Association Between Left Atrial Stiffness Index and Atrial Fibrillation Recurrence in Patients Undergoing Left Atrial Ablation

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Background—Atrial fibrillation (AF) is associated with significant abnormalities of left atrial (LA) systolic and diastolic function. This study describes a novel measure, LA stiffness index, that estimates LA diastolic function and its association with clinical outcomes of catheter ablation.

Methods and Results—A total of 219 AF patients referred for ablation (59% paroxysmal, mean CHA2DS2-VASc score 1.7±1.4) were enrolled. Atrial pressure and volume loops were prepared from invasive pressure measures and cardiac magnetic resonance imaging volumetric data during sinus rhythm for all patients. An LA stiffness index was created, defined by the ratio of change in LA pressure to volume during passive filling of LA (ΔP/ΔV). Patients were followed prospectively. Mean LA stiffness index for AF patients was 0.6±0.5 mm Hg/mL (paroxysmal AF 0.5±0.4 and persistent AF 0.7±0.6; P<0.001). Linear regression analysis showed a rise in the stiffness index with age, increasing at a rate of 0.02 mm Hg/mL per year (P<0.001). The LA stiffness index was higher in patients with previous LA ablation(s) for AF (0.5±0.35 versus 0.8±0.70; P<0.001). Forty of 160 patients had recurrence after AF ablation with a mean follow-up of 10.4±7.6 months. Patients with recurrence had higher stiffness index than those without recurrence (0.8±0.46 versus 0.4±0.22; P<0.001).

Conclusions—LA stiffness index, a novel measure to assess LA diastolic function, increases with age and is higher in persistent AF and in the setting of repeat AF ablation. Greater LA stiffness index was independently associated with recurrence of AF after LA ablation. (Circ Arrhythm Electrophysiol. 2016;9:e003163. DOI: 10.1161/CIRCEP.115.003163.)

Key Words: atrial fibrillation • catheter ablation • magnetic resonance imaging • recurrence
WHAT IS KNOWN

- Atrial fibrillation has a high recurrence rate after catheter ablation.
- Postablation recurrence has been associated with left atrial remodeling that results in fibrosis and contractile dysfunction.

WHAT THE STUDY ADDS

- The left atrial stiffness index is a novel measure that combines catheter-based pressure measurements with volumetric cardiac magnetic resonance imaging data to obtain estimates of atrial compliance from pressure–volume loops.
- Preprocedural left atrial stiffness index is a strong independent predictor of recurrence after ablation, suggesting a mechanistic link between fibrosis, reduced atrial wall compliance, and recurrent atrial fibrillation.

Other exclusion criteria included moderate to severe valvular heart disease on echocardiography and systolic dysfunction defined by LV ejection fraction of <45%.

Cardiac Magnetic Resonance Imaging

All patients underwent CMR examinations using a 1.5-Tesla magnetic resonance scanner (Avanto or Aera; Siemens, Erlangen, Germany) using either a 6-channel (Avanto) or an 18-channel (Aera) phased array body coil in combination with the integrated spine matrix coils. Cine steady-state free precession gradient-echo images were obtained (echo time 1.1–1.6 ms, repetition time 2.2–3.2 ms, in-plane resolution 1.4 × 1.4 mm, slice thickness 8 mm) in contiguous horizontal long-axis planes covering the entire left atrium. Spatial resolution and slice thickness were held constant on the 2 scanners. Thirty phases were obtained per cardiac cycle with a temporal resolution of 40 to 45 ms. Images were processed off-line using QMass MR software (version 7.2; Leiden University Medical Center, Leiden, The Netherlands) as previously reported.8 LA endocardial contours were manually drawn for 30 phases of the cardiac cycle in all slices covering the entire LA. The LA appendage was excluded. The complete LA volume was automatically calculated using the Simpson method for each of the 30 phases of the cardiac cycle as shown in Figure 1A and 1B for 2 representative patients.

Ablation Procedure and LAP

All patients underwent AF ablation using wide-area circumferential ablation technique as previously described.16 All ablation procedures were performed while patients were in sinus rhythm. Patients either presented in sinus rhythm or were cardioverted to sinus rhythm before the start of the ablation procedure. Briefly, a double transseptal puncture was performed under fluoroscopic guidance. LA hemodynamic measurements including LAP were recorded using the CardioLab Electrophysiology System (General Electric Medical Systems Inc, Milwaukee, WI) after the transseptal puncture before any ablation lesions or fluid infusion. Pulmonary vein angiograms were then obtained for each of the pulmonary veins. An endocardial map of the left atrium was created with an electroanatomic mapping system (CARTO; Biosense Webster Inc, Diamond Bar, CA) and superimposed on the preexisting CMR image of the chamber. Using a circular multipolar electrode mapping catheter (Lasso; Biosense Webster), pulmonary vein potentials were evaluated.

A 4-mm–tipped irrigated ablation catheter (Thermocool; Biosense Webster) was advanced under fluoroscopic guidance to the left atrium with routine hemodynamic and electrocardiographic monitoring. Circumferential lesions were applied surrounding the pulmonary veins. The procedural end point was complete isolation of the pulmonary veins with entrance and exit block confirmed by the Lasso catheter.

The LAP tracing was manually divided into 30 equal phases of a cardiac cycle as shown in Figure 1C and 1D. In detail, the LAP for 30 time increments during a single RR interval was recorded, and LAP peak (v wave), LAP nadir (y descent), and LAP mean were identified and confirmed using ECG correlations. The ΔP (dP) was calculated by the difference of LAP peak and LAP bottom (Pv−Px), corresponding to the change in pressure during the passive filling phase of atrial diastole.

LA Pressure–Volume Loop

The LA volume and pressure curves were registered by aligning the 30 phases of the cardiac cycle. The opening and closing of mitral valve were used as anchoring points to register the 2 curves. LA pressure–volume (PV) loops were made for all patients, and representative PV loops with different LA stiffness indices from 2 patients are seen in Figure 1E. Figure 2A shows a graphical representation of a theoretical normal LA PV loop, where point C is the closure of mitral valve in cardiac systole and point O is opening of mitral valve at the start of ventricular diastole. The PV loop can be divided into the 4 phases. The first phase is the relaxation of the LA after atrial contraction, with the start of ventricular systole associated with a drop in LAP but rise in volume. The second phase is the passive filling of LA while mitral valve is still closed, associated with a rise in LAP and volume according to the characteristics of LA myocardial compliance. The third phase is the passive emptying of LA by the opening of the mitral valve at the end of the ventricular contraction, associated with a drop in LAP and volume. The fourth phase is the atrial contraction with a rise in LAP and drop in LA volume. Figure 2B shows the changes expected in a PV loop obtained in a patient with a dilated and stiff LA.

To quantify LA diastolic function, we created the LA stiffness index that approximates the slope of the passive filling phase of LA diastole from PV loops. We defined the LA stiffness index as the amount of pressure (mm Hg) required to induce a unit change in LA volume (mL) during the passive filling phase. Arithmetically, this was defined as the ratio of change in LAP to the change in LA volume during passive filling of LA ( ΔP divided by ΔV) measured in mmHg/mL.

Outcome Measurement

Patients were followed closely after ablation. Antiarrhythmic drug therapy, if present at the time of ablation, was discontinued 3 months after ablation. Patients were evaluated for recurrence at 3, 6, and 12 months at follow-up clinic visits and telephone interviews. If symptoms suggestive of an arrhythmia occurred, patients were asked to undergo 24-hour Holter monitoring or 30-day event monitoring, depending on the frequency of their symptoms as previously reported.17 Recurrent AF was defined based on the 2012 Heart Rhythm Society Consensus Document as symptomatic or asymptomatic AF, atrial tachycardia, or atrial flutter of >30 seconds duration after a 3-month blanking period.2

Statistical Analysis

Continuous data were presented as a mean ± standard deviation, and categorical data were presented as percentages. The means were compared using t test, and binary data were analyzed using χ² tests. A P value of <0.05 was considered statistically significant. Statistical analyses were performed using STATA version 12 (StataCorp, College Station, TX). We used a multivariable Cox model for hazard ratios for AF recurrence. To provide detailed analyses of the dose–response relationship of LA stiffness index with AF recurrence, we modeled the...
LA stiffness index with restricted quadratic splines with knots at the 5th, 10th, and 95th percentiles of its distribution. In spline analyses, we used the 50th percentile of the LA stiffness index distribution as the reference value. The multivariate regression model for the hazard ratio plot included age, sex, body mass index, hypertension, atherosclerotic vascular disease, diabetes mellitus, and CHA2DS2VASC score.

Figure 1. Top row. The left atrial (LA) volume changes in a single cardiac cycle from one QRS complex to the next in a patient with a compliant LA (A) and a stiff LA (B). The LA volume shows a drop at the onset of ventricular diastole indicating opening of mitral valve that is followed by the quick drop in volume at the end during atrial contraction. C and D. LA pressure during a single cardiac cycle from the same patients as A and B, respectively. The cycle is from one QRS complex to another starting with x descent, followed by v wave and y descent. The rise of LA pressure at the end of the cycle is showing a wave of atrial contraction. Registration of the LA volume and pressure curves was done by identifying the point of mitral valve closing and opening. The resultant pressure–volume loops for the 2 patients are shown in the bottom (E).
Results

Patients Characteristics

A total of 257 patients were screened and 38 were excluded (35 patients because of failure to maintain sinus rhythm during CMR or ablation procedure, 2 patients had moderate mitral regurgitation, 1 had low LV ejection fraction, and none had a pulse rate difference of >10% at the time of LAP and volume assessment). There was a median of 5.5 hours delay between CMR acquisition and transseptal puncture (with 75% of the patients had ablation procedure within 12 hours of the scan; mean was 23.3±44.4 hours with skewness of 2.72). Only 2 patients required cardioversion during ablation procedure, with one of them coming in for redo-ablation and the other was in persistent AF group. Of 219 included in the study, 130 (59.4%) patients had paroxysmal and 89 (40.6%) had persistent AF; 160 (73.1%) had undergone ablation for the first time. Patients undergoing initial AF ablation in the cohort were selected for outcome analysis, whereas the patients with prior ablation were excluded from outcome analysis. The average CHA2DS2-VASc score was 1.7±1.4 (Table 1).

LA Volume and Pressure in AF

The mean LA volume was 131.1±29.9 mL; paroxysmal AF patients had significantly lower LA volumes than persistent AF patients (124.1±26.9 mL versus 143.1±30.6 mL; P<0.001). The mean ΔV (change in LA volume during passive filling phase of LA) for the entire cohort was 25.4±9.6 mL, with paroxysmal AF having significantly higher ΔV than persistent AF (26.9±9.2 versus 23.0±9.7 mL; P=0.002). The mean ΔV was also significantly higher for the first-time ablation patients compared with those undergoing repeat ablation (27.0±9.3 mL versus 21.1±9.1 mL; P<0.001).

The mean LAP for the entire cohort was 19.8±7.4 mm Hg. There was no significant difference in mean LAP between paroxysmal and persistent AF patients (17.4±5.8 versus 21.9±8.2 mm Hg; P=0.09). However, the mean ΔP (change in LAP during passive filling) for the entire cohort was 12.2±5.8 mm Hg with significantly lower ΔP for paroxysmal (11.4±4.9 mm Hg) compared with persistent AF patients (13.3±6.8 mm Hg; P=0.020). The ΔP was lower for the first-time ablation patients (11.6±5.2 mm Hg) compared with those with repeat ablations (13.7±7.1 mm Hg; P=0.020).

The mean LA stiffness index for the entire cohort was 0.6±0.5 mm Hg/mL. The stiffness index was lower in paroxysmal AF (0.51±0.4 mm Hg/mL) compared with persistent AF (0.73±0.6 mm Hg/mL; P<0.001). For the entire cohort, linear regression analysis showed an increase in LA stiffness index with age at a rate of 0.02 mm Hg/mL per year (P=0.010) as shown in Figure 3A. The LA stiffness index was higher in

Figure 2. A, Graphical representation of a typical left atrium (LA) pressure–volume loop. Point C is the closure of mitral valve in cardiac systole, and point O is opening of mitral valve at the start of ventricular diastole showing the 4 phases of the LA cardiac cycle. B, Measurement of LA stiffness index (ΔP/ΔV). The slope of phase 2 defines the LA stiffness. The LA stiffness index approximates the slope of phase 2 by taking the ratio of the change in pressure to the change in volume (ΔP/ΔV) that occurs during the passive filling phase. Here, phase 2 of the 2 patients are highlighted with red color line where solid red line of a compliant LA can be compared with a stiff LA with higher LA pressure (ΔP) and smaller corresponding change in volume (ΔV).
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patients with previous history of LA ablations for AF (first ablation patients 0.51±0.35 mm Hg/mL versus repeat ablation patients 0.83±0.70 mm Hg/mL; P<0.001) as shown in Figure 3B.

LA Stiffness Index Score and AF Ablation Outcome

The subcohort of initial ablation patients was stratified on the basis of LA stiffness index into 4 equal quartiles: group A had the stiffness index <0.27; group B between 0.27 and 0.45; group C between 0.45 and 0.65; and group D >0.65.

Of the 160 patients undergoing an initial ablation procedure, 120 (75%) patients remained free of AF with a mean follow-up of 10.4±7.6 months to primary outcome. The comparison of patients with recurrent AF versus those who remained in normal sinus rhythm is shown in Table 2. Patients who had recurrence were noted to have significantly higher

Table 1. Demographics of the Entire Cohort of Patients Undergoing Pulmonary Vein Isolation for Atrial Fibrillation

<table>
<thead>
<tr>
<th>Variables</th>
<th>Number of Ablations</th>
<th>P Value</th>
<th>AF Type</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>First</td>
<td>Repeat</td>
<td></td>
<td>Paroxysmal</td>
</tr>
<tr>
<td>Patients, n (219)</td>
<td>160</td>
<td>59</td>
<td>0.8910</td>
<td>130</td>
</tr>
<tr>
<td>Age, y</td>
<td>61.3±10.3</td>
<td>61.1±9.0</td>
<td>0.757</td>
<td>60.9±9.7</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>123</td>
<td>44</td>
<td>0.356</td>
<td>93</td>
</tr>
<tr>
<td>Race (white), n (%)</td>
<td>137</td>
<td>50</td>
<td>0.357</td>
<td>113</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>81</td>
<td>34</td>
<td>0.675</td>
<td>63</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>24</td>
<td>10</td>
<td>0.636</td>
<td>19</td>
</tr>
<tr>
<td>Atherosclerotic disease, n (%)</td>
<td>21</td>
<td>8</td>
<td>0.636</td>
<td>14</td>
</tr>
<tr>
<td>Chronic heart failure, n (%)</td>
<td>19</td>
<td>7</td>
<td>0.942</td>
<td>10</td>
</tr>
<tr>
<td>History of thromboembolism, n (%)</td>
<td>8</td>
<td>5</td>
<td>0.334</td>
<td>8</td>
</tr>
<tr>
<td>Obstructive sleep apnea, n (%)</td>
<td>43</td>
<td>10</td>
<td>0.115</td>
<td>31</td>
</tr>
<tr>
<td>CHA2DS2VASc score</td>
<td>1.6±1.4</td>
<td>1.8±1.3</td>
<td>0.059</td>
<td>1.6±1.3</td>
</tr>
<tr>
<td>Duration of AF, y‡</td>
<td>5.1±4.7</td>
<td>9.3±7.5</td>
<td>&lt;0.001</td>
<td>6.2±5.5</td>
</tr>
<tr>
<td>LV ejection fraction, %§</td>
<td>54.4±9.2</td>
<td>52.6±10.1</td>
<td>0.359</td>
<td>56.0±8.8</td>
</tr>
<tr>
<td>LA volume, mL</td>
<td>131.7±29.9</td>
<td>133.7±36.0</td>
<td>0.795</td>
<td>124.1±26.9</td>
</tr>
<tr>
<td>LA volume index, mL/m²</td>
<td>62.8±16.4</td>
<td>66.0±4.3</td>
<td>0.439</td>
<td>61.1±16.8</td>
</tr>
<tr>
<td>No. of ablations, n (%)</td>
<td>NA</td>
<td>0</td>
<td>0.57</td>
<td>96</td>
</tr>
<tr>
<td>First ablation</td>
<td>160</td>
<td>0</td>
<td>0.57</td>
<td>96</td>
</tr>
<tr>
<td>Second ablation</td>
<td>0</td>
<td>42</td>
<td>17 (28.8)</td>
<td>25 (19.2)</td>
</tr>
<tr>
<td>Third or more ablation</td>
<td>0</td>
<td>17</td>
<td>9 (6.9)</td>
<td>6 (9.0)</td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation; LV, left ventricle; and NA, not applicable.
*Atherosclerotic disease includes both coronary artery and peripheral vascular disease.
†History of thromboembolism includes history of embolic stroke and transient ischemic attacks.
‡AF duration is measured from the onset of the symptoms to the ablation procedure.
§The ejection fraction is from the preprocedure transthoracic echocardiogram that was reviewed to evaluate systolic dysfunction and mitral regurgitation.

Figure 3. A. Relationship between left atrial (LA) stiffness index and age. The LA diastolic function seems to get worse with increasing age. B. Box plot showing repeat ablation patients noted to have higher LA stiffness index compared with first-time ablation patients (P<0.001).

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LA stiffness index (0.83±0.46 mm Hg/mL) compared with patients who remained in sinus rhythm (0.40±0.22 mm Hg/mL; \( P < 0.001 \)).

The LA volume was 129.0±29.4 mL for patients who had no recurrence compared with 139.7±30.3 mL for patients with recurrence (\( P = 0.049 \)) for patients with first-time ablation. The paroxysmal AF patients who had no recurrence had a mean LA volume of 121.4±24.8 mL, which was significantly smaller than that of patients with recurrence (138.2±33.7 mL; \( P = 0.025 \)). The persistent AF patients had a nonsignificant difference in mean LA volume (144.8±32.0 mL) for those without recurrence compared with those with recurrence (140.6±28.7 mL; \( P = 0.60 \)).

For the 40 patients in LA stiffness group A (lowest quartile), 38 (95%) had no recurrence and only 2 (5%) patients had recurrence of AF after the blanking period. Of the 43 patients in group B, 4 (9.3%) recurred; of the 38 patients in group C, 11 (30.0%) recurred; and of the 39 patients in group D (highest quartile of LA stiffness), 23 (59.0%) patients had evidence of recurrence of AF. Figure 4 shows the Kaplan–Meier curves of AF-free survival of patients after ablation of the LA by the 4 quartile groups of LA stiffness index. Groups C and D continued to have recurrence during the follow-up period, whereas groups A and B had low recurrence rates.

On univariate analysis, recurrence of AF was significantly associated with increasing age and body mass index, diabetes mellitus, persistent AF, higher CHA2DS2VASc score, and LA stiffness index as shown in Table 2. Multivariate analysis adjusting for age, sex, body mass index, hypertension, diabetes mellitus, CHA2DS2VASc score, and persistent AF and LA volume revealed LA stiffness index to be an independent predictor of AF ablation outcome (Table 3). Figure 5 shows spline analyses where, after adjusting for multiple variables, hazard ratios for AF recurrence are illustrated as a function of the LA stiffness index using restricted quadratic splines.

**Discussion**

Here, we report a novel measure of LA diastolic dysfunction, the LA stiffness index, which is based on a combination of noninvasive volume measurements from CMR and invasive pressure measurements at the time of the LA ablation. This

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**Table 2. Clinical Characteristics of Patients With and Without the Recurrence of AF During the Follow-Up Period of the Study**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total</th>
<th>No Recurrence</th>
<th>AF Recurrence</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, n (%)</td>
<td>160</td>
<td>120 (75)</td>
<td>40 (25)</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>123 (76.9)</td>
<td>94 (78.3)</td>
<td>29 (72.5)</td>
<td>0.45</td>
</tr>
<tr>
<td>Race (white), n (%)</td>
<td>137 (85.6)</td>
<td>106 (88.3)</td>
<td>31 (77.5)</td>
<td>0.09</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>81 (50.6)</td>
<td>57 (47.5)</td>
<td>24 (60.0)</td>
<td>0.17</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>24 (15.0)</td>
<td>14 (11.7)</td>
<td>24 (15.0)</td>
<td>0.041</td>
</tr>
<tr>
<td>Atherosclerotic disease, n (%)</td>
<td>27 (16.9)</td>
<td>16 (13.3)</td>
<td>11 (27.5)</td>
<td>0.038</td>
</tr>
<tr>
<td>Chronic heart failure, n (%)</td>
<td>19 (12.4)</td>
<td>12 (10.3)</td>
<td>7 (12.4)</td>
<td>0.14</td>
</tr>
<tr>
<td>History of thromboembolism, n (%)</td>
<td>8 (5.0)</td>
<td>5 (4.2)</td>
<td>3 (7.5)</td>
<td>0.40</td>
</tr>
<tr>
<td>Obstructive sleep apnea, n (%)</td>
<td>43 (26.9)</td>
<td>30 (25.0)</td>
<td>13 (32.5)</td>
<td>0.29</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>29.3±6.4</td>
<td>28.6±6.1</td>
<td>31.2±6.7</td>
<td>0.025</td>
</tr>
<tr>
<td>Persistent AF, n (%)</td>
<td>64 (40)</td>
<td>39 (32.5)</td>
<td>25 (62.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>CHA2DS2VASc score</td>
<td>1.6±1.4</td>
<td>1.4±1.4</td>
<td>2.3±1.5</td>
<td>0.001</td>
</tr>
<tr>
<td>Duration of AF, y</td>
<td>5.1±4.7</td>
<td>5.4±5.0</td>
<td>3.9±3.7</td>
<td>0.10</td>
</tr>
<tr>
<td>LV ejection fraction, %</td>
<td>54.4±9.2</td>
<td>54.3±9.9</td>
<td>54.9±7.1</td>
<td>0.79</td>
</tr>
<tr>
<td>LA volume, mL</td>
<td>131.7±29.9</td>
<td>129.0±29.4</td>
<td>139.7±30.3</td>
<td>0.049</td>
</tr>
<tr>
<td>LA volume index, mL/m²</td>
<td>62.8±16.4</td>
<td>61.9±16.1</td>
<td>65.4±17.2</td>
<td>0.25</td>
</tr>
<tr>
<td>LA stiffness index</td>
<td>0.51±0.35</td>
<td>0.40±0.22</td>
<td>0.83±0.46</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation; LA, left atrium; and LV, left ventricle.
novel measure provides an estimate of the compliance of the LA myocardium by determining the ratio of change in volume to change in pressure during the passive filling phase of LA diastole. We have found that LA stiffness index is associated with persistent AF, history of prior ablation, and age. Importantly, LA stiffness index is a strong independent predictor of recurrence in patients undergoing an initial AF ablation.

The passive filling phase of the LAP volume curve reflects the inherent lusitropic properties of the LA myocardium. The passive filling phase starts when the LAP has dropped low enough to equilibrate with the pulmonary venous pressure and the reverse flow of atrial contraction into the pulmonary veins has subsided, leading to forward flow into the LA. The LA receives blood, and the pressure in the LA increases based on atrial wall compliance. The slope of this pressure and volume relationship is dependent on the change in the pressure in LA diastole. We have found that LA stiffness index is associated with persistent AF, history of prior ablation, and age. Importantly, LA stiffness index is a strong independent predictor of recurrence in patients undergoing an initial AF ablation.

The relationship between various clinical features such as age, repeat ablations, and persistent AF to the LA diastolic function seen in this study with LA stiffness index is in accordance with the other reports on LA diastolic function.19–21 Most studies on LA diastolic function have used echocardiographic speckle tracking to assess strain and indirectly evaluate myocardial compliance.19,22 Other groups have investigated the atrial diastolic function by CMR, again based entirely on changes in LA volume.23 The LA strain technique uses movement of the myocardium in a cardiac cycle and is unable to assess the LAP.21 Importantly, a recent report by Park et al4 showed that LA peak pressure is an independent predictor of outcome after ablation. However, LAP alone is not able to assess the elasticity of LA myocardium unless the relationship of both the pressure and the volume is identified.

In agreement with prior reports, we found that myocardial diastolic function deteriorates with age.24 Our results also show that LA diastolic function is worse in patients with prior CA. We suspect this is because of ablation-induced myocardial scarring, which has been reported previously.19 Postablative stiff LA syndrome has been described and is reported to occur in 1.4% of patients.25 LA stiffness in this study was defined by elevated estimated pulmonary artery pressure on transthoracic echocardiography, which could be confounded by the presence of pulmonary hypertension or congestive failure. Our results confirm higher LA stiffness index in recurrent AF patients. We postulate that patients with recurrence likely have a diseased left atrium, which manifests as high stiffness index. Alternatively, this could in part be because of a direct effect of extensive radiofrequency ablation causing scarring and resulting in a stiff LA. To differentiate between these two causes, a longitudinal study would be needed.

The outcome of AF ablation has been linked with LA diastolic dysfunction in many reports.19,20,26–28 Our results are in accordance with a study by Morris et al19 using LA strain pattern using echocardiographic measures, showing that AF ablation outcomes are correlated with the LA systolic and diastolic function. In another report, PV flow velocities measured by echocardiography were inversely associated with recurrence after CA in a relatively small study of 67 AF patients.20 Another small study on 63 patients using speckled tracking on echocardiogram showed LA longitudinal strain as an independent predictor of recurrence after CA for AF.24 A recent investigation by Motoki et al27 showed 42% recurrence after initial AF ablation after a median of 8 months of follow-up in 256 patients.28

Figure 5. Hazard ratios for atrial fibrillation (AF) recurrence as a function of the left atrial (LA) stiffness index: the solid black line indicates multivariable-adjusted hazard ratios for AF recurrence as a function of the LA stiffness index using restricted quadratic splines. The dashed lines delineate the upper and lower 95% confidence intervals. The horizontal gray dotted line indicates a hazard ratio of 1. The model was adjusted for age, sex, body mass index, type of AF, the presence of hypertension, coronary artery disease, peripheral vascular disease, diabetes mellitus, LA volume index, and CHA2DS2VASc score.
Left Atrial Stiffness and AF Recurrence

Khurram IM, Beinart R, Zipunnik P. This is a single-center, small size cohort that needs to be reproduced and verified. In this study, we were unable to compare the LA stiffness index with control groups because of the invasive nature of the LAP measurement that would pose inappropriate risk for control group. Hence, LA stiffness index is assessed in selective AF patients undergoing CA and cannot be generalized to the overall AF population. There is no gold standard available for LA diastolic function assessment to validate this method. However, the trends and findings seen in this study are in agreement with LA diastolic function studies reported previously.

Conclusions
The LA stiffness index is an objective measure of the LA myocardial compliance using PV loops from the left atrium. Increased LA stiffness, reflected by an increase in stiffness index, is a strong predictor of recurrence after AF ablation.

Sources of Funding
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Disclosures
Dr Nazarian is on the magnetic resonance imaging advisory panel (unpaid) for Medtronic and is a scientific advisor to and the principal investigator for research funding to Johns Hopkins University from Biosense Webster Inc.

References
8. Khurram IM, Beinart R, Zipunnikov V, Dewire J, Yarmohammadi H, Sasaki T, Spragg DD, Marine JE, Berger RD, Halperin HR, Calkins H, patients where an echocardiographic measure of global LA strain was associated with the maintenance of sinus rhythm. In this study, LA diastolic function was estimated by constructing PV loops for a large sample of AF ablation patients who were followed prospectively. The method described in this study is labor-intensive and therefore would be difficult to implement in the clinical routine. We think, however, that the current method could be useful for the validation of other noninvasive methods of LA diastolic dysfunction assessment, such as feature tracking echocardiography, CMR, or pulmonary vein flows.

PV loops have been well established for the ventricles and are used for the assessment of global mechanical function. However, PV loops are not well studied in the atrium. There have been few atrial PV loop studies on animal models with limited clinical data. LA stiffness index provides a new tool to assess the properties of the LA myocardium that may help predict procedural outcomes. The LA volume, persistent AF, and LAP have been shown to be predictors of recurrence of AF after AF ablation. Similarly, in our study, we found that LA stiffness index along with age, body mass index, LA volume, type of AF and comorbidities like diabetes mellitus and atherosclerotic vascular disease, and CHA2DS2-VASc score are predictive of recurrence in univariate analysis as shown in Table 2. However, once multivariable analysis was conducted, these factors lost their significance, leaving LA stiffness index as the sole predictors for recurrence in this population. This indicates that perhaps the likely mechanism through which these factors increase the risk of recurrence is through worsening atrial compliance as measured by LA stiffness index. More studies are needed to validate and establish LA stiffness index as a potential mechanistic tool for recurrence of AF after pulmonary vein isolation. We think increases in LA stiffness index are likely related to atrial fibrosis, and future studies investigating the structure–function relationship of stiffness index to atrial scar on CMR are warranted.

Limitations
The LA stiffness index is an objective measure but is dependent on invasive measurement of the LAPs, making it difficult to obtain on routine basis for all patients. CA of AF requires LA access and direct measurement of LAP, which makes it inappropriate to compare with healthy controls. The PV loops in this study are registering volume and pressure from 2 different studies obtained at 2 different time intervals although within a day of the scan, with most undergoing magnetic resonance imaging just before the procedure; this can potentially induce change in hemodynamics, increasing the risk of imprecise coupling. Patients who were not in sinus rhythm at the time of CMR or after septal puncture at LAP measurement were excluded from the study, which could result in bias because of exclusion of patients with potentially more severe disease. We did not exclude patients with ventricular diastolic dysfunction, given the important association of this disease with AF. Patients with LV diastolic dysfunction will be expected to have a higher stiffness index, given that elevated LV end-diastolic pressure will result in higher opening pressures for the mitral valve, increasing ΔP. This is a single-center, small size cohort that needs to be reproduced and verified. In this study, we were unable to compare the LA stiffness index with control groups because of the invasive nature of the LAP measurement that would pose inappropriate risk for control group. Hence, LA stiffness index is assessed in selective AF patients undergoing CA and cannot be generalized to the overall AF population. There is no gold standard available for LA diastolic function assessment to validate this method. However, the trends and findings seen in this study are in agreement with LA diastolic function studies reported previously.

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References


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