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

Running title: Cheung et al.; Adenosine-Induced Pulmonary Vein Ectopy and Recurrent AF

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Journal Subject Codes: [5] Arrhythmias, clinical electrophysiology, drugs; [22]
Ablation/ICD/surgery
Abstract:

Background - Adenosine (ADO) can unmask dormant pulmonary vein (PV) conduction following PV isolation. ADO can also induce ectopy in electrically silent PVs following isolation, possibly via activation of autonomic triggers. We sought to identify the implications of ADO-induced PV ectopy for atrial fibrillation (AF) recurrence following 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, ADO was administered and the presence of ADO-induced PV reconnection and PV ectopy were recorded. Dormant conduction was targeted with additional ablation. ADO-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 ADO-induced PV ectopy were significantly lower than patients without ADO-induced PV ectopy (63% vs. 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% vs. 76% at 1 year; log rank = 0.062). With multivariate analysis, ADO-induced PV ectopy was found to be the only independent predictor of AF after PV isolation (HR 1.90; 95% CI: 1.06 – 3.40; p = 0.032).

Conclusions - ADO-induced PV ectopy is a predictor of recurrent AF following PV isolation and may be a marker of increased susceptibility to autonomic triggers of AF.

Key words: adenosine, pulmonary vein isolation, atrial fibrillation, catheter ablation
Introduction

Since 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 following PV isolation remain substantial and have been linked in part to conduction recovery between previously isolated PVs and the left atrium.\(^4\),\(^5\) Adenosine (ADO) has been shown to induce transient reconnection of isolated PVs following ablation, consistent with dormant conduction between the PVs and the left atrium.\(^6\),\(^7\),\(^8\),\(^9\)

The role for additional ablation guided by ADO testing for dormant conduction is unclear. While one study showed similar rates of freedom from AF among patients with and without ADO-induced PV reconnection after dormant conduction was targeted\(^10\), another study found higher AF recurrence rates among patients with dormant conduction even after additional ablation.\(^11\)

Recently, we have shown that ADO can also induce PV ectopy in electrically silent PVs following isolation.\(^12\) The mechanism of ADO-induced PV ectopy following PV isolation is unclear, but we have postulated that this phenomenon may be due to the activation of autonomic triggers from the ADO bolus response. The clinical implications of ADO-induced PV ectopy have not been elucidated. We therefore sought to assess the prognostic significance of ADO-induced PV ectopy and ADO-induced dormant conduction for recurrent AF following PV isolation.

Methods

Study population

We evaluated 156 consecutive patients who were referred to Weill Cornell Medical Center – NewYork Presbyterian Hospital for first-time catheter ablation of paroxysmal or persistent
symptomatic drug-refractory AF. Paroxysmal AF and persistent AF were defined as per HRS Consensus Statement guidelines. 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 prior to the procedure. The procedure was performed as previously described. 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 (St. Jude Medical, St. Paul, MN) mapping system. Using intracardiac echocardiography (ICE) (Siemens AcuNav, Malvern, PA) guidance, double transseptal access was performed and circular mapping catheters were used for mapping and recording of PV potentials.

**Pulmonary vein 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/or 5-10 Ω impedance drop with temperature ≤ 42°C. After completion of the ablation lesion set, a circular mapping catheter was 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 following 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 following PV isolation and adenosine testing.

Adenosine testing

Following completion of the circumferential ablation lesion set with isolation of each PV, the presence of any dissociated PV ectopy was noted as previously described.\textsuperscript{12} ADO testing was then performed. A 12 mg intravenous bolus of adenosine was injected followed by a flush of 20 cc of normal saline. The presence of \textit{ADO-induced PV reconnection} was noted (Figure 1).

In addition, if spontaneous PV ectopy was not observed at baseline (i.e., isolated PVs post-ablation were electrically silent for \textgtr 5 minutes prior to ADO testing), the induction of PV ectopy following ADO administration was defined as \textit{ADO-induced PV ectopy} (Figure 2). All sites of ADO-induced PV reconnection were targeted for ablation. Repeat ADO testing was performed and residual dormant conduction was noted and re-targeted with additional ablation as needed.

At > 20 minutes following initial PV isolation, all PVs were re-interrogated for acute reconnection and additional ablation was performed as needed.

Follow-up

Patients were monitored with 7-14 day continuous mobile telemetry monitors 3, 6 and 12 months post 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 \textgtr 30 seconds after a 3-month blanking period post-ablation. At 3-6 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 (IQR: 25th percentile, 75th percentile) depending on normality of distribution. Comparison of continuous variables was performed using Student’s t test while comparison of categorical variables was performed using the Chi square 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 presence of ADO-induced PV reconnection and ADO-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. Cox proportional hazards regression model analysis was used to identify independent predictors 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 ADO-induced PV ectopy affecting 45 (30%) patients. Of the 63 PVs with ADO-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 ADO-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 ADO-induced PV reconnection affecting 64 of 581 (11%) PVs. All 64 PVs with dormant conduction were targeted with additional ablation. Successful abolition of dormant conduction shown by repeat ADO testing was seen with 59 (92%) PVs. Comparison of baseline characteristics of patients with and without ADO-induced PV ectopy and ADO-induced PV reconnection are summarized in Table 2.

**Association between ADO-induced PV ectopy and dormant conduction**

Patients with dormant conduction were more likely to have ADO-induced PV ectopy compared to patients without dormant conduction but this trend did not reach statistical significance (39% vs. 26%; p = 0.12). Of the 466 electrically silent PVs seen following PV isolation in all patients, 27% of the PVs with dormant conduction also had ADO-induced PV ectopy while 12% of PVs without dormant conduction had ADO-induced PV ectopy (p = 0.004). Of the 13 PVs that exhibited both ADO-induced PV reconnection and ADO-induced PV ectopy, 8 (62%) PVs had evidence of dormant exit conduction (Figure 3).

**Predictors of recurrent AF upon follow-up**

Over 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 anti-arrhythmic drugs at 1 year. Rates of freedom from AF among patients with ADO-induced PV ectopy were significantly lower when compared to patients without ADO-induced PV ectopy (63% vs. 76% at 1 year; log rank = 0.014) (Figure 4A). There was a non-significant trend towards lower rates of freedom from AF among patients with ADO-induced PV...
reconnection compared to patients without ADO-induced PV reconnection (64% vs. 76% at 1 year; log rank = 0.062) (Figure 4B). In a multivariate Cox regression model, ADO-induced PV ectopy was the only significant independent predictor of recurrent AF (HR 1.9; 95% CI: 1.06 – 3.40; p = 0.032) (Table 3). Analysis of the interaction effect between ADO-induced PV ectopy and PV reconnection was significant (p = 0.04), with a repeat Cox model showing the presence of ADO-induced PV ectopy and PV reconnection in combination as a significant predictor of recurrent AF (HR 2.9; 95% CI: 1.28 – 6.37; p = 0.01) (Table 3). The impact of the presence of ADO-induced PV ectopy and dormant conduction either in isolation or in combination on AF recurrence are summarized in Figures 5A and B.

**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 due to lack of significant symptoms or desire to try anti-arrhythmic 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 following the initial procedure. During the repeat procedure, 17 of 18 patients had evidence of chronic reconnection of at least one 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 dormant conduction 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 ADO-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 dormant conduction or ADO-induced PV ectopy at initial procedure.

**Discussion**

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

**ADO-induced PV ectopy as a marker for susceptibility to recurrent AF**

The mechanism behind the association between ADO-induced PV ectopy and AF recurrence after PV isolation is unclear. We previously postulated that ADO may lead to activation of autonomic activation of PV triggers. In a canine model, injection of acetylcholine into the ganglionated fat pad of the PV-left atrial junction can induce PV firing and acetylcholine and ADO are known to activate identical signal transduction cascades. Hence, ADO-induced PV ectopy may be partly due to the activation of parasympathetic triggers. Moreover, administration of ADO as an intravenous bolus can also have significant sympathomimetic effects. Sympathetic activation, together with parasympathetic activation, is an important component of autonomically-triggered PV firing in isolated canine preparations and in intact dogs. ADO 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.
Therefore, the presence of ADO-induced PV ectopy following PV isolation may be a marker of susceptibility to autonomic triggers of AF. Unlike dormant conduction which identifies isolated PVs that are prone to future chronic reconnection, ADO-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 component of AF ablation.\textsuperscript{20,21,22} 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.\textsuperscript{22,23,24} Several studies have suggested improved outcomes among patients who have successful vagal denervation during AF ablation.\textsuperscript{20,21}

**Dormant conduction and recurrent AF**

Results from initial retrospective studies have suggested that elimination of dormant conduction leads to reduced rates of recurrent AF.\textsuperscript{8,9} However, we found that despite additional ablation to target ADO-induced PV reconnection, patients with dormant conduction continued to have more recurrent AF, a finding consistent with those of Miyazaki et al.\textsuperscript{11} We found that 86% PVs with dormant conduction at initial procedure exhibited chronic reconnection upon repeat ablation. Moreover, a significant proportion of PVs that were chronically reconnected at repeat ablation did not exhibit dormant conduction at the initial procedure, consistent with a low negative predictive value of ADO-induced PV reconnection for predicting chronic reconnection. Our findings suggest that dormant conduction identifies a group of patients in whom durable PV isolation is not easily achieved regardless of additional ablation.

**Association between ADO-induced PV reconnection and ADO-induced PV ectopy**

We found a higher rate of ADO-induced PV ectopy among isolated PVs that had dormant
conduction compared to PVs without dormant conduction, although this difference was not significant when the comparison was performed on a per-patient basis. The reasons for this link are unclear as the mechanisms underlying the two phenomena are likely distinct. Areas of PVs with thicker musculature such as the carinal region have been shown to have a higher prevalence of dormant conduction, likely to due to 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 to PVs with limited and discrete connections. Therefore, PVs with extensive musculature may be more susceptible to both ADO-induced reconnection and ADO-induced ectopy. Through our analysis of PVs with both ADO-induced PV reconnection and ADO-induced PV ectopy, we were able to demonstrate the phenomenon of dormant PV exit conduction, which has not been previously described. Prior studies of ADO-induced PV reconnection have only examined dormant conduction as manifest by loss of entrance block. Our study provides evidence that ADO-induced PV reconnection can be bidirectional.

**Study limitations**

First, in an attempt to ensure that ADO-induced PV ectopy was due to ADO effect and not coincidental spontaneous PV firing, we excluded PVs that had any evidence of PV ectopy prior to ADO testing. However, due to the sporadic nature of spontaneous PV firing post-PV isolation, we cannot exclude the occurrence of PV ectopy during ADO administration that was independent of ADO effect. Second, we had a limited proportion of patients who underwent repeat ablation, which may have precluded our finding an association between ADO 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 ADO-induced PV ectopy and autonomically-mediated non-PV triggers. Fourth, in our study, ADO administration was performed following PV isolation without incorporation of a waiting period which may have affected the diagnostic yield of ADO testing. Finally, since we did not have implanted devices in all our study patients, AF recurrence could have been under-detected despite the use of mobile cardiac telemetry monitoring.

**Conclusions**

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

**Acknowledgments:** We would like to thank Dr. Richard B. Devereux for his assistance with review of the manuscript.

**Conflict of Interest Disclosures:** Dr. Jim W. Cheung has received speaker honoraria from Medtronic and fellowship grant support from Biosense Webster, Medtronic and St. Jude Medical. Dr. Christopher F. Liu has received speaker honoraria from St. Jude Medical. Dr. George Thomas has received speaker honoraria from St. Jude Medical. The rest of the authors have no relevant disclosures.

**References**


2. Chen SA, Hsieh MH, Tai CT, Tsai CF, Prakash VS, Yu WC, Hsu TL, Ding YA, Chang MS. Initiation of atrial fibrillation by ectopic beats originating from the pulmonary veins:


**Table 1.** Baseline characteristics of study patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Study pts (n = 152)</th>
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<tbody>
<tr>
<td>Age, mean (yrs)</td>
<td>60 ± 11</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>120 (79)</td>
</tr>
<tr>
<td>Paroxysmal atrial fibrillation, n (%)</td>
<td>96 (64)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>65 (43)</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>18 (12)</td>
</tr>
<tr>
<td>Congestive heart failure, n (%)</td>
<td>15 (10)</td>
</tr>
<tr>
<td>Ejection fraction, mean (%)</td>
<td>59 ± 11</td>
</tr>
<tr>
<td>Left atrial size, mean (cm)</td>
<td>4.2 ± 0.7</td>
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</table>
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 (+) pts (n = 45)</th>
<th>ADO-PV ectopy (-) pts (n = 107)</th>
<th>p value</th>
<th>Dormant conduction (+) pts (n = 44)</th>
<th>Dormant conduction (-) pts (n = 108)</th>
<th>p value</th>
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<tbody>
<tr>
<td>Age, mean (yrs)</td>
<td>60 ± 10</td>
<td>60 ± 11</td>
<td>0.83</td>
<td>62 ± 9</td>
<td>60 ± 11</td>
<td>0.26</td>
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<td>Male, 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>
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<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>
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<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>
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<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>
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<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>
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<td>EF, mean (%)</td>
<td>58 ± 10</td>
<td>60 ± 11</td>
<td>0.54</td>
<td>60 ± 11</td>
<td>59 ± 11</td>
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<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>
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ADO = adenosine; PV = pulmonary vein; AF = atrial fibrillation; HTN = hypertension, DM = diabetes mellitus, CHF = congestive heart failure, EF = ejection fraction; LA = left atrial
Table 3. Univariate and multivariate predictors of recurrent AF following a single ablation procedure

<table>
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<th>Unadjusted (univariate)</th>
<th>Adjusted (multivariate)</th>
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<td></td>
<td>Hazard ratio</td>
<td>95% CI</td>
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<tr>
<td>Age</td>
<td>1.00</td>
<td>0.97 – 1.03</td>
</tr>
<tr>
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<td>0.87 – 4.81</td>
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<tr>
<td>Paroxysmal AF</td>
<td>1.56</td>
<td>0.83 – 2.97</td>
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<tr>
<td>Hypertension</td>
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<td>0.57 – 1.79</td>
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<tr>
<td>Diabetes mellitus</td>
<td>1.51</td>
<td>0.71 – 3.25</td>
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<td>LVEF</td>
<td>1.00</td>
<td>0.98 – 1.03</td>
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<td>Left atrial size</td>
<td>1.31</td>
<td>0.86 – 1.99</td>
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<td>0.37 – 1.2</td>
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<tr>
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<td>0.97 – 3.10</td>
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<td>2.11</td>
<td>2.02 – 4.36</td>
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Analysis of interaction between ADO-induced PV ectopy and ADO-induced PV reconnection

<table>
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<tr>
<th></th>
<th>Hazard ratio</th>
<th>95% CI</th>
<th>p value</th>
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<tr>
<td>No ADO-induced PV ectopy or dormant conduction</td>
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<td></td>
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<tr>
<td>Dormant conduction only</td>
<td>1.77</td>
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<td>0.15</td>
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<tr>
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<td>2.12</td>
<td>1.00 – 4.98</td>
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<td>2.86</td>
<td>1.28 – 6.37</td>
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AF = atrial fibrillation; LVEF = left ventricular ejection fraction; ADO = adenosine
Figure Legends:

**Figure 1.** Adenosine-induced PV reconnection. Surface ECG leads I and V1 are displayed at the top. Electrograms (PV1,2 – PV19-20) from the PV ostium are shown at the bottom. ADO = adenosine; PV = pulmonary vein

**Figure 2.** Adenosine-induced PV ectopy. Surface ECG leads I and V1 are displayed at the top, coronary sinus electrograms (CS1,2 – CS9,10) are displayed in the middle and electrograms (PV1,2 – PV19-20) from the PV ostium are shown at the bottom. Administration of ADO results in AV block (*) and induction of two beats of dissociated PV ectopy (thin arrows). ADO = adenosine; PV = pulmonary vein

**Figure 3.** Restoration of bidirectional PV conduction with adenosine coincident with AV block following PV isolation. Recordings from the left inferior PV of a patient following PV. 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 following PV isolation with no evidence of dissociated PV ectopy. B. Following 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 two APCs (**). C. Follow-up recordings showing resumption of entrance block. First two sinus beats show PV entrance conduction followed by disappearance of PV reconnection. ADO = adenosine; CS = coronary sinus; PV = pulmonary vein; AV = atrioventricular.
**Figure 4.** Impact of ADO-induced PV ectopy and PV reconnection on freedom from AF after PV isolation. **A.** Kaplan Meier survival curves comparing freedom from AF among patients with and with ADO-induced PV ectopy. **B.** Kaplan Meier survival curves comparing freedom from AF among patients with and with ADO-induced PV reconnection.

**Figure 5.** Effect of ADO-induced PV ectopy and dormant conduction either in isolation or in combination on AF recurrence. Flow diagram (A) and Kaplan Meier survival curves for freedom from AF (B) for patients stratified according to presence or absence of ADO-induced PV ectopy and dormant conduction. *Pts = patients; DC = dormant conduction; ADO PVE = ADO-induced PV ectopy.*
ADO

AV Block

AVO-induced PV ectopy
Post-ADO

Resumption of entrance block
A

**Freedom from AT/AF Survival**

- ADO-induced PV ectopy (-)
- ADO-induced PV ectopy (+)

Log rank p = 0.014

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<th>Follow-up (ds)</th>
<th># pts at risk</th>
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<tr>
<td>0</td>
<td>107</td>
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<tr>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>180</td>
<td>60</td>
</tr>
<tr>
<td>360</td>
<td>10</td>
</tr>
<tr>
<td>540</td>
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152 study patients

ADO

80 (53%) pts
(-) ADO-induced PV reconnection
(-) ADO-induced PV ectopy

Follow up

18 (23%) pts recurrent AF

27 (18%) pts
(+) ADO-induced PV reconnection
(-) ADO-induced PV ectopy

10 (37%) pts recurrent AF

28 (18%) pts
(-) ADO-induced PV reconnection
(+) ADO-induced PV ectopy

11 (39%) pts recurrent AF

17 (11%) pts
(+ ADO-induced PV reconnection
(+ ADO-induced PV ectopy

9 (53%) pts recurrent AF
Adenosine-Induced Pulmonary Vein Ectopy as a Predictor of Recurrent Atrial Fibrillation Following 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. published online November 15, 2013;
Circulation: Arrhythmia and Electrophysiology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-3149. Online ISSN: 1941-3084

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