Adenosine-Induced Pulmonary Vein Ectopy as a Predictor of Recurrent Atrial Fibrillation After Pulmonary Vein Isolation

Jim W. Cheung, MD; Frank S. Lin, MD; James E. Ip, MD; Seth R. Bender, MD; Faisal K. Siddiqi, MD; Christopher F. Liu, MD; George Thomas, MD; Steven M. Markowitz, MD; Bruce B. Lerman, MD

Background—Adenosine can unmask dormant pulmonary vein (PV) conduction after PV isolation. Adenosine can also induce ectopy in electrically silent PVs after isolation, possibly via activation of autonomic triggers. We sought to identify the implications of adenosine-induced PV ectopy for atrial fibrillation (AF) recurrence after PV isolation.

Methods and Results—A total of 152 patients (age, 60±11 years; 63% paroxysmal AF) undergoing PV isolation for AF were studied. After each PV was isolated, adenosine was administered and the presence of adenosine-induced PV reconnection and PV ectopy were recorded. Dormant conduction was targeted with additional ablation. Adenosine-induced PV ectopy was seen in 45 (30%) patients, and dormant conduction was seen in 44 (29%) patients. After a median follow-up of 374 days, 48 (32%) patients had recurrent AF after a single ablation procedure. Rates of freedom from AF among patients with adenosine-induced PV ectopy were significantly lower than patients without adenosine-induced PV ectopy (63% versus 76% at 1 year; log rank, 0.014). Rates of freedom from AF among patients with dormant conduction were also lower than patients without dormant conduction (64% versus 76% at 1 year; log rank, 0.062). With multivariate analysis, adenosine-induced PV ectopy was found to be the only independent predictor of AF after PV isolation (hazard ratio, 1.90; 95% confidence interval, 1.06–3.40; \(P=0.032\)).

Conclusions—Adenosine-induced PV ectopy is a predictor of recurrent AF after PV isolation and may be a marker of increased susceptibility to autonomic triggers of AF. (Circ Arrhythm Electrophysiol. 2013;6:1066-1073.)

Key Words: adenosine • atrial fibrillation • catheter ablation

Because the identification of pulmonary vein (PV) ectopy as an important trigger of atrial fibrillation (AF),1,2 electrical isolation of PVs has been thought to be the cornerstone of ablative treatment of AF.3 However, recurrence rates of AF after PV isolation remain substantial and have been linked, in part, to conduction recovery between previously isolated PVs and the left atrium.4,5 Adenosine has been shown to induce transient reconnection of isolated PVs after ablation, consistent with dormant conduction (DC) between the PVS and the left atrium.4,5 The role of additional ablation guided by adenosine testing for DC is unclear. Although 1 study showed similar rates of freedom from AF among patients with and without adenosine-induced PV reconnection after DC was targeted,6 another study found higher AF recurrence rates among patients with DC even after additional ablation.7

Clinical Perspective on p 1073

Recently, we have shown that adenosine can also induce PV ectopy in electrically silent PVS after isolation.8 The mechanism of adenosine-induced PV ectopy after PV isolation is unclear, but we have postulated that this phenomenon may be because of the activation of autonomic triggers from the adenosine bolus response. The clinical implications of adenosine-induced PV ectopy have not been elucidated. Therefore, we sought to assess the prognostic significance of adenosine-induced PV ectopy and adenosine-induced DC for recurrent AF after PV isolation.

Methods

Study Population

We evaluated 156 consecutive patients who were referred to Weill Cornell Medical Center—New York Presbyterian Hospital for first-time catheter ablation of paroxysmal or persistent symptomatic drug-refractory AF. Paroxysmal AF and persistent AF were defined as per Heart Rhythm Society Consensus Statement guidelines.8 After exclusion of 4 patients who had <90 days of follow-up, a total of 152 patients was included in the final analysis. This study was approved by the Weill Cornell Medical College Institutional Review Board.

Electrophysiology Study

Written informed consent was obtained from all patients before the procedure. The procedure was performed as previously described.9 Procedures were performed under intravenous sedation (N=136) or general anesthesia (N=16). Electroanatomic mapping was performed using CARTO (Biosense Webster, Diamond Bar, CA) or Ensite NavX.
Cheung et al  Adenosine-Induced Pulmonary Vein Ectopy and Recurrent AF  1067

(St Jude Medical, St Paul, MN) mapping system. Using intracardiac echocardiography (Siemens AcuNav, Malvern, PA) guidance, double transseptal access was performed, and circular mapping catheters were used for mapping and recording of PV potentials.

**PV Isolation**

Radiofrequency ablation was performed using a 3.5-mm (Thermocool; Biosense Webster) or 4-mm (Safire Blue; St Jude Medical) open-irrigation ablation catheter advanced via an 8.5 Fr sheath. Circumferential ablation was performed around the left and right PVs with power ≤45 W (≤30 W and ≤30 seconds on the posterior wall) to achieve ≥75% reduction in electrogram amplitude and 5 to 10 Ω impedance drop with temperature ≤42°C. After completion of the ablation lesion set, a circular mapping catheter was used into each PV to assess for isolation. The endpoint of ablation was complete PV isolation with both (1) entrance block with dissociation of PV potentials or complete abolition of PV potentials and (2) exit block with absence of left atrial capture with high output pacing at each bipolar pair of the circular mapping catheter at the PV ostium. If the patient remained in AF after attainment of PV entrance block, DC cardioversion was performed to allow pacing to assess for exit block. In patients with persistent AF, additional ablation of complex fractionated electrograms and non-PV triggers elicited by isoproterenol testing was performed at the discretion of the operator after PV isolation and adenosine testing.

**Adenosine Testing**

After completion of the circumferential ablation lesion set with isolation of each PV, the presence of any dissociated PV ectopy was noted as previously described.12 Adenosine testing was then performed. A 12-mg intravenous bolus of adenosine was injected followed by a flush of 20 mL of normal saline. The presence of adenosine-induced PV reconnection was noted (Figure 1). In addition, if spontaneous PV ectopy was not observed at baseline (ie, isolated PVs after ablation were electrically silent for ≥5 minutes before adenosine testing), the induction of PV ectopy after adenosine administration was defined as adenosine-induced PV ectopy (Figure 2). All sites of adenosine-induced PV reconnection were targeted for ablation. Repeat adenosine testing was performed, and residual DC was noted and retargeted with additional ablation as needed. At >20 minutes after initial PV isolation, all PVs were reinterrogated for acute reconnection, and additional ablation was performed as needed.

**Figure 1.** Adenosine (ADO)–induced pulmonary vein (PV) reconnection. Surface ECG leads I, aVF, and V1 are displayed at the top. Electrograms (PV1–PV19) from the PV ostium are shown at the bottom.

**Figure 2.** Adenosine (ADO)–induced pulmonary vein (PV) ectopy. Surface ECG leads I and V1 are displayed at the top, coronary sinus electrograms (CS1–CS10) are displayed in the middle, and electrograms (PV1–PV19) from the PV ostium are shown at the bottom. Administration of ADO results in AV block (*) and induction of 2 beats of dissociated PV ectopy (thin arrows).
Follow-Up
Patients were monitored with 7- to 14-day continuous mobile telemetry monitors 3, 6, and 12 months after ablation or more frequently if symptoms were reported. Telephone follow-up was also performed at 6-month intervals to assess for recurrent symptoms. In patients with implanted devices (N=10), interrogations were performed at 3-month intervals to assess for arrhythmia recurrence. Recurrence of AF was defined as any atrial tachycardia or AF recorded lasting ≥30 seconds after a 3-month blanking period after ablation. At 3 to 6 months, if no recurrent AF was seen, cessation of antiarrhythmic drug therapy was recommended for all patients. Repeat ablation was recommended for all patients with symptomatic recurrent AF. During repeat ablation for recurrent AF, all PVs were mapped and the presence of chronic PV reconnection was recorded.

Statistical Analysis
Continuous variables are expressed as mean±SD or median (interquartile range [IQR], 25th percentile, 75th percentile) depending on normality of distribution. Comparison of continuous variables was performed using Student t test, whereas comparison of categorical variables was performed using the χ² test or Fisher exact test. Survival plots were generated using Kaplan–Meier survival analysis. Comparisons between survival curves were performed using the log-rank test. Clinical characteristics including the presence of adenosine-induced PV reconnection and adenosine-induced PV ectopy that were associated with recurrent AF with P value <0.10 were considered as candidates for the regression model of recurrent AF. The proportional hazard assumption was tested using graphical analysis of log–log survival curves. A P value of <0.05 was considered statistically significant. All statistical calculations were performed using SPSS version 19.0 (SPSS Inc, Chicago, IL).

Results
Baseline Characteristics and Prevalence of Adenosine-Induced PV Ectopy and Reconnection
The baseline characteristics of the study patients are displayed in Table 1. All 581 PVs in the 152 study patients were successfully isolated. After excluding 115 PVs with spontaneous PV ectopy at baseline, 63 of 466 (14%) PVs had evidence of adenosine-induced PV ectopy affecting 45 (30%) patients. Of the 63 PVs with adenosine-induced ectopy, 26 (41%) involved the left superior PV, 10 (16%) involved the left inferior PV, 19 (30%) involved the right superior PV, and 8 (13%) involved the right inferior PV. The duration of adenosine-induced PV ectopy was transient, lasting median 2 beats (IQR, 1–3; range, 1–19 beats). A total of 44 (29%) patients had evidence of adenosine-induced PV reconnection affecting 64 of 581 (11%) PVs. All 64 PVs with DC were targeted with additional ablation. Successful ablation of DC shown by repeat adenosine testing was seen with 59 (92%) PVs. Comparison of baseline characteristics of patients with and without adenosine-induced PV ectopy and adenosine-induced PV reconnection is summarized in Table 2.

Association Between Adenosine-Induced PV Ectopy and Dormant Conduction
Patients with DC were more likely to have adenosine-induced PV ectopy when compared with patients without DC, but this trend did not reach statistical significance (39% versus 26%; P=0.12). Of the 466 electrically silent PVs seen after PV isolation in all patients, 27% of the PVs with DC also had adenosine-induced PV ectopy, whereas 12% of PVs without DC had adenosine-induced PV ectopy (P=0.004). Of the 13 PVs that exhibited both adenosine-induced PV reconnection and adenosine-induced PV ectopy, 8 (62%) PVs had evidence of dormant exit conduction (Figure 3).

Predictors of Recurrent AF on Follow-Up
For median follow-up of 374 (IQR, 323–418) days, 48 (32%) patients had evidence of recurrent AF after a single procedure. Of the 104 patients without recurrent AF, 97 (93%) were not taking antiarrhythmic drugs at 1 year. Rates of freedom from AF among patients with adenosine-induced PV ectopy were significantly lower when compared with patients without

Table 2. Comparison of Patients With and Without Adenosine-Induced PV Ectopy and of Patient With and Without Adenosine-Induced PV Reconnection

<table>
<thead>
<tr>
<th></th>
<th>ADO-PV Ectopy (+) Patients (N=45)</th>
<th>ADO-PV Ectopy (-) Patients (N=107)</th>
<th>P Value</th>
<th>Dormant Conduction (+) Patients (N=44)</th>
<th>Dormant Conduction (-) Patients (N=108)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean, y</td>
<td>60±11</td>
<td>60±11</td>
<td>0.83</td>
<td>62±9</td>
<td>60±11</td>
<td>0.26</td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>41 (91)</td>
<td>79 (74)</td>
<td>0.02</td>
<td>34 (77)</td>
<td>86 (80)</td>
<td>0.75</td>
</tr>
<tr>
<td>Paroxysmal AF, n (%)</td>
<td>25 (56)</td>
<td>71 (66)</td>
<td>0.21</td>
<td>29 (66)</td>
<td>67 (62)</td>
<td>0.66</td>
</tr>
<tr>
<td>HTN, n (%)</td>
<td>20 (44)</td>
<td>45 (42)</td>
<td>0.79</td>
<td>23 (52)</td>
<td>42 (39)</td>
<td>0.13</td>
</tr>
<tr>
<td>DM, n (%)</td>
<td>6 (13)</td>
<td>12 (11)</td>
<td>0.71</td>
<td>7 (16)</td>
<td>11 (10)</td>
<td>0.32</td>
</tr>
<tr>
<td>CHF, n (%)</td>
<td>4 (9)</td>
<td>11 (10)</td>
<td>0.79</td>
<td>3 (7)</td>
<td>12 (11)</td>
<td>0.42</td>
</tr>
<tr>
<td>EF, n (%)</td>
<td>58±10</td>
<td>60±11</td>
<td>0.54</td>
<td>60±11</td>
<td>59±11</td>
<td>0.66</td>
</tr>
<tr>
<td>LA size, mean, cm</td>
<td>4.3±0.6</td>
<td>4.2±0.7</td>
<td>0.54</td>
<td>4.0±0.6</td>
<td>4.3±0.7</td>
<td>0.06</td>
</tr>
</tbody>
</table>

ADO indicates adenosine; AF, atrial fibrillation; CHF, congestive heart failure; DM, diabetes mellitus; EF, ejection fraction; HTN, hypertension; LA, left atrial; and PV, pulmonary vein.
adenosine-induced PV ectopy (63% versus 76% at 1 year; log rank, 0.014; Figure 4A). There was a nonsignificant trend toward lower rates of freedom from AF among patients with adenosine-induced PV reconnection when compared with patients without adenosine-induced PV reconnection (64% versus 76% at 1 year; log rank, 0.062; Figure 4B). In a multivariate Cox regression model, adenosine-induced PV ectopy was the only significant independent predictor of recurrent AF. Figure 3. Restoration of bidirectional pulmonary vein (PV) conduction with adenosine (ADO) coincident with AV block after PV isolation. Recordings from the left inferior PV of a patient after PV isolation. Surface ECG leads (I and V1) are displayed at the top, coronary sinus recordings in the middle, and PV recordings are at the bottom. A, Baseline recordings after PV isolation with no evidence of dissociated PV ectopy. B, After ADO administration, AV block is seen coincident with loss of PV entrance block (broad black arrows). Two beats of PV ectopy (*) are induced with evidence of PV exit conduction (dashed arrows) leading to 2 APCs (**). C, Follow-up recordings showing resumption of entrance block. First 2 sinus beats show PV entrance conduction followed by disappearance of PV reconnection.
AF (hazard ratio, 1.9; 95% confidence interval, 1.06–3.40; \( P = 0.032 \); Table 3). Analysis of the interaction effect between adenosine-induced PV ectopy and PV reconnection was significant \( (P = 0.04) \), with a repeat Cox model showing the presence of adenosine-induced PV ectopy and PV reconnection in combination as a significant predictor of recurrent AF (hazard ratio, 2.9; 95% confidence interval, 1.28–6.37; \( P = 0.01 \); Table 4). The effect of the presence of adenosine-induced PV ectopy and DC either in isolation or in combination on AF recurrence is summarized in Figure 5A and 5B.

**Repeat Ablation Findings**

A total of 19 of 48 (40%) patients with recurrent arrhythmia underwent repeat ablation. The reasons for lack of repeat ablation in 60% of patients were patient preference because of lack of significant symptoms or desire to try antiarrhythmic drugs. One patient had cavotricuspid isthmus ablation for atrial flutter. The remaining 18 patients had recurrent AF and underwent repeat ablation at mean 179 (IQR, 107–241) days after the initial procedure. During the repeat procedure, 17 of 18 patients had evidence of chronic reconnection of ≥1 PV, with a median of 2.0 (IQR, 1.8–4.0) PVs reconnected. Overall, the chronic PV reconnection rate was 65% involving 42 of 65 previously isolated PVs. The distribution of the 42 chronically reconnected PVs was 9 (21%) left superior PVs, 11 (26%) left inferior PVs, 10 (24%) right superior PVs, and 12 (29%) right inferior PVs. Among these 18 patients, 5 (28%) patients had DC at the initial procedure involving 7 PVs. Of these 7 PVs, 6 (86%) PVs were chronically reconnected at repeat procedure. A total of 5 (28%) had adenosine-induced PV ectopy at the initial procedure involving 5 PVs. Of these 5 PVs, 3 (60%) PVs were chronically reconnected at repeat procedure. A total of 33 PVs found to have chronic reconnection at repeat ablation did not exhibit either DC or adenosine-induced PV ectopy at initial procedure.

**Discussion**

In this study, we demonstrate that the presence of adenosine-induced PV ectopy is a predictor of recurrent AF after PV isolation. Moreover, despite a strategy of additional ablation to target DC after PV isolation, baseline adenosine-induced PV reconnection was associated with a trend toward increased AF recurrence. However, in a multivariate analysis, DC was not a significant predictor of recurrent AF.

**Adenosine-Induced PV Ectopy as a Marker for Susceptibility to Recurrent AF**

The mechanism behind the association between adenosine-induced PV ectopy and AF recurrence after PV isolation is unclear. We previously postulated that adenosine may lead to activation of autonomic activation of PV triggers.\(^{12}\) In a canine model, injection of acetylcholine into the ganglionated fat pad of the PV–left atrial junction can induce PV firing,\(^{13}\) and acetylcholine and adenosine are known to activate identical signal transduction cascades.\(^{14}\) Hence, adenosine-induced PV ectopy may be partly because of the activation of parasympathetic triggers. Moreover, administration of adenosine as an intravenous bolus can also have significant sympathomimetic effects.\(^{15,16}\) Sympathetic activation, together with parasympathetic activation, is an important component of autonomically triggered PV firing in isolated canine preparations and in intact dogs.\(^{17}\) Adenosine may lead to sympathetically induced increased Ca\(^{2+}\) transients and early afterdepolarizations, as well as parasympathetically induced action potential shortening that promotes autonomically triggered AF.\(^{18,19}\)

Therefore, the presence of adenosine-induced PV ectopy after PV isolation may be a marker of susceptibility to autonomic triggers of AF. Unlike DC, which identifies isolated PVs that are prone to future chronic reconnection, adenosine-induced PV ectopy may reflect intact vagal inputs to the heart which may trigger AF in the future via not only PV foci but also non-PV foci. The role of the autonomic nervous system in the pathogenesis of AF may be significant, and vagal denervation has been proposed by several groups to be an important factor in the prevention of AF.
Table 3. Univariate and Multivariate Predictors of Recurrent AF After a Single Ablation Procedure

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Unadjusted (Univariate)</th>
<th>Adjusted (Multivariate)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hazard Ratio</td>
<td>95% CI</td>
</tr>
<tr>
<td>Age, y</td>
<td>1.00</td>
<td>0.97–1.03</td>
</tr>
<tr>
<td>Men</td>
<td>2.04</td>
<td>0.87–4.81</td>
</tr>
<tr>
<td>Paroxysmal AF</td>
<td>1.56</td>
<td>0.83–2.97</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.01</td>
<td>0.57–1.79</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.51</td>
<td>0.71–3.25</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>0.84</td>
<td>0.30–2.34</td>
</tr>
<tr>
<td>LVEF</td>
<td>1.00</td>
<td>0.98–1.03</td>
</tr>
<tr>
<td>Left atrial size</td>
<td>1.31</td>
<td>0.86–1.99</td>
</tr>
<tr>
<td>Spontaneous PV ectopy</td>
<td>0.68</td>
<td>0.37–1.2</td>
</tr>
<tr>
<td>ADO-induced PV ectopy</td>
<td>2.03</td>
<td>1.14–3.61</td>
</tr>
<tr>
<td>ADO-induced PV reconnection</td>
<td>1.73</td>
<td>0.97–3.10</td>
</tr>
<tr>
<td>ADO-induced PV ectopy × ADO-induced PV reconnection</td>
<td>2.11</td>
<td>2.02–4.36</td>
</tr>
</tbody>
</table>

ADO indicates adenosine; AF, atrial fibrillation; CI, confidence interval; LVEF, left ventricular ejection fraction; and PV, pulmonary vein.

component of AF ablation. Approaches used to target ganglionic plexi for ablation include high-frequency stimulation, localization of fractionated atrial potentials, and direct visualization of fat pads via surgery. Several studies have suggested improved outcomes among patients who have successful vagal denervation during AF ablation.

Dormant Conduction and Recurrent AF

Results from initial retrospective studies have suggested that elimination of DC leads to reduced rates of recurrent AF. However, we found that despite additional ablation to target adenosine-induced PV reconnection, patients with DC continued to have more recurrent AF, a finding consistent with those of Miyazaki et al. We found that 86% of PVs with DC at initial procedure exhibited chronic reconnection on repeat ablation. Moreover, a significant proportion of PVs that were chronically reconnected at repeat ablation did not exhibit DC at the initial procedure, consistent with a low negative predictive value of adenosine-induced PV reconnection for predicting chronic reconnection. Our findings suggest that DC identifies a group of patients in whom durable PV isolation is not easily achieved regardless of additional ablation.

Association Between Adenosine-Induced PV Reconnection and Adenosine-Induced PV Ectopy

We found a higher rate of adenosine-induced PV ectopy among isolated PVs that had DC when compared with PVs without DC although this difference was not significant when the comparison was performed on a per-patient basis. The reasons for this link are unclear because the mechanisms underlying the 2 phenomena are likely distinct. Areas of PVs with thicker musculature, such as the carinal region, have been shown to have a higher prevalence of DC likely because of the difficulty of achieving transmural ablation lesions at those sites. Moreover, PV firing is more commonly seen in PVs with circumferential PV–left atrial connections when compared with PVs with limited and discrete connections. Therefore, PVs with extensive musculature may be more susceptible to both adenosine-induced reconnection and adenosine-induced ectopy. Through our analysis of PVs with both adenosine-induced PV reconnection and adenosine-induced PV ectopy, we were able to demonstrate the phenomenon of dormant PV exit conduction, which has not been previously described. Prior studies of adenosine-induced PV reconnection have only examined DC as manifest by loss of entrance block. Our study provides evidence that adenosine-induced PV reconnection can be bidirectional.

Limitations

First, in an attempt to ensure that adenosine-induced PV ectopy was because of adenosine effect and not coincidental spontaneous PV firing, we excluded PVs that had any evidence of PV ectopy before adenosine testing. However, because of the sporadic nature of spontaneous PV firing after PV isolation, we cannot exclude the occurrence of PV ectopy during adenosine administration that was independent of adenosine effect. Second, we had a limited proportion of patients who underwent repeat ablation, which may have precluded our finding that an association between adenosine testing results during initial ablation and chronic PV reconnection during repeat ablation. Third, we did not record non-PV triggers identified at initial and repeat ablation, which would have allowed investigation of a possible association between adenosine-induced PV ectopy and autonomously mediated non-PV triggers. Fourth, in our study, adenosine administration was performed after PV isolation without incorporation of a waiting period, which

Table 4. Analysis of Interaction Between ADO-Induced PV Ectopy and ADO-Induced PV Reconnection

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No ADO-induced PV ectopy or dormant conduction</td>
<td>Reference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dormant conduction only</td>
<td>1.77</td>
<td>0.82–3.83</td>
<td>0.15</td>
</tr>
<tr>
<td>ADO-induced PV ectopy only</td>
<td>2.12</td>
<td>1.00–4.98</td>
<td>0.05</td>
</tr>
<tr>
<td>ADO-induced PV ectopy and dormant conduction</td>
<td>2.86</td>
<td>1.28–6.37</td>
<td>0.01</td>
</tr>
</tbody>
</table>

ADO indicates adenosine; CI, confidence interval; and PV, pulmonary vein.
may have affected the diagnostic yield of adenosine testing. Finally, because we did not have implanted devices in all our study patients, AF recurrence could have been underdetected, despite the use of mobile cardiac telemetry monitoring.

Conclusions

After PV isolation, adenosine can induce not only transient PV reconnection but also PV ectopy in electrically quiescent PVs. We demonstrate that adenosine-induced PV ectopy is an independent predictor of AF recurrence after PV isolation. Further study is necessary to investigate whether adenosine-induced PV ectopy is a marker of susceptibility to autonomic triggers of AF.

Acknowledgments

We thank Dr Richard B. Devereux for his assistance with review of the article.

Disclosures

Dr Cheung has received speaker honoraria from Medtronic and fellowship grant support from Biosense Webster, Medtronic and St Jude Medical. Dr Liu has received speaker honoraria from St Jude Medical. Dr Thomas has received speaker honoraria from St Jude Medical. The other authors report no conflicts.

References


**CLINICAL PERSPECTIVE**

Although adenosine has largely been used to unmask dormant conduction between the pulmonary veins (PVs) and the left atrium after PV isolation, it has recently been shown that adenosine can also induce PV ectopy in electrically quiescent veins after ablation. The clinical significance of adenosine-induced PV ectopy after pulmonary vein isolation is unclear. In this study of 152 patients undergoing PV isolation for symptomatic atrial fibrillation, we examine the relationship between adenosine-induced PV ectopy and atrial fibrillation–free survival after PV isolation. We demonstrate that adenosine-induced PV ectopy is an independent predictor associated with almost double the risk of atrial fibrillation recurrence after PV isolation. We also find that even with additional ablation to target dormant conduction at initial PV isolation, adenosine-induced PV reconnection is associated with increased recurrent atrial fibrillation although this difference did not reach statistical significance. The mechanism behind the association between adenosine-induced PV ectopy and recurrent atrial fibrillation after PV isolation is unclear. The hypothesis that adenosine-induced PV ectopy may be a marker of increased susceptibility to autonomic triggers of atrial fibrillation warrants further investigation.
Adenosine-Induced Pulmonary Vein Ectopy as a Predictor of Recurrent Atrial Fibrillation After Pulmonary Vein Isolation

Jim W. Cheung, Frank S. Lin, James E. Ip, Seth R. Bender, Faisal K. Siddiqi, Christopher F. Liu, George Thomas, Steven M. Markowitz and Bruce B. Lerman

Circ Arrhythm Electrophysiol. 2013;6:1066-1073; originally published online November 15, 2013;
doi: 10.1161/CIRCEP.113.000796

Circulation: Arrhythmia and Electrophysiology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2013 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-3149. Online ISSN: 1941-3084

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circep.ahajournals.org/content/6/6/1066

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Arrhythmia and Electrophysiology can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Arrhythmia and Electrophysiology is online at:
http://circep.ahajournals.org//subscriptions/