Early stage of left atrium remodelling predicts better outcome in long-term follow-up of atrial fibrillation ablation

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Abstract

Background: Radiofrequency catheter ablation (RFCA) has been increasingly used for the treatment of patients with symptomatic atrial fibrillation (AF).

Aim: To identify simple pre-procedural success predictors of RFCA in patients with AF.

Methods and Results: It comprised 294 consecutive patients (mean age 54 ± 11 years, 71% male) with symptomatic AF (28% — paroxysmal with short episodes (< 12 h); 50% — paroxysmal with episodes ≥ 12 h and < 7 days; 11.5% — persistent; 10.5% — longstanding persistent), having undergone the first RFCA. Before RFCA, all patients underwent pulmonary vein (PV) anatomy imaging and echocardiographic left atrium diameter (LAD) evaluation. PV periostial or antral isolation guided by electroanatomical mapping was performed with additional lines or complex fractionated electrograms ablation (if required). Outcomes were defined as clinical success (complete or improvement) or failure. After a mean follow-up of 36.9 ± 13 months, clinical success was observed in 90.5% of patients, made up of 47.3% complete success, and 43.2% improvement. Patients with short AF episodes underwent fewer procedures (1.6 vs. 2, p = 0.026) and had the highest clinical (97.6%) and complete (63.9%) success rates. AF episodes < 12 h (p < 0.001), LAD < 4 cm (p = 0.01) and male gender (p = 0.002) independently predicted RFCA long-term clinical success. PV anatomy did not correlate with RFCA outcome. A trend was observed towards a larger number of procedures in patients with atypical PV anatomy (p = 0.059).

Conclusions: AF ablation should be performed in the early stage of AF, before structural remodelling development.

Key words: atrial fibrillation, radiofrequency catheter ablation, left atrium remodelling, pulmonary vein anatomy

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INTRODUCTION

Epidemiology shows an increasing number of patients suffering from atrial fibrillation (AF), which is connected with higher morbidity and mortality [1]. AF occurs in 5–15% of the population aged over 65 years [2].

Radiofrequency catheter ablation (RFCA) is of growing importance in AF treatment. Apart from an ongoing improvement in ablation methods and technical equipment, as well as high acute success rates, many studies show an increasing percentage of arrhythmia recurrences and a decreasing success rate in the long-term outcome [3–6]. Better prediction of successful procedures is therefore needed. However, the studies that have reported long-term outcomes of AF ablation are still limited [5, 7–10].

Previous studies have identified age, AF type [11], hypertension [12], obstructive sleep apnoea syndrome [13], metabolic syndrome [14], left atrium diameter (LAD) [12, 15], and LA volume [16] as predictors of RFCA outcome. However, the

role of atrial remodelling and its advancement has not been studied extensively in this respect. There have been limited studies evaluating the impact of pulmonary vein (PV) anatomy variations on RFCA success rate [16, 17].

There is sufficient data showing the correlation of LA structural remodelling and AF duration and type [18, 19], as well as LA dimensions [20, 21]. The prolongation of AF recurrent episodes time is a symptom of developing atrial electrical and contractile remodelling [22, 23]. We hypothesised that AF episodes shorter than 12 h, and proper LA size, predicted a higher success rate of RFCA and indicated an early stage of atrial remodelling. On the contrary, AF recurrences longer than 12 h indicate ongoing LA functional and structural remodelling.

The aim of our study was to evaluate the impact of AF type and AF episode duration, LAD, as well as PV anatomy on the clinical success of AF ablation in a long-term follow-up. The study was designed to look for a simple and practical parameter predicting ablation outcome that could be implemented in everyday practice for the majority of patients and by the majority of physicians.

METHODS
Study population

The analysis included consecutive patients with symptomatic, drug refractory AF who, following multi-slice computed tomography (MSCT) of PVs as well as transthoracic echocardiography (TTE), underwent a first session of RFCA between March 2006 and June 2009. AF was defined as paroxysmal AF (PAF — Group 1), persistent (Group 2) or longstanding persistent (Group 3), according to the HRS/EHRA/ECAS Consensus Document [24]. Group 1 was divided into two subgroups (A and B) depending on AF episode duration and the method of sinus rhythm restoration (i.e. spontaneous, antiarrhythmic drugs [AAD], or cardioversion). Group 1A was classified as PAF with episode duration < 12 h, and spontaneous or after 'pill in the pocket' AAD therapy termination. Group 1B was defined as PAF episodes ≥ 12 h to seven days, with spontaneous and/or after intravenous AADs termination. Group 2 was defined as AF persistent (from seven days up to one year or when cardioversions were done), and Group 3 was defined as AF longstanding persistent (> 1 year).

Exclusion criteria included: age < 18 and > 70 years, severe valve stenosis or insufficiency, prosthetic mitral valve or percutaneous mitral commissurotomy, clinically relevant hepatic dysfunction requiring specific therapy, clinically manifest thyroid dysfunction requiring therapy, hypertrophic cardiomyopathy, restrictive cardiomyopathy, and surgical ablation of AF in the past.

Minimal follow-up duration from the last procedure was 12 months. The study protocol was approved by the Institutional Review Board and Bioethics Committee of the Institute of Cardiology and an informed consent was obtained from each patient.

Pulmonary vein imaging

All patients underwent PV imaging by a 64-slice MSCT scanner (Siemens Dual Source Definition) before first RFCA. Variants of PV anatomy and anomalies were evaluated (number of veins, accessory veins, common trunks). PV anatomy variants were divided into typical and atypical. Typical PV anatomy was defined as separate drainage of four PVs (single left and right superior and interior PVs, without accessory veins). The presence of any variations (common trunks, accessory veins) was classified as atypical PV anatomy.

Transthoracic echocardiography

Two-dimensional, M-mode, and colour Doppler TTE were performed in the standard position and views, using VIVID 6. Echocardiograms were performed routinely before RFCA. In our study, the antero-posterior LAD measurement in the long parasternal axis was used. All examinations were done by experienced observers.

Ablation procedure

Two catheters were introduced via a transseptal puncture into the left atrium: a circumferential PV mapping catheter (Lasso™, Biosense and Webster, Inc., CA, USA) and a cooled tip ablation catheter (ThermoCool Navi-Star, Biosense-Webster, Inc., CA, USA). One catheter (Marinr®, Medtronic Inc., Minneapolis, MN, USA) was introduced into the coronary sinus through the femoral vein. During the procedure, patients were under continuous sedation (fentanyl and midazolam), and unfractionated heparin 80 IU/kg was administered.

All patients had a PV isolation procedure by periostial or antral ablation guided by CARTO mapping [25]. In persistent or longstanding persistent AF patients, a stepwise ablation approach was used [26]. The goal of PV isolation was the absence of any potentials on the circumferential PV mapping catheter. If there was no conversion to sinus rhythm, linear lesions (roof line, mitral line) and/or complex fractionated electrograms ablation was performed individually. Cavo-tricuspid isthmus line was performed in patients with a history and/or induction of typical atrial flutter.

Follow-up

Every patient had a clinical evaluation, classic 12-lead electrocardiogram (ECG) and 24-h Holter ECG registration or 14 day ECG telemonitoring during the follow-up in the outpatient clinic three, six and 12 months after ablation. Patients who lived some distance from our department had six- and 12- month follow-up appointments with their local cardiologist. In case of arrhythmia recurrence, they were referred to our centre for further follow-up visits. Between the scheduled visits and after the 12-month follow-up visit, all patients were asked to register any palpitations on 12-lead ECG. After the 12-month follow-up period, at least one 24-h Holter registration per year was required. Finally, a median of six 24-h Holter registrations

per patient (interquartile range [IQR] 5–7) were available for analysis. Long-term follow-up of all patients was carried out by telephone interview, according to the protocol accepted by the Institutional Review Board, and additionally a final 24-h or 12-lead ECG (sending by fax or e-mail) was mandatory.

The blanking period (first three months after ablation) was excluded from analysis. Antiarrhythmic drug therapy was stopped 3–6 months after ablation if a patient had remained asymptomatic. Patients with AF/atrial tachycardia (AT) recurrences were carefully diagnosed by repetitive ECGs, 24-h Holter, event Holter and/or continuous 14-day transtelephonic full disclosure ECG monitoring. Patients were qualified for a repeated procedure and/or pharmacological treatment, according to HRS Expert Consensus Document [24].

We divided our follow-up results into main sections: clinical success or failure. Clinical success was defined as complete success (absence of AF/AT recurrences ≥ 30 s without AADs) and improvement (≥ 70% reduction of AF recurrences with no AADs or absence of AF recurrences with previously ineffective AADs treatment). Clinical failure was defined as an absence of any success endpoints.

Statistical analysis

Categorical data was presented as frequencies and was compared with χ^2 statistics or Fisher's exact tests. The distribution of continuous data was analysed using the Kolmogorov-Smirnov test. Normally distributed variables were compared using Student's t test and one-way analysis of variance (Fisher's analysis of variance) test and were presented as the mean ± standard deviation. Post-hoc comparisons in the analysis of variance were made with the Tukey test. The Mann-Whitney, Wilcoxon, and Kruskal-Wallis analyses of variance tests were used for comparisons of variables with other than normal distributions; these were presented as the median and IQR (25–75 percentile) and/or minimal and maximal values. Receiver operating characteristic (ROC) curve was used for detailed LAD analysis. Logistic regression analysis was used to search for independent predictors of RFCA success. Accordingly, odds ratios (OR) were computed, with the respective 95% confidence intervals (CI). P values < 0.05 were considered significant. Statistical analyses were performed using the Statistical Package for Social Sciences, version 16.0 (SPSS, Chicago, IL, USA).

RESULTS
Baseline patients' characteristics

294 consecutive AF patients, 208 (71%) men, mean age 54 ± 11 (17–72) years, who met the required criteria were included in this study. All patients were symptomatic and had failed a mean of 1.5 ± 0.8 class I or III AADs prior to ablation procedure. Patients were divided into three groups and subgroups according to the criteria mentioned above: Group 1 — 229 (78%); Group 2 — 34 (11.5%); and Group 3 — 31 (10.5%) patients. Additionally, Group 1 was divided into two subgroups: A (n = 83, 28%) and B (n = 146, 50%). The characteristics of the study population are presented in Table 1.

Table 1. Patient population characteristics

	All patients	PAF < 12 h (Group 1A)	PAF ≥ 12 h (Group 1B)	AF persistent (Group 2)	AF longstanding (Group 3)	P
Number	294 (100%)	83 (28%)	146 (50%)	34 (11.5%)	31 (10.5%)	
Male gender	208 (71%)	52 (63%)	105 (72%)	31 (78%)	29 (83%)	NS
Age [years]	54.2 ± 11	50.2 ± 12	56.1 ± 10.5	57.7 ± 8.2	51.8 ± 11†	0.001
Hypertension	139 (47%)	35 (42.2%)	80 (54.8%)	14 (42.4%)	10 (32.3%)	0.063
Coronary artery disease	38 (13%)	10 (12%)	24 (16.4%)	3 (9.1%)	1 (3.2%)	0.198
Diabetes mellitus	25 (8.5%)	6 (7.2%)	12 (8.2%)	6 (18.2%)	1 (3.2%)	0.154
Other structural heart disease*	23 (7.8%)	2 (2.4%)	15 (10.3%)	2 (6.1%)	4 (12.9%)	0.121
Body mass index > 25 kg/m²	86 (29%)	21 (25.3%)	43 (29.5%)	12 (36.4%)	10 (32.3%)	0.667
Mean left atrium diameter [cm]	4.2 (range 2.7–6.1)	4.0 ± 0.6	4.1 ± 0.5	4.4 ± 0.3	4.6 ± 0.7‡	< 0.001
Typical PV anatomy	185 (63%)	51 (61.4%)	93 (63.7%)	23 (69.7%)	18 (58.1%)	0.783
Left common trunk	53 (18.1%)	19 (22.9%)	24 (16.4%)	3 (9.1%)	7 (22.6%)	0.286
Right middle PV	60 (20.4%)	17 (20.5%)	27 (18.5%)	7 (21.3%)	9 (29%)	0.360
Other right-sided PV	11 (3.7%)	3 (3.6%)	4 (2.7%)	2 (6%)	2 (6.5%)	0.275
Left middle PV	7 (2.4%)	1 (1.2%)	4 (2.7%)	0	2 (6.5%)	0.311

Data is presented as mean ± SD or number (per cent); *dilated cardiomyopathy, ischaemic cardiomyopathy with left ventricular ejection fraction > 30%, not significant valvular heart disease, congenital heart malformations with not significant left-to-right shunt); AF — atrial fibrillation; PAF — paroxysmal AF; PV — pulmonary vein
†Group 1A vs. Group 2 (p = 0.039); Group 2 vs. Group 3 (p = 0.031)
‡Group 1A vs. Group 2 (p = 0.003), Group 1A vs. Group 3 (p < 0.001), Group 1B vs. Group 2 (p = 0.018), Group 1B vs. Group 3 (p < 0.001)

Table 2. Results of ablation efficacy in different atrial fibrillation (AF) groups

Groups of AF	Clinical success [%]	Complete success/improvement [%]	Failure [%]
Group 1A	97.6	63.9/33.7	2.4
Group 1B	89.7	41.8/47.9	10.3
Group 2	84.8	42.4/42.4	15.2
Group 3	80.6†	32.3‡/48.4	19.4§
P	0.022	0.003/0.194	0.022

P value for trends between Groups 1A vs. 1B vs. 2 vs. 3
†Group 1A vs. 1B (p = 0.029), Group 1A vs. 2 (p = 0.009), Group 1A vs. 3 (p = 0.002)
‡Group 1A vs. 1B (p = 0.001), Group 1A vs. 2 (p = 0.035), Group 1A vs. 3 (p = 0.003)
§Group 1A vs. 1B (p = 0.029), Group 1A vs. 2 (p = 0.009), Group 1A vs. 3 (p = 0.002)

Follow-up

The mean follow-up duration in the whole cohort was 36.9 ± 13 (range 12–57) months. 551 RFCAs were performed with the median procedure number of two (IQR 1–2). A repetitive procedure was performed in 144 (49%) patients.

Clinical success was achieved in 256 (90.5%) patients, made up of a complete ablation success in 139 (47.3%) patients, and clinical improvement in the other 127 (43.2%) patients. RFCA failed in 28 (9.5%) patients. The number of procedures was the same in the clinical success and the clinical failure group (median 2 [IQR 1–2] vs. 2 [IQR 1–2], p = NS), although patients with complete success underwent a smaller number of procedures (median 1 [IQR 1–2] vs. 2 [IQR 1–2]; p = 0.009).

AF type and episode duration

Results of RFCA differed across groups (Table 2). The highest RFCA success rate was found in Group 1A (63.9% of the patients had a complete success; in 97.6% clinical success was achieved). There was a difference in RFCA efficacy between Groups 1A and 1B (complete success was observed in 63.9% vs. 41.8%, p = 0.001 and clinical success in 97.6% vs. 89.7%, p = 0.022). In Groups 1B and 2, complete and clinical success rates were similar (41.8% vs. 42.4%, p = 0.548 and 89.7% vs. 84.8%, p = 0.297, respectively). The percentage of Group 3 patients whose follow-up ended with complete success was considerably lower (32.3%).

The mean number of procedures was significantly lower in Group 1A compared to the other groups (1.6 ± 0.9 [median 1] vs. 2 ± 1.4 [median 2], p = 0.026).

Left atrial diameter

Mean LAD differed significantly between groups (p < 0.001), which is illustrated in Figure 1. In Group 1A, we observed the smallest mean LAD of 4.0 ± 0.6 cm vs. 4.2 ± 0.6 cm in the remaining patients (p = 0.001). Variables influencing an increase in the LA size are shown in Table 3.

There was a relationship between LAD and RFCA success rate. Complete success rate was higher in patients with smaller LAD (4.1 ± 0.6 cm vs. 4.2 ± 0.6 cm, p = 0.019).
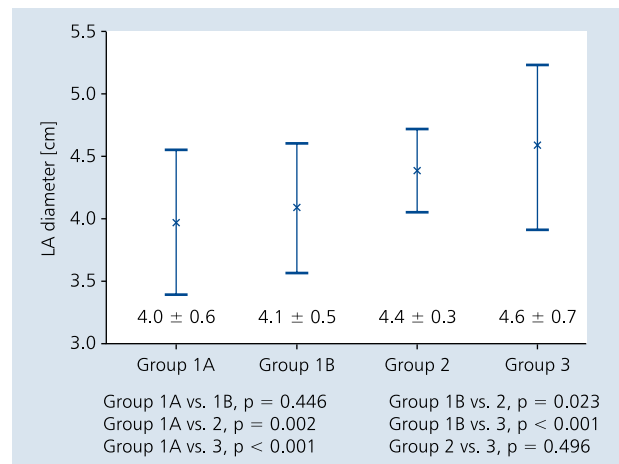

Group 1A vs. 1B, p = 0.446   Group 1B vs. 2, p = 0.023
Group 1A vs. 2, p = 0.002   Group 1B vs. 3, p < 0.001
Group 1A vs. 3, p < 0.001   Group 2 vs. 3, p = 0.496

Figure 1. Left atrium (LA) diameter in atrial fibrillation groups. Parameter [cm] was presented as mean (crosses) ± standard deviation

Moreover, LAD < 4.0 cm was observed significantly more often in patients with complete success of RFCA compared to others (43.2% vs. 28.2%, p = 0.005). Based on the ROC curve analysis, we determined LAD of 4.0 cm as a border value, which could be a predictor of RFCA complete success rate (Fig. 2).

Pulmonary venous anatomy

Typical PV anatomy was observed in 186 (63%) patients. PVs were equally distributed in groups (Table 1). There was no correlation between PV anatomy and clinical success/failure rates of RFCA (p = 0.4). However, there was a trend towards an increasing number of procedures in patients with atypical PV anatomy: median 1 (1–2) vs. 2 (1–2), p = 0.059.

Predictors of RFCA success rate

In univariate analysis, it turned out that in Group 1A (AF episodes < 12 h), LAD < 4 cm, male gender and age were potentially predictive factors of complete ablation success (Table 4). Multivariate analysis proved that short (< 12 h) AF episodes (OR = 2.95, 95% CI 1.68–5.2, p < 0.001),

Table 3. Factors significantly influencing left atrium enlargement

Variable	P
Age	0.001
Male gender	0.001
AF persistent	0.006
AF longstanding persistent	< 0.001
SHD	< 0.001
BMI > 25	0.006

AF — atrial fibrillation; BMI — body mass index; SHD — other structural heart disease (see explanation under Table 1)

LAD < 4.0 cm (OR = 1.98; 95% CI 1.17–3.35; p = 0.011), as well as male gender (OR = 2.37; 95% CI 1.36–4.16; p = 0.002) were independent predictors of complete ablation success. We would like to point out that PV anatomy had no impact on RFCA efficacy.
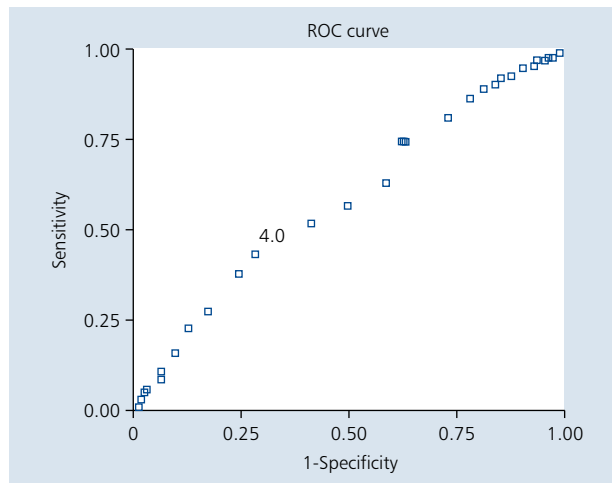

Figure 2. Receiver operating characteristic (ROC) curve analysis of left atrium diameter [cm] with highest sensitivity and specificity for predicting complete success rate of atrial fibrillation ablation (area under the ROC curve = 0.531)

DISCUSSION
Major findings

The correlation between the stage of LA structural remodelling and AF duration [18, 19], as well as LA dimensions, has been shown in experimental models [20, 21, 27], although the reported impact of the above on the clinical outcome after RFCA is inconsistent [12, 28]. We present new data documenting the impact of LA remodelling defined as duration and type of AF episodes as well as LAD, on ablation success rate.

Based on the results of this study, we suggest that parameters easy to obtain in everyday practice, such as AF episode duration < 12 h and LAD < 4.0 cm as well as male gender, are independent predictors of ablation success. The results of this study support experts' recommendations to treat AF in the early stage of the disease [29, 30].

A few studies have examined the impact of PV anatomy on the long-term success rate of AF ablation [16, 17]. Our results did not reveal any impact of PV anatomy on RFCA outcome, although we observed a trend for the number of procedures to increase in atypical PV anatomy.

Impact of LA remodelling advancement on RFCA outcome

In the natural history of focal AF, several stages of LA remodelling are observed. In the first stage, spontaneous termination of arrhythmia is frequent [22, 23]. Several factors, like inflammation, electrolytes disturbances, hypoxia, stress and effort

Table 4. Univariate correlates of radiofrequency catheter ablation complete success rate

Univariative analysis	Complete success	Improvement + failure	P
Mean age [years]	52.6 ± 12.4	55.6 ± 10.2	0.021
Male gender	77%	65.4%	0.019
Paroxysmal AF < 12 h	64.3%	35.7%	< 0.001
Paroxysmal AF ≥ 12 h	42.9%	57.1%	0.125
Paroxysmal AF	49.8%	50.2%	0.054
AF persistent	44.1%	55.9%	0.418
AF longstanding persistent	32.3%	67.7%	0.056
Hypertension	43.9%	50.6%	0.148
Diabetes mellitus type 2	7.2%	9.6%	0.297
Structural heart disease	9.4%	6.5%	0.240
Body mass index > 25	27.3%	30.8%	0.302
Left atrium diameter < 4.0 cm	57.7%	42.3%	0.005

AF — atrial fibrillation

as well as alcohol abuse play an important role in initiating and maintaining the arrhythmia. In the unchanged atrial muscle, the role of triggers and drivers (originating mainly in PV ostia) is dominating [31]. Other cofactors like hypertension, age, obstructive sleep apnoea, valvular diseases, and obesity may contribute to remodelling of the atria muscle. In the above cases, an increasing role of LA muscle substrate for AF maintenance is observed. The influence of AF duration on the structure of the atrial muscle is also well documented [18, 23]. The longer arrhythmia sustains, the more advanced the changes in the atrial muscle, beginning from reversible changes in the ionic channels to irreversible structural changes and fibrosis [19, 21, 32]. There is also evidence that damaged and fibrotic atria are more likely to fibrillate [33, 34]. Multidirectional injury and fibrosis of muscle fibres create substrate for a nonuniform anisotropic conduction, rotors or multiple wavelet and so-called fibrillatory conduction [19, 21].

Our study revealed that AF episodes lasting longer than 12 h correlate with incompletely reversible remodelling advancement and lead to subsequent AF recurrences after ablation procedure. The high success rate of RFCA in short-time AF recurrences suggests that LA remodelling is still reversible.

The success rate reported by different groups varies from 57 up to 79.5% [5, 9]. In a group of patients in whom ablation was performed in a similar way published by Weerasooriya et al. [10], a complete success rate of 63.9% was reported for repeated procedures in a five-year follow-up.

Predictors of clinical outcome

Prior studies, based on heterogeneous groups, have indicated age [7], obesity [13], diabetes mellitus [8], hypertension [12], and different cardiovascular co-morbidities [35], as predictors of AF recurrence after RFCA. In our study, age, body mass index (BMI) > 25 and cardiovascular co-morbidities alone did not predict RFCA efficacy. However, we observed their significant impact on LA enlargement. In our opinion, the cause of LA enlargement is multifactorial [28, 33, 36]. The above mentioned factors analysed separately are hard to quantify and might not be suitable for everyday qualification of patients (e.g. the presence of hypertension or specific blood pressure measurements; obesity or specific value of BMI etc.). In some patients, the coexistence of several co-morbidities might combine to form a multifactorial AF risk factor. Therefore, in our opinion, LAD reflects an impact of different co-morbidities together, and can be objectively quantified and measured.

In our study, we have used standard echocardiographic measurement of LA. Smaller LAD has been confirmed as a predictor of RFCA efficacy [12, 15] and AF termination by RFCA [6] in prior studies. However, some researchers have emphasised that LA volume determined by MSCT is more appropriate for LA size assessment [37] and correlated with long-term results of ablation [16]. It is worth mentioning that the studies cited above did not compare the impact of both

LAD and LA volume on AF ablation outcome. In our opinion, LAD is sufficient for predicting the success or failure, but significant enlargement of LAD alone should not disqualify from RFCA.

Our results did not reveal any impact of PV anatomy on the final long-term outcome. However, atypical PV anatomy could predispose to repeated procedures (p = 0.059). Nor have other studies revealed any impact on RFCA final success [16, 17]. To the best of our knowledge, this study examined PV anatomy visualised by 64-slice CT in one of the largest groups published. The findings of PV anatomy pattern and common PV variations are similar to those reported in previous studies on smaller groups which described a typical 4 — PV anatomy in 57–59% of patients, accessory PVs in 27–29%, and left common trunk in 16–17% [38, 39].

RFCA in AF patients with early stage of LA remodelling as a first choice therapy

According to current guidelines [40], AF ablation for PAF patients is recommended in cases of unsuccessful treatment with at least one AAD (IA), although ablation as the first line treatment is possible. Wazni et al. [15] and Tunner et al. [41] have shown that PV isolation might be the first-choice therapy for treating selected PAF patients, instead of AAD treatment. Antiarrhythmic drug therapy can prolong therapeutic process and result in LA remodelling advancement, as Winkle et al. [42] have reported. Results of the randomised MANTRA-PAF and RAAFT II trials support the 2010 recommendation that RFCA as first-line therapy for rhythm control in selected patients (especially with PAF and low risk of periprocedural complications) is a reasonable solution [43, 44].

An acceptable success rate in the long-term outcome and a lower procedure number in patients with short episodes of PAF encouraged us to propose ablation as a first-line early treatment strategy. Unsatisfactory results in longstanding persistent AF patients suggest cautious qualification for ablation in such a group. Our results are consistent with an early and comprehensive AF management approach, published in EHRA Consensus [29, 30], and with the published results of single-centre and randomised trials [15, 41–44].

Limitations of the study

In our study we have analysed the duration of AF episodes. We did not include duration from the beginning of AF symptoms for detailed analysis. We cannot exclude silent AF episodes of unknown duration, although all patients had symptomatic AF episodes and before ablation all patients have had Holter or long-term full disclosure ECG monitoring.

Nor can we exclude asymptomatic AF recurrences in the transtelephonic long-term follow-up, although all patients had a systematically scheduled ECG monitoring (24-h Holter or 14-day registration) over 12 months post ablation. Moreover, patients feeling palpitations were assigned to the clinical im-

provement group, although some of these episodes might not have been associated with AF recurrences. All these patients were closely followed up, with multiple Holter monitoring done if palpitations appeared.

CONCLUSIONS

The stage of LA remodelling measured as the duration of AF episode as well as echocardiographic measurement of LAD is a predictor of AF ablation success. RFCA success rate in AF patients with the early stage of LA remodelling is significantly higher than in more advanced remodelling groups. Our findings suggest that AF patients should be qualified for ablation treatment in the early stage of the disease before structural remodelling development.

Conflict of interest: none declared

References

1. Benjamin EJ, Wolf PA, D'Agostino RB et al. Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. Circulation, 1998; 98: 946–952.
2. Falk RH. Atrial fibrillation. N Engl J Med, 2001; 344: 1067–1078.
3. Cheema A, Vasamreddy CR, Dalal D et al. Long-term single procedure efficacy of catheter ablation of atrial fibrillation. J Interv Card Electrophysiol, 2006; 15: 145–155.
4. Cappato R, Calkins H, Chen SA et al. Worldwide survey on methods, efficacy, and safety of catheter ablation for human atrial fibrillation. Circulation, 2005; 111: 1100–1105.
5. Medi C, Sparks PB, Morton JB et al. Pulmonary vein antral isolation for paroxysmal atrial fibrillation: results from long-term follow-up. J Cardiovasc Electrophysiol, 2011; 22: 137–141.
6. O'Neill MD, Wright M, Knecht S et al. Long-term follow-up of persistent atrial fibrillation ablation using termination as a procedural endpoint. Eur Heart J, 2009; 30: 1105–1112.
7. Tzou WS; Marchlinski FE, Zado ES et al. Long-term outcome after successful catheter ablation of atrial fibrillation. Circ Arrhythm Electrophysiol, 2010; 3: 237–242.
8. Wokhlu A, Hodge DO, Monahan KH et al. Long-term outcome of atrial fibrillation ablation: impact and predictors of very late recurrence. J Cardiovasc Electrophysiol, 2010; 21: 1071–1078.
9. Ouyang F, Tilz R, Chun J et al. Long-term results of catheter ablation in paroxysmal atrial fibrillation: lessons from a 5-year follow-up. Circulation, 2010; 122: 2368–2377.
10. Weerasooriya R, Khairy P, Litalien J et al. Catheter ablation for atrial fibrillation: are results maintained at 5 years of follow-up? J Am Coll Cardiol, 2011; 57: 160–166.
11. Derejko P, Polańska M, Chojnowska L et al. Przezskórna ablacja migotania przedsionków prądem o wysokiej częstotliwości u pacjentów z kardiomiopatią przerostową: typ migotania a skuteczność zabiegu. Kardiol Pol, 2013; 71: 17–24.
12. Berruezo A, Tamborero D, Mont L et al. Pre-procedural predictors of atrial fibrillation recurrence after circumferential pulmonary vein ablation. Eur Heart J, 2007; 28: 836–841.
13. Jongnarangsin K, Chugh A, Good E et al. Body mass index, obstructive sleep apnea, and outcomes of catheter ablation of atrial fibrillation. J Cardiovasc Electrophysiol, 2008; 19: 668–672.
14. Tang RB; Dong JZ; Liu XP et al. Metabolic syndrome and risk of recurrence of atrial fibrillation after catheter ablation. Circulation, 2009; 73: 438–443.
15. Tanner H, Makowski K, Roten L et al. Catheter ablation of atrial fibrillation as first-line therapy: a single centre experience. Europace, 2011; 13: 646–653.
16. Hof I, Chilukuri K, Arbab-Zadeh A et al. Does left atrial volume and pulmonary venous anatomy predict the outcome of catheter ablation of atrial fibrillation? J Cardiovasc Electrophysiol, 2010; 20: 1005–1009.
17. Hunter RJ, Ginks M, Ang R et al. Impact of variant pulmonary vein anatomy and image integration on long-term outcome after catheter ablation for atrial fibrillation. Europace, 2010; 12: 1691–1697.
18. Wijffels MC, Kirchhof CJ, Dorland R, Allessie MA. Atrial fibrillation begets atrial fibrillation: a study in awake chronically instrumented goats. Circulation, 1995; 92: 1954–1968.
19. Verheule S, Tuyls E, van Hunnik A et al. Fibrillatory conduction in the atrial free walls of goats in persistent and permanent atrial fibrillation. Circ Arrhythm Electrophysiol, 2010; 6: 590–599.
20. Wożakowska-Kaplon B. Changes in left atrial size in patients with persistent atrial fibrillation: a prospective echocardiographic study with a 5-year follow-up period. Int J Cardiol, 2005; 101: 47–52.
21. Schotten U, de Haan S, Neuberger HR et al. Loss of atrial contractility is primary cause of atrial dilatation during first days of atrial fibrillation. Am J Physiol, 2004; 287: H2324–H2331.
22. Walczak F. Natural history of focal atrial fibrillation: the role of atrial remodeling. In: Walczak F, Szumowski Ł, Siebert J ed. Migotanie przedsionków: postacie, mechanizmy, rola ablacji. Serce dla arytmii. Fundacja na rzecz elektrofizjologii. 1st Ed. Warszawa 2008: 185–193.
23. Allessie M, Ausma J, Schotten U. Electrical, contractile and structural remodeling during atrial fibrillation. Cardiovasc Res, 2002; 54: 230–246.
24. Calkins H, Brugada J, Packer DL et al. HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation: recommendations for personnel, policy, procedures and follow-up. Heart Rhythm, 2007; 4: 816–861.
25. Hocini M, Sanders P, Jais P et al. Technique for curative treatment of atrial fibrillation. J Cardiovasc Electrophysiol, 2004; 15: 1471–1487.
26. Matsuo S, Lim K-T, Haissaguerre M. Ablation of chronic atrial fibrillation. Heart Rhythm, 2007; 4: 1461–1463.
27. Winkle RA, Mead RH, Engel G, Patrawala RA. Relation of early termination of persistent atrial fibrillation by cardioversion or drugs to ablation outcomes. Am J Cardiol, 2011; 108: 374–379.
28. Balk EM, Garlitski AC, Alsheikh-Ali AA et al. Predictors of atrial fibrillation recurrence after radiofrequency catheter ablation: a systematic review. J Cardiovasc Electrophysiol, 2010; 11: 1208–1216.
29. Kirchhof P, Lip GY, Van Gelder IC et al. Comprehensive risk reduction in patients with atrial fibrillation: emerging diagnostic and therapeutic options-a report from the 3rd Atrial Fibrillation Competence NETwork/European Heart Rhythm Association consensus conference. Europace, 2012; 14: 8–27.
30. Van Gelder IC, Haegeli LM et al. Rationale and current perspective for early rhythm control therapy in atrial fibrillation. Europace, 2011; 13: 1517–1525.
31. De Jong AM, Maass AH, Oberdorf-Maass SU et al. Mechanisms of atrial structural changes caused by stretch occurring before and during early atrial fibrillation. Cardiovasc Res, 2011; 89: 689–691.
32. Burstein B, Nattel S. Atrial fibrosis: mechanisms and clinical relevance in atrial fibrillation. J Am Coll Cardiol, 2008; 51: 802–809.
33. John B, Stiles MK, Kuklik P et al. Electrical remodeling of the left and right atria due to rheumatic mitral stenosis. Eur Heart J, 2008; 29: 2234–2243.
34. Allessie M. Stretch and speed: a complicated couple. J Cardiovasc Electrophysiol, 2011; 22: 402–404.
35. Helms AS, West JJ, Patel A et al. Relation of left atrial volume from three-dimensional computed tomography to atrial fibrillation recurrence following ablation. Am J Cardiol, 2009; 103: 989–993.

36. Meris A, Amigoni M, Uno H et al. Left atrial remodelling in patients with myocardial infarction complicated by heart failure, left ventricular dysfunction, or both: the VALIANT Echo study. Eur Heart J, 2009; 1: 56–65.

37. Hof I, Arbab-Zadeh A, Scherr D et al. Correlation of left atrial diameter by echocardiography and left atrial volume by computed tomography. J Cardiovasc Electrophysiol, 2009; 20: 159–163.

38. Mansour M, Holmvang G, Sosnovik D et al. Assessment of pulmonary vein anatomic variability by magnetic resonance imaging: implications for catheter ablation techniques for atrial fibrillation. J Cardiovasc Electrophysiol, 2004; 15: 387–393.

39. Marom EM, Herndon JE, Kim YH, McAdams HP. Variations in pulmonary venous drainage to the left atrium: implications for radiofrequency ablation. Radiology, 2004; 230: 824–829.

40. European Heart Rhythm Association; European Association for Cardio-Thoracic Surgery, Camm AJ, Kirchhof P, Lip GY et al. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). Eur Heart J, 2010; 19: 2369–2429.

41. Wazni OM, Marrouche NF, Martin DO et al. Radiofrequency ablation versus anti-arrhythmic drugs as first-line treatment of symptomatic atrial fibrillation. JAMA, 2005; 293: 2634–2640.

42. Winkle RA, Mead RH, Engel G et al. Prior antiarrhythmic drug use and the outcome of atrial fibrillation ablation. Europace, 2012; 14: 646–652.

43. Cosedis Nielsen J, Johannessen A, Raatikainen P et al. A randomized comparison of radiofrequency ablation and antiarrhythmic drug therapy as first line treatment in paroxysmal atrial fibrillation. N Engl J Med, 2012; 367: 1587–1595.

44. Morillo CA, Verma A, Connolly SJ et al. Radiofrequency Ablation vs. Antiarrhythmic Drugs as First-Line Treatment of Symptomatic Atrial Fibrillation: (RAAFT 2): a randomized trial. JAMA, 2014; 311: 692–700.

Wczesny etap przebudowy lewego przedsionka jako czynnik prognostyczny skuteczności ablacji migotania przedsionków w obserwacji odległej

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Streszczenie

Wstęp: Ablacja prądem o wysokiej częstotliwości (RF) jest zyskującą na znaczeniu metodą leczenia migotania przedsionków (AF). Jednak mimo ciągłego doskonalenia technik ablacji i wysokiego odsetka wczesnej skuteczności zabiegu, obserwacje odległe pokazują stopniowo zwiększający się odsetek nawrotów arytmii w czasie. Jednocześnie dane dotyczące odległych (> 3 lat) wyników ablacji podłoża AF są ograniczone. Kluczowy problem stanowi odpowiednia kwalifikacja do tego rodzaju leczenia, tj. ocena wskazań, stratyfikacja ryzyka okołozabiegowego i prognoza skuteczności terapii.

Cel: Celem pracy była ocena wpływu: rodzaju AF (napadowe [PAF], przetrwałe, długotrwałe przetrwałe), czasu trwania epizodów AF (< 12 h, ≥ 12 h), wielkości lewego przedsionka (LA) i anatomii żył płucnych (PV) na skuteczność ablacji RF podłoża AF w obserwacjach odległych.

Metody: Analizą objęto kolejnych pacjentów z AF objawowym, opornym na leki antyarytmiczne (AAD), u których wykonano pierwszą sesję ablacji RF podłoża AF w okresie od marca 2006 do czerwca 2009 r. Chorych podzielono na grupy w zależności od postaci AF i czasu trwania epizodu: grupa 1A — PAF z napadami < 12 h, grupa 1B — PAF z napadami od ≥ 12 h do 7 dni, grupa 2 — przetrwałe AF, grupa 3 — długotrwałe przetrwałe AF. U wszystkich osób wykonano 64-rzędową tomografię komputerową LA i PV oraz przezklatkowe badanie echokardiograficzne. U wszystkich pacjentów została przeprowadzona izolacja PV (periostialna lub antralna) z użyciem systemu elektroanatomicznego CARTO. U osób z przetrwałym i długotrwałe

przetrwałym AF zastosowano metodę stopniowania rozległości zabiegu (*stepwise ablation approach*). Wyniki odległej obserwacji po ostatniej sesji ablacji przedstawiono jako skuteczność kliniczną (skuteczność całkowita + poprawa) lub niepowodzenie. Całkowitą skuteczność zdefiniowano jako brak nawrotów AF/częstoskurczu przedsionkowego (AT) ≥ 30 s bez AAD, natomiast poprawę jako istotną redukcję nawrotów AF/AT (> 70%) bez AAD lub brak nawrotów AF w czasie stosowania nieskutecznych wcześniej AAD. Niepowodzeniem określano nieosiągnięcie żadnego z powyższych celów. Odległe wyniki skuteczności ablacji podsumowano na podstawie zgromadzonej dokumentacji medycznej uzupełnionej danymi z telefonicznego wywiadu przeprowadzonego wg protokołu zaakceptowanego przez Terenową Komisję Bioetyczną.

Wyniki: Do grupy badanej włączono 294 kolejnych osób spełniających powyższe kryteria. Średni wiek wynosił 54 ± 11 (17–72) lata; 71% (n = 208) badanych stanowili mężczyźni. Pacjenci zostali podzieleni na grupy: grupa 1A — 83 osoby (28%), grupa 1B — 146 (50%), grupa 2 — 34 (11,5%), grupa 3 — 31 (10,5%). Grupy różniły się istotnie pod względem wieku (p < 0,001) i średniej wielkości LA (p < 0,001). Średni czas obserwacji w całej grupie wynosił 36,9 ± 13 (12–57) miesięcy. Wykonano 551 ablacji; mediana liczby zabiegów wynosiła 2 (IQR 1–2). Kolejne zabiegi przeprowadzono u 144 (49%) pacjentów. Chorzy z grupy 1A wymagali kolejnych sesji ablacji rzadziej (1,6 *vs.* 2; p = 0,026) niż pozostali oraz wykazano u nich najwyższy odsetek klinicznej (97,6%) i całkowitej (63,9%) skuteczności zabiegu. Typową anatomię PV stwierdzono u 186 (63%) osób. Nie zanotowano istotnej korelacji między wariantami anatomicznymi PV a odległymi wynikami ablacji (p = 0,4). Zaobserwowano jedynie trend dotyczący większej liczby zabiegów u pacjentów z atypową anatomią PV; mediana 1 (1–2) vs. 2 (1–2); p = 0,059. Stwierdzono związek między wielkością LA a odległymi wynikami ablacji. Odsetek całkowitej skuteczności ablacji był wyższy u pacjentów z mniejszym LA (4,06 ± 0,55 cm *vs.* 4,22 ± 0,58 cm; p = 0,019). Na podstawie analizy krzywej ROC wyznaczono wielkość LA = 4,0 cm jako graniczną dla prognozowania skuteczności całkowitej ablacji. Analiza wieloczynnikowa potwierdziła, że krótkie napady AF (< 12 h) (OR = 2,95; 95% CI 1,68–5,2; p < 0,001), wielkość LA < 4 cm (OR = 1,98; 95% CI 1,17–3,35; p = 0,011) i płeć męska (OR = 2,37; 95% CI 1,36–4,16; p = 0,002) są niezależnymi predyktorami całkowitej skuteczności ablacji. Nie wykazano wpływu anatomii PV na skuteczność odległą ablacji AF.

Wnioski: Stopień zaawansowania przebudowy LA, wyrażony jako czas trwania epizodu AF i echokardiograficzny pomiar wielkości LA, jest niezależnym predyktorem skuteczności ablacji RF. Dlatego też wydaje się, że pacjenci z AF powinni być kwalifikowani do leczenia metodą ablacji RF we wczesnym okresie choroby, przed rozwojem nieodwracalnej przebudowy przedsionków.

Słowa kluczowe: migotanie przedsionków, przebudowa, ablacja RF, anatomia żył płucnych