Pre-Excistent Left Atrial Scarring in Patients Undergoing Pulmonary Vein Antrum Isolation
An Independent Predictor of Procedural Failure

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**OBJECTIVES**
The goal of this study was to assess the impact of left atrial scarring (LAS) on the outcome of patients undergoing pulmonary vein antrum isolation (PVAI) for atrial fibrillation (AF).

**BACKGROUND**
Left atrial scarring may be responsible for both the perpetuation and genesis of AF. A total of 700 consecutive patients undergoing first-time PVAI were studied. Before ablation, extensive voltage mapping of the left atrium (LA) was performed using a multipolar Lasso catheter guided by intracardiac echocardiography (ICE). Patients with LAS were defined by a complete absence of electrographic recording by a circular mapping catheter in multiple LA locations, and this was validated by electroanatomic mapping. All four pulmonary vein antra and the superior vena cava were isolated using an ICE-guided technique. Patients were followed at least nine months for late AF recurrence. Univariate and multivariate analyses were performed to assess the predictive value of LAS and other variables on outcome.

**METHODS**
A total of 700 consecutive patients undergoing first-time PVAI were studied. Before ablation, extensive voltage mapping of the left atrium (LA) was performed using a multipolar Lasso catheter guided by intracardiac echocardiography (ICE). Patients with LAS were defined by a complete absence of electrographic recording by a circular mapping catheter in multiple LA locations, and this was validated by electroanatomic mapping. All four pulmonary vein antra and the superior vena cava were isolated using an ICE-guided technique. Patients were followed at least nine months for late AF recurrence. Univariate and multivariate analyses were performed to assess the predictive value of LAS and other variables on outcome.

**RESULTS**
Of 700 patients, 42 had LAS, which represented 21 ± 11% of the LA surface area by electroanatomic mapping. Patients with LAS had a significantly higher AF recurrence (57%) compared with non-LAS patients (19%, p = 0.003). Also, LAS was associated with a significantly larger LA size, lower ejection fraction, and higher C-reactive protein levels. Univariate analysis revealed age, nonparoxysmal AF, and LAS as predictors of recurrence. Multivariate analysis showed LAS as the only independent predictor of recurrence (hazard ratio 3.4, 95% confidence interval 1.3 to 9.4; p = 0.01).

**CONCLUSIONS**
Pre-existent LAS in patients undergoing PVAI for AF is a powerful, independent predictor of procedural failure. Left atrial scarring is associated with a lower EF, larger LA size, and increased inflammatory markers. (J Am Coll Cardiol 2005;45:285–92) © 2005 by the American College of Cardiology Foundation

Electrical and structural remodeling of the atrium occurs in patients with atrial fibrillation (AF) and structural heart disease (1). In particular, studies have demonstrated that some patients with atrial arrhythmias have spontaneous atrial scarring characterized by discrete regions of low voltage (2). These changes in substrate may be responsible for both the perpetuation and genesis of AF. The mechanism for this scarring, as well as its relationship to clinical outcome, is not well known.

Catheter ablation of AF using the technique of pulmonary vein antrum isolation (PVAI) has emerged as an effective therapy for patients with symptomatic AF (3). However, although there have been numerous studies examining the predictors of AF recurrence after electrical cardioversion or with antiarrhythmic therapy (4,5), little is known about predictors of recurrence after PVAI. Specifically, it is unknown whether the presence of atrial scarring has any impact on post-PVAI outcome. Left atrial scarring (LAS) may serve as a substrate for slow conduction and intra-atrial re-entry, which may predispose to future atrial arrhythmia (6,7). Thus, the goals of this study were to characterize LAS and to assess its impact on the long-term procedural outcome in patients undergoing first-time PVAI for treatment of AF.

**METHODS**

**Study population.** Consecutive patients presenting to our institution for first-time PVAI for treatment of AF between January 2002 and August 2003 were included in this study. Patients presenting for repeat PVAI or with a history of any previous catheter ablation were excluded from the study. Patients with previous cardiac surgery were also excluded from the study. Patients selected for PVAI all had symptomatic AF, which was paroxysmal, persistent, or permanent and refractory to two or more antiarrhythmic drugs. A total of 700 patients were identified and included in the study. All patients gave written, informed consent before the mapping and ablation procedures, and collection of patient data was performed in accordance with institutional ethics guidelines.

**PVAI procedure.** All patients underwent PVAI using an intracardiac echocardiography (ICE)-guided technique, which is summarized here but described in extensive detail.
LA mapping and definition of scar. Before PVAI, all patients underwent detailed voltage mapping of the LA. Mapping was always performed in sinus rhythm whenever possible. For those patients in AF at the start of the procedure, external direct current cardioversion was performed to convert the patient to sinus rhythm to allow mapping. If necessary, more than one cardioversion was performed if AF recurred during mapping. In some patients with permanent AF who could not be cardioverted to sinus for even a few beats before ablation, mapping had to be performed in AF.

Because we do not routinely use an electroanatomic mapping system for PVAI, voltage mapping was initially performed in all patients using the 20-mm diameter decapolar circular (Lasso) mapping catheter. The catheter was used to map the entire LA, including the posterior wall, anterior wall, and roof, while staying outside of the PVs. Both ICE and fluoroscopy guided Lasso movement and position in the LA. Contact between the Lasso and atrial surface was confirmed using ICE. Bipolar electrograms (EGMs) were recorded and filtered at 30 to 400 Hz. Provided that the Lasso had good atrial contact, patients with LAS were identified by a complete absence of atrial EGMs seen in all 10 poles of the circular mapping catheter in at least three distinct Lasso positions in the LA. In order to validate our definition and more accurately quantify the extent of scarring, all patients in the LAS group enrolled after January 2003 had electroanatomic mapping of the LA performed using the CARTO system (Biosense Webster Inc.). For comparison, we also performed CARTO maps of the LA in a subset of consecutive patients in the non-LAS group (some of these CARTO maps were also performed as part of another study). Mapping was performed with a 4-mm-tip catheter (Navistar, Biosense Webster Inc.). For CARTO mapping, “scar” was defined as an absence of voltage or a bipolar voltage amplitude ≤0.05 mV indistinguishable from noise; low-voltage “abnormal” areas were defined as an amplitude ≤0.5 mV, as reported elsewhere (2,9). The CARTO system is able to measure the distance between any two points. Using the assumption that a scarred segment of LA could be divided into multiple smaller rectangular or trapezoidal shapes, the area of the segment could be approximated by summing the areas of the smaller shapes. This segment was then expressed as a percentage of the total approximated LA surface area (assessed by the same technique) excluding the tubular portion of the PVs. A similar technique has been previously reported for mapping the left ventricle (10).

Biochemical markers. All patients had serum drawn just before PVAI for assessment of C-reactive protein (CRP) and brain natriuretic peptide (BNP) levels. The CRP levels were assayed by immunonephelometry using the Dade Behring BNIII analyzer protocol (Dade Behring, Deerfield, Illinois). The BNP levels were determined using the assay by Biosite Diagnostics (San Diego, California).

Follow-up. After the procedure, patients continued anti-coagulation with warfarin to maintain an international normalized ratio of 2.0 to 3.0 for a minimum of three months. In all patients, antiarrhythmic medications were continued for two months after ablation and were chosen from one of sotalol, propafenone, flecainide, or dofetilide. Amiodarone was not used after ablation. Antiarrhythmic medications were discontinued in all patients after two months.

Late recurrence of AF was defined as AF occurring beyond two months after PVAI. Thus, success was defined as a lack of late AF recurrence off antiarrhythmic medication. All patients included in this study were followed up for a minimum of nine months after ablation and successfully underwent our follow-up procedures. All patients wore rhythm transmitters for a minimum of three months after
RESULTS

Patient characteristics with and without LAS. Of the 700 patients included in the study, 42 (6%) had LAS, as defined in the Methods section. The characteristics of the patients with and without LAS are listed in Table 1. A strong trend was observed in which a lower proportion of patients with LAS presented with paroxysmal AF (11\% of 42) compared with those without LAS (263 [40\%] of 658), but this difference was not quite statistically significant (p = 0.07). Patients with LAS had a significantly larger LA size compared with patients without LAS, with mean values of 4.9 ± 0.7 cm and 4.0 ± 0.8 cm, respectively (p = 0.03). The mean ejection fraction (EF) was also lower in patients with LAS compared with patients without it, with mean values of 49 ± 8% and 54 ± 7%, respectively (p = 0.03).

Late recurrence of AF after PVAI (beyond two months) was significantly higher in patients with LAS (24 [57\%] of 42) compared with patients without LAS (128 [19\%] of 658; p = 0.003). Kaplan-Meier curves describing late AF recurrence in patients with and without LAS are depicted in Figure 1. The mean time to late recurrence for patients with LAS was 101 ± 49 days versus 133 ± 40 days for patients without LAS (p = 0.17). Of the patients who recurred, 17 of 24 in the LAS group and 117 of 128 in the non-LAS group underwent a second procedure. After this second procedure, 3 (18\%) of 17 LAS patients and 57 (49\%) of 117 non-LAS patients remained free of AF. Using these second procedure success rates and assuming that all patients with recurrence underwent a second PVAI, the overall cure rate after two procedures would have been 52\% in LAS patients and 90\% in non-LAS patients.

As indicated in Table 1, the mean age, AF duration, and incidence of structural heart disease (any hypertensive, coronary, valvular, or cardiomyopathic disease) were no different in the two groups (p = NS for all). Isolation of all four PV antra was achieved in all of the patients in both LAS and non-LAS groups at the end of the ablation procedure (as described in the Methods section). Procedure time and total radiofrequency time did not differ between the groups (Table 1).

### Table 1. Characteristics of Patients With and Without Left Atrial Scarring

<table>
<thead>
<tr>
<th></th>
<th>LA Scar (n = 42)</th>
<th>No LA Scar (n = 658)</th>
<th>p Value</th>
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<tbody>
<tr>
<td>Age (yrs)</td>
<td>59 ± 13</td>
<td>53 ± 13</td>
<td>0.09</td>
</tr>
<tr>
<td>Paroxysmal AF (%)</td>
<td>11 (26%)</td>
<td>263 (40%)</td>
<td>0.07</td>
</tr>
<tr>
<td>AF duration (yrs)</td>
<td>7.0 ± 4.9</td>
<td>6.1 ± 5.4</td>
<td>0.39</td>
</tr>
<tr>
<td>Structural heart disease (%)</td>
<td>20 (48%)</td>
<td>289 (44%)</td>
<td>0.72</td>
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<tr>
<td>LA size (cm)</td>
<td>4.9 ± 0.7</td>
<td>4.0 ± 0.8</td>
<td>0.03*</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>49 ± 8%</td>
<td>54 ± 7%</td>
<td>0.03*</td>
</tr>
<tr>
<td>C-reactive protein (mg/l)</td>
<td>5.93 ± 7.75</td>
<td>0.31 ± 0.68</td>
<td>0.01*</td>
</tr>
<tr>
<td>Brain natriuretic peptide (pg/ml)</td>
<td>191 ± 92</td>
<td>110 ± 80</td>
<td>0.06</td>
</tr>
<tr>
<td>Procedure time (min)</td>
<td>168 ± 47</td>
<td>162 ± 40</td>
<td>0.27</td>
</tr>
<tr>
<td>RF time (min)</td>
<td>47 ± 25</td>
<td>45 ± 28</td>
<td>0.48</td>
</tr>
<tr>
<td>AF recurrence (%)</td>
<td>24 (57%)</td>
<td>128 (19%)</td>
<td>0.003*</td>
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</table>

*Significant value (p < 0.05). Data are presented as the mean value ± SD or number (%) of patients.

AF = atrial fibrillation; LA = left atrial; RF = radiofrequency.

The mean follow-up time for all patients in this study was 15.8 ± 7.8 months.

**Statistical analysis.** All data are reported as the mean value ± SD, unless otherwise indicated. A collection of the characteristics of patients with and without LAS and univariate analysis to assess the predictive value of clinical variables on AF recurrence was performed using the unpaired, independent samples t test for continuous variables, and the chi-square test for categorical variables. Multivariate analysis was performed using Cox regression analysis, with a determination of a hazard ratio and its 95\% confidence interval (CI) for each variable in the model. Survival curves describing freedom from AF in LAS and non-LAS patients were determined using the Kaplan-Meier method. Survival curves were compared using the log-rank test. A p value of <0.05 was considered significant for all statistical determinations. All analyses were performed using SPSS software version 11.0 (SPSS, Chicago, Illinois).
Biochemical markers with and without LAS. The CRP and BNP results for patients with and without scar are compared in Table 1. The CRP levels were significantly higher in patients with LAS compared with patients without it. The LAS patients had a mean CRP level of $5.93 \pm 7.75 \text{ mg/l}$, as compared with $0.31 \pm 0.68 \text{ mg/l}$ in patients without LAS ($p < 0.01$). There was a strong trend toward higher BNP levels in patients with LAS, but this did not reach statistical significance. The mean BNP level was $191 \pm 92 \text{ pg/ml}$ in LAS patients compared with $110 \pm 80 \text{ pg/ml}$ in non-LAS patients ($p = 0.06$). The mean serum creatinine was no different between the LAS and non-LAS groups ($1.1 \pm 0.3 \text{ vs. } 1.2 \pm 0.4 \text{ mg/dl}$, $p = 0.51$). The percentage of patients taking statins and angiotensin-converting enzyme inhibitors also did not differ between the two groups ($p = \text{NS}$ for both).

Electroanatomic mapping of LAS. Of the 42 patients with LAS included in the study, 19 underwent electroanatomic mapping with CARTO. A total of 115 consecutive CARTO maps were performed in patients without LAS. A mean of 164 $\pm 68$ points was acquired for each map. Mapping had to be performed in AF for 2 (10%) of 19 and 8 (7%) of 115 of LAS and non-LAS patients, respectively. The presence of multiple, large regions of scar (as defined earlier) was confirmed in all of the CARTO maps for LAS patients. Scar covered an average of $21 \pm 11\%$ of the estimated LA surface area. In LAS patients, scar was also associated with extensive low-voltage regions. A representative example of a CARTO voltage map in a patient with LAS is shown in Figure 2. In contrast, very small, isolated regions of scar were identified in only 6 (5%) of 115 non-LAS patients, covering <5% of the estimated LA area. This small subset did not significantly differ in clinical characteristics from the rest of the non-LAS group. Mean voltage in LAS patients was $1.3 \pm 0.4 \text{ mV}$ compared with $2.1 \pm 0.6 \text{ mV}$ in non-LAS patients ($p = 0.02$). When the voltage data from patients in refractory AF are excluded, mean voltage in LAS patients was $1.4 \pm 0.4 \text{ mV}$, as compared with $2.2 \pm 0.7 \text{ mV}$ in non-LAS patients ($p = 0.03$).

Univariate predictors of late AF recurrence. Univariate predictors of late AF recurrence are detailed in Table 2. There were a total of 152 recurrences in the total population of 700 patients. Of the variables analyzed, only the presence of LAS, age, and nonparoxysmal AF were found to be significant predictors of late AF recurrence. The presence of LAS was the most significant of the univariate predictors. Twenty-four (16%) of 152 patients with recurrence had LAS, as compared with 18 (3%) of 548 of patients without recurrence ($p = 0.002$). Patients with recurrence were older
than patients without recurrence (52 ± 11 years; p = 0.01). More patients with recurrence also had nonparoxysmal AF (75% vs. 57%, p = 0.047). Other variables, including LA size, EF, gender, AF duration, and number of antiarrhythmic medications that failed, were not significantly different in the recurrence and non-recurrence groups. We did not find a significant difference in CRP or BNP levels in patients with and without recurrence.

The same univariate predictors were found to be significant in the subset of patients with CARTO maps as for the entire cohort.

Multivariate predictors of late AF recurrence. Multivariate predictors of late AF recurrence are depicted in Figure 3. Only the presence of LAS was a significant independent predictor of late AF recurrence when combined with other clinical variables in Cox regression modeling. The hazard ratio for recurrence in patients with LAS was 3.4 (95% CI 1.3 to 9.4, p = 0.01). Age and nonparoxysmal AF were not found to be significant independent predictors. The hazard ratio for age (per decade) was 1.33 (95% CI 0.86 to 2.10, p = 0.21); for nonparoxysmal AF, it was 1.57 (95% CI 0.80 to 2.68, p = 0.18).

DISCUSSION

Main findings. This study describes an important risk factor for AF recurrence in patients who have undergone AF catheter ablation. In patients undergoing PVAI for AF, LAS is a powerful, independent predictor of long-term recurrence after the procedure. In fact, using multivariate analysis, LAS was the only variable that significantly predicted post-PVAI AF recurrence. Not only is LAS associated with a higher AF recurrence rate, but it is also associated with a larger left atrial size, lower EF, and higher levels of both CRP and BNP. Left atrial scarring detected by contact voltage mapping with a multipolar circular catheter also correlates to substantial surface areas of scar and abnormal atrium, as detected by three-dimensional electroanatomic mapping. This study presents quite a large cohort of PVAI patients to systematically examine the risk factors for AF recurrence after the procedure. It also uniquely identifies scarring in the LA as a risk factor for AF recurrence in the post-PVAI population.

Because our PVAI technique and that of many others do not routinely use electroanatomic mapping, we initially identified LAS patients using a Lasso catheter. An absence of EGM was chosen for an objective definition that is easily reproducible and applicable in both sinus rhythm and AF. The observation that CARTO mapping confirmed the

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<th>Table 2. Univariate Predictors of Late Atrial Fibrillation Recurrence</th>
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<tr>
<td>Scar (n)</td>
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<tr>
<td>Age (yrs)</td>
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<tr>
<td>Nonparoxysmal AF (n)</td>
</tr>
<tr>
<td>Male gender (n)</td>
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<tr>
<td>AF duration (yrs)</td>
</tr>
<tr>
<td>Antiarrhythmic drugs failed (n)</td>
</tr>
<tr>
<td>Structural heart disease (n)</td>
</tr>
<tr>
<td>LA size (cm)</td>
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<tr>
<td>Ejection fraction (%)</td>
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<td>C-reactive protein (mg/l)</td>
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<td>Brain natriuretic peptide (pg/ml)</td>
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*Significant value (p < 0.05). Data are presented as the number (%) of patients or mean value ± SD.

Abbreviations as in Table 1.

Figure 3. Multivariate predictors of late atrial fibrillation (AF) recurrence as assessed by Cox regression analysis. Hazard ratios are indicated by the square points, and the 95% confidence interval (CI) is indicated by the solid horizontal lines. P values for each variable are indicated at the right. Only left atrial (LA) scarring was found to be an independent predictor, with a hazard ratio of 3.4 (95% CI 1.3 to 9.4, p = 0.01). EF = ejection fraction; HD = heart disease.
presence of extensive scar versus none/minimal in LAS versus non-LAS patients, respectively, validates our method of defining LAS patients.

Very small, isolated scar was found in a small minority of non-LAS patients. This is not surprising given that scarring may be a prevalent phenomenon. The fact that this group did not differ significantly from the rest of the non-LAS cohort suggests that only patients with a larger scar burden are at risk of procedural failure.

**Relationship of LAS to other AF predictors.** Several of the risk factors for AF recurrence that we identified have been reported in other clinical settings. Age, EF, nonparoxysmal AF, and LA size have all been shown to predict AF recurrence after cardioversion and in other clinical settings (4,5,11,12). In the only other large series of AF ablation patients, only LA size was shown to be a univariate predictor of post-ablation recurrence in permanent AF patients (13). However, we found that when combined with LAS in a multivariate model, none of these variables was an independent predictor of recurrence. That is because we demonstrated that nonparoxysmal AF, lower EF, and larger LA size were all related to LAS. Patients with LAS also trended toward being older. By combining several features that are known to predict AF recurrence, LAS becomes a very powerful predictor. Left atrial scarring may be the final link that characterizes a population at highest risk of recurrence after PVAI.

**Relationship of LAS to recurrence.** From our data, we cannot conclude whether LAS is the direct cause of AF recurrence or whether it is an associated condition. However, our findings are consistent with other studies that have reported on the association between scarring and AF. Increased amounts of atrial fibrosis are found in the atria of AF patients (14) and have been directly implicated as a cause of increased AF prevalence in postoperative patients (7). This is because scarring is likely an important etiologic factor in AF persistence. Chronic atrial fibrosis and scarring alter intraatrial conduction and increase atrial effective refractory periods (2,6). Altered conduction and barriers formed by the scar may form the critical circuits for intra-atrial re-entry that promote AF persistence. Indeed, atrial fibrosis may be more important than electrical substrate changes for the maintenance of AF (15,16).

By altering the atrial substrate, scarring may increase vulnerability to AF induction by sources apart from the PV antral area. Ectopy beyond the PV region less commonly triggers AF (17), perhaps because of longer coupling intervals and reduced firing frequency (18), which cannot easily induce AF in normal tissue. This explains why isolation of the PV antra is curative of AF in 80% to 90% of patients. However, atrial fibrosis can lead to AF induction by burst or premature atrial pacing that otherwise fails to cause AF in normal hearts (19,20). Scar may also predispose patients to left atrial flutters caused by left or right atrial triggers, which in turn may degenerate into AF. Even the incidence of non-PV region sources may be higher with fibrosis. Myopathic atrial cells can demonstrate abnormal triggered activity (21,22), and atrial remodeling can increase the rate and organization of depolarization waves emanating from focal sources, promoting formation of intraatrial rotors (23). Thus, it is very plausible that the LAS directly contributes to PVAI failure.

Scarring did not lead to procedural failure because of an inability to achieve the end point of PV isolation. The procedures were not technically more demanding in scar patients, with durations and fluoroscopy times very similar to those of nonscar patients. If anything, patients with scar presenting for their first or second ablation had fewer PV potentials than those without scar, which is not surprising given that these patients have much less electrically active tissue to begin with.

The possibility that LAS is simply an associated “by-stander” in patients with AF recurrence must also be considered. Atrial fibration itself causes structural changes within the atrium (24), so LAS may simply reflect preexisting AF burden. Furthermore, we do not know the exact pathologic correlate of LA scar. Although fibrosis is most likely, other substrates cannot be ruled out. Atrial amyloid, for example, may be a stronger predictor of AF than fibrosis (25).

**Etiology of LAS.** Several mechanisms have been implicated in the formation of scar in the atrium. Chronic AF itself may result in structural remodeling (24). Patients with CHF may develop diffuse fibrotic changes in the atrium secondary to a pan-myocardial remodeling effect (2). However, there is an increasing amount of data showing that inflammatory mediators and vasoactive peptides may play a key causative role in atrial structural remodeling (26,27).

Therefore, it is intriguing that we observed a higher mean CRP level in patients with LAS. This is consistent with other data demonstrating an association between CRP and the risk of future AF (28) and failure of cardioversion for AF (29). It is possible that elevated CRP levels represent a pro-inflammatory state that is directly responsible for atrial scar formation. Inflammation may directly cause atrial fibrosis via oxidative damage (26). Furthermore, therapies that reduce CRP levels, such as statins, can decrease structural changes and AF burden in animal models (30). However, whether elevations in CRP are causative or simply a marker of atrial remodeling cannot be definitively determined by our data.

Levels of BNP were also higher in patients with LAS, although this difference barely missed being statistically significant (p = 0.06). Brain natriuretic peptide is associated with worsening cardiac function and is prognostic of cardiovascular events (31). However, it too may play a direct role in cardiac remodeling, along with other peptides such as angiotensin II (27). Our data thus present novel clinical associations that may form the basis for further study into the etiology of atrial scar formation.

**Clinical implications.** By identifying patients with LAS at the time of PVAI, operators can immediately predict a high
chance of procedural failure. Based on this finding, it may be possible to alter therapy in this select group to maximize success. Patients with LAS may require routine detailed mapping of the scar with ablation of all potential isthmuses that can cause intra-atrial re-entry to minimize recurrence. A second procedure does not appreciably increase the cure rate, so perhaps repeat PVAI should not be routinely offered. The goal of total freedom from antiarrhythmic therapy may also need to be revised in this group, and combination ablation with long-term drug therapy may be the most effective approach. Finally, adjuvant therapy with statins and/or angiotensin-converting enzyme inhibitors in LAS patients may prove promising in helping to limit and perhaps reverse scar formation and AF burden.

**Study limitations.** The overall success rates reported in the non-LAS patients here are somewhat lower than but consistent with recent reports by our group. We report one- and two-procedure success rates of 81% and 90%, respectively, versus 83% to 85% and 93% to 98% by Khaykin et al. (8). The high end of the success rates in their report represents patients with purely lone AF, as opposed to this non-LAS cohort, which is a heterogeneous group with structural heart disease. Furthermore, our current report includes patients treated by multiple operators (currently five) in contrast to previous reports where one operator was predominantly doing PVAI.

Furthermore, LAS is a risk factor that can only be determined invasively at the time of the procedure. Left atrial scarring cannot be used to preempt PVAI in patients at very high risk of recurrence. It would be ideal if a combination of clinical variables, ECG criteria, and a noninvasive imaging technique could predict scar before PVAI.

The prevalence of scar reported in our “control” group may be lower than expected. This may reflect a selection bias given that fewer than one-half the patients had structural heart disease, and the majority had preserved EF. Also, our definition of scar is based on voltage mapping alone and not on the ability to capture at high-output pacing. Although this may be a limitation, the definition of scar using voltage alone has been validated (33) and used extensively in previous studies (2,10). It may also be technically challenging to access and maintain good contact with the Lasso in some parts of the LA, particularly the septal aspect of the anterior wall. However, these areas do not represent large portions of the LA, and despite the challenges, we have been able to map these regions consistently in patients. Finally, the length of follow-up and biases inherent to cohort studies may limit our conclusions. However, our post-PVAI cohort represents one of the longer follow-up durations published to date.

**Conclusions.** Pre-existent LAS in patients undergoing PVAI for AF is a powerful, independent predictor of procedural failure. Left atrial scarring is associated with a lower EF, larger LA size, and increased inflammatory markers. This study serves as a basis for further investigation into the cause of LAS and its exact relationship to AF recurrence.

**REFERENCES**