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Ability of Left Atrial Distensibility After Radiofrequency Catheter Ablation to Predict Recurrence of Atrial Fibrillation

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| 1 | Ability of Left Atrial Distensibility after Radiofrequency Catheter Ablation to Predict |
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| 2 | Recurrence of Atrial Fibrillation |
| 3 | |
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| 19 | Running head: Left atrial distensibility |

| 1 | Abstract: This study sought to assess the left atrial (LA) functional recovery after |
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| 2 | radiofrequency catheter ablation (RFCA) for atrial fibrillation (AF) and to evaluate the |
| 3 | determining factor of procedural success of RFCA using a novel preload stress |
| 4 | echocardiography. A total of 111 patients with AF were prospectively recruited. The |
| 5 | echocardiographic parameters were obtained during the leg-positive pressure (LPP) maneuver |
| 6 | both at baseline and mid-term after RFCA. As an index of LA distensibility, the LA expansion |
| 7 | index was calculated as (LAV _{max} - LAV _{min}) \times 100 / LAV _{min} . During a median follow-up period |
| 8 | of 14.2 months, AF recurrence was observed in 23 (20.7%) patients. In LA functional |
| 9 | parameters at baseline, only the Δ LA expansion index was significantly larger in the success |
| 10 | group (16 ± 11% vs. 4 ± 9%, P<0.05). At mid-term follow-up, the Δ LA expansion index |
| 11 | significantly increased to $32 \pm 19\%$ (P<0.05), together with structural LA reverse remodeling |
| 12 | only in the success group. Moreover, the Δ stroke volume index during the LPP stress test |
| 13 | significantly increased only in the success group (from 2.3 \pm 1.3 mL/m² to 3.1 \pm 4.8 mL/m², |
| 14 | P < 0.05). In a multivariate analysis, left ventricular ejection fraction (hazard ratio 0.911, |
| 15 | <i>P</i> <0.05) and baseline Δ LA expansion index (hazard ratio 0.827; <i>P</i> <0.001) were independent |
| 16 | predictors of AF recurrence. In conclusion, the baseline Δ LA expansion index during LPP |
| 17 | stress is a reliable marker for predicting procedural success after RFCA. Moreover, |
| 18 | maintenance of sinus rhythm resulted in an improvement of the preload reserve after RFCA. |
| 19 | Keywords: leg-positive pressure stress, left atrial distensibility, left atrial fibrosis. |

| 1 | The principal role of the left atrium (LA) is to modulate left ventricular (LV) |
|----|--|
| 2 | diastolic filling and cardiac performance through reservoir, conduit, and booster pump |
| 3 | functions, ¹ without an elevation in LA pressure. In patients with atrial fibrillation (AF), these |
| 4 | essential functions are significantly impaired, leading to LA remodeling. Structural LA |
| 5 | remodeling progressively leads to myocardial dysfunction and subsequent electrical |
| 6 | alterations in the cardiomyocytes, ² creating an AF-prone fibrotic substrate, ³ which promotes |
| 7 | trigger driven paroxysmal to substrate dependent persistent AF. The purpose of this study was |
| 8 | to assess the relationship between maintenance of sinus rhythm and functional LA reverse |
| 9 | remodeling mid-term after radiofrequency catheter ablation (RFCA). Moreover, we also |
| 10 | investigated the determinant factor for predicting procedural success of RFCA by preload |
| 11 | stress echocardiography using a novel leg-positive pressure (LPP) maneuver. |
| 12 | Methods |
| 13 | This prospective study included 111 consecutive patients with AF who underwent |
| 14 | RFCA at the Kobe University Hospital and Tokushima University Hospital from October |
| 15 | 2018 to March 2020. The exclusion criteria for this study were (1) a suboptimal quality of |
| 16 | echocardiographic images, (2) history of venous thrombosis or pulmonary embolism, (3) |
| 17 | severe orthopedic traumatic disease in the lower limbs, and (4) symptomatic decompensated |
| 18 | heart failure. Moreover, the patients with more than moderate valvular heart disease were |
| 19 | excluded from this study. Use of medications, including antihypertensive drugs, was kept |

| 1 | constant during the study period. This study was approved by the local ethics committee of |
|----|---|
| 2 | the involved institutions, and written informed consent was obtained from all participants. |
| 3 | As shown in the study protocol (Figure 1), all echocardiographic studies were |
| 4 | performed within three days after RFCA (baseline) and at 3-6 months postoperatively (mid- |
| 5 | term follow-up). Measurements were obtained in accordance with the current guidelines of |
| 6 | the European Association of Cardiovascular Imaging/the American Society of |
| 7 | Echocardiography. ⁴ LV ejection fraction (EF) and volumes were calculated by means of the |
| 8 | modified biplane Simpson's method. LA volumes were measured at two time phases: when |
| 9 | LA expanded to the maximum volume at end-systole (LAV $_{max}$) and when LA reduced its |
| 10 | volume just after the booster-pump phase (LAV $_{min}$). As shown in Figure 2, the LA expansion |
| 11 | index was calculated as $(LAV_{max} - LAV_{min}) \times 100/LAV_{min}$. ⁵ The transmitral early diastolic (E) |
| 12 | and atrial wave (A) velocities were measured using pulsed-wave Doppler recordings. ⁶ Early |
| 13 | diastolic (e') mitral annular velocity was measured using spectral tissue Doppler imaging with |
| 14 | a sample volume placed at the septal and lateral mitral annulus, and the averaged value was |
| 15 | calculated to estimate the LV filling pressure. ⁶ Stroke volume (SV) was measured at the LV |
| 16 | outflow tract. |
| 17 | Speckle-tracking analysis was performed using dedicated software (TOMTEC- |
| 18 | ARENA; TOMTEC Imaging Systems GmbH, Unterschleissheim, Germany). The average |
| | |

19 values of the longitudinal strain from three LV apical views were calculated to obtain the LV

| 1 | global longitudinal strain (LV-GLS). As for the speckle-tracking analysis of the LA |
|----|--|
| 2 | myocardium, LA-focused apical four- and two-chamber images were obtained. A |
| 3 | predominant positive wave that peaked at LV systole was expressed as LA-GLS. ⁷ |
| 4 | For the preload stress test, commercially available LPP equipment (Dr Medomer |
| 5 | DM-5000EX, Medo Industries Co, Ltd, Tokyo, Japan) was used. The LPP stress maneuver |
| 6 | has been described previously in detail. ^{8,9} Briefly, it was designed to provide a continuous |
| 7 | external pressure around both lower limbs using dedicated airbags at 90 mmHg pressure, |
| 8 | which has been proven to safely provide an increase in cardiac preload. ⁹ Echocardiographic |
| 9 | measurements were obtained both at rest and during LPP stress, and the changes in the |
| 10 | measured parameters were calculated as the difference (Δ). |
| 11 | Electrical mapping and ablation were performed using the CARTO3 system |
| 12 | (Biosense Webster, Diamond Bar, CA, USA) as a guide after the integration of a three- |
| 13 | dimensional model of the anatomy of the LA and pulmonary veins obtained from pre- |
| 14 | interventional computed tomography. RFCA was performed in a "point-by-point" manner, |
| 15 | and the pulmonary veins were isolated by wide-area circumferential ablation. Patients were |
| 16 | followed closely after RFCA and evaluated for recurrence at 3, 6, and 12 months during |
| 17 | follow-up clinic visits. Procedural success was defined as freedom from documented AF |
| 18 | lasting more than 30 seconds after the 3-month blanking period. ¹⁰ |
| 19 | Continuous variables were expressed as mean values and standard deviation for |

| 1 | normally distributed data and as median and interquartile range for non-normally distributed |
|----|---|
| 2 | data. Categorical variables were expressed as frequencies and percentages. Independent |
| 3 | sample t -test or Mann-Whitney U test was used to compare variables between groups. The |
| 4 | paired <i>t</i> -test or Wilcoxon signed-rank test was used to compare differences in parameters |
| 5 | between the two time-points, as appropriate. The initial univariate logistic regression analysis |
| 6 | to identify univariate factors for identifying AF recurrence was followed by a multivariate |
| 7 | analysis using a stepwise selection, with the P -value for entry into the model set at <0.10. All |
| 8 | tests were two-tailed, and a <i>P</i> -value<0.05 was considered statistically significant. All analyses |
| 9 | were performed using MedCalc version 16.5.0 (MedCalc Software; Ostend, Belgium). |
| 10 | Results |
| 11 | The baseline clinical characteristics of the 111 patients with AF are summarized in |
| 12 | Table1. Approximately 50% of the patients had paroxysmal AF, and the remaining half had |
| 13 | persistent or long-standing persistent AF. Hypertension was the most common comorbidity, |
| 14 | followed by diabetes, heart failure, and stroke. The mean CHA ₂ DS ₂ -VASc score was 2.4±1.5. |
| 15 | The baseline characteristics of the patients with paroxysmal and persistent AF are provided in |
| 16 | the Supplementary Table. |
| 17 | During a median follow-up period of 14.2 (12.2-18.4) months, AF recurrence was |
| 18 | observed in 23 patients, and the remaining 88 patients were allocated to the success group. |
| | |

| 1 | patients at the mid-term follow-up. For these cases, measurements were averaged from three |
|----|---|
| 2 | non-consecutive beats with a cycle length within 10%-20% of the average heart rate. |
| 3 | No significant differences were observed between the groups in terms of age, |
| 4 | CHA2DS2-VASc score, AF type, comorbidities, and laboratory data including brain natriuretic |
| 5 | peptide level at baseline (Table 1). With respect to the hemodynamic and echocardiographic |
| 6 | parameters, although the recurrence group was more likely to have larger LV volumes and |
| 7 | LAVI and lower LVEF, there were no significant differences in LA functional parameters, |
| 8 | including LA-GLS, LA stiffness index, and LA expansion index at baseline (Table 2). |
| 9 | During LPP stress, LV volume, LVEF, LAVI, E/e' ratio, and SVi significantly |
| 10 | increased in both groups as a result of the increased preload (Table 2). Of note was that, |
| 11 | although LA-GLS and LA expansion index significantly increased during LPP stress, these |
| 12 | responses were blunted in the recurrence group. Consequently, the Δ LA expansion index was |
| 13 | significantly larger in the success group at the baseline preload stress assessment (Table 2). |
| 14 | Follow-up echocardiography was performed at 6.1 (3.6-6.4) months after RFCA. As |
| 15 | for LA parameters, LA-GLS, LAVI, and LA stiffness index all significantly improved at the |
| 16 | mid-term follow-up after RFCA in the success group. Notably, the LA expansion index |
| 17 | increased only in the success group (Table 2 and Figure 3). Moreover, LV structural and |
| 18 | functional reverse remodeling was also observed at mid-term follow-up after RFCA, as |
| 19 | evidenced by the improvement in LV-GLS, increase in e' velocity, and decrease in E/e' ratio |

| 1 | only in the success group. Meanwhile, these beneficial effects of functional and structural |
|----|--|
| 2 | reverse remodeling were blunted in the recurrence group (Table 2). |
| 3 | At the mid-term follow-up, the LA expansion index significantly increased during |
| 4 | LPP stress in the success group, but not in the recurrence group (Table 2 and Figure 4). |
| 5 | Together with the improvement in LA distensibility, SVi significantly increased during LPP |
| 6 | stress without any elevation in LV filling pressure in the success group (Table 2 and Figure 4), |
| 7 | indicating a significant improvement in the preload reserve. In contrast, in the recurrence |
| 8 | group, the increased response of SVi was significantly blunted even at the expense of a |
| 9 | significant increase in E/e' ratio during the LPP stress test (Table 2 and Figure 4). |
| 10 | The hazard ratios (HRs) and 95% confidence intervals (CI) for each baseline clinical, |
| 11 | hemodynamic, and echocardiographic variables to predict AF recurrence are shown in Table |
| 12 | 3. In a multivariate logistic regression analysis, although baseline LAVI and use of |
| 13 | antiarrhythmic drugs were not selected as independent predictors of AF recurrence, LVEF and |
| 14 | baseline Δ LA expansion index during LPP stress were selected as the independent |
| 15 | determinants of AF recurrence after RFCA. |
| 16 | A receiver operating characteristic curve analysis identified the optimal cut-off value |
| 17 | of LVEF to be 56.3%, and the Δ LA expansion index to be 13.7%, respectively (Figure 5). |
| 18 | Discussion |
| 19 | In the clinical course of AF, LA remodeling can be considered as time-dependent |

| 1 | structural, functional, and electrical alterations. ¹ These different types of LA remodeling are |
|----|--|
| 2 | closely interrelated and progressively interact with each other, ¹¹ resulting in alterations in the |
| 3 | tissue architecture, including microscopic fibrotic remodelling ³ and macroscopic atrial |
| 4 | dilatation. In these progressive pathological processes, LA fibrosis appears to play a central |
| 5 | role in the development and maintenance of AF, by causing the heterogeneity of electrical |
| 6 | conduction and a predisposition to re-entry. ^{2,3} Moreover, as the fibrotic burden increases, non- |
| 7 | compliant LA would no longer be able to exert sufficient reservoir function; ultimately, LA |
| 8 | acts as merely a passive conduit, that is LA fibrotic cardiomyopathy. ^{12,13} In this way, LA |
| 9 | distensibility progressively deteriorates in parallel with LA myocardial fibrosis; therefore, LA |
| 10 | reservoir function has recently gained attention for its clinical role in patients with AF. |
| 11 | Khurram et al. studied 219 patients with AF referred to RFCA by analyzing LA pressure- |
| 12 | volume loops and found that LA stiffness was a strong independent predictor of AF |
| 13 | recurrence in patients undergoing RFCA. ¹⁴ Moreover, Hsiao et al. prospectively studied a |
| 14 | total of 2,200 patients who complained of dyspnea and they clearly demonstrated that the |
| 15 | echocardiographic LA expansion index was associated exponentially with the incidence of |
| 16 | persistent AF. ⁵ These previous investigators underscored the importance that impaired resting |
| 17 | LA distensibility was attributed to the development or recurrence of AF. Nevertheless, from a |
| 18 | pathophysiological point of view, the stiffness characteristics of a chamber are not static, or |
| 19 | dynamic capacity to distend itself in response to increased blood volume without increasing |

| 1 | internal pressure. In this study, the baseline ΔLA expansion index could accurately predict AF |
|----|--|
| 2 | recurrence presumably because the dynamic property of chamber distensibility could reflect |
| 3 | the degree of LA myocardial fibrosis more accurately than static parameters. |
| 4 | In this study, not only a structural but a significant functional improvement in LA |
| 5 | was observed after maintaining a sinus rhythm. These results may imply that the restoration |
| 6 | of a sinus rhythm could not merely terminate the vicious cycle of electrical, structural, and |
| 7 | functional remodeling, but reverse it. During the LPP stress test at the mid-term follow-up, the |
| 8 | Δ LA expansion index dramatically improved in the success group, accompanied by an |
| 9 | increased SV in response to the increased preload. These beneficial hemodynamic responses |
| 10 | may suggest the restoration of the ability to reserve significant blood volume in the LA |
| 11 | chamber without an elevation in LA pressure during the reservoir phase, consequently |
| 12 | resulting in sufficient LV diastolic filling and increased SV. However, structural and |
| 13 | functional reverse remodeling was not observed in the recurrence group. In this subgroup, it is |
| 14 | speculated that the fibrotic burden of the LA myocardium might be too advanced to the extent |
| 15 | that LA myocardial damage was no longer reversible. Therefore, the increased cardiac preload |
| 16 | no longer properly reserved in the stiff LA. Instead, it merely led to an elevation in LA |
| 17 | pressure, diastolic LV underfilling, and eventually reduced preload reserve. |
| 18 | Although RFCA is an established therapy for AF, its recurrence rate is reported to be |
| 19 | 10-40% for paroxysmal AF and as high as 60-80% for persistent AF; ¹⁵ therefore, appropriate |

| 1 | patient selection is a burning topic in this field. Theoretically, impaired LA distensibility |
|----|--|
| 2 | would be closely related to the fibrotic burden; thus, patients with AF may undergo RFCA |
| 3 | before the Δ LA expansion index is impaired for successful RFCA. The assessment of the |
| 4 | Δ LA expansion index may be helpful in predicting patient outcomes, providing an appropriate |
| 5 | strategy for RFCA, and making clinical decisions regarding post-procedural medical therapy. |
| 6 | This study has some limitations. First, because this study exclusively focused on the |
| 7 | LA reservoir function, we were unable to assess other atrial functional parameters, including |
| 8 | LA conduit and booster pump functions or right atrial function. Moreover, the pulmonary |
| 9 | veins and their variations were not anatomically assessed in this study. Second, the LPP |
| 10 | maneuver may not be available in all electrophysiological laboratories. Because passive leg- |
| 11 | lifting stress is reported to be able to provide significant cardiac preload and can be used for |
| 12 | the risk stratification of patients with heart failure, ¹⁶ further studies using this easy-to-use |
| 13 | preload stress are expected to validate our findings. |
| 14 | In conclusion, the baseline ΔLA expansion index during LPP stress |
| 15 | echocardiography was found to be a reliable marker to predict procedural success after |
| 16 | RFCA. Moreover, maintaining the sinus rhythm has been shown to induce a virtuous cycle of |
| 17 | LA reverse remodeling and improvement in preload reserve. These results may have |
| 18 | substantial implications in appropriate patient selection, emerging therapies after RFCA, risk |
| 19 | stratification, and postoperative follow-up. |

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| 8 | | |
| 9 | | |

1 Figure legends

| 2 | Figure 1. Study protocol |
|----|--|
| 3 | Transthoracic echocardiography and LPP stress echocardiography were performed within 3 |
| 4 | days after RFCA (baseline) and at 3-6 months after RFCA (mid-term). |
| 5 | RFCA, radiofrequency catheter ablation; TTE, transthoracic echocardiography; LPP, leg- |
| 6 | positive pressure. |
| 7 | |
| 8 | Figure 2. Schematic presentation of the measurement of the LA expansion index |
| 9 | The LA expansion index was calculated as (LAV_max - LAV_min) \times 100 / LAV_min both at rest and |
| 10 | during LPP stress. Subsequently, the Δ LA expansion index was calculated by subtracing the |
| 11 | expansion index at rest from that obtained during LPP stress. Moreover, the Δ LA expansion |
| 12 | index was measured both at baseline and mid-term follow-up. |
| 13 | LA, left atrial; LAV, left atrial volume; LPP, leg-positive pressure. |
| 14 | |
| 15 | Figure 3. Changes in resting LA functional and structural parameters from baseline to |
| 16 | the mid-term follow-up after RFCA for both the success and recurrence groups |
| 17 | Each plot and bar represents mean and standard deviations. |
| 18 | LA, left atrium; RFCA, radiofrequency catheter ablation; GLS, global longitudinal strain; |

19 LAVI, left atrial volume index.

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| J | L |
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| 2 | Figure 4. Changes in ΔLA expansion index and ΔSVi from baseline to the mid-term |
|----|--|
| 3 | follow-up after RFCA in both success and recurrence groups |
| 4 | In the success group, both the ΔLA expansion index and ΔSVi significantly increased from |
| 5 | baseline to the mid-term follow-up after RFCA, yet no significant changes were observed in |
| 6 | the recurrence group. |
| 7 | LA, left atrium; SVi, stroke volume index; RFCA, radiofrequency catheter ablation. |
| 8 | |
| 9 | Figure 5. ROC curve analysis for differentiating procedural success after RFCA |
| 10 | The baseline ΔLA expansion index was revealed to have a high discriminative potential for |
| 11 | predicting procedural success after RFCA. |
| 12 | ROC, receiver operating characteristic; RFCA, radiofrequency catheter ablation; LA, left |
| 13 | atrial. |
| 14 | |

Figure 1

(A)



(B)



(C)



Catheter ablation

✓ Laboratory examination

Baseline

- Immediately after catheter ablation
- ✓ TTE : rest + LPP

Mid-term follow-up

- ✓ 3-6 months after catheter ablation
- ✓ TTE : rest + LPP





Figure 4 Δ SVi Δ LA expansion index *P* < 0.05 n.s (%) (mL/m²) *P* < 0.05 30 5 4 4.7 3.1 32 ±4.0 20 ±4.8 3 ±19 2.4 n.s 2 ±4.3 3 2.3 10 土.7 16 ±1.3 Δ Mid-term **Mid-term** 1 ±11 ± 9 **Baseline Baseline** 0 0 **Success** Recurrence **Success** Recurrence





| | Cut-off | ACU (95% CI) | Sensitivity | Specificity | P value |
|--------------------------------------|---------|--------------|-------------|-------------|---------|
| LVEF (%) | 56.3 | 0.663 | 52.2 | 88.6 | <0.05 |
| Baseline ΔLA expansion index | 13.7 | 0.813 | 100 | 45.8 | <0.001 |

| | All patients | Success | Recurrence | |
|---|---------------|---------------|---------------|-----------------|
| Variables | (N = 111) | (N = 88) | (N = 23) | <i>P</i> -value |
| Age (years) | 67±9 | 67±10 | 67±8 | 0.97 |
| Body mass index (Kg/m ²) | 25±4 | 25±4 | 24±3 | 0.54 |
| Body surface area, (m ²) | 1.7 ± 0.2 | $1.7{\pm}0.2$ | $1.7{\pm}0.2$ | 0.69 |
| CHA ₂ DS ₂ -VASc score | 2.4±1.5 | 2.3±1.5 | 2.6±1.4 | 0.42 |
| Types of Atrial Fibrillation | | | | |
| Paroxysmal | 58 (52%) | 49 (56%) | 9 (39%) | 0.16 |
| Persistent/Long-standing persistent | 53 (48%) | 39 (44%) | 14 (61%) | 0.18 |
| Comorbidities | | | | |
| Heart failure | 12 (11%) | 7 (8%) | 5 (22%) | 0.06 |
| Hypertension | 65 (59%) | 55 (63%) | 10 (43%) | 0.10 |
| Diabetes | 29 (26%) | 24 (27%) | 5 (22%) | 0.70 |
| Stroke | 12 (11%) | 9 (10%) | 3 (13%) | 0.70 |
| Laboratory data | | | | |
| Hemoglobin (g/dL) | 13±1 | 13±1 | 13±2 | 0.76 |
| Creatinine (mg/dL) | $0.9{\pm}0.2$ | $0.9{\pm}0.2$ | $0.9{\pm}0.2$ | 0.37 |
| Estimated glomerular filtration rate (mL/min/1.73m ²) | 65±13 | 65±13 | 61±12 | 0.17 |
| Brain natriuretic peptide (pg/mL) | 76 (31-141) | 58 (29-144) | 108 (75-138) | 0.22 |

Table1. Baseline clinical characteristics of the patients with atrial fibrillation

Data are presented as n, mean \pm SD, n (%), or median (interquartile range).

Table 2. Comparisons of haemodynamic and echocardiographic parameters during leg-positive pressure stress both at baselineand mid-term follow-up

| | | Suco | cess | | Recurrence | | | | |
|--|-----------|--------------------------|------------|--------------------------|------------|--------------------------|------------|--------------------------|--|
| | Ba | seline | Mid-ter | m follow up | Ba | aseline | Mid-ter | m follow up | |
| Variable | Rest | Leg-positive pressure | Rest | Leg-positive pressure | Rest | Leg-positive pressure | Rest | Leg-positive pressure | |
| Hemodynamics | | | | | | | | | |
| Systolic blood pressure (mmHg) | 126±18 | 129±19* | 124±20 | 123±17 | 127±18 | 124±14 | 120±21 | 121±18 | |
| Diastolic blood pressure (mmHg) | 73±14 | 76±14* | 67±16† | 68±14 | 74±9 | 72±18 | 68±21 | 70±17 | |
| Heart rate (bpm) | 71±13 | 69±10* | 67±10† | 64±9* | 71±15 | 69±12* | 66±14 | 65±18 | |
| Stroke volume index (mL/m ²) | 39±11 | 42±12* | 37±9† | 41±10* | 42±11 | 46±12* | 36±7† | 40±8* | |
| Δ Stroke Volume index (mL/m ²) | 2. | 2.3±1.3 | | 3.1±4.8† | | 4.7 ± 4.0 | | 2.4±4.3‡ | |
| Echocardiographic indices | | | | | | | | | |
| Left ventricular volume index (mL/m ²) | | | | | | | | | |
| End-diastole | 47±10 | 51±11* | 47±12 | 54±14* | 56±12‡ | 61±16* | 52±15 | 59±15* | |
| End-systole | 17±5 | 18±5 | 18±6 | 20±7* | 24±10‡ | 25±12 | 21±8‡ | 22±10 | |
| Left ventricular mass index (g/m ²) | 8 | 6±27 | 82 | 2±21† | 9 | 95±23 | 91 | 7±27‡ | |
| Left ventricular ejection fraction (%) | 63±6 | 65±5* | 63±5 | 65±5* | 58±9‡ | 61±11 | 60±8 | 65±8* | |
| Left atrial volume index (mL/m ²) | 40±12 | 45±13* | 34±9† | 40±10* | 47±16‡ | 52±17* | 43±16†‡ | 48±18* | |
| | 1.6 | 1.5 | 1.2 | 1.3 | 1.9 | 2.0 | 1.5 | 1.5 | |
| E/A rano | (1.1-2.2) | (1.2-2.4) | (0.9-1.6)† | (1.0-1.6)* | (1.5-2.5) | (1.5-2.5) | (1.0-2.2)† | (1.2-1.8) | |
| e' velocity (cm/sec) | 7.3±1.7 | 7.6±2.0* | 7.4±1.7† | 7.6±1.7 | 7.6±2.0 | 7.6±2.1 | 7.5±2.3 | 7.2±2.6 | |
| E/e' ratio | 11±3 | 13±5* | 10±3† | 11±4 | 12±5 | 13±5* | 11±4 | 14±10* | |

| $\Delta E/e$ ' ratio | 1.2 ± 2.1 | | 1.0 | $1.0{\pm}2.2$ | | 1.5 ± 2.3 | | 3.4±7.5‡ | |
|---|-------------|--------|---------------|---------------|-------|---------------|-------|----------|--|
| Tricuspid regurgitation-pressure gradient | 22+0 | 2/1+8 | 10+0+ | <i>??</i> ⊥0* | 25+7 | 24+8 | 21+10 | 22+10 | |
| (mmHg) | 2319 | 24±0 | 1 <i>9</i> ⊥9 | | 2311 | 24±0 | 21±10 | 22-10 | |
| Tricuspid annular plane systolic excursion (mm) | 22±4 | 23±4 | 22±4 | 23±4* | 23±4 | 24±5 | 22±4 | 24±5 | |
| Inferior vena cava diameter (mm) | 14±4 | 16±4* | 12±4† | 14±3* | 14±4 | 15±3 | 12±3† | 14±3* | |
| Left ventricular-global longitudinal strain (%) | 13±4 | 13±4 | 15±4† | 15±4 | 12±3 | 13±3 | 13±5 | 13±5 | |
| Left atrial-global longitudinal strain (%) | 17±6 | 19±5* | 21±6† | 23±7* | 15±6 | 16±6* | 16±6‡ | 17±5 | |
| Left atrial expansion index (%) | 40±27 | 56±28* | 61±30† | 93±34* | 37±14 | 40±14* | 34±17 | 36±18* | |
| Δ Left atrial expansion index (%) | 16 | ±11 | 32= | ±19† | 3.7 | ± 9.0 ‡ | 2.6 | ±6.5‡ | |

**P*<0.05 vs. rest, †*P*<0.05 vs. baseline, ‡*P*<0.05 vs. success

Data are presented as n, mean \pm SD, n (%), or median (interquartile range).

| | Un | ivariate analys | sis | Multivariate analysis | | | |
|---|-------|-----------------|---------|-----------------------|-------------|---------|--|
| Variables | | 95% CI | P value | HR | 95% CI | P value | |
| Clinical variables | | | | | | | |
| Age (y) | 0.999 | 0.952-1.049 | 0.97 | | | | |
| Gender (male) | 0.857 | 0.314-2.340 | 0.76 | | | | |
| CHA ₂ DS ₂ -VASc score | 1.120 | 0.821-1.528 | 0.47 | | | | |
| Type of atrial fibrillation (paroxysmal) | 0.512 | 0.201-1.306 | 0.16 | | | | |
| Brain natriuretic peptide concentration, pg/mL | 1.001 | 0.997-1.004 | 0.73 | | | | |
| Radiofrequency catheter ablation strategy | 1 150 | 0 620 2 121 | 0.64 | | | | |
| (pulmonary vein isolation) | 1.139 | 0.030-2.131 | 0.04 | | | | |
| Prescription of antiarrhythmic drugs | 3.301 | 1.233-8.838 | < 0.05 | | | | |
| Baseline echocardiographic variables | | | | | | | |
| Left ventricular ejection Fraction (%) | 0.906 | 0.847-0.968 | < 0.01 | 0.900 | 0.831-0.974 | < 0.05 | |
| Left atrial volume index (mL/m ²) | 1.040 | 1.004-1.077 | < 0.05 | | | | |
| E/e' ratio | 1.022 | 0.899-1.161 | 0.74 | | | | |
| Left ventricular-global longitudinal strain (%) | 0.928 | 0.814-1.058 | 0.26 | | | | |
| Left atrial-global longitudinal strain (%) | 0.923 | 0.818-1.042 | 0.19 | | | | |
| Left atrial expansion index (%) | 0.994 | 0.974-1.014 | 0.58 | | | | |
| Variables under leg-positive pressure stress | | | | | | | |
| Δ Left atrial expansion index (%) | 0.831 | 0.754-0.915 | < 0.001 | 0.900 | 0.753-0.931 | < 0.001 | |

Table 3. Univariate and multivariate logistic regression analysis to predict AF recurrence

HR, hazard ratio; CI, confidential interval.

All other abbreviations as in Table 1 and 2.