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PREDICTION OF LOW-VOLTAGE AREAS IN THE LEFT ATRIUM IN PATIENTS WITH NON-VALVULAR ATRIAL FIBRILLATION BY NON-INVASIVE MARKERS

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Aim. To develop a method for predicting the area of low-voltage area (LVA) in the left atrium (LA), associated with the minimum and maximum expected effectiveness of primary radiofrequency ablation (RFA) in patients with non-valvular atrial fibrillation (AF) using non-invasive predictors.

Methods. A longitudinal single-center study included 150 symptomatic non-valvular AF pts aged 20-72 years (median 59.0 [51.0; 64.0]), including 63 women (42%) hospitalized for primary RFA; 119 pts (79.3%) had paroxysmal and 31 (20.7%) - persistent AF. All pts initially underwent general clinical examination, transesophageal and advanced transthoracic echocardiography, estimation of NT-proBNP (pg/ml) and growth differentiation factor 15 (GDF-15, pg/ml) in the blood. Electroanatomical mapping was performed in sinus rhythm before RFA. The area of LVA (<0.5 mV) was calculated as percentage of total LA area. Left ventricular (LV) ejection fraction (LVEF) was >50% in all pts.

Results. LVA area varied from 0 to 95.3%, median was 13.7% [5.1; 30.9]. Depending on LVA area, pts were divided into 3 groups: 36 pts (<5%) in gr. 1; 74 pts (5-30%) in gr. 2; 40 pts (>30%) in gr. 3. Increase of LVA area was associated with age, presence, and severity of congestive heart failure (CHF), persistent AF, CHA₂DS₂-VASc score ≥3 points, increase of LA volume, LV hypertrophy and increase of NT-proBNP and GDF-15 levels. In univariate analysis, LVA area <5% was associated with NT-proBNP level <125 pg/ml, absence of obesity and CHF, lower LA volume index (<28 ml/m²). Independent predictors of LVA <5% were: NT-proBNP <125 pg/ml, absence of obesity and LA volume index ≤28 ml/m². The model was of good quality, C-statistics was 0.775 (p<0.001). In univariate analysis, LVA area >30 % was associated with age >60 years, NT-proBNP >125 pg/ml, GDF-15 >840 pg/ml, persistent AF, presence of LV hypertrophy, LVEF ≤60%, LA volume index ≥ 32 ml/m². Independent predictors of LVA >30% were: LA volume index ≥32 ml/m², GDF-15 >840 pg/ml, and LVEF ≤60%. The model was of good quality, C-statistics was 0.752 (p<0.001).

Conclusion. Evaluation of noninvasive parameters, including clinical characteristics, echocardiographic parameters, and blood levels of NT-proBNP and GDF-15, allows prediction of electroanatomical substrate in left atrium in pts with non-valvular AF referred to primary RFA.

Key words: atrial fibrillation; electroanatomical mapping; low voltage areas; radiofrequency ablation; left atrial fibrosis

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Atrial fibrillation (AF) is the most common arrhythmia associated with a 5-fold increased risk of stroke and a 2-fold increased risk of death [1]. Catheter ablation (CA) is superior to drug therapy in terms of sinus rhythm restoration and improved quality of life when choosing a treatment strategy for AF and is reasonably safe in the hands of experienced operators [1]; however, the return of arrhythmias within the first year after CA after a three-month blind period is as high as 25-40% [2]. This necessitates the need to improve patient selection by identifying subgroups of patients with different expected CA performance [3].

Left atrial (LA) fibrosis is known to underlie the electroanatomical substrate of AF [1, 4]; while its size deter-

mines the stability of AF [5, 6] and the effectiveness of CA [6, 7]. Current methods used to assess fibrosis, including magnetic resonance imaging (MRI) with delayed contrast [8, 9] and endocardial bipolar electroanatomic mapping (EAM) with low-voltage areas (LVA) delineation [10, 11], correlate well with each other [12]. Studies using both methods have shown that the severity of LA fibrosis greater than 30% of the LA area may serve as an independent predictor of recurrent AF after CA [6, 13]. Nevertheless, the high economic and labor costs of MRI and the additional increase in the risk of complications associated with prolongation of CA time in case of EAM performance make it difficult to apply these methods in widespread clinical

practice. This explains the relevance of the problem of developing methods for predicting the severity of LVA using available noninvasive methods of investigation in patients with AF referred for CA.

The aim of the study was to develop a method to predict the area of LVA in the LA associated with the minimum and maximum expected efficacy of primary radiof-requency ablation (RFA) in patients with non-valvular AF using non-invasive markers.

METHODS

A single-center study included 150 patients with symptomatic nonvalvular AF consecutively hospitalized at the Tyumen Cardiology Research Center for primary RFA, aged 20 to 72 years (median 59.0 [51.0; 64.0]), including 63 women (42%) and 87 men. Paroxysmal AF was present in 119 patients (79.3%) and persistent AF in 31 (20.7%).

Exclusion criteria were as follows: LA auricular thrombosis during transesophageal echocardiography (Echo), myocardial infarction or coronary artery interventions within the last 6 months, left ventricular ejection fraction (LVEF) below 50%, acute or chronic comorbidities in decompensation, chronic obstructive pulmonary disease, patient refusal to participate in the study, pregnancy.

All patients initially, before RFA, underwent general clinical examination, deployed transthoracic Echo, transesophageal Echo, endocardial bipolar EAC, and determination of blood levels of N-terminal brain natriuretic propeptide (NT-proBNP, pg/mL) and growth differentiation factor 15 (GDF-15, pg/mL).

Transthoracic Echo was performed in accordance with the current recommendations of the American Society of Echo and the European Association for Cardiovascular Imaging [14]; chamber sizes and volumes, left ventricular (LV) systolic and diastolic functions were evaluated. The studies were performed using a Vivid E9 ultrasound scanner (General Electric Medical Systems, USA). The presence of left ventricular hypertrophy (LVH) was considered as a criterion for the presence of LV myocardial mass index (LVMM index) exceeding the value of 95 g/m² for women and 115 g/m² for men. The types of LV geometry were determined based on LVMM index and relative LV wall thickness values [14].

Endocardial bipolar voltage LA mapping was performed in sinus rhythm as the first stage of primary RFA, and electrical cardioversion was performed beforehand in persistent AF. CARTO 3 3D navigation system (Biosense Webster), Thermocool Smart Touch ablation electrodes with 3.5 mm interelectrode spacing, and LASSO multipole

Fig. 1. Results of voltaic electroanatomic mapping of the left atrium of patients with different area of low-voltage areas (indicated by color other than purple): a - area <5%, b - from 5 to 30%, c ->30%.

circular mapping electrodes (Biosense Webster) with 2-5-2 mm interelectrode spacing were used to construct the electroanatomical map. When using the point-to-point method, at least 250 points taken at stable contact of the electrode with the endocardium of the LA were taken to construct the LA map. LA voltage analysis was performed by an experienced electrophysiologist in the postoperative period. LVAs were defined by the presence of 3 or more adjacent points with voltages <0.5 mV [13], and the total area of LVAs was calculated as % of the total area of the LA. The regions of the mitral valve and pulmonary vein apertures were excluded when calculating the total LA area.

Blood level of NT-proBNP (reference value below 125 pg/mL) was determined using an analyzer IMMU-LITE 2000 (Siemens Diagnostics, USA) by enzyme-linked immunosorbent assay. GDF-15 level (pg/mL) was determined on a Stat Fax 4200 microplate photometer (USA) by quantitative method (direct enzyme immunoassay) using the analytical kit «Human GDF-15/MIC-1 ELISA» (Bio-Vender, Czech Republic) for research purposes (range of determinations from 35 to 2240 pg/mL). According to the instructions, medians in different age groups can be taken as reference levels: 378-648 pg/mL for men and 444-653 pg/mL for women.

The diagnoses of arterial hypertension, ischemic heart disease, and chronic heart failure (CHF) were established in accordance with the current recommendations of the Russian Society of Cardiology. Body mass index \geq 30 kg/m² was adopted as the criterion for obesity.

Statistical processing of data was performed using IBM SPSS Statistics 21 and Statistica 12.0 programs. The distribution of quantitative variables was examined using the Shapiro-Wilk test. In normal distribution, data are presented as mean M and standard deviation (SD); in other distribution, data are presented as median (Me) and interquartile range [25%; 75%]. ANOVA analysis of variance and Kraskell-Wallis test were used for comparative analysis depending on the distribution of data. Qualitative data were compared by Pearson's χ^2 test. Bonferroni correction was applied for multiple comparisons. Univariate and multivariate logistic regression were used to examine the association of variables and to find independent predictors of LVA area. Cutoff values of quantitative variables were searched for by ROC analysis. The quality of the models was assessed using C-statistics, sensitivity, and specificity. Results were evaluated at the p <0.05 level as statistically significant and as tending to significant differences at the p < 0.1 level.

The study was conducted in accordance with the provisions of the Declaration of Helsinki, the study protocol was

approved by the local ethics committee (protocol #176 dated November 23, 2021). Informed consent to participate in the study was obtained from all study subjects.

RESULTS

According to EAM data, the area of LVA ranged from 0 to 95.3%, with a median of 13.7% [5.1; 30.9]. According to the area of LVA, patients were divided

Table 1. Clinical and demographic characteristics and echocardiographic indices in groups with different low-voltage zone (LVA) areas

		Group 1 (LVA <5%) (n=36)	Group 2 (LVA 5-30%) (n=74)	Group 3 (LVA >30%) (n=40)	Reliability of differences
Age, years		55.0 [47.5; 61.5]	58.0 [52.0; 64.0]	61.5 [53.5; 65.0]	P=0.017, P ₁₋₂ =0.289, P ₁₋₃ =0.013, P ₂₋₃ =0.321
Female gender, n (%)		11 (30.6)	31 (41.9)	21 (52)	P=0.153, P ₁₋₂ =0.251, P ₁₋₃ =0.154, P ₂₋₃ =0.278
Arterial hypertension, n (%)	Yes	29 (80.6)	61 (82.4)	38 (95)	P=0.658, P ₁₋₂ =0.811,
	No	7 (19.4)	13 (17.6)	2 (5)	$P_{1-3}=0.126, P_{2-3}=0.058$
Coronary artery disease, n (%)	Yes	12 (33.3)	30 (40.5)	19 (31.2)	P=0.954, P ₁₋₂ =0.465,
	No	24 (66.7)	44 (59.5)	21 (68.8)	$P_{1-3}=0.455, P_{2-3}=0.474$
Prior myocardial infarction, n (%)	Yes	0	2 (2.7)	1 (2.5)	P=0.914, P ₁₋₂ =0.319,
	No	36 (100)	72 (97.3)	39 (97.5)	$P_{1-3} = 0.615, P_{2-3} = 0.949$
Heart failure, n (%)	Yes	29 (80.6)	40 (54.1)	15 (37.5))	P=0.001, P ₁₋₂ =0.007,
	No	7 (19.4)	34 (45.9)	25 (62.5)	$P_{1-3} = 0.001, P_{2-3} = 0.091$
Paroxysmal AF, n (%)		33 (91.7)	61 (82.4)	25 (62.5)	P=0.005, P ₁₋₂ =0.197,
Persistent AF, n (%)		3 (8.3)	13 (17.6)	15 (37.5)	$P_{1-3}=0.005, P_{2-3}=0.018$
Diabetes mellitus, n (%)	Yes	4 (11.1)	8 (10.8)	5 (12.5)	P=0.999, P ₁₋₂ =0.962,
	No	32 (88.9)	66 (89.2)	35 (87.5)	$P_{1-3} = 0.963, P_{2-3} = 0.786$
Obesity, n (%)	Yes	22 (61.1)	28 (37.8)	19 (47.5)	P=0.701, P ₁₋₂ =0.050.
	No	14 (39.9)	46 (62.2)	21 (52.5)	$P_{1-3}=0.172, P_{2-3}=0.592$
Smoking, n (%)	Yes	31 (86.1)	67 (90.5)	38 (95)	P=0.412, P ₁₋₂ =0.484,
	No	5 (13.9)	7 (9.5)	2 (5)	$P_{1-3}=0.412, P_{2-3}=0.400$
CHA ₂ DS ₂ -VASc ≥3, n (%)		6 (16.7)	20 (27.0)	17 (43.6)	P=0.033, P ₁₋₂ =0.230. P ₁₋₃ =0.033, P ₂₋₃ =0.075
GFR, ml/min/1.73 m ²		82.5 [64.0; 94.5]	83.0 [69.0; 96.0]	87.0 [69.0; 94.0]	P=0.925, P ₁₋₂ =999, P ₁₋₃ =0.954, P ₂₋₃ =0.922
NT-proBNP, pg/mL		64.6 [25.9; 107.0]	93.0 [44.4; 194.0]	132.5 [75.7; 361.0]	P=0.012, P ₁₋₂ =0.239, P ₁₋₃ =0.008, P ₂₋₃ =0.273
GDF-15, pg/mL		694.0 [552.5; 1026]	767.5 [622.5; 934.0]	924.5 [758.5; 1162]	P=0.035, P ₁₋₂ =1.000. P ₁₋₃ =0.071, P ₂₋₃ =0.070
LA volume index, ml/m ²		27.2±7.0	31.3±8.5	35.1±9.9	P=0.001, P ₁₋₂ =0.048, P ₁₋₃ =0.000. P ₂₋₃ =0.063
LVMM index, g/m ²		79.8 [72.3; 89.2]	86.5 [76.1; 96.9]	95.2 [83.9; 115.4]	P=0.006, P ₁₋₂ =0.497, P ₁₋₃ =0.005, P ₂₋₃ =0.072
LESD index, mm/m ²		14.5±1.9	15.2±2.1	16.5±3.2	$P_{1-3} = 0.003, P_{1-2} = 0.370.$ $P_{1-3} = 0.002, P_{2-3} = 0.029$
LV ejection fraction, %		64.0±5.6	64.5±7.3	61.4±6.9	$P_{1-3} = 0.229, P_{2-3} = 0.063$
Normal LV geometry, n (%)		17 (47.2)	44 (59.5)	11 (27.5)	P=0.0024,
Concentric LV remodelling		13 (36.1)	19 (25.7)	10 (25.0)	$P_{1-2}=0.377,$
Concentric LVH, n (%)		4 (11.1)	4 (5.4)	10 (25.0)	$P_{1-3}^{1-2}=0.002,$
Eccentric LVH, n (%)		2 (5.6)	7 (9.5)	9 (22.5)	P ₂₋₃ =0.001,
LVH, n (%)	Yes	6 (16.7)	11 (14.9)	19 (47.5)	P=0.0003, P ₁₋₂ =0.806,
	No	30 (83.3)	63 (85.1)	21 (52.5)	P ₁₋₃ =0.0002, P ₂₋₃ =0.0002

Note: hereinafter, AF - atrial fibrillation; LV - left ventricle; GFR - glomerular filtration rate; LA - left atrium; LVMM - left ventricular myocardial mass; LVESD - LV end-systolic diameter; LVH - LV hypertrophy.

into 3 groups: group 1 (<5%) - 36 patients, group 2 (5-30%) - 74 patients, group 3 (>30%) - 40 patients. Figure 1 shows examples of electroanatomical charts of patients with different areas of LVA.

The clinical and demographic characteristics and Echo parameters of the patients in the different groups, as well as the results of multiple comparisons, are summarized in Table 1. Patients from different groups did not differ in the frequency of use and spectrum of antiarrhythmic drugs, oral anticoagulants, ACE inhibitors, and ARA.

In general, it should be noted that an increase in LVA was associated with increasing age, presence of CHF, an increase in the proportion of patients with persistent AF, presence of 3 or more CHA₂DS₂-VASc scores, an increase in LA diameter and volume indices, LVMM index and presence of LVH, and an increase in the levels of both biomarkers, NT-proBNP and GDF-15 (Table 1). In the group with minimal LVA area, there was a tendency to decrease the proportion of obese patients.

To find predictors of minimal (<5%) and pronounced (>30%) LVA area, variables that showed statistically significant differences or a trend toward them in the comparative between-group analysis were included in the single-factor logistic regression analysis. For quantitative variables, thresholds separating patients with LVA area <5% and >30% with optimal sensitivity-to-specificity ratios were additionally determined using ROC analysis. Final prediction models were searched for using multivariate logistic regression analysis, which included variables that had a significant association with minimum (<5%) or maximum (>30%) LVA area, as measured by single-factor regression analysis. In selecting the final model, optimal levels of C-statistics, sensitivity and specificity were chosen as criteria. The results are presented in Tables 2 and 3.

According to the results of multivariate regression analysis, the likelihood of having minimal (<5%) LVA area was 4.712-fold higher in patients with NT-proBNP levels less than 125 pg/mL and LA volume index \leq 28 mL/m² 4.363-fold, and 78% lower in the presence of obesity. In assessing the quality of the model, the C-statistic of the model is 0.775 (p<0.001), with a sensitivity of 66.0% and specificity of 76%, which corresponds to good quality.

Thus, the likelihood of having a LVA area >30% is 3-fold higher in patients with GDF-15 levels >840 pg/mL and with an LVEF \leq 60%, and 2.8-fold higher in the presence of an LA volume index \geq 32 mL/m². The C-statistic was 0.752 (p <0.001), the sensitivity was 60%, and the specificity of the model was 79%, which corresponds to a good quality model.

DISCUSSION

Predicting the area of LVA in the LA is important in a personalized approach to the choice of therapeutic tactics in patients with AF because it gives an idea of the severity of atrial cardiomyopathy [15] and the size of the electroanatomic substrate of AF before planned RFA [7, 13].

The results of the DECAAF study showed that the efficacy of RFA decreased with increasing severity of LA fibrosis assessed by MRI, and the recurrence rate of AF with an area of LA fibrosis >30% reached 69.4% at 15 months after RFA [6]. G.A.Begg et al. found that the area of LVA >30% can also be a predictor of AF recurrences during the first year after RFA [13], therefore we chose this index as a criterion corresponding to marked fibrosis.

Among clinical-instrumental parameters and biomarkers, we have identified factors associated with the increase of LVA area in LA: age, presence of CHD, persistent form of AF, presence of 3 or more points on the CHA₂DS₂-VASc scale, increased NT-proBNP and GDF-15, increased LA volume index, presence of LVH, decreased LV systolic function. Independent predictors of LVA area >30% associated with expected poor RFA performance [13] were: LA volume index ≥32 mL/m², LVEF ≤60%, GDF-15 >840 pg/mL.

Comparison of our results with the data of previous studies confirmed the significance of the index characterizing LA dilatation as the main predictor of LVA. The DR-FLASH scale developed by Kosiuk et al. (2015) [16] for predicting LVA and identifying patients for possible LA substrate modification includes LA diameter >45 mm. The similar APPLE scale proposed by J.Kornej et al. (2018) included a LA diameter >43 mm [17], which was replaced by an LA volume index \geq 39 ml/m² in the modified APPLE scale [18]. Since the description of the LA size does not accurately reflect the anatomy of the LA and, consequent-

Table 2.

Results of single-factor and multivariate analyses to find predictors of low-voltage zones <5%

Single-factor analysis Multivariate analysis Variables В OR [95% CI] В OR [95% CI] p p Age >60 years -0.8110.130 0.444 [0.156; 1.268] NT-proBNP <125 pg/mL 1.394 0.020 4.032 [1.241; 13.101] 1.550 0.019 4.712 [1.294; 17.158] GDF-15 < 745 pg/mL 1.025 0.044 2.786 [1.028; 7.545] _ -1.498 0.013 Presence of obesity -1.1810.027 0.307 [0.107; 0.877] 0.224 [0.069; 0.729] Persistent AF -0.693 0.306 _ 0.500 [0.133; 1.887] -1.580 0.017 Presence of CHD 0.206 [0.056; 0.758] _ CHA_2DS_2 -VASc ≥ 3 points -0.8290.219 0.437 [0.116; 1.637] LVESD index (mm/m²) -0.156 0.177 0.856 [0.683; 1.073] LA volume index ≤28 ml/m² 1.122 0.027 1.473 0.010 3.072 [1.138; 8.295] 4.363 [1.418; 13.423]

Примечание: здесь и далее ОШ - отношение шансов; ДИ - доверительный интервал.

ly, the degree of LA dilatation, this was considered in the modified APPLE scale [18]. Our data suggest that LA volume index may be an independent predictor of both minimal and severe LVA area, but with different cutoff values of \leq 28 mL/m² and \geq 32 mL/m², respectively. The association of LA dilatation with the severity of LA fibrosis is well established and corresponds to the degree of progression of atrial cardiomyopathy in patients with AF [15].

According to the literature, the most frequent predictors of LVA are age [16-19], female gender [16, 17, 19, 20] and persistent form of AF [16-18, 20]. According to our results, age ≥60 years and persistent AF were associated with LVA area >30%, according to single-factor analysis, but were not included as independent predictors in the final model. Female gender in our study did not show itself as a predictor of fibrosis, which is probably due to the peculiarities of the study group.

The second independent predictor of severe (>30%) LVA area was LVEF $\leq 60\%$. In contrast to the study by J.Kornej et al. (2018) [17], according to the results of which LVEF <50% was included in the APPLE scale as an independent predictor of LVA, our study included only patients with LVEF \geq 50%. Our data are consistent with the results of the study by G.J.Wehner et al. [21]. A study by these authors of the association of Echo study data with outcomes in a large population of cardiovascular patients showed that the lowest mortality (nadir of mortality) was associated with an LVEF in the range of 60-65% rather than a level of 50% [21]. This is also consistent with the current view that the cohort of patients with CHF with LVEF ≥50% is heterogeneous «in form and content» [22]. [22]. Our results, according to which the probability of a marked LVA area >30% (as a surrogate marker of LA fibrosis) increases at LVEF ≤60%, may also explain the decreased efficacy of antifibrotic drugs (valsartan+sacubitril or sodium-glucose cotransporter type 2 inhibitors) at LVEF >60% [22].

Biomarkers as potential predictors of LVA have been investigated in several studies. The study by V.A.Rossi et al. established the association of elevated NT-proBNP level with the presence of LVA in the LA [20]. In our study,

normal NT-proBNP level was an independent predictor of minimal LVA area, and elevated NT-proBNP level was associated with severe (>30%) LVA area, according to single-factor analysis.

The association of GDF-15 level with the size of the LVA in the LA area was previously shown in a pilot study on 86 patients with non-valvular AF referred for primary RFA: GDF-15 level >767.5 pg/mL was a predictor of LVA area >20% [23]. In this study, on a larger group of patients, GDF-15 levels >840 pg/mL were associated with a larger area of LVA, >30%. This is consistent with the claim that GDF-15 expression and concentration in blood reflects an integral signal of cellular stress, organ dysfunction and biological aging of the cardiovascular and renal systems [24, 25]. GDF-15 is now a recognized biomarker of interstitial fibrosis: its level correlates with diffuse and focal myocardial fibrosis assessed by MRI [26].

According to our data, the ideal patient with AF referred for RFA should not be obese. Experimental studies have proven that in chronic obesity, the substrate for the development of AF may be fatty infiltration of the posterior wall of the LA by epicardial fat, which leads to decreased and inhomogeneous voltages [27]. This is consistent with the results of the study by V.A. Ionin et al.: there was a 4.5-fold increase in the relative risk of AF recurrence after RFA with an increase in epicardial fat thickness >6.4 mm in patients with AF and metabolic syndrome [28].

Thus, prediction of the area of LVA in patients with nonvalvular AF referred for primary RFA is an important component of a personalized approach to the choice of the optimal treatment strategy because it gives an idea of the severity of atrial cardiomyopathy [15] and the size of the electroanatomic substrate of AF before the planned RFA [7, 13].

CONCLUSION

Evaluation of noninvasive parameters including clinical characteristics, echocardiographic parameters, and levels of circulating blood NT-proBNP and GDF-15 can predict the severity of electroanatomic substrate in the LA in patients with nonvalvular AF referred for primary RFA.

Table 3.

Results of single-factor and multivariate analysis on finding predictors of low-voltage zones >30%

Single-factor analysis Multivariate analysis Variables В OR [95% CI] В OR [95% CI] p Age >60 years 1.118 0.017 3.060 [1.218; 7.690] -NT-proBNP > 125 pg/mL 0.962 0.038 2.618 [1.054; 6.505] GDF-15 >840 pg/mL 1.118 0.017 3.060 [1.218; 7.690] 1.108 0.029 3.030 [1.121; 8.189] Persistent AF 1.045 0.040 2.843 [1.048; 7.715] Presence of CHD 0.789 0.088 2.201 [0.890; 5.439] CHA_2DS_2 -VASc ≥ 3 points 0.856 0.086 2.353 [0.886; 6.255] LV ESD index ≥15.8 mm/m² 0.993 0.049 2.700 [1.004; 7.262] -1.225 0.011 LV hypertrophy 3.405 [1.321; 8.773] 3.958 [0.966; 16.223] Concentric LVH 1.376 0.056 0.021 Eccentric LVH 1.440 4.222 [1.247; 14.301] --LVEF ≤60% 1.460 0.003 4.308 [1.657; 11.199] 1.107 0.036 3.024 [1.073; 8.522] 1.219 0.049 2.799 [1.004; 7.799] LA volume index ≥32 ml/m² 0.011 3.385 [1.328; 8.626] 1.029

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