Catheter Ablation of Ganglionated Plexi in Patients with Adenosine Triphosphate Induced Atrial Fibrillation After Pulmonary Vein Isolation

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Abstract

Aims: Intravenous ATP may induce atrial fibrillation (AF). ATP shares similar receptor-effector coupling systems with acetylcholine. However, the association between an ATP injection and the hyperactivity of the intrinsic cardiac autonomic nervous system, known as ganglionated plexi (GPs), are not well-understood. We described a series of patients with non-pulmonary vein (PV) trigger sites provoked by an ATP injection, and assessed the feasibility of a ganglionated plexus (GP) ablation. **Methods**: Five hundred and ninety-nine consecutive patients (69% men; mean age, 68 ± years, 60% paroxysmal AF) were retrospectively examined. A total of 7 patients (1.2%) that had ATP-induced AF following a PV isolation were enrolled in this analysis. **Results**: The distribution of the foci overlapped the GP location; the coronary sinus (CS) in six patients, right atrial posterior wall (RAPW) adjacent to the interatrial groove in 2, mitral annulus in 2, ligament of Marshall in 1, right septum below the foramen ovale in 1 and left atrial posterior wall in 1, respectively. Among those trigger foci, we confirmed a vagal response by high frequency stimulation in the CS and RAPW in six and two patients, respectively. After a median RF time of 2.9 minutes (range 2.5 to 11.3) targeting those foci, six patients who received a repeat ATP injection became non-inducible. **Conclusion**: ATP-induced AF after a PV/Box isolation was associated with hyperactivity of atrial GP. The GP ablation was effective in this rare, but challenging situation.

Introduction

The pulmonary veins (PV) are the most frequent trigger source of atrial fibrillation (AF) and PV isolation is the cornerstone of catheter ablation for AF.[1] Non-PV foci are occasionally identified during the ablation procedure, and isoproterenol (ISP) are commonly utilized to elicit the AF triggers.[2]

An intravenous injection of adenosine triphosphate (ATP) or adenosine has been used to unmask dormant conduction following isolation of pulmonary veins (PVs).[3] It has also been known that intravenous ATP may induce AF.[4] ATP produced the same cardiac effects and share similar receptor-effector coupling systems with acetylcholine.[5] ATP injection enhances parasympathetic activity followed by responsive sympathetic hyperactivity. However, the association between ATP injection and hyperactivity of the intrinsic cardiac autonomic nervous system, known as ganglionated plexus (GP) were not well-understood.

In this retrospective study, we describe a series of patients with non-PV trigger site provoked by ATP injection, and assess the feasibility of GP ablation.

Methods

Study population

Five hundred and ninety-nine consecutive patients (69% men; mean age, 68 ± years, 60% paroxysmal AF) who underwent a total of 686 ablation procedures (including 538 of the first procedures, and 148 of redo procedures) for AF from January 2015 to April 2020 were retrospectively examined. A total of 7 patients (1.2%) showed ATP-induced AF following PV isolation were enrolled in this analysis. All antiarrhythmic drugs, including amiodarone, were discontinued for at least five half-lives before the procedure.

Written informed consent for the procedure was obtained from all patients. The institutional review board approved this retrospective study protocol.

EP Study and Ablation Procedure

All procedures were performed in the fasting state under general anesthesia with mechanical ventilation through a laryngeal mask airway. After introducing the vascular access, intravenous heparin was initiated to maintain the activated coagulation time over 300 seconds throughout the procedure.

A duodecapolar catheter (BeeAT, Japan Lifeline Co., Tokyo, Japan) was placed in the coronary sinus (CS) through the right internal jugular vein. The proximal eight electrodes of this catheter covered the septum of the right atrium (RA) and superior vena cava (SVC). We performed transseptal puncture with the guidance of the intracardiac ultrasound. After the puncture, a single 8.5 Fr steerable catheter (Agilis, St. Jude Medical, St. Paul, MN, USA) and two pre-shaped catheters (8Fr SL0, St. Jude Medical, St. Paul, MN, USA) were inserted into the left atrium (LA). Three-dimensional electroanatomic mapping system (EnSite NavX, St. Jude Medical, St. Paul, MN, USA and Carto 3, Biosense Webster, Irvine, CA, USA) were used in all patients.

All patients underwent PV isolation with or without posterior wall isolation (i.e., BOX isolation). We preferentially performed BOX isolation; however, considering the type of AF (paroxysmal or non-paroxysmal) and the spatial relationship between the esophagus and the LA posterior wall, a standard PV isolation was adopted in some patients. The ablation catheter and double Lasso mapping catheters were each advanced into the LA. Radiofrequency (RF) ablation was applied via an irrigated tip catheter to encompass the left and right PVs for PV isolation and encompass all PVs together with the posterior wall for BOX isolation. The endpoint of the PVI and BOX isolation was a bidirectional conduction block between the LA and each isolation area.

SVC isolation was also performed in patients who has long SVC myocardial sleeve ($>$ 2 cm). The endpoint of SVC isolation was a bidirectional conduction block between RA and SVC. To prevent diaphragmatic paralysis, we performed pace mapping to identify the site with diaphragmatic capture. RF ablation was applied in a point-by-point manner at the earliest activation site of SVC potentials during sinus rhythm.

Cavotricuspid isthmus (CTI) ablation was performed in all patients except for the patients who underwent a prior ablation procedure for AF. The endpoint of CTI ablation was a bidirectional conduction block across the CTI.

The other ablation strategies such as linear ablation, ablation targeting complex atrial fractionated electrocardiogram (CFAE), or low voltage area were at the operator's discretion.

Intravenous ATP Challenge

We performed ATP challenge testing after a 60-minute waiting time since initial documentation of PV/BOX isolation.

Intravenous ATP (20 mg) was administered with immediate saline flush during an intravenous ISP infusion (0.5 to 1.0 μg/min). The dose of ISP infusion was adjusted to increase the heart rate over 100 beats per minute. The ATP effect was confirmed by the presence of temporary bradycardia and a decrease in blood pressure.

Double Lasso catheters were placed at the antrum of four PVs and/or SVC during the ATP challenge. If dormant PV conduction was identified, additional RF energy was applied to establish complete PV/BOX and/or SVC disconnection. Repeat ATP injections during ISP infusion were performed to reconfirm the complete disconnection of them.

Mapping the non-PV, non-Box, and non-SVC trigger

In this case series, ATP challenge testing reproducibly provoked AF.

We tried to identify the trigger sites considering the anatomical distribution of the GP around both atria. We carefully observed the initial beats at the onset of the induced AF. If we supposed the trigger PACs should come from GP regions, we proved the presence of GP by applying high-frequency stimulation (HFS) (20 Hz) at the suspected trigger region. A positive response was defined as an increase in the R-R interval by $> 50\%$ during AF.[6] The sites with positive responses to HFS were marked on the 3-D mapping system, and then we applied RF ablation there at the power of 30 to 35 watts for 30 to 60 seconds. Following each RF application, HFS was repeated at the same site to confirm that the positive response was eliminated. RF applications were repeated if the positive response to HFS was still elicited.

When the trigger foci were thought to be not associated with GP regions, we put the Lasso catheters close to the suspected region and repeated ATP injection for detailed mapping. We performed additional ablation to eliminate the foci if it could be identified.

We introduced this "GP-based approach" since Case 2. In Case 1, we tried to identify the trigger sites, observing the first beats that initiated AF. CFAE was also targeted to reduce the total number of electric cardioversion and ATP testing. Finally, we administered ATP at least twice to verify the noninducibility of AF, if possible.

Post-procedural Follow up

After discharge, all patients underwent a 24-hour Holter monitoring every three months for one year and every six months thereafter. Patients were advised to return to our hospital or nearby clinics to record a 12-lead electrocardiogram when patients experienced symptoms suggestive of AF recurrence. Otherwise, patients were offered to undergo additional 24-hour Holter monitoring or patient-driven event monitor (HCG-801, Omron Healthcare Co., Kyoto, Japan) according to the duration and frequency of the symptoms. In patients with a cardiac implantable electronic device, AF recurrence was also monitored with the device. AF recurrence was defined as the appearance of sustained AF or atrial tachycardia (AT) lasting more than 30 seconds. The first three months after the procedure was the blanking period.

Data Disclosure

The data underlying this article will be shared on reasonable request to the corresponding author.

Results

The baseline characteristics of patients are summarized in Table 1. All of the study patients were male, and the mean age was 50 ± 17 years. All of the patients had paroxysmal AF. Two patients had a prior history of anterior myocardial infarction, and one patient was diagnosed with idiopathic ventricular fibrillation and had an implantable cardioverter-defibrillator. The remaining four patients have no underlying heart disease. The mean LA diameter was 35.6 ± 5.0 mm, and the mean left ventricular ejection fraction was $60\pm12\%$ by echocardiography. Two patients (Case 1 and 2) underwent a prior AF ablation procedure. In their previous procedures, ATP injection did not induce AF in Case 1, and in Case 2, ATP was administered during ongoing AF.

Ablation performed before and after ATP injection

The results of the procedure are summarized in Table 2. Before ATP challenge testing, we performed Box isolation in 4 patients and PV isolation in the remaining three patients. SVC isolation was also performed in

4 patients, and mitral isthmus linear ablation, low voltage area ablation, and CFAE ablation were performed in one patient each.

Spontaneous reconnection and ATP provoked dormant conduction of the isolated veins were documented in 2 patients each. In Case 6, GP ablation within the CS eliminated the ATP-induced AF irrespective of the dormant conduction of the left PV (Figure 1).

The ablation sites following the observation of ATP-induced AF were illustrated in Figure 3. The foci included CS in six patients, RA posterior wall adjacent to the interatrial groove in 2, lateral mitral annulus in 2, ligament of Marshall in 1, RA septum below the foramen ovale in 1, and LA posterior wall below the Box lesion in 1, respectively. Among these trigger foci, we confirmed the vagal response by HFS in CS and RA posterior wall in six and two patients (Figures 1 and 2).

After a median RF time of 2.9 minutes (range 2.5 to 11.3) targeting these foci, all the six patients who received repeat ATP injection became non-inducible except for one patient (Case 1) who did not undergo the GP-based approach.

Complications

HFS within the CS inadvertently captured the ventricle and induced ventricular fibrillation in one patient (Case 7, Figure 4). We immediately performed external electrical defibrillation then successfully terminated the ventricular fibrillation.

Another patient developed the right phrenic nerve injury (Case 4). It was attributable to the RF application during SVC isolation and eventually resolved over two years after the procedure.

Postablation Follow-Up

During a mean follow-up period of 32.5±22.9 months (4.0 to 63.1) after the index procedure, five patients were free from AT/AF without anti-arrhythmic drugs.

One patient (Case 3) had a recurrence as AT 6 months after the first procedure. In the second procedure, we confirmed the reconnection of the 4 PVs and rapid firing originating from the right PV. ATP administration following re-isolation of all PVs never induced AF. The patient was free from atrial tachyarrhythmia after the second procedure.

In another patient (Case 2), remote monitoring of ICD documented a few episodes of AF 11 months after the index (i.e., second) procedure. The patient was asymptomatic because all episodes occurred at mid-night or early morning and terminated within one to two minutes. We did not perform the third procedure; however, there had been no AF episode for over four years since these AF episodes.

Discussion

This retrospective case series describes non-PV, non-BOX, and non-SVC trigger sites provoked by ATP injection and demonstrates the effectiveness of the GP-based approach. The main findings of this study were:

The incidence of ATP-induced AF after PV/Box isolation and SVC isolation was 1.2%.

ATP-provoked trigger foci were distributed in particular sites, which overlapped with the distribution of GP.

Among these trigger foci, we proved the presence of GP by the vagal response to HFS in CS and RA posterior wall in six and two patients. CS- and RA-GP ablation suppressed the ATP-induced AF with a modest amount of RF application.

HFS within CS had a risk of ventricular fibrillation induction.

Incidence and Clinical significance of ATP-induced AF

Previous studies reported that the incidence of ATP/Adenosine-induced AF was 29.6 and 47% before PV isolation;[7, 8] and 5.6 to 13% after PV isolation.[9, 10, 11] Most of these foci located in PV and SVC. When excluding non-PV/non-Box and non-SVC foci, the incidence of ATP-induced AF was 2.5% and 15% before PV isolation; and 2.4% to 7.4% after PV isolation in these studies. These were still higher than the incidence of the present study.

The difference in the incidence of ATP-induced AF from non-PV foci was mainly due to various induction protocols. Tutuianu et al. used adenosine of 18 or 36 mg for induction,[8] equivalent to about 34 or 68 mg of ATP according to each molecular weight. The excessive dose may lead to provoke non-clinical and non-specific triggers. The dose of ATP and isoproterenol in the present study was lower than previous studies because the purpose of ATP injection was to unmask dormant conduction between LA and the isolated areas, not to induce AF.

Tutuianu et al. also reported that adenosine much more frequently induced non-PV triggered AF as compared with ISP (3 to 20 mcg/min); then, they concluded that there was no correlation between non-PV triggers with ATP and arrhythmia recurrence.[8]

In contrast, Kuroi et al. administered 30 mg of ATP after PVI and identified that ATP-provoked AF originating from the atria (not from SVC) was the independent predictor of a recurrence of arrhythmia even after the repeat procedure.[10]

Tao et al. administered 20 mg of ATP before PVI, and they revealed that ATP-induced AF was documented from the same site as the spontaneous AF in 41% of patients.[7]

Similar to the incidence of AF induction, the difference in the induction protocols might lead to a discrepancy in the clinical significance. The different patient populations and a limited number of cases who undergo the repeat procedure to confirm the relationship between the AF recurrence and the ATP-provoked foci also might be related to the discrepancies.

In our study patients, only 20 mg of ATP injection following PV/Box isolation (and SVC isolation in 4 of 7 patients) reproducibly induced AF. Therefore, mapping and ablation of non-PV/non-Box foci were thought to be mandatory, and the ablation resulted in favorable clinical outcomes.

Association between GP and ATP-induced AF

Pharmacologically, adenosine shortens atrial action potential duration and refractory period mainly through the activation of specific G protein-coupled adenosine A1 receptors and the downstream outward potassium channel, which is also regulated by acetylcholine via M2 muscarinic receptors.[5]

Anatomical studies have shown that about a half of atrial ganglia are present on the surface of the RA adjacent to the intertribal groove (posterior RA GP), around the SVC (superior RA GP), and about one-third of atrial ganglia are present between the inferior vena cava, CS ostium and around CS (posteromedial LA GP).[12, 13]

Previous clinical studies have suggested that adenosine/ATP could provoke the RA or CS triggers more frequently as compared to ISP.[8, 11]

Zhang et al. reported that about 70% of ATP-provoked triggers were located in SVC. They postulated the hyperactivity of the SVC–aorta–GP induced by ATP could lead to rapid firing from the SVC.[9]

Thus, considering the pharmacological mechanisms of ATP, the anatomical characteristics of GP, the distribution of the ATP-induced foci observed in previous studies, and the efficacy of the GP-based approach in our patients, ATP-induced AF following PV/Box and SVC isolation must be associated with the hyperactivity of GP.

Ablation strategy for ATP-induced AF

According to the current expert consensus statement on catheter and surgical AF ablation, if a reproducible initiation of AF from non-PV foci after PV isolation, focal ablation at the site of origin should be considered.[14] However, localization and elimination of non-PV AF triggers can be challenging because of the transient nature of non-PV triggers and diverse locations to perform focal ablation.

Zhang et al. reported the foci triggering AF could not be localized because of the transient effect of ATP in 10 out of 39 patients.[9] Kuroi et al. reported the patients with atrial AF foci had worse clinical outcomes than patients with SVC foci.[10]

Thus, these previous studies imply the difficulty of identifying the precise foci from the initial beat using the current mapping techniques. Some of these unidentified or residual foci might be associated with GP. In our study patients, we could eliminate non-PV foci by the GP-based approach without performing detailed activation mapping. In this context, targeting the GP site, not the presumably earliest site, might be a useful alternative ablation strategy in patients with ATP-induced AF.

However, we should recognize the high specificity but low sensitivity of the vagal response to HFS.

Calò et al. demonstrated the efficacy of GP ablation in RA in patients with vagal paroxysmal AF. Thirty-four patients were randomly assigned for a selective ablation at sites with positive HFS response or an extensive approach at anatomic sites of GP. They concluded that the anatomical ablation of RA GPs is effective in about 70% of patients.[15] They did not perform PV and SVC isolation in both groups, whereas we employed the GP-based approach after PV/Box and SVC isolation. These lesion sets should affect some parts of the posterior and superior RA GP. Therefore extensive anatomic ablation of posterior and superior RA GP might not be necessary for our patients.

Recently, cardioneuroablation targeting the fractionated atrial potentials during sinus rhythm, called AF-Nest, has been applied to vagal AF.[16, 17] Pachon et al. demonstrated a mean of 33.6±13 AF-Nest ablation completely abolished the vagal response induced by pulsed electric field delivered from the internal jugular vein.[17]

If our approach did not suppress the ATP-induced AF, we should consider performing these extensive ablation techniques. These extensive or anatomical ablations have potential risks of complications such as inappropriate sinus tachycardia and risks of recurrence as atrial tachycardia caused by formation of an arrhythmogenic substrate or critical channels among the cloud-like lesions.

Nevertheless, prospective randomized controlled study is warranted to determine the optimal ablation strategy for ATP-induced AF after PV/Box and SVC isolation.

Risk of ventricular fibrillation by HFS in the coronary sinus

In Case 7, HFS within the CS inadvertently captured ventricular myocardium leading to ventricular fibrillation (Figure 4A, B). Po et al. advised against HFS delivered within 2 cm of the ventricle to avoid inducing ventricular fibrillation.[6] The CS runs along the mitral annulus so that the catheter within the CS would be located close to the ventricular myocardium. We carefully performed trial pacing at 20 V before HFS to confirm the stimulus would not capture the ventricle. However, the respiratory motion of the heart or ventricular refractoriness due to rapid ventricular responses under ISP infusion might result in either transient capture or loss of capture. Hence, the ablation of AF-Nests might be an alternative to HFS within the CS.

Limitations

First, this was a single-center retrospective study with a small number of cases. As the inherent limitation of the retrospective study, the study protocol regarding the ablation and ATP challenge were not consistent among the patients. For instance, one patient did not undergo HFS (Case 1); another patient (Case 6) did not undergo repeat ATP injection at the end of the procedure. Second, HFS was not systematically performed in all the non-PV trigger sites. However, some of the non-PV trigger sites, such as the Marshall tract or distal portion of CS, might not necessarily provoke the vagal response to HFS because of the low sensitivity

of HFS and the effect of prior PV/Box isolation on the interaction among the GPs.[6, 18]Third, we did not include the patients with ATP-induced frequent atrial premature complexes.

Finally, the relationship between the episodes of AF and vagal tone predominance was not thoroughly reviewed. Therefore, further studies are warranted to elucidate the association between ATP-induced AF and vagal AF.

Conclusion

ATP-induced AF after PV/Box and SVC isolation was associated with the hyperactivity of atrial GP. The GP-based approach was effective for this not common but challenging situation.

Conflict of interest: none declared.

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Figure Legends

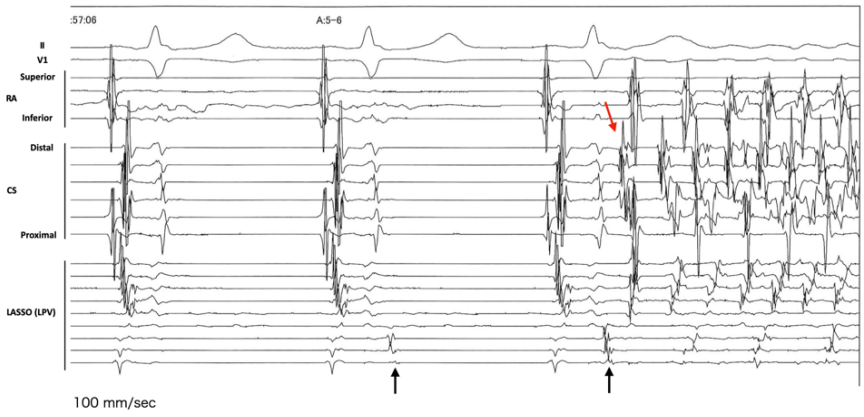
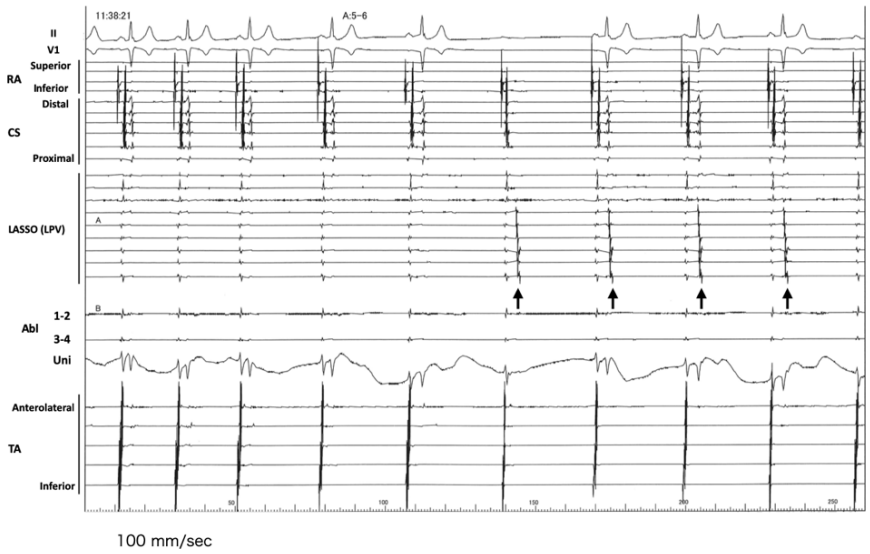


Figure 1. A 64-year-old male with type 2 diabetes mellitus and a prior history of anterior myocardial infarction (Case 7).

ATP injection after the initial PV isolation revealed dormant left PV conduction (black arrow) and also simultaneously induced AF by the trigger PACs from the CS (red arrow).

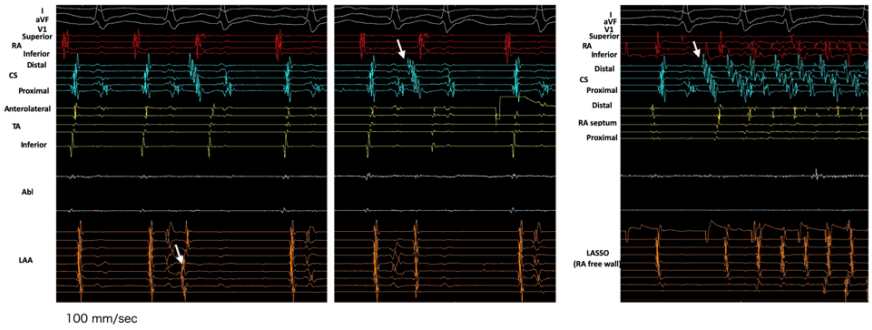
B and C . Therefore, we performed HFS within the CS, which elicited vagal responses at five sites. Brown tags are ablation lesions. Yellow and orange markers indicate the sites with a positive and negative response to HFS, respectively.



D . RF ablation at these sites eliminated the ATP-induced AF despite the residual dormant conduction of the left PV (black arrow). We applied RF ablation at the posterior segment of the left PV to achieve re-isolation. Finally, we confirmed that ATP induced neither AF nor dormant PV conduction.

ATP = adenosine triphosphate; PV = pulmonary vein; AF = atrial fibrillation; PACs = premature atrial complexes; CS = coronary sinus; HFS = high frequency stimulation.

Figure 2. A 23-year-old male with idiopathic ventricular fibrillation (VF) who underwent the second ablation procedure for paroxysmal AF (Case 2).



In the first procedure, we performed PV isolation, SVC isolation, and CTI ablation. However, AF persisted and immediately recurred soon after electric cardioversion. Therefore we performed GP ablation around PVs (posterior Left GP, anterior right GP, and superior left GP) and linear ablation between the superior PVs (i.e., roofline). The ATP challenge was performed during ongoing AF and not repeated after the restoration of sinus rhythm. In the second procedure, we performed re-isolation of the reconnected right PV and SVC.

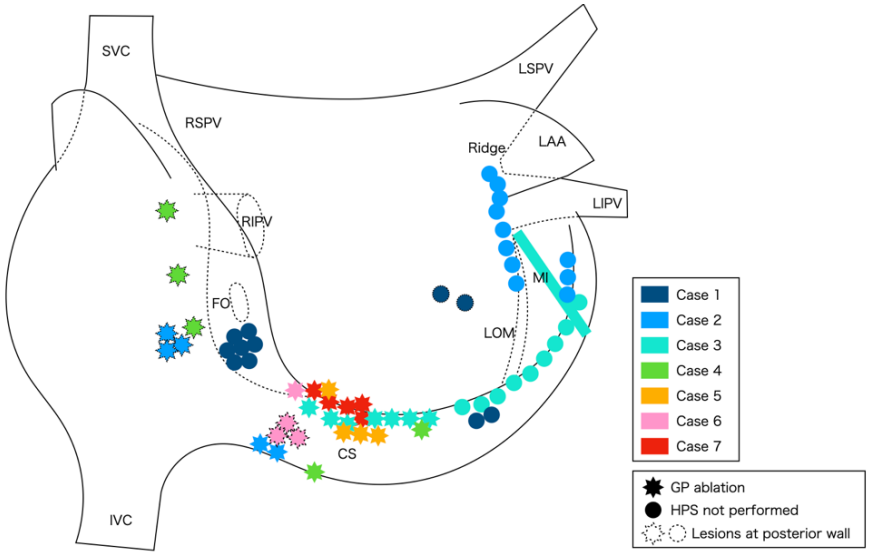
Isoproterenol infusion induced frequent PACs from multiple foci (white arrows in the left and middle panel). ATP injection induced AF from multiple foci (white arrows in the right panel) without dormant conduction of the isolated veins. We identified the trigger foci in the distal portion of CS and the left PV and LA appendage ridge. Radiofrequency ablation along the ligament of Marshall and lateral aspect of the mitral annulus (opposed to the distal CS) suppressed these PACs.

A bolus administration of ATP still induced AF. The first beat initiating AF was documented at the CS ostium and RA septum (white arrows).

C . Therefore, we performed HFS within the CS and RA septum. Vagal responses by HFS were observed at three sites in the RA septum adjacent to the interatrial groove and two sites near the CS ostium (blue tags in the right panels). Following the RF ablation at these sites, AF was no longer inducible by ATP provocation.

TA = tricuspid annulus. Other abbreviations are the same as Figure 1 and 2.

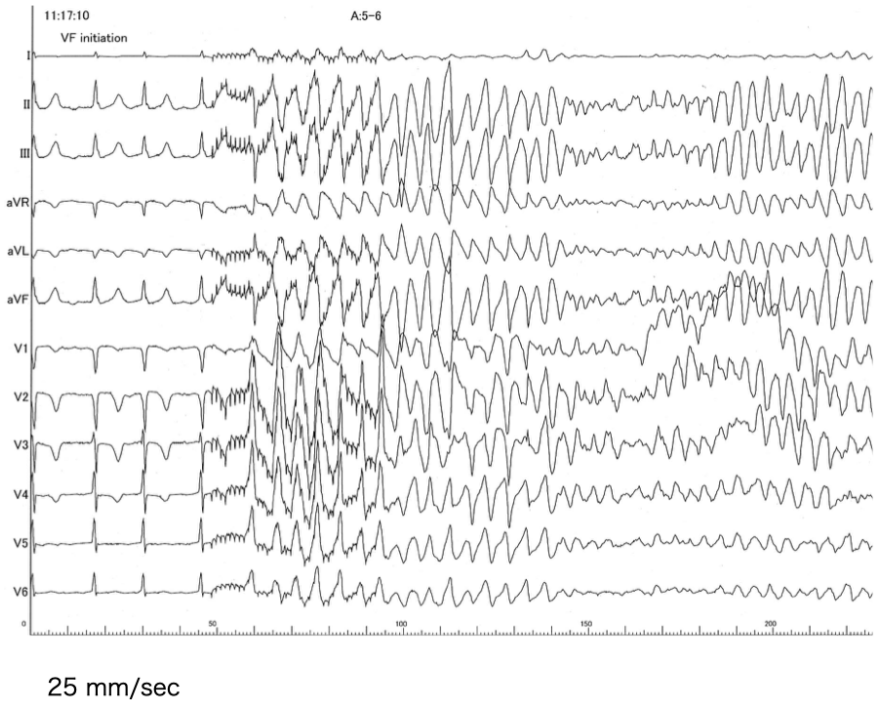
Figure 3. Distributions of the ablation sites following the observation of ATP-induced AF.



Eight-rayed stars indicate the ablation sites with a positive response to high-frequency stimulation (HFS). Round tags indicate the ablation sites without performing HFS. Dotted lesions were applied to the posterior wall at the each site.

LSPV = left superior pulmonary vein (PV); RSPV = right superior PV; LAA = left atrial appendage; RIPV = right inferior PV; LIPV = left inferior PV; MI, mitral isthmus; FO = foramen ovale; LOM = ligament of Marshall; CS = coronary sinus; IVC = inferior vena cava. Other abbreviations are the same as Figure 1 and 2.

Figure 4. Ventricular fibrillation induced by high-frequency stimulation (HFS) within the coronary sinus.



Twelve-leads electrocardiogram during the HFS.

Intracardiac recordings before and during the HFS. Ventricular potentials were noticeable at the distal bipolar electrode of the ablation catheter.

C . Trial pacing 10 seconds before the HFS. Pacing from the ablation catheter at 150 beats per minute did not capture the ventricular myocardium except for the initial three stimuli.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Age, yr	74	22	45	55	55	38	64
Gender	Male	Male	Male	Male	Male	Male	Male
Underlying heart disase	Anterior OMI	Idiopathic VF	none	none	noen	none	Anterior OMI
Type of AF	Paroxsymal	Paroxsymal	Paroxsymal	Paroxsymal	Paroxsymal	Paroxsymal	Paroxsymal
Prior AF ablation	Y	Y	N	N	N	N	N
CHF	N	N	N	N	N	N	Y
Hypertension	Y	N	N	N	N	N	N
Diabetes	N	N	N	N	N	N	Y
Stroke or TIA	N	N	N	N	N	N	N
Estimated GFR, ml/min	64.1	95.4	79.8	82.9	79.5	79.5	38.0
BNP, pg/ml	35	7.0	99.6	23.1	21.8	4.7	63.7
LA dimension, mm	39	27	42	31	37	36	37
LVEF, %	70	58	62	73	63	60	35
Beta blocker	N	N	N	Y	N	Y	Y
ACE-inhibitor / ARB	Y	N	N	N	N	N	Y
Statin	Y	N	N	N	N	N	N
Antiarrhythmic drug	pilsicainide	amiodarone	N	N	N	N	N

Table 1. Baseline characteristics of the study patients

OMI denotes old myocardial infarction; VF, ventricular fibrillation; AF, atrial fibrillation; CHF, congestive heart failure; TIA, transient ischemic attack; GFR, glomerular filtration rate; BNP, brain natriuretic peptide;

LA, left atrial; LVEF, left ventricular ejection fraction; ACE-i, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Ablation in the previous procedure	Box-I MI line CTI	PVI Roof line SVC-I GP around PV CTI	None	None	None	None	None
Ablation before ATP injection	Box-I MI line	right PVI SVCI	Box-I CTI	Box-I SVCI LVA in left roof CTI	Box-I SVCI CFAE in LA CTI	PVI SVCI CTI	PVI CTI
Reconnected vein (spontaneous / ATP provoked)	LA PW (spontaneous)	None	None	Right PV (Spontaneous)	None	SVC (ATP-provoked)	Left PV (ATP-provoked)
Ablation after ATP-induced AF	CFAE in MA & PW below Box lesion Right septum	LOM region Lateral MA GP in CS & RA	MI line CAFE along CS GP in CS	GP in CS & RA	GP in CS	GP in CS	GP in CS
Response to ATP at the end of the procedure	AF inducible	Non-inducible	Non-inducible	Non-inducible	Non-inducible	Not assessed	Non-inducible
Total RF time, minutes	30.0	23.7	64.2	51.7	55.3	46.1	19.4
RF time following ATP-induced AF, minutes	5.2	11.3	10.1	2.8	2.6	2.5	2.9
Number of RF sites following ATP-induced AF	11	15	20	6	5	5	5

Table 2. Summary of the ablation procedure

Box-I indicates Box isolation; MI, mitral isthmus; CTI, cavotricuspid isthmus; PVI, pulmonary vein isolation; SVCI, superior vena cava isolation; GP, ganglionated plexus; ATP, adenosine triphosphate; LVA, low voltage area; CFAE, complex fractionated atrial electrocardiogram; LA, left atrium; MA, mitral annulus; PW, posterior wall; LOM, ligament of Marshall; CS, coronary sinus; RA, right atrium; RF, radiofrequency ablation; AF, atrial fibrillation