmia syndromes, which may predispose the atrial tissue to the arrhythmogenic substrate necessary for AF development [4].

A subset of paediatric patients with AF referred to as having lone atrial fibrillation presents without any identifiable structural heart disease or other secondary causes. This rare condition raises the possibility of a genetic predisposition to AF [5]. Emerging evidence suggests that mutations in genes related to ion channels, gap junctions, and atrial myopathy may contribute to AF development in otherwise healthy children [6]. However, the precise genetic mechanism remains poorly understood, necessitating further investigation.

Atrial cardiomyopathies, characterised by structural and functional abnormalities of the atrial myocardium, also play a critical role in AF pathogenesis in the paediatric population. These abnormalities may be subtle and difficult to detect, yet they contribute significantly to the arrhythmogenic potential of the atrial tissue [7]. Understanding the interaction between atrial myopathy and AF in children is crucial for improving diagnostic accuracy and developing targeted therapeutic strategies.

Despite the growing body of literature on paediatric AF, significant gaps remain in our understanding of its pathogenesis, clinical course, and optimal management. Paediatric patients' unique physiological and developmental characteristics pose challenges in extrapolating adult treatment paradigms to this population. This study addressed these gaps by comprehensively analysing paediatric AF cases from a tertiary paediatric cardiology centre, focusing on the epidemiology, management, and outcomes.

2. Materials and Methods

Study Design and Ethical Considerations

This retrospective study was conducted at a tertiary care centre specialising in paediatric cardiology. The Institutional Review Board (IRB) of Unidade Local de Saúde São José approved the study protocol. Given the study's retrospective nature, the IRB waived the requirement for informed consent. This study adhered to the ethical principles outlined in the Declaration of Helsinki.

In line with the General Data Protection Regulation (GDPR) and national data protection laws, stringent measures have been implemented to protect patient privacy. All data were anonymised before analysis, and access to the data was restricted to authorised personnel. Data handling and storage complied with the institutional protocols, ensuring the confidentiality and security of all information.

Patient Selection

The study population consisted of paediatric patients aged 0-18 years diagnosed with atrial fibrillation (AF) between January 2015 and December 2023. Patients were identified through a comprehensive review of electronic health records (EHRs). The inclusion criteria required a confirmed diagnosis of AF, as documented by 12-lead electrocardiogram (ECG), Holter monitoring,

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or event monitoring records. Patients were excluded if their records lacked sufficient documentation to confirm AF diagnosis.

Data Collection and Management

The data were extracted using a structured form designed to ensure consistency and accuracy. The following variables were collected.

- **Demographic information:** age at diagnosis, sex, ethnicity, and relevant family history. Additionally, the presence of associated diagnoses such as genetic conditions or congenital heart disease (CHD) was documented. For patients with CHD, details regarding surgical interventions, the presence of residual lesions (e.g. valvular regurgitation, atrial dilation), and postoperative outcomes were recorded.
- **Clinical Presentation:** Information on presenting symptoms (e.g. palpitations, dizziness, syncope), duration of symptoms before diagnosis, and potential triggers of AF (e.g. exercise and infections) was collected.
- **Diagnostic Findings:** The diagnostic evaluation included data from ECG, Holter monitoring, or event monitoring, documenting the type and frequency of arrhythmia episodes. Additionally, findings from advanced imaging modalities such as echocardiography and cardiac magnetic resonance imaging (MRI) were gathered to assess structural heart disease. Specific attention was paid to identifying residual lesions, valvular dysfunction (e.g. mitral regurgitation), atrial dilation, and ventricular function (systolic and diastolic). Cardiac MRI was also used to evaluate myocardial fibrosis through late gadolinium enhancement (LGE).
- **Laboratory and Imaging Results:** Laboratory results, including electrolytes, thyroid function tests, and relevant genetic testing, were reviewed to identify potential metabolic or endocrine triggers for AF. Advanced imaging studies, particularly cardiac MRI, were prioritised to assess the detailed cardiac anatomy, function, and presence of myocardial fibrosis, which may have implications for AF pathophysiology.
- **Electrophysiological Study (EPS) Data:** For patients who underwent an electrophysiological study (EPS), data regarding the study's findings, including the inducibility of arrhythmias, electrophysiological characteristics of the atria, and outcomes of any ablation procedure, were collected.
- **Treatment Modalities:** Information on the treatment approaches was documented, including pharmacological therapies (e.g. antiarrhythmic drugs and anticoagulants), non-pharmacological interventions (e.g. electrical cardioversion, catheter ablation), and surgical treatments. The outcomes of EPS and ablation procedures were specifically noted, as were any complications associated with these interventions.
- **Clinical Outcomes:** Clinical outcomes included resolution of AF, recurrence rates, and complications, such as stroke or heart failure. Long-term follow-up data were collected to assess the durability of the treatment outcomes and the need for further intervention.

Statistical Analysis

Descriptive statistics were used to summarise the demographic and clinical characteristics of the study population. Continuous variables were presented as mean ± standard deviation (SD) or median with interquartile range (IQR), depending on their distribution. Categorical variables were summarised as frequencies and percentages.

3. Results

3.1. Demographics and Clinical Presentation

The study cohort comprised 36 paediatric patients diagnosed with atrial fibrillation (AF), with a mean age at presentation of 15 years (range 10-18 years). The majority of the patients were male (58%; n=21). Nearly half of the diagnoses (47.2%; n=17) were made in the emergency department, where patients primarily presented with symptoms of tachycardia and palpitations. Detailed demographic and clinical characteristics of the cohort are summarised in Table 1.

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Table 1. Patient demographics and diagnosis context.

Variable	N=36
Baseline characteristics	
Age (y), median	15
Male sex, n (%)	21 (58%)
Coexisting conditions	
Structural Congenital HD	6 (16,7%)
Structural Acquired HD	19 (52,8%)
Cardiomyopathy	1 (2,8%)
Rhythm Diseases	3 (8,3%)
Dysautonomia	1 (2,8%)
Without known cardiac disease	6 (16,7%)
Family history of AF, n (%)	0 (0%)
Context of diagnosis	
Emergency, n (%)	17 (47,2%)
During cardiac catheterization, n (%)	2 (5,6%)
Post-surgical, n (%)	4 (11,1%)
Incidental finding, n (%)	13 (36,1%)

3.2. Underlying Conditions

A significant proportion of the cohort (86.1%, n=31) had underlying cardiovascular conditions. Acquired heart disease, particularly rheumatic heart disease (RHD), was the most common (52.8%; n=19), followed by congenital structural heart disease (16.7%; n=6), and rhythm disturbances (Wolff-Parkinson-White Syndrome) (11.1%; n=4). Additionally, a small subset of patients were diagnosed with dysautonomia and cardiomyopathy (2.8% each; n=1). Lone atrial fibrillation, defined as AF without identifiable structural or functional heart disease, was present in 16.7% of the cases (n=6).

Structural heart disease

Among the patients with RHD, isolated mitral valve involvement, predominantly stenosis, was observed in 57.9% (n=11). Of these, seven patients had undergone mechanical mitral valve replacement. Rheumatic mitro-aortic disease was identified in seven patients, with stenosis as the predominant lesion. Four patients underwent surgery involving mechanical mitral valve replacement and aortic valve plasty.

The cohort also included six patients with congenital heart anomalies: complete atrioventricular septal defect (n=2), pulmonary valve atresia with ventricular septal defect (n=1), univentricular heart with double-inlet left ventricle and malposition of the great arteries (n=1), truncus arteriosus type I (n=1), and a combination of atrial and septal defects with patent ductus arteriosus in one patient

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diagnosed with Shprintzen-Goldberg syndrome. All patients with congenital heart defects had undergone surgical correction.

3.3. Treatment strategies

At the initial presentation, 41.7% (n=15) of the cohort required immediate intervention to manage atrial fibrillation (AF), while 27.8% (n=10) spontaneously reverted to sinus rhythm. Primary interventions included electrical cardioversion (53.3%; n=8) and pharmacological conversion with amiodarone (46.7%; n=7). The treatment modality was not specified in 30.6% (n=11) of cases (Table 2).

Following the initial AF episode, 80.6% (n=29) of patients were prescribed pharmacological therapy. Monotherapy was the most common approach, utilised in 69% (n=20) of the cases, with amiodarone (25%) and digoxin (22%) as the preferred agents. Oral anticoagulation was initiated in 63.9% (n=23) of the cohort, particularly in those with rheumatic heart disease (RHD) (n=20) and congenital structural heart disease (n=3). Warfarin was the most frequently prescribed anticoagulant, while in two cases of lone AF, rivaroxaban was used.

All patients with Wolff-Parkinson-White (WPW) syndrome or other accessory pathways underwent successful catheter ablation of the accessory pathway as the first-line treatment. These procedures, performed using either radiofrequency or cryoablation techniques, demonstrated high success rates, with no further need for antiarrhythmic therapy. The ablations targeted various accessory pathways, including the lateral left, posteroseptal, and mid-septal pathways, resulting in complete resolution of WPW-associated arrhythmias.

All patients with lone AF underwent electrophysiological studies, followed by catheter ablation. The ablation strategy primarily involved antral isolation of the pulmonary veins. Radiofrequency ablation was performed in 40% of these cases, while the remaining patients underwent single-shot cryoablation. Notably, in two patients, extensive areas of low voltage were identified in the left atrium, prompting further genetic investigations, although these remained inconclusive. Additionally, in one patient, triggers were identified and ablated from the superior vena cava.

Before the ablation procedures, all patients underwent a preprocedural transthoracic echocardiogram to assess left ventricular ejection fraction and left atrial dimensions. Computed tomography (CT) with left atrial segmentation was also performed to evaluate the left atrial anatomy and to exclude intracardiac thrombi. Oral anticoagulation was continued until the procedure, with warfarin or direct oral anticoagulants (DOACs) used at therapeutic doses, omitting one dosage prior to ablation. Antiarrhythmic drugs were discontinued for at least five half-lives before the procedure. Ablations were performed under conscious sedation with continuous oxygen saturation and ECG monitoring.

The ablation protocol varied, depending on the mapping system used. For patients treated with the CARTO system (Biosense Webster, Irvine, California, USA), ablations were performed using the ThermoCool SmartTouch® SurroundFlow catheter. For those treated with the NavX Precision system (Abbott, Abbott Park, Illinois, USA), the FlexAbility Ablation Catheter Sensor Enabled was used. In patients who underwent cryoablation, the Arctic Front™ cryoablation system (Medtronic) was used along with the Achieve Mapping Catheter (Medtronic) for precise mapping and ablation.

The ablation procedure involved the following steps: positioning a decapolar catheter through the right femoral vein to the coronary sinus for guidance, performing a transseptal puncture under fluoroscopic guidance, and employing three-dimensional mapping systems (either CARTO or NavX Precision) to map the right and left atria. Ablations were then performed using point-by-point lesions to achieve antral isolation of pulmonary veins. In cases in which cryoablation was used, single-shot techniques were employed for pulmonary vein isolation.

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Table 2. Treatment strategies.

Therapy	n	%
Initial approach		
Unknown	11	30,6
Needed intervention	15	41,7
Amiodarone	7	46,7
External electric cardioversion	8	53,3
Spontaneous resolution	10	27,8
Long-term approach		
Pharmacological treatment	29	80,6
Monotherapy	20	69
Digoxin	8	22
Amiodarone	9	25
Flecainide	2	6
Sotalol	1	3
Multiple	9	31
Amiodarone + digoxin	5	14
Flecainide + beta-blocker	4	11
Without pharmacological treatment	7	19

3.4. Recurrence

The overall efficacy of rhythm control strategies in our cohort was 50%, with a low recurrence rate of 3.8 % (n = 3) for atrial fibrillation (AF). Recurrences were identified in two patients with lone AF, one of whom was being treated with a beta-blocker and the other with amiodarone. Additionally, one recurrence occurred in a patient with congenital structural heart disease (Truncus arteriosus type I) who was receiving a combination of a beta-blocker and digoxin.

3.5. Outcomes and complications

The follow-up period revealed a significant loss of data, with 19 patients—primarily those with rheumatic heart disease (RHD) and originating from Portuguese-speaking African countries—being lost to follow-up after returning to their home countries. Among the observed complications, ischaemic stroke was the most frequent, occurring in three patients. All stroke cases involved patients with RHD. One patient had unoperated left atrial dilation, another had a mitral prosthesis, and the third had undergone mitral valvuloplasty, but was noncompliant with oral anticoagulation therapy.

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These findings underscore the importance of sustained follow-up and adherence to anticoagulation therapy to prevent complications, particularly in patients with underlying rheumatic heart disease.

4. Discussion

Atrial fibrillation (AF) is the most common arrhythmia in adults and is strongly associated with well-established risk factors, such as hypertension, valvular heart disease, and advancing age [8, 9]. However, its occurrence in paediatric populations is rare, with a prevalence of less than 0.05% before the age of 30 [2]. In children, AF is often linked to underlying conditions such as congenital heart disease (CHD), rheumatic heart disease (RHD), cardiomyopathy, and inherited arrhythmia[1, 5].The rarity of paediatric AF, coupled with its association with congenital and acquired heart conditions, underscores the importance of targeted research to improve the understanding and treatment of this age group. This study contributes to the growing body of the literature by providing a detailed examination of AF in children, focusing on its epidemiology, underlying conditions, management strategies, and outcomes.

AF and Underlying Conditions

Our findings corroborate those of previous studies, indicating that AF in children is frequently associated with underlying cardiovascular conditions. In our cohort, 86.1% of the patients had a cardiovascular-related underlying condition, with acquired heart disease, particularly RHD, being the most prevalent (52.8%). This is consistent with earlier reports that identified RHD as a leading cause of AF in paediatric populations, especially in regions with high rates of rheumatic fever[10]. Although Portugal is typically not classified as a high-burden country for RHD, it receives a significant number of migrants from regions where RHD remains prevalent. Consequently, our findings underscore the importance of recognising and managing RHD-related AF in nonendemic regions. This highlights the need for preventive measures against rheumatic fever to reduce the burden of AF in affected children, especially in those who may be underserved or from migrant populations.

In line with other studies, we also observed that CHD was a significant contributor to AF in children [3, 11].Congenital defects, such as atrial septal defects, and more complex lesions, such as truncus arteriosus, were present in 16.7% of our patients. Mandalenakis et al. demonstrated that children with CHD have a 22-fold increased risk of developing AF compared with the general population, even though the absolute risk remains low during childhood [12]. Our findings further support the notion that children with CHD require long-term surveillance, as AF may manifest earlier in life, particularly after surgical interventions that alter atrial anatomy[13]. This is crucial in the management of children with complex congenital anomalies, where surgical correction can introduce new arrhythmogenic substrates, thereby increasing the likelihood of AF.

WPW Syndrome and Accessory Pathways

Our study identified a notable prevalence of Wolff-Parkinson-White (WPW) syndrome in 8.3% of the patients, with AF being a common presenting arrhythmia. The literature reports that 16-26% of patients with WPW may experience spontaneous degeneration of atrioventricular reentrant tachycardia (AVRT) into AF, which poses a significant risk due to the potential for rapid ventricular responses and progression to ventricular fibrillation [14]. In our cohort, all patients with WPW underwent successful catheter ablation of their accessory pathways, leading to the resolution of AF and eliminating the need for ongoing antiarrhythmic medication. This aligns with other studies that recommend catheter ablation as a first-line treatment for WPW-associated AF to prevent life-threatening arrhythmias and improve long-term outcomes [14].

Lone Atrial Fibrillation

We observed a higher prevalence of lone AF in our paediatric cohort (16.7%) than in previously reported data, such as the study by El-Assaad et al., which suggested a prevalence of 7.5 per 100,000 children [5]. This discrepancy may be partly attributable to the size of our study population and the potential geo-social factors that are specific to our patient cohort. Lone AF, which is characterised by the absence of identifiable structural heart disease or other conditions, presents a significant

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diagnostic and therapeutic challenge. Recent studies suggest that atrial fibrosis may play a crucial role in the pathogenesis of AF even in young patients [7].

In our study, two patients with lone AF exhibited extensive areas of low voltage in the left atrium, indicative of underlying atrial fibrosis. One patient with no family history of arrhythmia or cardiomyopathy underwent cardiac MRI, which revealed isolated late gadolinium enhancement of the posterior wall of the left atrium, a finding previously described in patients with MYH7 variants associated with extensive left atrial fibrosis in the context of paroxysmal AF [6]. Although genetic testing in our patients did not yield definitive results, these findings support the hypothesis that lone AF may represent an early manifestation of atrial-selective cardiomyopathy, where the primary pathology lies within the atria rather than secondary to other cardiac conditions [15].

Emerging evidence links genetic variants, particularly those affecting sodium and potassium channels, cardiomyopathy-related genes (such as TTN), gap-junction channels, and transcription factors, to the development of AF in younger populations [6, 16]. These findings underscore the importance of a comprehensive evaluation, including advanced imaging and genetic testing, in paediatric patients presenting with lone AF to better understand the underlying mechanisms and guide appropriate management.

The Role of the Autonomic Nervous System in Atrial Fibrillation

In addition to structural and genetic factors, the autonomic nervous system (ANS) is increasingly recognised as playing a pivotal role in the pathogenesis of atrial fibrillation. Dysautonomia, characterised by an imbalance or dysfunction in the autonomic regulation of the heart, has been implicated in the initiation and maintenance of AF. The ANS influences atrial electrophysiology through its sympathetic and parasympathetic branches, which can alter atrial refractoriness and conduction velocity, thereby creating a substrate conducive to AF.[17, 18]

In our cohort, we observed one patient diagnosed with dysautonomia, a condition that may contribute to AF through heightened sympathetic activity or vagal tone. Studies have shown that increased sympathetic activity can lead to atrial ectopy and shortens atrial refractory periods, while increased vagal tone can promote reentrant circuits by slowing conduction [19]. This autonomic imbalance may serve as a trigger for AF episodes, particularly in patients without structural heart disease. Understanding the role of the ANS in AF, especially in younger patients with conditions like dysautonomia, could help refine therapeutic strategies, such as targeting autonomic modulation through pharmacological or interventional approaches

Given the complex interplay between the autonomic nervous system and AF, further research is warranted to explore how dysautonomia and related autonomic dysfunctions might contribute to the pathogenesis of AF in paediatric populations. This could lead to more targeted therapies aimed at autonomic regulation, potentially reducing AF burden in these patients.

Management and Outcomes

In terms of management, we found that electrical cardioversion (53.3%) and amiodarone therapy (46.7%) were the most commonly used initial interventions. These strategies align with the current recommendations for acute AF management in paediatric populations. However, the low recurrence rate observed in our cohort (3.8%) is particularly noteworthy, especially when compared with recurrence rates reported in other studies, which tend to be higher [1, 20]. This discrepancy may be attributable to the high proportion of patients in our cohort who underwent catheter ablation, particularly those with WPW syndrome, in whom ablation effectively eliminated the substrate for AF recurrence.

Oral anticoagulation was initiated in 63.9% of our patients, primarily in those with RHD and congenital heart defects. The use of warfarin was more common in our cohort, reflecting the specific patient population, including those with mechanical valve replacements due to RHD. However, the occurrence of ischaemic stroke in three patients with RHD despite anticoagulation underscores the challenges in managing stroke risk in this high-risk group. This finding is consistent with the literature emphasising the importance of anticoagulation in preventing thromboembolic events in children with AF and underlying heart diseases [1, 5, 20]. Nonetheless, the high rate of data loss in our cohort, primarily due to patients returning to their home countries, limits our ability to fully assess long-term outcomes and complications.

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Future Directions and Clinical Implications

Our study highlights several important considerations in the management of paediatric AF. First, the high prevalence of AF in children with RHD and CHD underscores the need for early detection and targeted intervention in these high-risk groups. Second, the success of catheter ablation in managing WPW-associated AF suggests that early intervention may be beneficial for preventing recurrence and improving long-term outcomes. Finally, the emerging recognition of lone AF as a potential manifestation of early atrial cardiomyopathy calls for further research on the genetic and molecular mechanisms underlying AF in young patients.

Larger multicentre studies with robust follow-up are essential to better understand the natural history of paediatric AF and optimise treatment strategies. The integration of advanced imaging techniques, such as cardiac MRI and genetic testing, may provide further insights into the pathophysiology of AF in this population, paving the way for personalised therapeutic approaches. Clinically, our study underscores the importance of early and comprehensive management of paediatric AF to prevent complications and improve long-term outcomes in this vulnerable patient group. Addressing the challenges associated with follow-up and data retention will be crucial for future research efforts to ensure that the findings are generalisable and that paediatric AF management continues to evolve based on robust evidence.

Limitations

The retrospective design of this study, conducted within a single tertiary paediatric cardiology centre, provides valuable insights into AF outcomes in paediatric patients, although it inherently limits the ability to establish causation between the observed factors. The relatively small sample size and significant data loss, particularly due to patients being lost to follow-up, limit the generalisability of the findings and the ability to draw definitive conclusions regarding long-term outcomes. Additionally, the lack of uniformity in treatment protocols across the cohort may have influenced the results, underscoring the need for standardised approaches in future research. These limitations highlight the need for larger multicentre studies to validate these findings and further investigate the underlying mechanisms and optimal management strategies for paediatric AF.

5. Conclusions

In our study population, AF was predominantly associated with underlying structural heart disease; however, nearly 15% of patients presented with lone AF, indicating that AF can occur without a prior cardiac substrate. Although AF has a high rate of conversion to sinus rhythm, most patients require long-term antiarrhythmic therapy, reflecting the chronic nature of the condition. Neurological complications, particularly ischaemic strokes, were a significant concern, but were limited to patients with underlying heart disease, emphasising the importance of careful management in this subgroup. Further multicentre studies with larger patient cohorts are essential to better understand the aetiology, risk factors, and optimal therapeutic interventions for paediatric AF. These future studies could provide more comprehensive data to guide clinical practice and improve outcomes in children affected by this complex arrhythmia.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board (IRB) of Unidade Local de Saúde São José (Ethics Committee approval number 974/2020). Ethical approval was obtained prior to the commencement of the study, ensuring that all procedures adhered to the ethical standards set forth in the Declaration.

Informed Consent Statement: Patient consent was waived due to the retrospective nature of the study. As the study involved the analysis of previously collected medical records and did not require direct interaction with patients, obtaining individual consent was deemed impractical and unnecessary. Additionally, all data were

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anonymised prior to analysis to protect patient confidentiality, in compliance with institutional guidelines and data protection regulations.

Data Availability Statement: The data supporting the reported results in this study are not publicly available due to privacy and ethical restrictions. The study involved patient medical records, and the data were anonymised to protect patient confidentiality in accordance with institutional guidelines. Access to the data is restricted and may be available from the corresponding author upon reasonable request, subject to approval by the Institutional Review Board and in compliance with applicable data protection regulations.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Mills LC, Gow RM, Myers K, Kantoch MJ, Gross GJ, Fournier A, et al. Lone atrial fibrillation in the pediatric population. Can J Cardiol. 2013;29(10):1227-33. doi: 10.1016/j.cjca.2013.06.014.
2. Hubrechts J, Vô C, Boulanger C, Carkeek K, Moniotte S. Atrial fibrillation in a pediatric patient caused by an unusual malignant etiology: A case report. Front Pediatr. 2023;11:1051041. doi: 10.3389/fped.2023.1051041.
3. Martín de Miguel I, Ávila P. Atrial Fibrillation in Congenital Heart Disease. Eur Cardiol. 2021;16:e06. doi: 10.15420/ecr.2020.41
4. Gourraud JB, Khairy P, Abadir S, Tadros R, Cadrin-Tourigny J, Macle L, et al. Atrial fibrillation in young patients. Expert Rev Cardiovasc Ther. 2018;16(7):489-500. doi: 10.1080/14779072.2018.1490644
5. El-Assaad I, Al-Kindi SG, Saarel EV, Aziz PF. Lone Pediatric Atrial Fibrillation in the United States: Analysis of Over 1500 Cases. Pediatr Cardiol. 2017;38(5):1004-9. doi: 10.1007/s00246-017-1608-7.
6. Marcoux E, Sosnowski D, Ninni S, Mackasey M, Cadrin-Tourigny J, Roberts JD, et al. Genetic Atrial Cardiomyopathies: Common Features, Specific Differences, and Broader Relevance to Understanding Atrial Cardiomyopathy. Circ Arrhythm Electrophysiol. 2023;16(12):675-98. doi: 10.1161/CIRCEP.123.003750.
7. Cunha PS, Laranjo S, Heijman J, Oliveira MM. The Atrium in Atrial Fibrillation - A Clinical Review on How to Manage Atrial Fibrotic Substrates. Front Cardiovasc Med. 2022;9:879984. doi: 10.3389/fcvm.2022.879984.
8. Andrade J, Khairy P, Dobrev D, Nattel S. The clinical profile and pathophysiology of atrial fibrillation: relationships among clinical features, epidemiology, and mechanisms. Circ Res. 2014;114(9):1453-68. doi: 10.1161/CIRCRESAHA.114.303211.
9. Chen Q, Yi Z, Cheng J. Atrial fibrillation in aging population. Aging Med (Milton). 2018;1(1):67-74. doi: 10.1002/agm2.12015
10. Shenthar J. Management of atrial fibrillation in rheumatic heart disease. Heart Rhythm O2. 2022;3(6Part B):752-9. doi: 10.1016/j.hroo.2022.09.020
11. Hernández-Madrid A, Paul T, Abrams D, Aziz PF, Blom NA, Chen J, et al. ESC Scientific Document Group , Arrhythmias in congenital heart disease: a position paper of the European Heart Rhythm Association (EHRA), Association for European Paediatric and Congenital Cardiology (AEPC), and the European Society of Cardiology (ESC) Working Group on Grown-up Congenital heart disease, endorsed by HRS, PACES, APHRS, and SOLAECE. *EP Europace*. 2018;20(11):1719–53. doi: 10.1093/europace/eux380.
12. Mandalenakis Z, Rosengren A, Lappas G, Eriksson P, Gilljam T, Hansson PO, et al. Atrial Fibrillation Burden in Young Patients With Congenital Heart Disease. Circulation. 2018;137(9):928-37. doi: 10.1161/CIRCULATIONAHA.117.029590.
13. Moe TG, Abrich VA, Rhee EK. Atrial Fibrillation in Patients with Congenital Heart Disease. J Atr Fibrillation. 2017;10(1):1612. doi: 10.4022/jafib.1612.
14. Centurion OA. Atrial Fibrillation in the Wolff-Parkinson-White Syndrome. J Atr Fibrillation. 2011;4(1):287. doi: 10.4022/jafib.287.
15. Cunha PS, Antunes DO, Laranjo S, Coutinho A, Abecasis J, Oliveira MM. Case report: Mutation in NPPA gene as a cause of fibrotic atrial myopathy. Front Cardiovasc Med. 2023;10:1149717. doi: 10.3389/fcvm.2023.1149717.
16. Nielsen JB, Thorolfsdottir RB, Fritsche LG, Zhou W, Skov MW, Graham SE, et al. Biobank-driven genomic discovery yields new insight into atrial fibrillation biology. Nat Genet. 2018;50(9):1234-9. doi: 10.1038/s41588-018-0171-3.
17. Oliveira M, da Silva MN, Geraldes V, Xavier R, Laranjo S, Silva V, et al. Acute vagal modulation of electrophysiology of the atrial and pulmonary veins increases vulnerability to atrial fibrillation. Exp Physiol. 2011;96(2):125-33. doi: 10.1113/expphysiol.2010.053280.
18. Ferreira M, Laranjo S, Cunha P, Geraldes V, Oliveira M, Rocha I. Orthostatic Stress and Baroreflex Sensitivity: A Window into Autonomic Dysfunction in Lone Paroxysmal Atrial Fibrillation. J Clin Med. 2023;12(18). doi: 10.3390/jcm12185857

 doi:10.20944/preprints202408.1276.v1

19. Oliveira M, Postolache G, Geraldes V, Silva V, Laranjo S, Tavares C, et al. [Acute electrophysiological modulation of the atria and pulmonary veins: effects of sympathetic and parasympathetic interaction on atrial fibrillation inducibility]. Rev Port Cardiol. 2012;31(3):215-23. doi: 10.1016/j.repc.2012.01.007
20. Furst ML, Saarel EV, Hussein AA, Wazni OM, Tchou P, Kanj M, et al. Medical and Interventional Outcomes in Pediatric Lone Atrial Fibrillation. JACC Clin Electrophysiol. 2018;4(5):638-48. doi: 10.1016/j.jacep.2018.02.014