Journal of Electrocardiology 56 (2019) 38–42

Contents lists available at ScienceDirect

Journal of Electrocardiology

journal homepage: www.jecgonline.com

Correlation of P-wave properties with the size of left atrial low voltage areas in patients with atrial fibrillation

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ARTICLE INFO

Keywords:
Atrial fibrillation
Left atrial scarring
12-lead surface ECG
Catheter ablation

ABSTRACT

Background: Left atrial low voltage areas (LVA) are associated with increased recurrence rates of atrial fibrillation (AF) after catheter ablation and can be a potential ablation target during the procedure. Therefore, noninvasive prediction of the presence and the distribution of LVA may help physicians to predict ablation outcomes and to guide antiarrhythmic management.

Material and methods: Seventy-three consecutive patients with atrial fibrillation undergoing first time left atrial ablation for paroxysmal or persistent AF were enrolled. P-wave properties (amplitude and duration) were measured in all limb and precordial leads in pre-interventional sinus rhythm surface ECGs and correlated with total LVA size. LVA were detected via high density low voltage maps of the left atrium in sinus rhythm. LVA were then manually encircled, their total size was calculated and given as a percentage of the total LA surface area.

Results: A significant, inverse correlation with LVA size was shown for P-wave amplitude for leads I, II, aVR, aVF, V1, V4, V5 and V6. Additionally, a significant positive correlation between LVA size and P-wave duration was shown for leads V1, V2 and V3.

As the strongest correlation was shown for the amplitude in lead I ($R = -0.578$), this lead was used to find a potential cutoff for LVA prediction. The best cut-off for a P-wave amplitude in lead I to predict severe scarring (defined as LVA size >35%, according to UTAH stadium IV) was 0.062 mV with an area-under-the receiver-operating-characteristic curve of 0.935, a sensitivity of 85% and a specificity of 88%.

Conclusions: P-wave duration and amplitude show significant correlations with LVA size and may be used as a noninvasive tool to predict severe scarring. Amplitudes in lead I smaller than 0.062 mV were found to be predictive of LVA >35%.

Introduction

Catheter ablation has become an substantial part of rhythm control strategies when treating patients with paroxysmal and persistent atrial fibrillation [1]. Nevertheless, success rates remain unsatisfactory with recurrence rates of up to 50% after 12 months and a high need of 20–40% of repeat procedures [2–5].

Several studies have demonstrated that the presence and the extent of left atrial low voltage areas (LVA) are strongly associated with decreased longterm success rates after catheter ablation [6–11]. These success rates may be improved by creating linear or circular lesions targeting these LVA in addition to the isolation of the pulmonary veins [12,13]. Therefore, simple and reliable methods for preprocedural identification of LVA are of great importance to help physicians to predict outcomes and to select an appropriate ablation strategy.

Among patients with left atrial scarring, both P-wave amplitude and duration might be altered due to scarring and inhomogeneous spreading of the electrical wavefront.

Thus, we hypothesized that analysis of P-wave properties might serve as a tool for noninvasive prediction of LVA among patients with atrial fibrillation.

Material and methods

Study characteristics

This study included 73 consecutive patients who underwent first time catheter ablation of paroxysmal or persistent atrial fibrillation. Only patients who presented in sinus rhythm prior to the ablation were included in order to perform P-wave analysis. Patients with cardiac pacemakers, low-quality ECG's, severe tachy- or bradycardia at

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https://doi.org/10.1016/j.jelectrocard.2019.06.008
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the time of recording were not included in the study. All patients were enrolled at the Charité-University medicine hospital in Berlin.

Electroanatomical mapping and radiofrequency ablation

After the exclusion of intracardiac thrombi by transesophageal echocardiography, left atrial ablation procedures were performed under conscious sedation with intravenous midazolam and propofol. First, a 10-pole diagnostic catheter (Inquiry, Abbott cardiovascular, Abbott Park, IL, USA) was introduced into the coronary sinus. In all cases, double transseptal puncture was performed, followed by the introduction of two catheters via two long left atrial sheats (Agilis and SLO 8.5 Fr sheath, St- Jude Medical, Saint Paul, MN, USA): one 10-pole circular mapping catheter (Inquiry Optima, Abbott cardiovascular, Abbott Park, IL, USA, or LassoNav, Biosense Webster Inc., Diamond Bar, CA) with an electrode size of 1 mm and an interelectrode spacing of 7–7–7 mm and a 3.5 mm open irrigated ablation catheter (Tacticath, Abbott cardiovascular, Abbott Park, IL, USA, or Navistar ThermoCool, Biosense Webster Inc., Diamond Bar, CA). Heparin was administered to reach an activated clotting time of 300–400 s.

For all patients, high density electroanatomical maps of the left atrium, the pulmonary veins and the left atrial appendage were acquired with the use of the NavX Ensite Velocity system (NavX; Abbott cardiovascular, Abbott Park, IL, USA) or the CARTO-3 system (Biosense Webster, Diamond Bar, CA, USA). Mapping points were acquired with a 10-pole circular mapping catheter. All maps were recorded in sinus rhythm with an interpoint interpolation of 10 mm, a model filling threshold of 10 mm and a low-voltage cutoff of 0.5 mV [14]. Electrogram stability was analyzed for ensuring sufficient contact between catheter and endocardium. LVA were manually encircled, summarized and calculated as total and as percentage of the whole left atrial area (excluding pulmonary veins, Fig. 1).

P-wave analysis

Preprocedural 12-lead surface ECG's were recorded in sinus rhythm using a Schiller AT-102 system (Schiller, Baar, Switzerland) with noise filtering. Only high quality-ECG's were used in this study. P-wave duration and amplitude were analyzed with high magnification (200–400%) in all limb and precordial leads. For each lead, three distinct P-waves were measured by a single technician who was blinded to clinical data and the size of LVA found later during the ablation procedure. Mean values were used for analysis.

P-wave amplitude was measured from the top of the wave to the lower part of the isoelectric line (defined as TP interval) using Cardio Caliper software (Cardio Caliper, Iconico, New York, USA; Fig. 1). P-wave duration was measured between the junction of the P-wave with the isoelectric line.

Statistical analysis

Categorical variables are presented as absolute numbers and percentages and were compared by using Pearson's χ^2 test. Continuous variables are shown as mean ± standard deviation (SD). For normally distributed data, relationship between LVA size and P-wave properties was calculated with Pearson's correlation coefficient and Spearman for skewed data.

Cutoffs with respect to severe left atrial scaring (>35 vs. <35%) for P-wave duration and amplitude were calculated using receiver-operating-

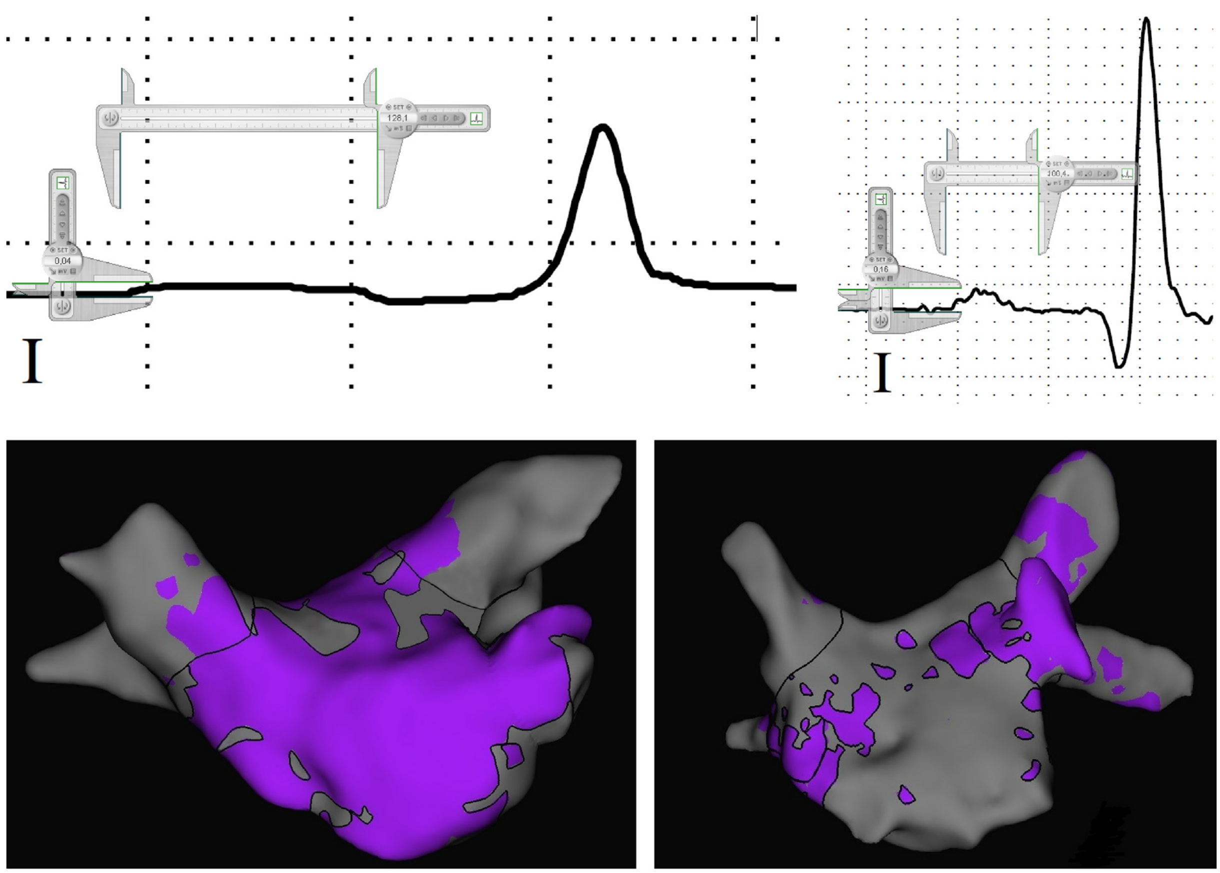

Fig. 1. Measurement of left atrial low voltage areas and P-wave amplitude and duration in lead I. The first electroanatomical map shows a highly scarred atrium (87%, AP-view) with a corresponding P-wave amplitude of 0.04 mV and duration of 136 ms. For measurement purposes, mainly non-scarred areas were encircled. The second example has less scarring (10%, AP-view) with P-wave amplitude of 0.16 mV and duration of 100 ms.

characteristic (ROC) analysis. Additionally, AUC including 95% CI, sensitivity and specificity were calculated.

A *P* value of ≤0.05 was considered to be statistically significant. No Bonferroni correction has been performed due to the explorative character of this study.

All calculations were performed using SPSS® for Windows Version 25.0 (SPSS Inc.).

Results

Study cohort

The included 73 consecutive patients had a mean age of 63.07 ± 10.35 years. Acute procedural success (defined as entrance and exit block) was achieved in all cases. Tables 1 and 2 show clinical and electrophysiological characteristics of our study cohort.

Correlation of P-wave properties with low voltage areas

Low voltage areas showed a mean size of 21.82 ± 31.42 cm^2. Severe scarring was defined according to UTAH stadium IV (total LVA size of >35%) and was observed in 13 patients (17.8%) [15].

For every patient, P-wave duration and amplitude were measured for three consecutive P-waves in all twelve leads. Table 3 shows average P-wave values of our study cohort.

Comparison between P-wave amplitude and total LVA percentage showed a significant inverse correlation for leads I, II, aVR, aVF, V1, V4, V5 and V6. For the duration of the P-waves a significant positive correlation with LVA percentage was revealed for leads V1, V2 and V3 (Table 3).

As the strongest correlation was shown for the amplitude in lead I (R = −0.578; $p < 0.001$), this lead was used to find a potential cutoff for LVA prediction. The best cut-off to predict severe scarring (defined as total LVA size >35%, UTAH stadium IV) was 0.062 mV with an area-under-the receiver-operating-characteristic (ROC) curve of 0.935 (95% CI 0.861–1.000), a sensitivity of 85% and a specificity of 88% (Fig. 2). 18 patients (24.7%) showed a pre-interventional P-wave amplitude <0.062 mV in lead I (Fig. 3).

Discussion

Main findings

This study evaluated the relationship between left atrial LVA and surface-ECG P-wave properties. For the first time, P-wave duration and amplitude in all 12 leads were correlated to LVA size. P-wave amplitude in leads I, II, aVR, aVF, V1, V4, V5 and V6 and P-wave duration in leads V1, V2 and V3 showed a significant correlation with the percentage of LVA. Another novel finding is that preprocedural P-wave amplitude <0.062 mV in lead I can predict severe left atrial scarring, defined as LVA >35%.

Table 1
Patient characteristics.

Number of patients	73
Age, mean ± SD (years)	63.07 ± 10.35
Female patients, n (%)	31 (42%)
BMI, mean ± SD (kg/m^2)	28.02 ± 4.91
Hypertension, n (%)	53 (72.6%)
Diabetes mellitus, n (%)	15 (20.5%)
Coronary heart disease, n (%)	17 (23.3%)
Paroxysmal atrial fibrillation, n (%)	56 (76.7%)
LA diameter, mean ± SD (mm)	40.11 ± 4.69
LVEF, mean ± SD (%)	58.00 ± 4.88

LA = left atrial; LVEF = left ventricular ejection fraction.

Table 2
Electroanatomical properties of the study cohort.

Total left atrial area, mean ± SD (cm^2)	116.23 ± 25.31
Mapping points, mean ± SD	616.07 ± 423.67
Left atrial LVA (total), mean ± SD (cm^2)	21.82 ± 31.42
Left atrial LVA (percentage of total area), mean ± SD (cm^2)	18.36 ± 23.70
Patients with LVA < 5%, n (%)	28 (38.4%)
Patients with LVA 5–20%, n (%)	25 (34.2%)
Patients with LVA 20–35%, n (%)	7 (9.6%)
Patients with LVA > 35%, n (%)	13 (17.8%)

LVA = low voltage area.

Clinical relevance

Noninvasive identification of presence and extent of LVA via P-wave analysis can be important for a mainly two reasons.

Firstly, as mentioned earlier, it is well known that both presence and extent of LVA found in electroanatomical mapping procedures can predict arrhythmia recurrence. Recurrence after catheter ablation is significantly higher among patients with LVA compared to patients without LVA (57% vs. 19%, $p = 0.003$) [6]. For patients with left atrial scarring >30%, freedom from atrial fibrillation also is lower (28%) compared to scarring <5% (76%) [9]. Therefore, it is desirable to establish noninvasive tools to predict LVA for patient selection and education.

Secondly, preprocedural identification of patients with substantial left atrial LVA is important for choosing an appropriate ablation method. Single-shot ablation techniques like Laser- or Cryo-balloon devices are unsuitable for LVA modification. Therefore, if ECG analysis indicates a high probability for severe scarring, RF ablation might be selected as a preferred ablation strategy [16].

Alternatively, left atrial scarring could be identified noninvasively via late gadolinium enhancement magnetic resonance imaging (MRI) [7]. In clinical routine, the use of MRI as preprocedural tool for left atrial scar detection is limited by its low availability, high costs and the frequent presence of pacemakers and defibrillators unsuitable for MRI.

Clinical risk scores, like the DR-FLASH score [17], are also used as noninvasive tools for LVA identification. In contrast to our approach, this method is based on multiple findings, including echocardiography, clinical characteristics and laboratory tests, and is only tested to detect the presents of any LVA, not their extent.

P-wave analysis on surface-ECG predicting left atrial scarring: Previously published studies.

Electrical activity among scarred atria is unstructured and inhomogeneous. Not only due to scarred areas, but also because of colliding activation fronts, a smaller amplitude and prolonged P-wave on surface ECG may emerge [18]. In general, the amplitude of any ECG-wave is the result of both the amount of viable myocytes and the vector of the wavefront. Impairment of those two factors may have caused our observed results.

Two studies evaluated the relationship of surface-ECG P-wave properties and left atrial scarring in patients with atrial fibrillation.

One single center study including 525 consecutive patients analyzed P wave properties (duration and amplitude) in leads I, II, III, aVL, aVF and V1 and their correlation with total left atrial mean voltage. A correlation was found for P-wave amplitude in lead I, already indicating that P-wave amplitude may be suitable for correlation with the size of low voltage areas and prediction of severe scarring as shown in our study [18].

Another single center study with 72 patients demonstrated that total P-wave duration (measured between earliest deflection from baseline to the latest return in any lead) correlated well with LVA ($r = 0.78$, $p < 0.0001$ with 0.5 mV cutoff for LVA). ROC analysis revealed that the presence of any LVA could be predicted with P-wave duration >150 ms (sensitivity 94.3%, specificity 91.7) [19]. We also found a significant correlation between duration in leads V1, V2 and V3 and the percentage of LVA, although calculated correlations were not as strong as for amplitude in lead I. The reason might be that for our analysis, P-wave duration was measured for each lead separately, as the goal was to establish a

Table 3
Correlation of P-wave amplitude and duration to left atrial low voltage areas (as percentage of total left atrial area).

ECG lead	Amplitude, mean ± SD (mV)	*R* (*p-value*)	Duration, mean ± SD (ms)	*R* (*p-value*)
Lead I	0.08 ± 0.03	**−0.578** (<**0.001**)	109.75 ± 14.73	0.121 (0.458)
Lead II	0.11 ± 0.04	**−0.450** (<**0.001**)	118.20 ± 18.65	0.052 (0.693)
Lead III	0.09 ± 0.03	−0.192 (0.145)	114.16 ± 19.71	0.211 (0.203)
Lead aVR	−0.09 ± 0.03	**0.388** (**0.001**)	113.38 ± 14.05	−0.026 (0.855)
Lead aVL	0.06 ± 0.22	−0.114 (0.440)	108.60 ± 14.01	0.065 (0.779)
Lead aVF	0.98 ± 0.04	**−0.288** (**0.022**)	114.37 ± 16.39	−0.007 (0.960)
Lead V1	0.07 ± 0.03	**−0.292** (**0.038**)	118.00 ± 22.00	**0.363** (**0.004**)
Lead V2	0.08 ± 0.03	−0.202 (0.154)	106.82 ± 23.05	**0.267** (**0.048**)
Lead V3	0.10 ± 0.03	−0.196 (0.128)	113.66 ± 18.32	**0.262** (**0.043**)
Lead V4	0.09 ± 0.03	**−0.374** (**0.002**)	115.90 ± 22.84	0.151 (0.266)
Lead V5	0.08 ± 0.02	**−0.363** (**0.004**)	118.01 ± 18.52	0.137 (0.324)
Lead V6	0.07 ± 0.02	**−0.370** (**0.004**)	119.82 ± 17.94	0.103 (0.490)

Significant values are highlighted.

predictor that only uses the P-wave properties of a single lead to simplify the approach.

Limitations

Surface-ECG P-waves can be altered by many factors. Although we recorded all ECG's in a still, lying position under temporary breathing arrest, electrical noise and anatomical differences like the size and thickness of the patient's chest wall might have altered P-wave properties. It is also known that P-wave duration can be influenced by heart rate and the autonomic nervous system [20]. In order to detect subtle changes in P-wave amplitude, appropriate amplification, high magnification, good quality and noise filtering are crucial.

Also, since standardised measurement is important especially when using high magnification, we suggest to use the lower part of the isoelectric line for P-wave analysis.

We used a cutoff of 35% of LVA, as this size was shown to be significantly associated with AF recurrence. Yet this cutoff was determined via MRI measuring LA fibrosis [15]. As the discussion if LVA of 35% found in MRI represent the same amount of fibrosis seen in electroanatomical mapping is still ongoing, the importance of these areas may be under- or overestimated.

Finally, all maps were acquired using a circular pulmonary vein mapping catheter. Although this multipole catheter accelerates the mapping process, we could not analyze wall contact pressure to ensure endocardial contact [21]. Instead, we relied on stable electrograms as surrogate for sufficient contact between catheter and endocardium.

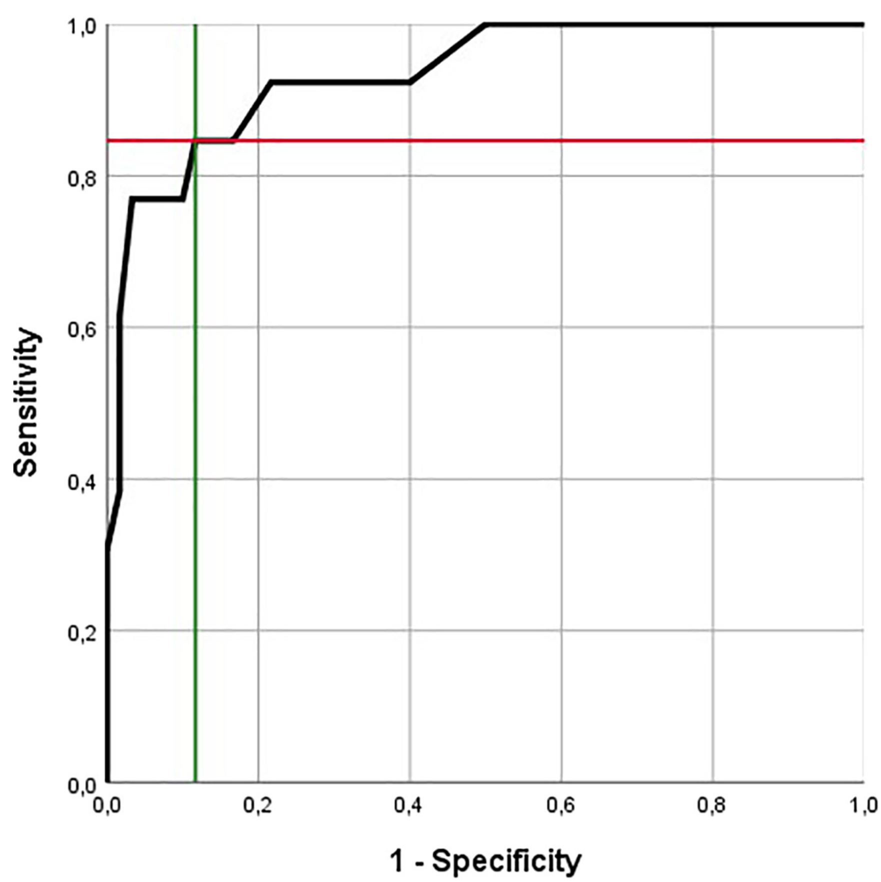

Fig. 2. Receiver under operator-curve to predict severe left atrial scarring. The cut-off value to predict left atrial scarring >35% was an amplitude of 0.062 mV in lead I with a sensitivity of 85% (horizontal red line) and a specificity of 88% (vertical green line).

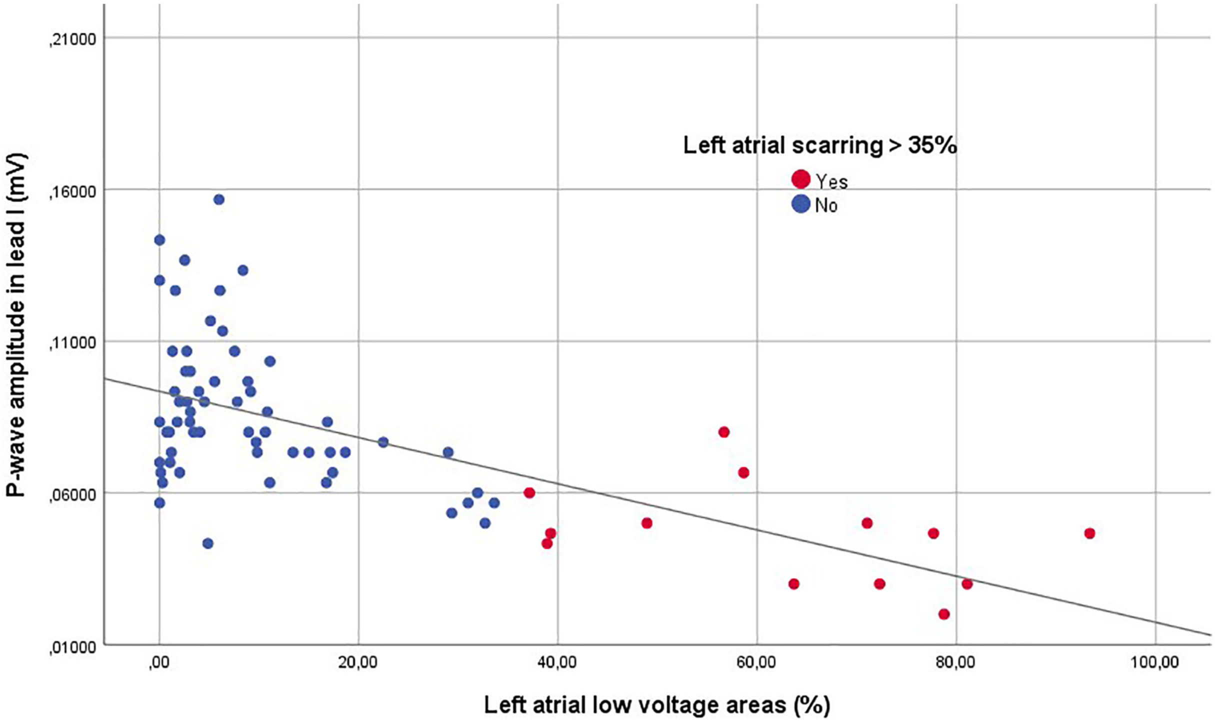

Fig. 3. Scatter plot between left atrial scarring and P-wave amplitude in lead I. Correlation between P-wave amplitude in lead I and left atrial low voltage areas (percentage) with regression line. This scatter plot shows a significant negative correlation ($R = -0.578$, $p < 0.001$).

Although high density voltage maps were acquired, overestimation of LVA is possible.

Conclusions

Both P-wave amplitude and duration of several leads correlate significantly with the extent of left atrial low voltage areas. P-wave amplitude in lead I showed the highest correlation and can predict severe left atrial scarring (>35%) with a cutoff of 0.062 mV, sensitivity of 85% and specificity of 88%. This noninvasive method to identify patients with severe left atrial scarring might help physicians to choose ablation strategy.

Declaration of Competing Interest

None.

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