rugada syndrome (BS) is characterized by an ST-segment elevation in the right precordial leads of the electrocardiogram (ECG) and a high incidence of sudden cardiac death in patients with structurally normal hearts.1 It has been reported that approximately 20% of patients with BS develop supraventricular arrhythmias, and atrial fibrillation (AF) is associated in 10–20% of those cases.1,2 However, attempting medical control of the AF in those patients can be challenging because some antiarrhythmic drugs may increase the risk of sudden cardiac death.1

Idiopathic paroxysmal AF has been demonstrated to be triggered by atrial premature beats (APBs) originating from the pulmonary veins (PVs)3 and catheter ablation to electrically isolate the PVs from the left atrium (LA) has been established as an effective technique for controlling paroxysmal AF.4–8 Because PV isolation (PVI) often eliminates the need for antiarrhythmic drugs to treat AF, this procedure may be an especially attractive option for treating AF in patients with a Brugada ECG pattern. However, the efficacy of PVI is unknown in such patients, so the purpose of this study was to investigate the safety and efficacy of this technique.

Methods

Patient Characteristics

The subjects were 6 consecutive patients exhibiting a Brugada ECG at baseline who underwent an electrophysiologic study and catheter ablation for symptomatic AF. All patients had frequent attacks of paroxysmal (at least once a week) or persistent AF. The baseline characteristics of these patients, including the age, sex, echocardiographic parameters, presence of structural heart disease, Brugada ECG pattern, and nature of the clinical AF, were recorded. All patients gave written, informed consent before the procedure.

Electrophysiologic Study

The procedure was performed under sedation with intravenous propofol in the fasting state. For mapping and pacing, standard multielectrode catheters were placed in the coronary sinus and His bundle region. The transseptal procedure was performed with fluoroscopic or intracardiac echocardiography guidance. Catheterization into the LA...
was performed with a single-puncture, double-transseptal catheterization technique or 2 punctures, triple-transseptal catheterization technique (2 sheaths over 1 puncture site and the 3rd sheath via a 2nd puncture site) using an 8-Fr SL1 or 2 sheath (St Jude Medical, AF Division, Minnetonka, MN, USA). Intravenous heparin was administered to maintain an activated clotting time >300 s after the atrial transseptal procedure. The ostial diameters of all 4 PVs were measured by selective angiography in all cases as previously reported. The diameter of the PV ostium was measured across the PV antrum in each of the 2 projections (left and right anterior oblique views), and the mean value was obtained.

PVI Technique

In order to electrically isolate the PVs from the LA, either circumferential PV antrum isolation (CPVAI) or an encircling ipsilateral PVs isolation (EIPVsI) was performed using an electroanatomic mapping system (CARTOTM, Biosense-Webster, Diamond Bar, CA, USA) and multipolar circular mapping catheters. In the CPVAI, circumferential radiofrequency (RF) lesions were created approximately 1 cm away from the circular catheter positioned at the PV ostium. For the EIPVsI method, a 3-dimensional shell representing the LA was first constructed by an electroanatomic mapping system (Fig 1). RF current was then applied approximately 1 cm away from the double circular catheters positioned at the PV ostia to encircle the left- and right-sided ipsilateral PVs (Fig 1). RF energy was delivered to maintain an electrode temperature of less than 40°C with a maximum power setting of 40 W using a 3.5-mm tip irrigated ablation catheter or with a target temperature of 55°C and maximum power setting of 40 W using a 4-mm tip non-irrigated ablation catheter. The end-point of these ablation techniques was complete PV electrical disconnection and non-inducibility of "spontaneous" AF during isoproterenol infusion (2–4 μg/min) and burst atrial pacing (to a cycle length as short as 200 ms).

Follow-up

Follow-up was performed at 2 weeks, 1 month and every month thereafter, using 24-h Holter and cardiac recordings. All patients who reported symptoms were given an event monitor to document the cause of the symptoms. Computed tomography was performed before and 3–4 months after the ablation procedure to assess the PVs for stenosis.

Results

Clinical Characteristics

The baseline characteristics of the 6 patients are shown in Table 1 (5 males, 1 female; age range 42–61 years). The echocardiographic dimension of the LA was 32–38 mm and left ventricular ejection fraction 55–75%. None of the patients had any structural heart disease. The baseline ECG demonstrated a type I Brugada pattern in 1 patient, a type II pattern in 4 patients, and a type III pattern in 1 patient.

Table 1 Clinical and Electrocardiographic Details of the Study Group

<table>
<thead>
<tr>
<th></th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
<th>Patient 5</th>
<th>Patient 6</th>
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<tr>
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<td>III</td>
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<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
<td></td>
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<tr>
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<td>(–)</td>
<td>(–)</td>
<td>(–)</td>
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<td>(–)</td>
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<td>(–)</td>
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</table>

ECG, electrocardiogram; LA, left atrium; LVEF, left ventricular ejection fraction; SHD, structural heart disease; N/A, not available; VF, ventricular fibrillation; ICD, implantable cardioverter-defibrillator.
Efficacy of PVI in PAF Patients With Brugada ECG

In all but 1 (Patient 4) of the patients exhibiting a type II or III Brugada ECGs, the administration of a sodium-channel blocker (pilsicainide 1 mg/kg over 10 min, IV\textsuperscript{10,11}) converted the ECG to a type I pattern (Fig 3). Patient 4 alone had a family history of sudden cardiac death. Half of the patients had experienced syncope and in 2 of those patients, ventricular fibrillation was induced by programmed electrical stimulation. An implantable cardioverter-defibrillator (ICD) had been implanted in the 2 patients (Patients 2 and 6), who satisfied the criteria for BS\textsuperscript{1} and in the 1 patient (Patient 4) without a type I Brugada ECG, but with a history of syncope and family history of sudden death. All 3 patients had experienced inappropriate shocks from their ICD because of rapidly conducted AF. Five patients exhibited a paroxysmal form of AF and 1 had a persistent form. The AF duration was 3 weeks to 8 years. All the patients also had typical, cavotricuspid isthmus-dependent atrial flutter.
Electrophysiologic Study and Catheter Ablation

The electrophysiologic findings and the results of catheter ablation are summarized in Table 2. The mean ostial diameter was 19.7±1.9 (17.4–22.4), 16.9±2.3 (13.2–19.8), 15.1±1.9 (13.3–18.0), and 16.8±2.1 (13.4–19.9) mm for the left superior PVs, right superior PVs, left inferior PVs, and right inferior PVs, respectively. At baseline, the heart rhythm was sinus rhythm in 2 patients, AF in 3 patients, and typical atrial flutter in 1 patient (Patient 1, Fig 2). In the 2 patients with sinus rhythm, AF was induced by burst atrial pacing from the coronary sinus and no APBs were observed after the spontaneous termination of AF. In the patient with atrial flutter, a cavotricuspid isthmus ablation was first performed and no APBs were observed after the termination of atrial flutter. In 2 of the 3 patients with AF, it was terminated spontaneously before ablation and thereafter no APBs were observed throughout the procedure. In the remaining patient with AF, PV ablation was performed during AF. CPVAI was performed in 2 patients and EIPVsI in the remaining patient. In the 1 patient undergoing EIPVsI during AF, the AF terminated during the ablation of the left PVs. Successful PV electrical disconnection was achieved for all the PVs in all the patients (Figs 4,5). Neither vagal responses nor ST-segment elevation during PVI were observed in any of the patients. Thereafter, burst atrial pacing from the coronary sinus with an isoproterenol infusion induced AF in 1 patient and typical atrial flutter in another patient. In the patient with the induced AF,
cardioversion was performed and neither spontaneous AF nor APBs were observed after restoration of sinus rhythm. In the patient with the induced typical atrial flutter, a cavotricuspid isthmus ablation was performed and thereafter neither spontaneous AF nor APBs were observed. Cavotricuspid isthmus ablation was also performed in all of the other patients. The mean duration of RF application to complete the PV electrical disconnection was 56±11 (42–72) min. The total procedure and fluoroscopy times were 146±11 (128–157) and 49±6 (42–58) min, respectively.

Follow-up
During follow-up, 5 of the 6 (83%) patients were free of symptomatic AF without any antiarrhythmic drugs after the first procedure. The remaining patient (Patient 6) had an early recurrence of AF and a newly developed atrial tachycardia (AT) after the first procedure and a 2nd procedure was performed immediately. Recovery of an electrical connection was observed in the 3 PVs and a few RF applications delivered at the conduction gaps with electrophysiologic guidance achieved successful electrical disconnection in all the PVs. However, even after that, clinical AT was still induced by burst atrial pacing from the coronary sinus. Detailed mapping of the LA revealed that the tachycardia was a focal AT originating from the mitral isthmus. After the AT was eliminated by a few RF applications, neither AF nor AT was induced despite burst atrial pacing with isoproterenol infusion. Finally, during the follow-up period (11±6, 5–20 months) after the last procedure, 6 of 6 (100%) patients were free of any symptomatic atrial arrhythmias without any antiarrhythmic drugs. No PV stenosis was observed and no other complications occurred.

Discussion
It is well known that AF is often observed in patients with BS and it can be a difficult clinical problem for those patients because attempts to control the AF with antiarrhythmic medications may increase the risk of sudden cardiac death. In addition, the use of an ICD may be complicated by inappropriate shocks because of the rapidly conducted AF in these patients. Because of these concerns, non-pharmacological therapy to eliminate the AF is especially attractive for patients with BS. Though a type I ECG, which is characterized by a coved-typed ST-segment elevation of ≥2 mm (0.2 mV) followed by a negative T wave, is necessary for a definitive diagnosis of BS, the ECG pattern can be dynamic and is often concealed. Therefore, AF patients with type II or III Brugada ECGs, which are characterized by a ST-segment elevation with a saddleback appearance and high takeoff of the ST-segment elevation ≥2 mm, trough displaying an ST elevation ≤1 mm, and then either a positive or biphasic T wave (type II) or either a saddleback or coved appearance with an ST-segment elevation <1 mm (type III): may also be at risk for adverse effects of antiarrhythmic drugs. To the best of our knowledge, this is the first report to investigate the safety and efficacy of PVI in AF patients with a Brugada ECG pattern. We demonstrated that PVI was highly effective and safe in AF patients with a Brugada ECG, similar to other patients with idiopathic AF. These findings suggest that PVI is a potential first-line therapy for symptomatic AF in patients with a Brugada ECG.

Morita et al reported that atrial vulnerability is enhanced in patients with BS and that abnormal atrial conduction may be an electrophysiologic basis for the induction of AF in patients with BS. However, the mechanism of AF occurrence in the patients with BS or with a Brugada ECG alone remains unclear. In the present study there was no evidence that AF originated from the PVs in any of the patients; however, PVI alone eliminated AF completely in all of them. It has been reported that arrhythmogenic PVs for AF...
exhibit a dilatation of the ostium and in all of the present patients, the PV ostial diameters were larger than those of the arrhythmogenic PVs in the previous report. These findings also suggest that the PVs in all the patients in this study might have been arrhythmogenic for AF.

We cannot discuss the efficacy and safety of the PVI in each of the stratifications because the clinical characteristics regarding BS were variable in the present patients. Further studies are needed to clarify this issue, but we believe that the results of this study have significant clinical implications.

**Conclusion**

In this small group of patients with a Brugada ECG pattern, PVI appeared to be safe and effective, suggesting that this therapy deserves consideration for highly symptomatic individuals with paroxysmal and persistent AF.

**References**


