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The Right Atrial Area as a New Factor to Predict Successful Pulmonary Vein Isolation: an Emergent Predictor Variable

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ABSTRACT

Up to now, few factors have been identified to predict successful pulmonary vein isolation, none of which with high predictive values. The objective of our study was to compare different predictive factors of atrial fibrillation recurrence after pulmonary vein isolation, including new parameters of the right atrium (area and index volume). We retrospectively analysed data from 66 patients and included echocardiogram parameters performed within 18 months prior to the ablation procedure. We excluded patients with left ventricular dysfunction (defined as a left ventricular ejection fraction < 50%); previous diagnostic of cardiomyopathy; severe valvular heart disease; severe pulmonary hypertension; or those with poor image quality in the echocardiogram. We considered atrial fibrillation recurrence to be the presence of atrial fibrillation of 30 seconds or longer demonstrated by a standard electrocardiogram or in a 24-hour Holter electrocardiogram within a year after the ablation procedure. We found that the right atrium area (odds ratio = 1.52; 95% confidence interval 0.95–2.43, P = 0.08) and a previous pulmonary vein isolation procedure (odds ratio = 0.21; 95% confidence interval 0.04–1.01, P = 0.05) were nearly statistically significant predictors of successful atrial fibrillation ablation at one year. Although our study was limited because of a low number of patients and because it is a retrospective analysis, we found that a higher right atrial area may be related to the late recurrence of atrial fibrillation. This tendency may be useful in predicting patient outcomes.

KEYWORDS: Atrial fibrillation; Pulmonary vein isolation; Heart atria.

INTRODUCTION

Atrial fibrillation (AF) is the most common cardiac arrhythmia in developed countries.

Recent guidelines[1] recommend rhythm control by pulmonary vein isolation (PVI) using radiofrequency or cryoablation for symptomatic patients with failure or intolerance to antiarrhythmic drug therapy (ADT), as a first-line rhythm control

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therapy based on patient preference, when tachycardia-induced cardiomyopathy is highly probable or in patients with reduced left ventricular ejection fraction[2].

The absence of symptomatic AF recurrence is the primary efficacy outcome in most studies.

For this reason, a lot of predictive factors for AF recurrence have emerged. The most important ones are the underlying cardiovascular disease, such as hypertension, complicated heart disease (including valvular heart disease), older age, persistent as opposed to paroxysmal AF, the volume of procedures performed at the centre, untreated obstructive sleep apnoea, obesity, increasing plasma B-type natriuretic peptide level, or left atrial (LA) dilation[3-9].

Considering the perspective that long-standing AF could produce atrial cardiopathy[10,11], which may be the cause of LA dilation and its predictive role in PVI outcomes, we have speculated that it could also cause right atrial (RA) enlargement in the absence of other factors, such as severe right valve disease or severe pulmonary hypertension. Consequently, this could also be used as a predictive factor for AF recurrence after PVI.

METHODS

We retrospectively analysed data from our hospital database from 2010 to 2019. We included adult patients with 18 years old and older with a VPI and an echocardiogram performed both in our hospital who were followed in our center for 12 months after the ablation procedure. We included echocardiogram parameters of patients whose echocardiogram had been performed within 18 months prior to the ablation procedure. We excluded patients with left ventricular dysfunction (defined as a left ventricular ejection fraction < 50%), previous diagnosis of cardiomyopathy (including ischaemic, hypertrophic, restrictive, constrictive or tachycardia-mediated cardiomyopathy), previous diagnosis of severe valvular heart disease, severe pulmonary hypertension, or those with poor image quality in the echocardiogram.

All cryoablation procedures were performed in a fasting state and under deep sedation. A transesophageal echocardiogram was performed in every patient, prior to vein access, in order to exclude left appendage thrombi. After transseptal puncture, bolus heparin (100 mg/kg weight) and infusion were administrated to obtain activated clotting time (ACT) of 300-350 seconds.

All procedures were performed with first and second-generation Medtronic Cryoablation Catheters. Pulmonary vein potentials were recorded with Achieve circular mapping catheter. According to the protocol at our centre and with CryoDOSING study[12], one 180-second application was performed if time to isolation was less than 60 seconds, and one 240-second application was performed if time to isolation was 60-100 seconds. If there were no isolation after 100 seconds of application, this was stopped, and the balloon was repositioned. No bonus applications were given. If there were a lack of pulmonary vein signals, one 180-second or 240-second application was given depending on the achieved temperature. After the last application, entrance and exit isolation was checked in all veins.

The ablation procedure was only focused on PVI and did not consider other targets for ablation. Patients with previous PVI were considered if they had a single previous ablation with radiofrequency energy, not taking into consideration how much time ago it was performed.

For the measurements, we followed the recommendations of the American Society of Echocardiography and the guidelines of the European Association of Cardiovascular Imaging[13], and we considered the most common measurements of both atrium (lenght of the LA, index volume of both the LA and RA and RA area) (Fig. 1). The endpoint was AF recurrence after a year from the procedure.

For the analysis, AF recurrence was considered as the presence of AF of 30 seconds or longer, demonstrated by a standard electrocardiogram or in a 24-hour Holter electrocardiogram within a year after the PVI procedure.

For statistical analysis, we first checked compliance with the normality assumptions and then applied the normal distribution. For the comparative tests, we used the Student's t-test. Significant variables in the univariant analysis (those with $p \leq 0.06$) were considered for prediction tests. The predictive model was estimated according to a logistic regression model for a case-control study.

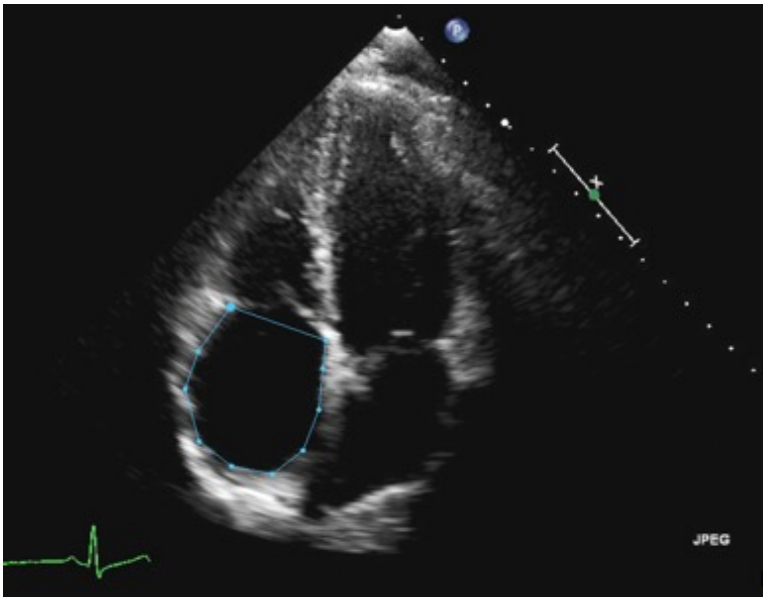

Figure 1. Measurement of the right atrial area in four-chamber apical view at end-systole.

RESULTS

We recorded patient data from our database from 2010 to 2019, which included 206 patients. Approximately 70% of the population did not meet the inclusion criteria, mainly due to the presence of basal cardiomyopathy (23.8%), severe valvular heart disease (8.5%), poor image quality (1.5%) or the fact that the echocardiogram had been performed outside the considered timeframe (34.2%), resulting in 66 patients included in the analysis.

The Tables 1 and 2 show the univariant and multivariant analysis.

Table 1. Univariant analysis*.

Variable	Patients with AF recurrence N = 28	Patients without AF recurrence n = 38	Significance (p-value)
Age (years)	58.43 ± 1.77	58.76 ± 1.96	0.45
Body mass index (kg/m^2)	30.25 ± 2.57	28.92 ± 0.80	0.29
Obstructive sleep apnoea (%)	10.71% (3)	5.26% (2)	0.21
Estimated GFR (mL/min/1.73 m^2)	76.0 ± 4.07	80.84 ± 2.84	0.16
Type of AF (%) persistent vs. paroxismal	57.14% (16)	34.21% (13)	0.03
Treatment with ACEi/AIIRA (%)	28.57% (8)	18.42% (7)	0.17
Treatment with antiarrhythmics drugs. (%)	67.86% (19)	73.68% (28)	0.31
Previous PVI procedure (%)	10.71% (3)	26.32% (10)	0.06
LVEF (%)	60.4	62.1	0.19
TAPSE (mm)	23.6	21.9	0.16
Lenght of the LA (mm)	41.96 ± 3.55	34.03 ± 1.97	0.03
Index volume of the LA (mL/m^2)	44.97 ± 3.29	36.69 ± 2.44	0.02
Index volume of the RA (mL/m^2)	33.38 ± 1.84	29.89 ± 2.14	0.12
RA area (cm2)	22.18 ± 1.17	19.31 ± 0.63	0.02

AF: atrial fibrillation; GFR: glomerular filtration rate; ACEi/AIIRA: angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers; PVI: pulmonary vein isolation; LVEF: left ventricular ejection fraction; TAPSE: tricuspid annular plane systolic excursion; LA: left atrium; RA: right atrium; *numerical variables are presented with mean and standard deviation, and binomial variables are presented with percentage and total number of patients.

Table 2. Multivariant analysis*.

Variable	Odds ratio	Confidence interval 95%	Significance (p-value)
Type of AF (persistent vs. paroxysmal)	2.26	0.71–7.13	0.17
Previous PVI procedure	0.21	0.04–1.01	0.05
Lenght of the LA	1.01	0.97–1.05	0.72
Index volume of the LA	1.02	0.98–1.06	0.23
RA area	1.52	0.95–2.43	0.08

AF: atrial fibrillation; *numerical variables are presented with mean and standard deviation, and binomial variables are presented with percentage and total number of patients; PVI: pulmonary vein isolation; LA: left atrium; RA: right atrium.

Five variables obtained statistical significance in univariate analysis: the type of AF (persistent vs. paroxysmal), a previous PVI procedure, the lenght of the LA, the index volume of the LA, and the RA area. Although some of them, as previously mentioned, are well-known predictors of recurrence of AF, the area of the RA was also shown to be a predictor with p = 0.02, not so the indexed volume of the RA which had p = 0.12.

In the logistic regression model, we did not find any variable that statistically significantly predicted the recurrence of AF. The two best predictors were a previous PVI procedure (OR = 0.21; 95% confidence interval – 95%CI 0.04–1.01, P = 0.05), and the RA area (OR = 1.52, 95%CI 0.95–2.43, P = 0.08).

For the RA area, the area under the receiver operating characteristics (ROC) curve was 0.61, which is considered nearly acceptable to discriminate recurrence of AF with a cut-off value of 23.5 cm^2 as the best for differentiating patients who would have a recurrence from those would not (sensitivity = 0.36, and specificity = 0.79) (Fig. 2).

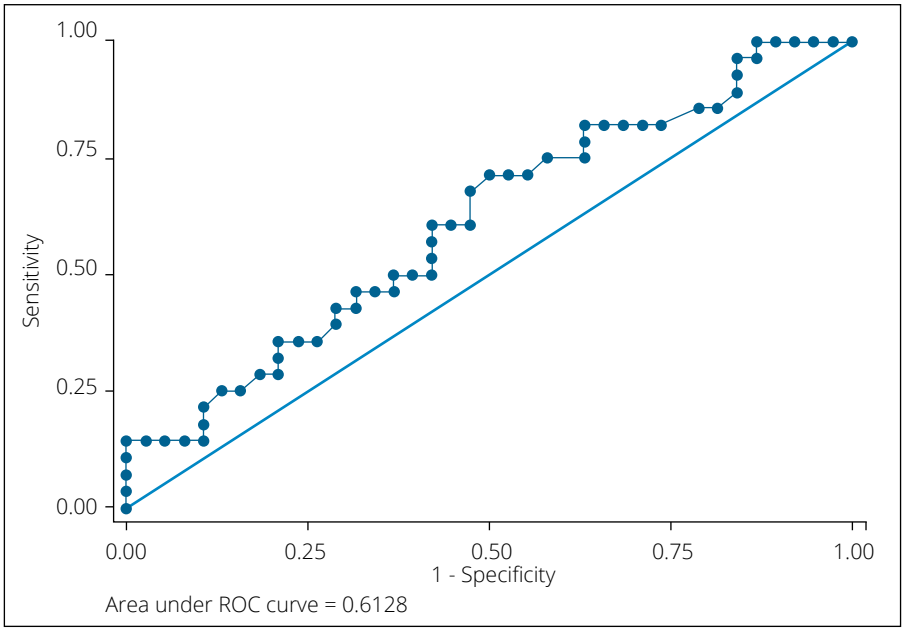

Figure 2. Receiver operating characteristics curve for right atrium area and risk of atrial fibrillation recurrence after pulmonary vein isolation.

DISCUSSION

This was a retrospective, observational, and single-centre study involving patients with a PVI procedure and predictive factors for AF recurrence at one year. We found that a lower RA area and a previous PVI procedure were predictors for non-recurrence of AF. However, both of them were nearly statistically significant.

According to our results, we want to highlight other studies which also consider that RA parameters play a role in AF recurrence.

Akutsu et al.[14] used a 64-slice multidetector computed tomography to assess RA and LA volumes before PVI in 65 patients. They found that both volumes were equally associated with post-PVI AF recurrence, showing a RA volume higher than 87 cc or a LA volume higher than 99 cc, with sensitivity of 81.3% for both values.

Moreover, Luong et al.[15] reported that RA volume indexed to body surface area was superior to LA volume indexed to body surface area for the prediction of AF recurrence at six months after direct current cardioversion. The measures were assessed by an echocardiogram within six months prior to cardioversion.

Xie et al.[16] found that higher RA volume indices (maximum and minimum) assessed by cardiac magnetic resonance were independently associated with incident AF after adjustment for conventional cardiovascular risk factors and LA parameters in the Multi-Ethnic Study of Atherosclerosis.

Takagi et al.[17] analyzed 245 patients with AF who had undergone PVI. RA and LA volumes were determined by contrast-enhanced computed tomography considering the atrial volume of ≥ 110 mL as atrial remodelling. They reported that RA remodeling is a useful predictor of clinical outcome (follow-up period of 12 months) after PVI.

Our study supports this association between atriopathy, especially of the RA, and increased risk of recurrence of AF after PVI. Its main advantage and so far unpublished hypothesis is that we used echocardiogram for RA measurements. We consider it a more affordable, easier and more readily available method for RA assessment.

On the other hand, the study has several limitations. First, it was performed at a single centre, although we considered it a good and representative sample of the general population with AF. Second, as a retrospective study, the data collection was more susceptible to errors; in fact, we excluded 68% of our initial population. We are aware that this is the main concern of the series, but given that the data review was performed retrospectively and after applying the exclusion criteria and extending the time window in which the echocardiogram was performed, we cannot ignore the high percentage of patients not included. Third, the echocardiograms were not performed at the same time as the PVI procedure, so we do not know the exact measurements of the echo parameters, and due to the broad margin of time selected for data inclusion (18 months), data correlation is more difficult. We arbitrarily chose this timeframe to allow the inclusion of the highest number of patients with the limitation of a broad window. Finally, we also admit that well-known predictive factors for late recurrence, such as LA volume or length, were not significant in our population. In our patients, only the RA area, rather than volume, was relevant possibly due to the small sample size and possible measurement errors which may have occured because the echocardiograms were not standarised for the purpose of this study.

For all these reasons, we consider that the hypothesis tested in our study should be validated in randomized clinical trials, specifically designed to test this association between RA dilatation measured by transthoracic echocardiography and the recurrence of AF after PVI.

CONCLUSION

We present the RA area as a new predictive factor for AF recurrence at one year after a PVI procedure with a cut-off point on the ROC curve of 23.5 cm^2 as the best for differentiating patients who would have a recurrence from those who would not. We also found that a previous PVI predicts a higher success of the ablation procedure. Although not statistically significant, these tendencies might encourage the inclusion of the RA area into the recurrence risk stratification factors considered for PVI procedures and further investigation into the role of long-standing AF and atriopathy including RA enlargement.

AUTHORS' CONTRIBUTION

Conceptualization: Aguilera Agudo C, Castro Urda V, Toquero Ramos J; **Formal Analysis:** Aguilera Agudo C; **Writing – Original Draft:** Aguilera Agudo C, Castro Urda V, Toquero Ramos J, Jiménez Sánchez D, Veloza Urrea D,

García-Izquierdo Jaén E, Pham Trung C, Moñivas Palomero V, Mingo Santos S, Fernández Lozano I; **Writing – Review & Editing:** Aguilera Agudo C, Castro Urda V, Toquero Ramos J, Jiménez Sánchez D, Veloza Urrea D, García-Izquierdo Jaén E, Pham Trung C, Moñivas Palomero V, Mingo Santos S, Fernández Lozano I.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author, upon reasonable request.

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CONFLICT OF INTERESTS

There are no potential conflicts of interest, including related consultancies, shareholdings nor funding grants.

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Not applicable.

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