Influence of left atrial size on the outcome of pulmonary vein isolation in patients with atrial fibrillation

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Abstract

Background: Atrial fibrillation (AF) is the most frequent sustained supraventricular tachyarrhythmia. Radiofrequency (RF) ablation is one of the options used to prevent the recurrence of AF. Despite thorough studies, the relation between left atrial (LA) size and the results of RF ablation remains controversial.

Aim: To estimate the relation between LA size assessed by echocardiography and the AF recurrence rate after pulmonary vein isolation (PVI).

Methods: Our analysis comprised 175 AF patients subjected to PVI between June 2011 and March 2012. Inclusion criteria comprised: symptomatic AF with no reversible cause, and age < 70, LA < 5.5 cm (anteroposterior). PVI was performed with a 4-mm non-irrigated catheter or irrigated catheter and circular mapping catheter (electroanatomic mapping with LocaLisa or CARTO systems). Recurrence was defined as any atrial tachyarrhythmia episode that lasted more than 30 s after three months of blanking period. Standard echocardiographic post-ablation anteroposterior LA measurements were performed with additional parameters such as systolic and diastolic LA area and volume (on sinus rhythm).

Results: The analysis included 198 procedures performed in 175 patients. Median follow-up time was 17 months. Median age was 56 years. After the first procedure, AF recurred in 88 (52.4%) patients. Efficacy after the last procedure was 55.2% (43.5% for persistent AF and 59.7% for paroxysmal AF). No significant relation between any of the LA parameters and the recurrence rate was found. Cox univariate and multivariate analysis revealed only very early AF recurrence as a prognostic factor for AF recurrence in the long term.

Conclusions: In patients with AF, no relation could be observed between the recurrence rate after PVI and the echocardiographic LA measurement parameters.

Key words: atrial fibrillation (AF), AF ablation, left atrial size, pulmonary vein isolation

INTRODUCTION

Atrial fibrillation (AF) is the most common tachyarrhythmia in clinical practice [1]. Radiofrequency (RF) catheter ablation is one of several therapeutic options used to prevent the recurrence of AF and remains the most effective treatment for drug-refractory patients. Catheter ablation (pulmonary vein isolation [PVI] is the basis of the procedure) is recommended as an alternative to antiarrhythmic drug therapy for patients with symptomatic recurrent paroxysmal AF on antiarrhythmic drug therapy, provided the procedure is performed by an experienced operator [2].

Despite progress in ablation techniques, AF recurrences remain common, resulting in a substantial percentage of patients requiring repeated procedures. Several factors have been shown to influence the recurrence rate after catheter ablation, one of them being the size of the left atrium (LA) [3]. Previous studies have revealed that echocardiographic parameters of LA can predict episodes of AF and estimate...
the success rate of cardioversion, thromboembolic risk and the long-term maintenance of sinus rhythm after traditional electrical cardioversion [4]. Numerous analyses have been conducted to assess the relationship between LA diameter and AF recurrence rate after catheter ablation [3]. Despite these studies, the influence of LA size on the result of ablation remains controversial and conflicting results can easily be found in the literature.

The aim of our study was to test the relations between several parameters of LA size assessed by echocardiography and the AF recurrence rate after PVI in a large cohort of patients.

METHODS
We carried out retrospective analysis of consecutive patients with paroxysmal or persistent AF who underwent PVI between June 2011 and March 2012. The patients qualified for PVI had symptomatic nonvalvular AF, a history of unsuccessful antiarrhythmic drug (group Ic or III), and age below 70 years. Exclusion criteria were: hyperthyroidism, significant mitral valve disease, LA anteroposterior diameter (measured in the parasternal long-axis view) over 5.5 cm, or severe disease with life expectancy below one year. One day after the catheter ablation, the patients underwent echocardiographic assessment of LA size, including:

— measurement of LA anteroposterior diameter obtained during left ventricular end-systole in the parasternal long-axis view;
— measurement of LA longitudinal and transverse diameters obtained during left ventricular end-systole in the apical four-chamber view;
— measurements of LA area obtained during left ventricular end-systole and end-diastole in the apical four-chamber view;
— estimation of LA volume during left ventricular end-systole and end-diastole, based on the biplane Simpson method, using LA planimetry in apical four-chamber and two-chamber views.

All measurements were performed in accordance with the 2006 guidelines on chamber quantification published by the European Association of Echocardiography (now known as the European Association of Cardiovascular Imaging) in collaboration with American echocardiographic societies [5]. Echocardiographic examination was performed using the Philips iE33 system (Philips Medical Systems, Andover, MA, USA).

Ablation strategy
One quadripolar catheter was placed in the coronary sinus and one in the right ventricle. The LA was accessed through a single or double transseptal puncture (or patent foramen ovale, if present), and a 10-pole circumferential 15–25 mm Lasso ( Biosense Webster, Diamond Bar, CA, USA) or Optima (St. Jude Medical, Minnetonka, MN, USA), and 4-mm non-irrigated tip ablation (Marinr, Medtronic, Minneapolis, MN, USA) or irrigated Navistar ThermoCool (Biosense Webster, Diamond Bar, CA, USA) catheters were used for mapping and RF ablation. After transseptal puncture, the patients were heparinised throughout LA access (target activated clotting time 300–400 s). Fluoroscopy and an electroanatomic system (CARTO or Localisa) were used to navigate the catheters. The following settings were used while delivering RF energy: non-irrigated tip ablation — temperature limit of 55°C and a power limit of 35 W; irrigated tip ablation — temperature limit 48°C, power limit 35 W and 30 W on posterior wall. All electrograms were displayed on an electrophysiological recording system. The endpoint of the procedure was the isolation of pulmonary vein potentials in all pulmonary veins. If the patient was on AF, cardioversion was performed to verify the isolation during sinus rhythm.

Follow-up
According to guidelines, a recurrence of AF was defined as any atrial tachycardia lasting more than 30 s with a three-month blanking period applied [6]. In all patients, antiarrhythmic drugs were discontinued immediately after catheter ablation. Treatment with vitamin K antagonist was continued for two months (patients with score CHA2DS2VASc 0–1) or indefinitely (CHA2DS2VASc 2 and more). During the first year after the ablation, six days of electrocardiography Holter monitoring was recommended. Further monitoring was performed at the discretion of the outpatient cardiologist. Final follow-up was based on patient visits, analysis of Holter monitoring and/or other patient documentation, and telephone contact. In the case of recurrence, the decision whether to repeat the procedure was based on clinical symptoms and patient preferences.

Statistical analysis
We assumed a rate of AF recurrence of 50% in the study group during the follow-up. Completion of follow-up was estimated as 90%. To detect a 1.8-fold increase of the risk of AF recurrence in patients with LA enlargement with an 80% power, at least 172 patients were needed. Categorical data was presented as percentages and frequency, continuous variables as median values and interquartile ranges (IQR). To compare particular groups, Fisher’s exact test and Mann-Whitney U test were performed for categorical variables and continuous variables, respectively. To determine the predictors of AF recurrence, univariate and multivariable Cox proportional-hazards regressions were performed. According to LA measurements, two separate analyses were performed, one for measured values and the second for values adjusted for body surface area (BSA). BSA assessment was based on Mosteller’s formula [7]. In multivariable Cox proportional-hazards regression, the adjusted LA diameter, adjusted LA systolic and diastolic areas, and all factors with a p value lower than 0.05 in univariate regression were included. Statistical significance was consid-
Results

One hundred and seventy five patients who underwent 198 procedures (1.13 procedures per patient) between June 2011 and March 2012 were included in the analysis; seven patients were lost to follow-up (4%), so the final group comprised 168 patients. Follow-up after the last procedure was available for 165 patients (patients with a follow-up shorter than three months after the last procedure were not analysed). Median age of the group was 56 years (IQR 50–62). Major characteristics of the group are shown in Table 1.

After a median follow-up of 17 months after the first PVI procedure, 88 patients had recurrences (52.4%). No significant relations between any of the LA parameters and the recurrence rate were found, even after indexation for BSA (Table 2).

The efficacy after the last procedure (median follow-up 12 months, IQR 5–17) was 55.2% and was higher in paroxysmal atrial fibrillation.atrial fibrillation; CAD — coronary artery disease; CI — confidence interval; HR — hazard ratio

Table 1. Major characteristics of the study group (data is presented as median [interquartile range] or n (%) when applicable). Univariate analysis of the clinical factors

<table>
<thead>
<tr>
<th>Group characteristic</th>
<th>Univariate analysis (after the first procedure)</th>
<th>Univariate analysis (since the last procedure)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR 95% CI P</td>
<td>HR 95% CI P</td>
</tr>
<tr>
<td>Female gender</td>
<td>53 (31.5%)</td>
<td>53 (31.5%)</td>
</tr>
<tr>
<td>Age</td>
<td>56 (50–62)</td>
<td>56 (50–62)</td>
</tr>
<tr>
<td>Body mass index</td>
<td>29.3 (26.0–32.3)</td>
<td>29.3 (26.0–32.3)</td>
</tr>
<tr>
<td>Age at onset of AF</td>
<td>50 (41–55)</td>
<td>50 (41–55)</td>
</tr>
<tr>
<td>Persistent AF</td>
<td>48 (28.6%)</td>
<td>48 (28.6%)</td>
</tr>
<tr>
<td>CAD</td>
<td>12 (7.2%)</td>
<td>12 (7.2%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>93 (56.0%)</td>
<td>93 (56.0%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>15 (9.0%)</td>
<td>15 (9.0%)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>9 (5.4%)</td>
<td>9 (5.4%)</td>
</tr>
<tr>
<td>Lone AF</td>
<td>36 (22.1%)</td>
<td>36 (22.1%)</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>55 (32.9%)</td>
<td>55 (32.9%)</td>
</tr>
<tr>
<td>AF at hospital</td>
<td>55 (34.8%)</td>
<td>55 (34.8%)</td>
</tr>
</tbody>
</table>

Table 2. Left atrium measurements — univariate analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Whole group</th>
<th>Univariate analysis (after the first procedure)</th>
<th>Univariate analysis (since the last procedure)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>HR 95% CI P</td>
<td>HR 95% CI P</td>
</tr>
<tr>
<td>LA APD [cm]</td>
<td>4.3 (3.9–4.6)</td>
<td>1.19 0.74–1.94 0.47</td>
<td>1.24 0.72–2.17 0.44</td>
</tr>
<tr>
<td>LA APD [cm] ≥ 4.3</td>
<td>73 (53.7%)</td>
<td>1.23 0.76–2.02 0.40</td>
<td>1.17 0.69–1.99 0.56</td>
</tr>
<tr>
<td>LA SA</td>
<td>17.6 (13.3–20.7)</td>
<td>1.03 0.99–1.07 0.20</td>
<td>1.03 0.98–1.08 0.26</td>
</tr>
<tr>
<td>LA DA</td>
<td>24.4 (20.6–27.4)</td>
<td>1.01 0.97–1.06 0.57</td>
<td>1.02 0.97–1.07 0.39</td>
</tr>
<tr>
<td>LA ESV</td>
<td>53 (37–64)</td>
<td>1.01 0.99–1.02 0.34</td>
<td>1.01 0.99–1.02 0.19</td>
</tr>
<tr>
<td>LA EDV</td>
<td>84 (68–95)</td>
<td>1.00 0.99–1.01 0.57</td>
<td>1.01 0.99–1.02 0.33</td>
</tr>
<tr>
<td>LA APD/1 m² BSA</td>
<td>2.07 (1.91–2.26)</td>
<td>1.59 0.60–4.20 0.35</td>
<td>1.57 0.52–4.78 0.43</td>
</tr>
<tr>
<td>LA SA/1 m² BSA</td>
<td>8.44 (6.56–10.11)</td>
<td>1.08 0.99–1.17 0.09</td>
<td>1.08 0.98–1.19 0.13</td>
</tr>
<tr>
<td>LA DA/1 m² BSA</td>
<td>11.78 (10.16–13.51)</td>
<td>1.06 0.97–1.15 0.23</td>
<td>1.07 0.97–1.19 0.19</td>
</tr>
<tr>
<td>LA ESV/1 m² BSA</td>
<td>25.79 (19.15–31.45)</td>
<td>1.01 0.99–1.03 0.35</td>
<td>1.01 0.99–1.04 0.26</td>
</tr>
<tr>
<td>LA EDV/1 m² BSA</td>
<td>40.25 (33.91–46.68)</td>
<td>1.01 0.99–1.03 0.54</td>
<td>1.01 0.99–1.04 0.39</td>
</tr>
</tbody>
</table>

APD — anteroposterior diameter; BSA — body surface area; CI — confidence interval; DA — diastolic area; HR — hazard ratio; EDV — end-diastolic volume; ESV — end-systolic volume; SA — systolic area; LA — left atrium

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ysmal AF patients (71/119 patients; 59.7%) than in persistent AF patients (20/46 patients; 43.5%).

No significant relations between any of the LA parameters and the recurrence rate were found (also after indexation for BSA, Table 2).

In univariate Cox regression analysis after the first PVI, only very early AF recurrence (during hospitalisation) was a prognostic factor for AF recurrence in the long term. In the same analysis after the last PVI, also persistent AF was significantly linked with AF recurrences (Table 1).

In multivariate Cox regression analysis, only AF recurrence during hospitalisation was a significant predictor of later recurrences after catheter ablation (Table 3). None of the parameters of the LA were linked with the recurrence rate after catheter ablation (due to the small number of patients with LA volume, only anteroposterior dimension, systolic and diastolic LA area were included).

**Complications**

One (0.6%) PVI procedure was complicated with cardiac perforation and subsequent cardiac tamponade. We observed no other peri- or intraprocedural complications. One (0.6%) patient was reported with cerebral stroke 14 months after the procedure.

**DISCUSSION**

The major result of our study is that in patients with AF undergoing ablation, with LA smaller than 5.5 cm (antero-posterior diameter), LA size did not affect the results of PVI. Also, the results were the same after a single, or after numerous, procedures.

We aimed to test the relationships between echocardiographic parameters of LA and results of PVI because echocardiographic measurements are cheap and easy to obtain in clinical practice, non-invasive and do not use X-rays (which could be important in patients treated invasively with catheter ablation). Several parameters were chosen based on the literature and current recommendations [5, 8].

The results regarding the possible effect of the LA diameter on the outcome of AF ablation are still contradictory. In a systematic review, Balk et al. [9] have shown that of 20 studies testing the relationship between LA diameter and AF recurrence after catheter ablation, only four have reported statistically significant independent associations. On the other hand, the most recent meta-analysis of 22 studies with 3,750 patients showed that the LA diameter is significantly associated with the risk of AF recurrence after single catheter ablation [3].

The difference between ours and previously published results could be due to preprocedural selection — most of the earlier studies did not impose an upper limit of LA size as an excluding factor [9]. We believed that the risk of recurrence in patients with a very large LA was high, so we excluded those patients from the invasive treatment. Nevertheless, the latest data shows in fact that the results of PVI in patients with very large LA and non-paroxysmal AF are rather good (54% efficacy of antiarrhythmic drugs after 12 months) [10], as are the results of AF ablation in patients with severe disease of mitral valve (with an obvious secondary LA enlargement) [11].

A parameter much better reflecting the real size of LA is LA volume, measured with multidetector computed tomography (MDCT). It was consequently a significant independent predictor of AF recurrence after PVI, at least in the short term (median period of observation: 12–19 months) [12–15]. The discrepancy between the observations with echocardiography and the MDCT LA parameters is probably due to the relatively poor correlation between the echocardiographic LA diameter and the LA volume from MDCT [12, 16].

Our results testing the LA volume (systolic and diastolic) or the LA area do not show any trend in univariate or multivariate Cox regression analysis. Thus we cannot confirm the results published earlier that echocardiographically measured LA volume impacts upon the outcome of PVI [17].

**Limitations of the study**

Our group had good statistical power, was homogenous and well described. Nevertheless, several limitations of the study limit its value. Firstly, the retrospective nature of the analysis. Secondly, the open-labelled echocardiographic measurements. We used real-life measurements that were not
standardised, and their inter- and intraobserver variability was not determined. And finally, the follow up. Despite efforts to standardise the follow-up for all patients, numerous patients had only one or two Holter monitorings during the follow-up period, which could have overestimated our success rate. Although echocardiographic measurements were performed during the first day after ablation, it is unlikely that this fact might significantly influence the results.

**CONCLUSIONS**

In patients with AF undergoing PVI, with the LA diameter below 5.5 cm, the LA diameter, area, or volume (echocardiographic measurements) do not affect the long-term outcome of PVI.

**Conflict of interest:** E. Koźluk: Medtronic — proctorship in atrial fibrillation ablations; P. Lodziński: Biosense-Webster — proctorship in atrial fibrillation ablations.

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Wpływ wielkości lewego przedsionka na skuteczność izolacji żył płucnych u pacjentów z migotaniem przedsionków

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Streszczenie

Wstęp: Migotanie przedsionków (AF) jest najczęstszą utrwaloną tachyarytmią nadkomorową. Jedną z metod zapobiegania nawrotom AF jest ablacją prądem o wysokiej częstotliwości. Mimo dokładnej analizy w dostępnym piśmiennictwie nie wykazano jednoznacznego związku między ocenianą echokardiograficznie wielkością lewego przedsionka (LA) a częstością nawrotów AF po zabiegu izolacji żył płucnych (PVI).

Cel: Celem pracy była ocena związku między wymiarem LA ocenianym echokardiograficznie a skutecznością zabiegu PVI.

Metody: Grupę badaną stanowiło 175 pacjentów poddanych zabiegowi PVI w okresie od czerwca 2011 r. do marca 2012 r. Kryteria włączenia obejmowały: objawowe AF bez uchwytnej odwracalnej przyczyny, wiek < 70 lat, wymiar LA < 5,5 cm (przednio-tylny). Zabieg PVI wykonywano za pomocą klasycznego cewnika z 4-mm końcówką lub cewnikiem chłodzonym na podstawie zapisów z okrężnego cewnika mapującego (system elektroanatomiczny LocaLisa lub CARTO). Nawrót arytmii definiowano jako wystąpienie po 3-miesięcznym okresie wygaszania jakiejkolwiek tachyarytmii przedsionkowej trwającej ponad 30 s. Po zabiegu PVI przeprowadzono standardową ocenę echokardiograficzną LA w wymiarze przednio-tylnym oraz dodatkowo powierzchni skurczowej i rozkurczowej oraz objętości LA (pomiary podczas rytmu zatokowego).

Wyniki: Analizie poddano 198 procedur PVI u 175 pacjentów. Mediana okresu obserwacji wyniosła 17 miesięcy, a mediana wieku badanej grupy — 56 lat. Nawrót AF po pierwszej procedurze wystąpił u 88 (52,4%) osób. Skuteczność z uwzględnieniem ostatniego zabiegu PVI wyniosła 55,2% (43,5% w grupie przetrwałego AF, 59,7% w grupie napadowego AF). Nie stwierdzono istotnego statystycznie związku między żadnym z analizowanych parametrów LA i nawrotem AF. Na podstawie analizy wieloczynnikowej Coxa stwierdzono, że jedynym czynnikiem progностycznym nawrotu AF w okresie obserwacji odległej jest bardzo wczesny nawrót AF po zabiegu PVI.

Wnioski: W grupie pacjentów z AF nie wykazano zależności między nawrotem AF po zabiegu PVI a echokardiograficznymi parametrami LA.

Słowa kluczowe: migotanie przedsionków, ablacja migotania przedsionków, wielkość lewego przedsionka, izolacja żył płucnych

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