

## Early Pulmonary Vein Conduction Recovery After Catheter Ablation Of Atrial Fibrillation

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### Abstract

**Background:** Pulmonary vein electrical isolation (PVI) is an effective treatment for atrial fibrillation (AF). However, recurrence of pulmonary vein (PV) conduction after ablation may limit long-term success. Early identification and treatment of acute PV conduction recovery during initial ablation may have an impact on subsequent clinical results.

**Objective:** "To" assess the prevalence of acute PV conduction recovery during the observation time after PV isolation for paroxysmal AF, and to evaluate the impact of re-isolation treatment on long-term clinical results.

**Methods:** 76 patients with paroxysmal AF were randomized to 2 groups to undergo PVI. Group A (Study Group: 38 patients): 30 minutes of observation were given following PV isolation for detection of acute PV-reconnection, with re-ablation of reconnected PVs. Group B (Control Group: 38 patients). Ablation procedure was done either by conventional method or using 3D electro-anatomical mapping. Symptoms, ECG and Holter monitoring were used to evaluate the clinical effectiveness of ablation. Any episode of symptomatic or asymptomatic atrial tachyarrhythmia that lasted more than 30 seconds documented with ECG or Holter monitoring was considered a recurrence.

**Results:** There was no statistically significant difference in age, sex, AF history, previous AF ablation, structural heart diseases & antiarrhythmic drug history among both groups. In the study group, 14 patients (36.8%) showed no PV reconnection, while 24 patients (63.2%) showed acute PV reconnection within 30 minutes. The LSPV showed the highest rate of acute PV reconnection during the observation period (66.6% of patients showing PV reconnection). AF recurred in only 6 patients (15.8%) in the study group in comparison to 20 patients (52.6%) having AF recurrence post-ablation in the control group. Among 24 patients of the study group, who showed PV reconnection which was re-isolated, only 4 patients (16.7%) had AF recurrence on follow up. In patients who did not show PV reconnection (14 patients), only 2 patients (14.3%) had AF recurrence on follow up.

**Conclusions:** Re-isolation of recovered PV conduction contributed to the improvement in the success rate of ablation for paroxysmal AF.

### Introduction

Atrial fibrillation is a common supraventricular tachyarrhythmia characterized by uncontrolled atrial activation with consequent deterioration of atrial mechanical function. It is the most common sustained cardiac rhythm disturbance, increasing in prevalence with age.<sup>[1]</sup> It has been well established that pulmonary vein (PV) triggering or driving is the dominant mechanism for paroxysmal atrial fibrillation (AF)<sup>[2]</sup>, and circumferential PV isolation (CPVI) is the main approach for AF elimination.<sup>[3]</sup> Considerable evidence points to the importance of pulmonary vein (PV) electrical isolation in the treatment of atrial fibrillation (AF) with catheter ablation procedures.<sup>[4]</sup> However, the recurrence rate of the procedure has been reported up to 30% after initial ablation, and PV conduction recovery accounts for 80% of AF recurrence, according to remapping results during a second procedure.<sup>[5]</sup> Although it is well recognized that recovery of pulmonary vein (PV) conduction is common among patients who fail atrial fibrillation (AF) ablation, little is known about the precise time course of recurrence.<sup>[6]</sup> Re-isolation of recovered

PV conduction can improve the success rate, making this of great importance to reduce the prevalence of PV re-connection after the initial procedure.<sup>[7]</sup>

### Aim of the study

This study aims to assess the prevalence of acute PV conduction recovery during the observation time after PV isolation for paroxysmal AF, and to evaluate the impact of re-isolation treatment on long-term clinical results.

### Patients and Methods

This study was carried on seventy six patients presenting to the Cardiology department at Ain Shams University Hospitals with atrial fibrillation dedicated for radiofrequency catheter ablation. Patients had pulmonary vein isolation using radiofrequency ablation done in the period from August 2009 till January 2012. Patients were randomly assigned to 2 groups. Group A (Study Group: 38 patients): 30 minutes of observation were given following PV isolation for detection of acute PV-reconnection, with re-ablation of reconnected PVs. Group B (Control Group: 38 patients): the procedure was terminated as soon as PV isolation was achieved, with no time given for observation of PV conduction recovery. Transesophageal echocardiography was performed to exclude left atrial thrombi. Written informed consent was obtained in all cases.

### Electrophysiological study

After proper local anesthesia, left subclavian vein puncture was done

### Key Words

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for introduction of a decapolar 6Fr catheter in coronary sinus. Left femoral venous puncture was done for introduction of a quadripolar 6 Fr catheter at His region (landmark for trans-septal puncture). Right femoral vein was punctured twice for two long sheaths of 8Fr caliber to be introduced from trans-septal punctures into LA cavity, one for the circular decapolar mapping catheter (Lasso catheter), and the other sheath for ablation catheter. In some cases, 1 trans-septal puncture was only done. 10,000 IU of heparin were given immediately after successful trans-septal punctures followed by continuous flushing with pressurized heparinized saline along the side of both long sheaths to avoid thrombus formation during this procedure with close follow up of activated clotting time (ACT) to be adjusted to be 300-400 seconds. Selective pulmonary vein angiography was done using 6F 3.5 Judkin's right coronary catheter or multi-purpose catheter.

### Ablation Procedure

#### Conventionally guided catheter ablation:

Ablation was done using open irrigation 3.5 mm-tip ablation catheter in the power controlled mode. Continuous irrigation was achieved using automated irrigation pump (Cool Flow<sup>®</sup>, Biosense Webster). Lasso catheter was positioned across the ostium of each PV aiming at recording pulmonary vein potentials (PVPs). The ablation catheter was positioned at the PV ostium or more precisely towards the antral aspect of each PV. Differential CS pacing was usually done for more discrimination of PVPs from LA signals during isolation of left-sided PVs. RF ablation was done segmentally all through the PV ostium aiming at diminishing PVPs in amplitude or making it takes a rounded far-field appearance. RF energy applied was typically 25-30 Watts with external irrigation flow rate of 15-18 ml/min. RF current was applied continuously with repositioning of the catheter tip every 30-60 seconds. "Complete PV isolation" was defined as the elimination of conduction of PV muscle in all pulmonary veins, as judged on the basis of either disappearance or dissociation of PV potentials.

#### CARTO 3D Electro-anatomical Mapping:

Continuous circumferential lesions were created encircling the left and right PV ostia or antra guided by the CARTO system using a 3.5 mm-tip open irrigation ablation catheter (Navistar<sup>™</sup> Thermocool<sup>™</sup> Biosense Webster). Integration of CT image into CARTO Mapping System was done. CT image fusion with 3D CARTO map was done in most of the cases ablated by CARTO technique. The CT image was imported into the system using CARTO- Merge<sup>™</sup> technique.

#### Observation for PV conduction recovery and re-ablation

For cases in Group A: PV conduction recovery was recorded after 30 minutes by re-positioning a decapolar circular mapping catheter in the left superior and inferior PV. Another 30 minutes of observation time were given for waiting and recording the right PV re-connection. At the end of the observation time, all the recovered PVPs were re-ablated aiming at complete re-isolation of the recovered PV. For cases in Group B: The procedure was terminated as soon as PV isolation was achieved, with no time given for observation of PV conduction recovery.

#### Post AF Ablation Management & Follow Up

Reporting of data was based on a consistent initial post-ablation blanking period of three months after the procedure. Follow up for the patients was done for a duration of 6 months after the procedure to detect long term success rate including the following data: history taking as regards recurrence of the symptoms, surface ECG was

taken at 1 day, 7 days, 1 month, 2 months, 4 months, and 6 months after the procedure. Holter monitoring was done in patients with recurrent symptoms to evaluate any arrhythmic events. Cases were always asked to record their ECG when symptomatic.

Any episode of symptomatic or asymptomatic atrial tachyarrhythmia that lasted more than 30 seconds documented with ECG or Holter monitoring was considered a recurrence.

#### Data Management and Analysis

The collected data was revised, coded, tabulated and introduced to a PC using Statistical package for Social Science (SPSS 15.0.1 for windows; SPSS Inc, Chicago, IL, 2001). Data were presented and suitable analysis was done according to the type of data obtained for each parameter. Student T Test was used to assess the statistical significance of the difference between two study group means. Chi-Square test was used to examine the relationship between two qualitative variables. Fisher's exact test was used to examine the relationship between two qualitative variables when the expected count is less than 5 in more than 20% of cells.  $P < 0.05$  was considered significant &  $P < 0.01$  was considered highly significant.

#### Results

There was no statistically significant difference in age, sex, AF history, previous AF ablation, structural heart diseases & antiarrhythmic drug history among both groups as shown in [Table 1]. Echocardiographic parameters (LV systolic function, presence of diastolic dysfunction, ventricular hypertrophy, mitral valve disease) were similar in both groups except for left atrial dimensions which were significantly lower in the study group with mean LA  $35.5 \pm 4.8$  mm, ranging from 27-46 mm. In the control group mean LA dimension was  $40.2 \pm 7.9$  mm, ranging from 26-53 mm. This difference was statistically significant with P value of 0.002.

Conventional ablation was done in 34 patients (89.5%) in the study group vs. 32 patients (84.2%) in the control group with no statistical significance. CARTO technique was used in 4 patients (10.5%) in the study group (2 of them were done using CARTO Merge technique) in comparison to 6 patients (15.8%) in the control (all of them were done by CARTO Merge). Regarding ablation strategy, 34 patients (89.5%) were ablated by segmental approach in the study group, 4 patients (10.5%) ablated by circumferential approach. In the control group, in 32 patients (84.2%) segmental approach was used, in 6 patients (15.8%) circumferential approach was used.

Additional lines of ablation were done in 6 patients in the study group (16.7%) in which ablation of cavo-tricuspid isthmus was done in 2 patients, 3 patients had additional ablation along mitral isthmus, & a patient received additional ablation line in SVC for isolation of potentials seen by Lasso catheter situated in SVC. In the control group, 4 patients (10.5%) received additional ablation line. 3 patients received additional ablation line at LA roof. One other patient had ablation along left atrial isthmus between LIPV & mitral annulus. During ablation procedure, 14 patients (36.8%) from the study group developed AF, 6 of which (42.9%) were spontaneously cardioverted to normal sinus rhythm during proceeding ablation, while 8 patients of them (57.1%) required external DC shock delivery. In the control group, 16 patients (42.1%) developed AF during the procedure, 8 of which (50%) were spontaneously cardioverted to normal sinus rhythm during the ablation, while the other 8 patients (50%) needed external DC shock delivery.

Fluoroscopy time was lower in the control group ( $111.3 \pm 40.8$

**Table 1:** showing relation between LA size, PV diameter sum & PV average diameter to AF recurrence in all patients.

	Recurrence of AF						
	No			Yes			P-value
	Mean	±SD	Median	Mean	±SD	Median	
LA (mm)	36.26	5.71	35.50	37.85	6.53	38.00	0.278
PV Diameter Sum	57.27	12.97	55.25	61.33	13.24	61.60	0.337
PV Average Diameter	16.52	2.61	16.07	15.85	1.09	15.63	0.225

Conventional ablation was done in 34 patients (89.5%) in the study group vs. 32 patients (84.2%) in the control group with no statistical significance. CARTO technique was used in 4 patients (10.5%) in the study group (2 of them were done using CARTO Merge technique) in comparison to 6 patients (15.8%) in the control (all of them were done by CARTO Merge). Regarding ablation strategy, 34 patients (89.5%) were ablated by segmental approach in the study group, 4 patients (10.5%) ablated by circumferential approach. In the control group, in 32 patients (84.2%) segmental approach was used, in 6 patients (15.8%) circumferential approach was used.

minutes) compared to the study group ( $135 \pm 32.4$  minutes). This difference was highly significant as P value was 0.006. Also total procedural time was lower in the control group ( $222.6 \pm 54.3$  minutes) compared to the study group ( $258.9 \pm 74.6$  minutes) which was also statistically significant as P value was 0.018.

#### Results of observation period of PVs in study group

In the study group, 14 patients (36.8%) showed no PV reconnection, while 24 patients (63.2%) showed acute PV reconnection within 30 minutes. The LSPV showed the highest rate of acute PV reconnection during the observation period. PV reconnection occurred in 16 patients (66.6% of patients showing PV reconnection) in LSPV. 4 patients (16.6%) showed PV reconnection in LIPV, 2 patients (8.3%) showed PV reconnection in RSPV. Left common PV showed PV reconnection in 4 patients (16.6%) while no patients had PV reconnection in either RIPV or in right common PV.

Regarding AF recurrence post-ablation, AF recurred in only 6 patients (15.8%) in the study group (in which 30 minutes were given for each PV to detect re-connection) in comparison to 20 patients (52.6%) having AF recurrence post-ablation in the control group. This result was highly statistically significant with P value of 0.001. Among 24 patients of the study group, who showed PV reconnection which was re-isolated, only 4 patients (16.7%) had AF recurrence on follow up. In patients who did not show PV reconnection (14 patients), only 2 patients (14.3%) had AF recurrence on follow up. In patients who did not show PV reconnection (14 patients), only 2 patients (14.3%) had AF recurrence on follow up. This shows that AF recurrence rates did not differ between group of patients who showed reconnection & were re-isolated & those who did not show PV reconnection (P value 0.10).

Complication rates were similar in both groups occurring in 4 patients in each group (10.5%). They all varied between mild pericardial effusion & local bleeding from puncture site after the procedure. One striking complication in one of the control group patients, Lasso catheter (15 mm diameter) which was stuck to postero-medial papillary muscle of MV apparatus with failed all trials to remove the catheter. Patient underwent surgery for removal of the catheter.

#### Discussion

Catheter ablation of AF is now a realistic therapeutic option for patients with paroxysmal AF.<sup>[8]</sup> Electrical isolation of all pulmonary veins is the endpoint of ablation.<sup>[9]</sup> It has been demonstrated that the majority of the patients who fail initial ablation procedure have resumption of PV conduction.<sup>[10]</sup> The recurrence rate of the procedure has been reported up to 30% after initial ablation, and PV conduction recovery accounts for 80% of AF recurrence, according to remapping results during a second procedure. Re-isolation of recovered PV conduction improves the success rate to 90%, making this of great importance to reduce prevalence of PV re-connection after the initial procedure.<sup>[5]</sup> A more recent study provided important additional evidence by comparing PV conduction in patients with a successful ablation procedure to those who failed the initial ablation. These investigators showed that in the majority of patients who remain in sinus rhythm; off antiarrhythmic drugs; after AF ablation, no recurrence of PV conduction occurs. In contrast, almost all the patients with AF recurrence show recurrent PV conduction.<sup>[11]</sup>

In the current study, 14 patients (36.8%) showed no PV reconnection, while 24 patients (63.2%) showed acute PV reconnection within 30 minutes. Among all pulmonary veins recorded (136 vein ostia), 26 veins (19.2%) showed PV reconnection. In the Cheema et al. study, after successful isolation of the PVs, repeat circular electrode recordings from each PV were obtained at 30 and 60 minutes. Recurrence occurred in 13 patients (93%) of the study. Recurrence was observed 30 minutes into the monitoring period in 17 veins (33%) with nine additional veins (17%) showing first recurrence at 60 minutes into monitoring period.<sup>[6]</sup> This can be explained by the fact that in the current study, the cohort of patients had predominantly paroxysmal AF; in contrast to the Cheema et al. study that comprised predominantly non-paroxysmal AF patients.<sup>[6]</sup>

Incidence of PV reconnection was higher in the current study if compared to the Wang et al. study. Continuous circumferential lesions were created in the Wang et al. study using CARTO system (Biosense Webster).<sup>[12]</sup> This step was not performed in our current study as circumferential ablation was done in only 4 patients in study (recheck) group while most of the patients were conventionally

**Table 2:** showing relation between LA size, PV diameter sum & PV average diameter to AF recurrence in study group patients.

	Recurrence of AF						
	No			Yes			P-value
	Mean	±SD	Median	Mean	±SD	Median	
LA (mm)	35.44	5.08	35.50	35.67	2.88	37.00	0.879
PV Diameter Sum	55.28	14.28	53.50	73.00	18.48	73.00	0.038
PV Average Diameter	16.07	2.62	15.28	16.03	2.05	16.03	0.976

ablated. Although in Wang et al. study additional 30 minutes of observation (reaching total 60 minutes observation) were included in Group C<sup>[12]</sup> in comparison to the current study in which only 30 minutes of observation were given, but incidence of PV reconnection was higher in the current study.

Regarding the PVs most commonly showing reconnection in the current study, LSPV was the PV that showed highest incidence of reconnection. It occurred in 16 patients (66.6% of patients showing PV reconnection). Then comes the LIPV reconnection which occurred in only 4 patients. Also left common PV reconnection occurred in 4 patients in our study. This is in agreement with the results of Sauer et al. who showed that the left superior PV was the most likely vein to acutely recover conduction compared with the other veins although percentage of LSPV reconnection differed from our study.<sup>[13]</sup> This also matches with the results of Cheema et

cure was achieved in 119 (56%) of 213 patients who demonstrated acute PV reconnection compared with 124 (59%) of 211 patients without acute PV reconnection observed (P value: 0.97).<sup>[13]</sup>

Upon comparing the group of patients in which observation time was given for PV reconnection (recheck group), to the group of patients in which no time was given for observation, the current study found that there was a great significant difference between both groups. AF recurrence rates post-ablation was 15.7% in recheck group (with 84.3% of patients free of symptoms), in comparison to 52.6% in control group (with 47.4% of control group patients free of symptoms). This was highly significant with P value of 0.003. Rate of arrhythmia recurrence was nearly the same in patients who were offered additional observational time in both our study & Wang et al. study, especially in the group in which 30 minutes of observation were given, exactly like protocol of our study group.<sup>[12]</sup>

**Table 3: showing relation between LA size, PV diameter sum & PV average diameter to AF recurrence in study group patients.**

	Recurrence of AF						
	No			Yes			P-value
	Mean	±SD	Median	Mean	±SD	Median	
LA (mm)	37.72	6.58	36.00	38.50	7.21	39.50	0.730
PV Diameter Sum	61.64	8.52	64.40	56.66	7.39	61.60	0.180
PV Average Diameter	17.51	2.42	17.10	15.77	.56	15.63	0.052

Fluoroscopy time was lower in the study group (111.3 ± 40.8 minutes) compared to the control group (135 ± 32.4 minutes). This difference was highly significant as P value was 0.006. Also total procedural time was lower in the study group (222.6 ± 54.3 minutes) compared to the control group (258.9 ± 74.6 minutes) which was also statistically significant as P value was 0.018.

al. study, when they showed that recurrence of conduction was more commonly observed at 30 minutes in the LSPV as compared to other veins (57% vs 23%, P = 0.02). A first recurrence at 60 minutes was observed in 21% of LSPVs as compared to 15% in other veins (P = 0.63).<sup>[6]</sup>

Any PV recurrence was also higher in two superior pulmonary veins as compared to inferior pulmonary veins<sup>[6]</sup> which was the case in the current study in which reconnection occurred more in superior PVs. This finding may be due to impaired catheter stability and energy delivery because of the complex anatomy involving the segment of PV ostium adjacent to the left atrial appendage, where a ridge of tissue dividing the structures is present. This anatomical feature is not present on the right-sided veins and could account for the differential rate of reconnection. Another possibility may be related to the difficulty in ablating the thickened tissue fibers involving this region, which includes the ligament of Marshall that borders the left PV structures.<sup>[13]</sup>

#### Follow Up of AF Recurrence Post-ablation

In the current study, AF recurrence rates post-ablation was 14.3% in patients who showed no PV reconnection (2 patients), 16.7% in (4) patients who showed PV reconnection (which was dealt with by re-isolation) with P value 0.100. All cases of recurrence were in the form of AF recurrence with no cases showing post-ablation flutter or atrial tachycardia. In the current study, there was no difference in AF recurrence between patients who showed reconnection and were re-isolated & those who did not show any PV reconnection. This means that observation period is beneficial in any situation whether PVs were reconnected or not, because it will confirm PV isolation (in case of no reconnection) or will raise the attention for the need for re-isolation (in case of reconnection).

This comparison & its results were similar to that done in the Sauer et al. study that compared patients showing reconnection with patients who did not show reconnection. After a single procedure, AF

PV conduction recovery was the dominant cause of AF recurrence after the initial ablation procedure and accounted for 80% of AF recurrence. PV conduction recovery after the initial PV isolation procedure could be classified into acute recovery and chronic recovery, according to the time it occurred. It is postulated that their respective mechanisms differ from each other. Acute PV conduction recovery might be attributable to discontinuous or non-transmural lesions and chronic PV conduction recovery might be caused by the restoration of a few atrial myocardium cells which survived initial ablation.<sup>[12]</sup>

Theoretically, re-ablation of recovered PV conduction could produce trans-mural lesions, reduce living atrial tissues along lesion lines, and thus contribute to lowering of the prevalence of chronic PV conduction recovery and improving long-term success rate.<sup>[12]</sup> The follow up results of the current study showed that the success rate in the study (recheck) group was significantly higher than that in control group. The results of the Wang et al. study also showed that the prevalence of acute PV conduction recovery varied according to different observation time spent on evaluating it. Theoretically, the longer the observation time was, the higher the prevalence of PV re-connection would be. Unfortunately, it was impossible to spend unlimited observation time on evaluating PV re-connection, so it was advisable to set a limited window of observation.<sup>[12]</sup>

The results of the current study are of potential clinical importance. These findings, combined with the results of prior studies, which have shown that the outcome of AF ablation correlate strongly with PV isolation, provides evidence to support incorporation of a 30- to 60-minutes monitoring period into AF ablation protocols.<sup>[11]</sup>

#### Conclusions

The prevalence of acute PV conduction recovery was not low after PV isolation, which mostly occurred within 30 min after initial isolation. LSPV was the PV that showed highest incidence of reconnection. It occurred in 66.6% of patients showing PV reconnection.

Observational time (30 minutes) given for detection of acute PV reconnection was of great benefit. Re-isolation of all veins that demonstrated early reconnection improved the long-term single procedure outcomes of AF ablation. The results of this study suggest that better strategies to permanently isolate the pulmonary veins are needed.

### Conflict Of Interests

None.

### Disclosures

None.

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