

# Work-up and management of lone atrial fibrillation: results of the European Heart Rhythm Association Survey

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The purpose of this European Heart Rhythm Association (EHRA) survey was to explore the work-up and management of lone atrial fibrillation (AF) among the European centres. Thirty-two European centres, all members of the EHRA electrophysiology (EP) research network, responded to this survey and completed the list of questions. The prevalence of lone AF has been reported to be  $\leq 10\%$  by 19 (60%) of the participating centres. The presence of isolated left atrial enlargement and left ventricular diastolic dysfunction represent heart disease according to 50 and 84% of the centres, respectively, and exclude the diagnosis of lone AF. Fifty-nine per cent of responders do not routinely consider genetic testing in lone AF patients. The initial therapeutic approach in symptomatic paroxysmal lone AF is antiarrhythmic drug therapy as reported by 31 (97%) of the centres. Pulmonary vein isolation only is the first ablation strategy for patients with symptomatic persistent lone AF at 27 (84%) of the responding centres. Assessment for sleep apnoea, obesity, and intensive sports activity in lone AF is performed at 27 (84%) centres. In conclusion, this EP Wire survey confirms that the term 'lone AF' is still used in daily practice. The work-up typically includes screening for known risk factors but not genetic testing. The preferred management of paroxysmal lone AF is rhythm control with antiarrhythmic drugs, whereas pulmonary vein isolation is the first ablation strategy for the majority of patients with symptomatic persistent lone AF.

**Keywords** Atrial fibrillation • Lone atrial fibrillation • Antiarrhythmic drugs • Ablation • Management • EHRA survey • EP wire

## Introduction

The term 'lone' atrial fibrillation (AF) was introduced in 1954 by Evans and Swann to describe AF patients for whom no apparent heart disease could be found during subsequent investigations.<sup>1</sup> Current guidelines define lone AF as AF in younger adults (age  $< 60$  years) with no clinical history or echocardiographic evidence of concomitant cardiovascular or pulmonary conditions or an acute trigger. Given this broad definition on the one hand and the ongoing effort to create a mechanistic classification for AF in a specific patient on the other hand, the goal of this European Heart Rhythm Association (EHRA) survey is to explore the use of the term 'lone AF' and the work-up and management of this clinical entity in the European countries.

## Methods and results

Thirty-two European centres, all members of the EHRA electrophysiology (EP) research network, responded to this survey and completed the questionnaire. Twenty-six of them are university hospitals (81%), two non-university, and four private hospitals. The main cardiology section in which responders are working is catheter ablation in 24 out of 32 (75%), device implantation in 6 (19%), and general cardiology in 2 (6%).

The prevalence of lone AF defined according to the current guidelines has been reported  $< 5\%$  by 6 (19%) of the centres, 5–10% by 13 (41%), 11–20% by 9 (28%), 21–30% by 3 (9%), and  $> 30\%$  by 1 centre (3%). Six out of 32 (19%) responders believe that the historical term 'lone AF' should not be used anymore in clinical practice.

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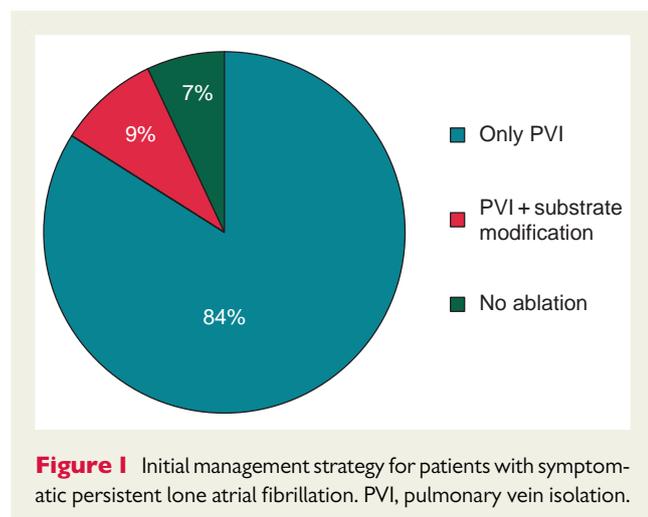
In the context of lone AF, the guidelines on AF diagnosis and management specifically mention only echocardiography in addition to the patient history and clinical examination but additional diagnostic tests are performed by a significant proportion of the responding centres: 12-lead electrocardiogram in 20 (62%) of the centres, exercise testing in 8 (25%), coronary angiography in 2 (6%), and a cardiac computed tomography scan in 1 centre (3%). Sixteen (50%) of 32 centres consider an isolated left atrial (LA) enlargement as a sign of heart disease which excludes the diagnosis of lone AF. The same holds true for isolated ventricular diastolic dysfunction as reported by 27 (84%) of the centres.

The majority (19 of 32, 59%) of the responders do not routinely use genetic testing in patients with lone AF, whereas 10 (31%) do so only when there is a family history of AF; 3 (9%) of the centres do not have access to genetic testing.

According to 22 (69%) of the centres, the risk for stroke in lone AF should be re-assessed annually and 9 (28%) reassess the patient's risk on a biannual basis.

The primary therapeutic approach in symptomatic paroxysmal lone AF is antiarrhythmic drug therapy at the majority of responders (31 of 32, 97%). In most centres (27 of 32, 84%), the initial ablation strategy for patients with symptomatic persistent lone AF is pulmonary vein isolation, while 3 (9%) of the centres add substrate modification to pulmonary vein isolation (2 centres perform linear lesions and 1 centre adds ablation of complex fractionated electrograms (CFAE) (Figure 1). Two responders (7%) do not perform ablation. Regarding patients with persistent lone AF, five (16%) of the centres perform a Cox maze III surgical procedure if catheter-based endocardial LA ablation fails and one centre does so after antiarrhythmic drug failure. Twenty-six (81%) never consider surgery for patients with lone AF. Seventeen (53%) of the centres (53%) differentiate their therapeutic approach in vagal and adrenergic lone AF.

The systematic evaluation and (if indicated) ensuing treatment of risk factors for lone AF among participating centres was also analysed in this EP Wire. Twenty-seven out of 32 centres (84%) are doing so for sleep apnoea, obesity, and intensive sports activity, and 30 (94%) screen for the occurrence of supraventricular tachycardia as a trigger for AF.



## Discussion

Due to the ambiguity of the current definition of lone AF leading to significant variations in what several researchers termed 'lone AF' and advances in the knowledge of AF mechanisms and aetiologies, some working groups state that 'lone AF' has no mechanistic or clinical basis and therefore should be avoided.<sup>2</sup> This was also reflected in this EP Wire as almost 20% of the responding centres do not use this terminology anymore. As a result, the proportion of AF considered to be 'lone AF' decreased from ~30% to <5%.<sup>2,3</sup> In this survey, 60% of the participating centres have reported the prevalence of lone AF in their practice to be ≤10%.

It remains a matter of debate whether an isolated LA enlargement represents heart disease and therefore excludes a diagnosis of lone AF. Left atrial enlargement is a well-known risk factor for cardiovascular events in AF patients, among others.<sup>4,5</sup> Atrial fibrillation may be caused by LA dilatation but AF itself can also result in LA enlargement.<sup>6</sup> Interestingly, 50% of the centres believe that LA enlargement represents underlying heart disease. To what extent ventricular diastolic dysfunction excludes lone AF is still an area of research. Several investigators have highlighted the dynamic and complex relationship between arterial hypertension, left ventricular hypertrophy, ventricular diastolic dysfunction, LA dilatation and AF.<sup>7</sup> It is clear from this EP Wire that the vast majority (84%) of the centres consider ventricular diastolic dysfunction as overt heart disease.

Several studies have demonstrated the heritability of AF.<sup>8–11</sup> A family history of lone AF exposes individuals to a 3.5-fold greater risk of developing arrhythmia themselves.<sup>12</sup> Lone AF has been associated with mutations in several cardiac ion channels, signalling molecules, and structural proteins.<sup>13,14</sup> It remains difficult to predict how the results of genetic counselling would influence the diagnosis of lone AF and how it may help optimize the treatment of arrhythmia.<sup>15</sup> This has been reflected by the results of this EP Wire as 59% of responders do not routinely consider genetic testing and 31% only do so when there is a family history of AF.

According to the recent guidelines, in patients with paroxysmal AF and no or minimal structural heart disease rhythm control can be achieved by antiarrhythmic drugs (dronedron, flecainide, propafenone, or sotalol) or catheter ablation depending on the patient's choice.<sup>16</sup> Nevertheless, several randomized trials compared catheter ablation of AF with antiarrhythmic drug therapy as the first-line rhythm control management.<sup>17–19</sup> They all reported a superior efficacy of catheter ablation up to 24 months of follow-up as well as an improvement in quality of life. However, late recurrences of AF after catheter ablation are common and the major complication rates including major complications of this procedure cannot be overlooked.<sup>16,20</sup> This may in part explain why 97% of the responding centres opt for antiarrhythmic drug treatment as the first therapeutic approach in symptomatic paroxysmal lone AF patients. When catheter ablation is performed in patients with persistent lone AF, the guidelines state that operators should consider more extensive ablation based on linear lesions or CFAE. This EP Wire has revealed that only 9% of centres choose to perform linear lesions or CFAE ablation in addition to pulmonary vein isolation in this kind of patients. Most likely due to its complexity and technical challenge, the standalone Cox maze III surgical treatment of persistent lone AF patients is only adopted by a minority of

responding centres (16%) after failure of endocardial LA ablation or antiarrhythmic drug therapy.<sup>21,22</sup>

Reassessment of risk factors is important in patients with lone AF as many patients develop cardiovascular disease during follow-up.<sup>23</sup> Obesity is a known risk factor for AF, with a 3–8% increased risk of AF with each unit increase in body mass index.<sup>24</sup> The incidence of lone AF has also been correlated with sports activity. Marathon running and the practice of >1500 lifetime hours of sport have been associated with a higher risk of lone AF.<sup>25</sup> Due to its effect on the autonomic balance and several haemodynamic parameters, sleep apnoea has been linked to a higher incidence of lone AF and a lower success rate of ablation therapies.<sup>26,27</sup> This EP Wire has shown that 84% of the centres perform a systematic assessment of these risk factors in patients with lone AF.

## Conclusions

This EP Wire survey confirms that the term 'lone AF' is still used in daily practice. The work-up typically includes screening for known risk factors but not genetic testing. The preferred management of paroxysmal lone AF is rhythm control with antiarrhythmic drugs. Pulmonary vein isolation only is the first ablation strategy for the majority of patients with symptomatic persistent lone AF.

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