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Selected echocardiographic and blood pressure parameters including ventricular-arterial coupling in predicting atrial fibrillation recurrence after pulmonary vein isolation: preliminary study

Short title: Ventricular-arterial coupling and atrial fibrillation recurrence

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INTRODUCTION

Pulmonary vein isolation (PVI) is the primary invasive treatment for patients with paroxysmal atrial fibrillation (AF) [1]. However around 10%–35% patients in the first year require redo procedure due to AF recurrence [2]. Predicting these recurrences is crucial in cardiac electrophysiology but remains challenging despite advances in ablation techniques. Several factors, including patient characteristics and procedural variables, complicate this prediction [3,4]. Ventricular-arterial coupling (VAC) is essential in understanding cardiac adaptations and AF recurrence post-PVI. This study examines the role of VAC dynamics in predicting AF recurrence post-PVI, aiming to identify factors influencing treatment efficacy.

METHODS

We prospectively recruited 49 patients (13 women and 36 men, aged 40–75 years) with paroxysmal AF scheduled for PVI at the University Hospital in Krakow. The study was conducted in 2019–2021. Participants had no other cardiovascular diseases, maintained sinus rhythm upon admission, preserved left ventricular (LV) ejection fraction, and normal carotid-femoral pulse wave velocity (PWV). The study, approved by the Jagiellonian University Ethics Committee, followed the Helsinki Declaration. All participants provided informed consent. Medical history, comorbidities, AF history, attack frequency and intensity, medication use, and lifestyle data were collected via standardized questionnaire, along with anthropometric and demographic data. PVI was performed using cryoballoon pulmonary vein catheter ablation method. Recurrence of atrial fibrillation was assessed by patients' symptoms on follow-up visit and by 72-hour Holter ECG monitoring performed within a month preceding the follow-up visit. Recurrence of AF was defined as recurrence of arrhythmia confirmed by Holter ECG monitoring or persistent attacks of arrhythmia in patients with negative observation for AF in Holter ECG.

Transthoracic echocardiography was performed to assess LV end diastolic volume, LV end systolic volume, stroke volume, left atrium volume indexed to the subjects' body surface area (LAVI) and LV global longitudinal strain (GLS). During echocardiographic recording of blood flow velocity in LV outflow tract the brachial peripheral systolic blood pressure and brachial pulse wave were simultaneously recorded. From the brachial signal the aortic pulse wave and subsequently the central systolic blood pressure were estimated. The PWV was computed as a quotient of the measured distance covered between the two recorders and the transit time measured. We calculated classical parameter of VAC which reflects an interplay between the heart and the arterial system as a ratio of arterial elastance and LV elastance. Arterial elastance (E_a) was measured as a ratio of end-systolic pressure (ESP) and stroke volume, where ESP was estimated as peripheral systolic blood pressure multiplied by 0.9 [5]. LV elastance (E_{es}) was calculated as a ratio of ESP and LV end systolic volume [4]. Finally, the E_a/E_{es} ratio was calculated. Additionally, we calculated the newly proposed VAC parameter — PWV to GLS ratio. In fasting patients, during recruitment and follow-up visit, venous blood samples were taken, and standard laboratory tests were performed including N-terminal pro-B-type natriuretic peptide. Additionally on baseline visit matrix metalloproteinases 3 and 9 (MMP-3, MMP-9) were assessed.

Statistical analysis

Statistical analysis was carried out in R software, version 4.0.5 and version 9.4 (SAS Institute, Cary, NC, US). A full and comprehensive description of the statistical methods can be found in Supplementary material.

RESULTS AND DISCUSSION

Patients ($n = 49$) with a mean age of 57.9 years, who underwent their first PVI, after mean (standard deviation) 13 month (2.5) follow-up reported heightened engagement in physical activity ($P = 0.008$), alleviated European Heart Rhythm Association symptoms ($P = 0.001$), and reduced use on antiarrhythmic medications ($P = 0.004$). They had lower N-terminal pro-B-type natriuretic peptide level (148 pg/ml vs. 108 pg/ml; $P = 0.047$), while blood pressure remained within normal range throughout the observation period (baseline characteristics of the patients can be found in Supplementary material, *Tables S1* and *S2*). Following PVI, there was a decrease in LV volume at end-diastole and end-systole, as well as a decrease in LAVI (41 ml/m² vs. 37.6 ml/m²; $P = 0.012$). Additionally, there was an improvement in LV GLS (−19.0% vs. −19.7%; $P = 0.036$), an increase in Ea (1.77 mm Hg/ml vs. 1.95 mm Hg/ml; $P = 0.020$), and an increase in Ees (2.77 mm Hg/ml vs. 3.2 mm Hg/ml; $P = 0.002$), however the other VAC components such as Ea/Ees and PWV/GLS ratios changes were not statistically significant. During the study follow-up, 24.5% of patients experienced AF recurrence. This result was comparable to results in other studies [2, 6]. Ea/Ees ratio was higher in patients without atrial fibrillation recurrence in a one-year follow-up (**Table 1**), but the baseline value was not a predictor of AF recurrence in regression model ($P = 0.47$). Baseline LAVI emerged as the sole predictor of AF recurrence in multivariable models table (Supplementary material, *Table S3*). Given the limited sample size of the study, the results of the logistic regression analysis should be interpreted with caution. Rather than being regarded as definitive conclusions, they should be viewed as a set of hypotheses that require further investigation.

AF recurrence after PVI is influenced by patient characteristics, procedural aspects, and post-procedural management. Key patient factors include age, type of AF, duration of arrhythmia, and comorbidities like hypertension, diabetes, obesity, sleep apnoea, kidney disease, and structural heart disease [7]. Procedural factors include incomplete pulmonary vein isolation, gaps in ablation lines, and non-pulmonary vein triggers [7]. Fibrotic changes, atrial remodelling, and complex fractionated electrograms raise AF recurrence risk [8]. Post-

procedural compliance with antiarrhythmic medications and other prescribed therapies is essential for maintaining sinus rhythm.

Epidemiological studies demonstrate a strong link between AF and heart failure with preserved ejection fraction (HFpEF), moreover AF is considered as one of the primary precedents and predictors of the development HFpEF [9]. The early changes in VAC observed in patients with AF are likely to progress to the development of HFpEF. The impairment of VAC is related to inflammatory and mechanical overload caused by arterial hypertension and other co-morbidities. In HFpEF increased arterial stiffness increases the LV late systolic pressure. The increase in Ea is a result of endothelial dysfunction, decreased nitric oxide production and vasoconstriction [5]. The increase in Ees arises from impaired diastolic function and a decrease in the contractile reserve of the left ventricle [5]. Therefore, AF is associated with early deterioration of VAC. In our study Ea/Ees was significantly lower in patients with recurrence of AF and the main contributor of this observation was an increase in left ventricular elastance while arterial elastance increased to lesser extent. This change may indicate potentially irreversible myocardial remodeling due to arrhythmia itself. In other studies, the aortic stiffness was an important risk factor in patients with AF and contributed to higher AF recurrence post-PVI [10].

Additionally, enlarged left atrium (LA) size correlates with increased post-PVI AF recurrence risk, with LA diameter and volume serving as indicators of LA structural remodeling, potentially triggered by the arrhythmia itself, promoting AF initiation and persistence [10, 11]. Moreover, individuals with larger LA may require more energy and longer application durations during PVI, with severe LA scarring predisposing to AF recurrence due to re-conduction between the LA and pulmonary veins.

CONCLUSION

Left atrial enlargement was found to be the independent predictor of PVI efficacy. Improvement of selected VAC parameters was observed after one-year follow-up post ablation procedure with better Ea/Ees in patients without AF recurrence. However, further studies are required to determine whether VAC is suitable for predicting AF ablation efficacy.

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/polish_heart_journal.

Article information

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Table 1. Comparison of VAC parameters in patients without atrial fibrillation versus patients with arrhythmia recurrence in a one-year follow-up

Parameters	Free from AF recurrence post-PVI	AF recurrence	P-value
Number	37	12	
VAC components			
Ea, mm Hg/ml	1.97 (0.4)	1.92 (0.6)	0.41
Ees, mm Hg/ml	3.10 (0.9)	3.83 (1.4)	0.07
Ea to Ees ratio	0.68 (0.2)	0.53 (0.1)	0.01

PWV to GLS ratio	-0.48 (0.1)	-0.43 (0.1)	0.19
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Data are presented as mean (SD)

Abbreviations: AF, atrial fibrillation; Ea, arterial elastance; Ees, left ventricle elastance; GLS, global longitudinal strain; PWV, pulse wave velocity; VAC, ventricular-arterial coupling