

# Long-term outcome of pulmonary vein isolation in patients with paroxysmal atrial fibrillation and Brugada syndrome

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## Aims

The therapeutical management of atrial fibrillation (AF) in the setting of Brugada syndrome (BS) might be challenging as many antiarrhythmic drugs (AADs) with sodium channel blocking properties might lead to the development of ventricular arrhythmias. This study sought to evaluate the clinical outcome in a consecutive series of patients with BS having undergone pulmonary vein (PV) isolation by means of radiofrequency (RF) or cryoballoon (CB) ablation and the efficacy of catheter ablation for preventing inappropriate interventions delivered by implantable cardioverter defibrillators (ICD) on a 3-year follow up.

## Methods and results

Twenty-three consecutive patients with BS (13 males; mean age was  $47 \pm 18$  years) having undergone PV isolation for drug-resistant paroxysmal AF were enrolled. Eleven patients (48%) had an ICD implanted of whom four had inappropriate shocks secondary to rapid AF. Over a mean follow-up period of  $35.0 \pm 25.4$  months (median 36 months) the freedom from AF recurrence after the index PV isolation procedure was 74% without AADs. Patients with inappropriate ICD interventions for AF did not present further ICD shocks after AF ablation. No major complications occurred.

## Conclusion

Catheter ablation is a valid therapeutic choice for patients with BS and paroxysmal AF considering the high success rates, the limitations of the AADs and the safety of the procedure, and it should be taken into consideration especially in those patients presenting inappropriate ICD shocks due to rapid AF.

## Keywords

Atrial fibrillation • Brugada syndrome • Pulmonary vein isolation • Cryoballoon • Radiofrequency • Inappropriate shock

## Introduction

Brugada syndrome (BS) is characterized by a distinct electrocardiographic pattern consisting of a right bundle branch block-like morphology and ST elevation in the right precordial leads in patients

without structural heart disease carrying the risk of sudden cardiac death (SCD) due to malignant ventricular arrhythmias.<sup>1</sup> Atrial fibrillation (AF) is the most common supraventricular arrhythmia in patients with BS, with a reported prevalence of 3–20%.<sup>2–5</sup> Pharmacological treatment of AF in the setting of BS might be challenging as many

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## What's new?

- The present study analysed the largest population of patients with Brugada syndrome and paroxysmal atrial fibrillation treated with catheter ablation over a long-term follow up.
- The freedom from recurrence of atrial fibrillation was 74% during a 3-year follow up and without antiarrhythmic drugs.
- Patients with inappropriate ICD interventions due to AF did not present further ICD shocks after catheter ablation.
- No major complications occurred in the study population.

antiarrhythmic drugs (AADs) with sodium channel blocking properties might lead to the development of ventricular arrhythmias. Moreover, patients with BS and implantable cardioverter-defibrillator (ICD) might experience inappropriate shocks due to AF with rapid ventricular response.

Pulmonary vein (PV) isolation is nowadays the cornerstone of percutaneous transcatheter ablation for drug-resistant paroxysmal AF.<sup>6</sup> However, PV isolation is not frequently performed in this patients' population as it is still unclear whether PV triggering is the underlying pathophysiological mechanism of AF in BS. Indeed, management of BS patients with symptomatic paroxysmal AF as well the choice of the optimal ablation strategy to treat these patients remains controversial. Available data reporting the effectiveness of PV isolation for paroxysmal AF among patients with BS are sparse<sup>7-9</sup> and have included small groups over a restricted follow-up duration.

In this study, we describe the clinical outcome on a 3 years follow-up period in a consecutive series of patients with BS having undergone PV isolation by means of radiofrequency (RF) or cryoballoon (CB) ablation.

## Methods

### Study population

Since 1992, all patients diagnosed with BS and their relatives tested for the syndrome have been included in a registry and followed-up in a prospective fashion. All patients included gave informed consent to participate in the registry. The ethical committee of the UZ Brussel-VUB has approved the study protocol. Individuals having undergone PV isolation by the means of RF or cryoenergy in our centre were consecutively included in this study. Patients were affected by drug-resistant paroxysmal AF prior to ablation. Paroxysmal AF was defined as the occurrence of recurrent episodes of AF self-terminating within 7 days. Physical examination, medical history and baseline electrocardiogram (ECG) were obtained in all patients before the invasive procedure.

To exclude the presence of thrombi in the left atrial appendage, transesophageal echocardiography was performed before the procedure, along with a transthoracic echocardiography (TTE) enabling assessment of left atrial (LA) and left ventricular dimensions as well as valve function.

### Pre-procedural management

Left atrial anatomy, PV drainage patterns, ostium shape, and dimensions were measured by means of pre-procedural multislice cardiac computed tomographic (CT) imaging. The CT scan protocol as well as the

parameters used to evaluate the abovementioned parameters have been extensively described previously.<sup>10</sup>

### Ablation procedure

Pulmonary vein isolation was performed by means of a RF energy source or CB ablation.

#### Radiofrequency ablation

Radiofrequency ablation was performed under general anaesthesia. After having achieved a double transeptal access, an electroanatomical map of the LA with the Carto system (Biosense Webster, Inc.) was created in all patients. Radiofrequency ablation was then performed with an open irrigated cool tip 3.5 mm catheter (Navistar, Biosense Webster, Inc., Diamond Bar, CA, USA). Before ablation all PVs were mapped by means of a circular mapping catheter (CMC) (Lasso, Biosense Webster, Inc., Diamond Bar, CA, USA) in order to evaluate the baseline electrical activity. After map completion, RF energy was applied through a 3.5 mm irrigated tip ablation catheter (Navistar, Thermocool™, Biosense Webster, Inc., Diamond Bar, CA, USA) in a power-controlled mode with a power limit of 35 W and a maximum temperature of 48°C. Power was decreased to 25W when ablating on the posterior wall in order to avoid oesophageal injury. No additional ablation lines were performed. All procedures were performed without contact-force technology.

#### Cryoballoon ablation

Briefly, after having achieved LA access, via a steerable 15 Fr sheath (FlexCath Advance®, Medtronic®, Minneapolis, MN, USA), a circular mapping catheter (Lasso, Biosense Webster, Inc., Diamond Bar, CA, USA) or a 20-mm diameter octapolar inner lumen mapping catheter (ILMC) (Achieve, Medtronic, MN, USA) were used to obtain baseline electrical information. A 28 mm CB (Arctic Front or Arctic Front Advance, Medtronic®, Minneapolis, MN, USA) was advanced over the ILMC up to the left atrium, inflated and positioned in the PV ostium of each vein. Among 14 CB ablation procedures, 5 (29%) were performed using first-generation CB (Arctic Front, Medtronic®) and the remaining 12 (71%) were performed using the second-generation CB (Arctic Front Advance, Medtronic®). Then, CB ablation procedure was performed as previously described.<sup>11</sup>

#### Repeat ablation procedure

After index PV isolation, all patients experiencing ATas, except those who became responsive to previously ineffective drugs or with short-lasting asymptomatic arrhythmic episodes, underwent a repeat ablation using a RF irrigated-tip CF catheter. Briefly, the CMC was positioned in each venous ostium to assess and identify potential reconnection. The location of gaps was defined as the site of reconnection in four different atrial regions. Once localized, RF applications were applied until isolation, which was also evaluated 30 min after. Radiofrequency applications were performed with an open irrigated-tip catheter with CF monitoring (Thermocool, SmartTouch™, Biosense-Webster, Inc., Diamond Bar, CA, USA) in a power-controlled mode with a power limit of 35 W and at a maximum temperature of 48°C. A 25 W power was limited to the posterior sites. Contact-force data were continuously monitored throughout the procedure.

Patients experiencing reconnection underwent re-PV isolation. In case of atrial tachycardia (AT), the mapping system allowed to identify the underlying mechanism. After AT termination, re-PV isolation was performed. After discharge, patients were scheduled for follow-up visits and all documented AT episodes >30 s after the index procedure were considered as a recurrence.

## Post-procedural management

Patients were discharged the day after ablation if clinical status was stable. After the intervention, patients were continuously monitored with ECG telemetry for at least 18 h. Before hospital discharge, all patients underwent transthoracic echocardiography in order to exclude pericardial effusion and a chest X-ray. Oral anticoagulation was started or restarted the evening of ablation and continued for at least 3 months. Anti-arrhythmic therapy was administered for 2 months following the procedure and discontinued if the patient was free of AF relapse.

## Follow-up

Clinical follow-up consisted of physical examination, ECG and 24 h Holter recording performed at 3, 6 and 12 months and every 6 months after the first year. Follow up of ICDs was performed every 6 months in the outpatient clinic, combined with remote device monitoring provided by the cardiac device company. All episodes of AF recurrence, including the ones occurring in the blanking period, were taken into consideration for the final analysis. All documented episodes of atrial tachyarrhythmias lasting  $\geq 30$  s were considered as a recurrence.

## Statistical analysis

Continuous variables are expressed as mean  $\pm$  SD or median and range as appropriate. Categorical variables are expressed as absolute and relative frequencies. Comparisons of continuous variables were done with Student's *t*-test or the Mann-Whitney *U* test as appropriate. The Chi-square test or Fisher's exact test was used to compare categorical variables as appropriate. Event-free survival was estimated by the method of Kaplan-Meier and compared by the log-rank test. A 2-tailed probability value of  $<0.05$  was deemed significant. Statistical analyses were conducted using the SPSS software (SPSS v20, Chicago, IL, USA).

## Results

### Baseline characteristics

Among 671 patients with BS included in our database, 79 individuals (12%) experienced documented episodes of paroxysmal AF. Among them, a total of 23 consecutive patients (44%) with BS (13 males; mean age was  $47 \pm 18$  years) underwent PV isolation for drug-resistant paroxysmal AF since November 2007. Baseline clinical characteristics of the study population are shown in *Table 1*. Mean LVEF was  $59 \pm 4\%$  and mean LA diameter was  $38 \pm 7$  mm.

### Medical history

In four patients (17%) a baseline spontaneous Brugada ECG type 1 was documented. In the other 19 patients (83%) BS was diagnosed after ajmaline challenge. Among the study population, seven patients (30%) had a family history of SCD and 1 patient (4%) had a previous episode of aborted sudden cardiac arrest due to ventricular fibrillation (VF). Nine patients (39%) reported a history of previous syncope and two patients (22%) were completely asymptomatic before experiencing AF. An electrophysiologic (EP) study was performed in 19 patients (83%) before the ablation procedure. The genetical test was performed in 11 patients (48%) and SCN5A gene mutations was found in 18% of all the genetical tests ( $n = 2$ ). Importantly, no specific genetic profiles have been identified in those patients with both BS and AF. Electrocardiogram and electrophysiological parameters are shown in *Table 2*. During programmed ventricular stimulation, sustained ventricular arrhythmias were induced in three patients (16%).

**Table 1** Clinical characteristics of the study population

Age (years)	47.2 $\pm$ 18.0
Male	13 (57%)
Family history of SCD	7 (30%)
Previous SCA	1 (4%)
History of syncope	9 (39%)
Spontaneous type 1 pattern	4 (17%)
Previous ICD implantation	15 (65%)
Inappropriate ICD interventions <sup>a</sup>	4 (27%)
LVEF (%)	59.5 $\pm$ 4.1
LA diameter (mm)	38.2 $\pm$ 6.9

Categorical variables are expressed as absolute and percentage (in brackets). Continuous variables are expressed as mean  $\pm$  SD. SCD, sudden cardiac death; SCA, sudden cardiac arrest; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; LA, left atrial.

<sup>a</sup>Percents refer to patients with ICD.

**Table 2** Electrocardiographic and EP parameters

PR interval (ms)	180.1 $\pm$ 36.4
QRS duration (ms)	121.2 $\pm$ 31.2
QTc interval (ms)	401.9 $\pm$ 37.9
AH interval (ms)	85.7 $\pm$ 26.9
HV interval (ms)	47.5 $\pm$ 10.9
cSNRT (ms)	402.2 $\pm$ 133.5

Continuous variables are expressed as mean  $\pm$  SD. cSNRT, corrected sinus node recovery time.

Furthermore, one patient underwent cavotricuspid isthmus ablation for atrial flutter prior to AF ablation. Fifteen patients (65%) had a previous ICD implantation and inappropriate shocks for rapid AF were documented in four of them (27%). Ten patients (67%) were implanted with a dual chamber device (DDD-ICD) and five (33%) with a single-chamber defibrillator (VVI-ICD). In 14 patients, the device was programmed as follows: VF detection  $>222$  bpm with shock therapy (35J $\times$ 6) and ventricular tachycardia (VT) detection  $>200$  bpm. In the remaining patient presenting a previous episode of aborted SCD, the device was programmed as follows: VF detection  $>222$  bpm with shock therapy (35J $\times$ 6) and VT detection  $>200$  bpm with anti-tachycardia pacing (ATP $\times$ 3) followed by shock therapy (20J $\times$ 1, 35J $\times$ 4). For this patient, pharmacologic therapy with sotalol and bisoprolol failed to maintain sinus rhythm and avoid inappropriate ICD interventions. Furthermore, reprogramming the device by switching off the VT zone detection was not able to avoid inappropriate ICD interventions that were caused by episodes of fast AF which met the rate threshold criteria for VF leading to an ensuing shock.

Ten patients (43%) already started to experience documented AF  $15.7 \pm 11.2$  months (median 15.5 months) before the diagnosis of BS; in the remaining 13 patients (57%) the first diagnosis of AF was done after a mean time of  $31.7 \pm 27.1$  months (median 32 months) from the diagnosis of BS. The mean number of failed class II or III AADs was  $1.3 \pm 0.6$ . Previous ineffective anti-arrhythmic therapy consisted of sotalol in 19 patients (83%). The remaining four patients received

**Table 3** Comparison between patients having undergone radiofrequency ablation procedures compared with those having undergone cryoballoon procedures

	Radiofrequency ablation (n=6)	Cryoballoon ablation (n=17)	P value
Age (years)	48.5 ± 10.6	45.4 ± 20.3	0.8
Male	2 (33%)	11 (65%)	0.2
Family history of SCD	3 (50%)	4 (24%)	0.3
Previous SCA	0 (0%)	1 (6%)	0.5
History of syncope	1 (17%)	8 (47%)	0.2
Spontaneous type 1 pattern	2 (33%)	2 (12%)	0.2
Previous ICD implantation	3 (50%)	12 (71%)	0.4
LVEF (%)	59.2 ± 4.3	59.6 ± 4.1	0.8
LA diameter (mm)	35.6 ± 6.0	39.8 ± 7.1	0.2
Procedural time (min)	89.2 ± 54.6	67.8 ± 14.7	0.2
Fluoro time (min)	17.7 ± 11.2	13.2 ± 7.8	0.3
Follow up (months)	37.5 ± 35.3	32.4 ± 17.3	0.6

Categorical variables are expressed as absolute and percentage (in brackets). Continuous variables are expressed as mean ± SD. SCD, sudden cardiac death; SCA, sudden cardiac arrest; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; LA, left atrial.

treatment with sotalol and betablockers ( $n = 3$ ; 13%), amiodarone ( $n = 1$ ; 4%). No patient received chronic treatment with oral sodium-channel blockers for the prophylaxis of paroxysmal AF.

### Procedural characteristics

A total of 92 PVs were depicted on the pre-procedural CT scan. No left common ostia were identified. At the time of the procedure, all patients were in sinus rhythm.

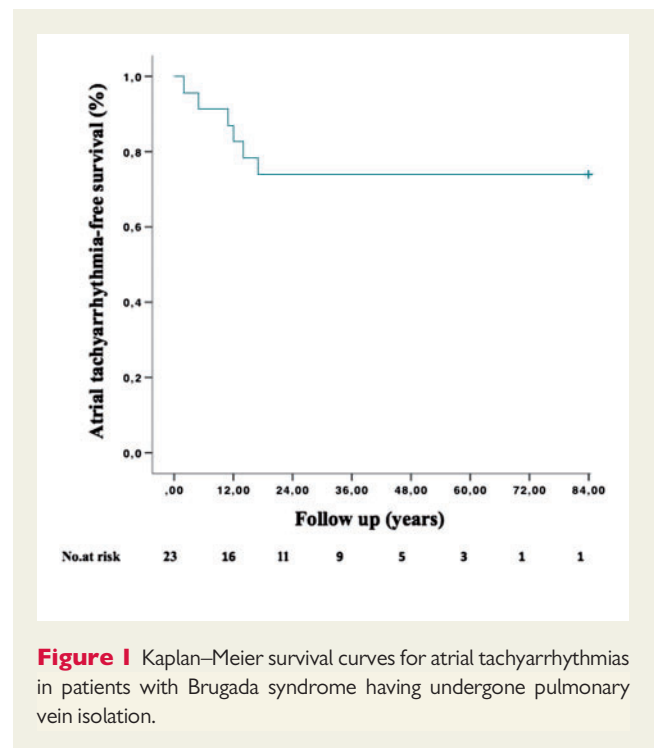
Among the study population, six patients (26%) underwent a procedure using RF energy, the remaining patients received a CB ablation ( $n = 17$ ; 74%). No ST-segment elevation was observed during PV isolation in any of the patients. Patients' characteristics for each group are listed in Table 3.

### Radiofrequency ablation

Mean procedural and fluoroscopy times were  $89.2 \pm 54.6$  and  $17.7 \pm 11.2$  min, respectively. Radiofrequency ablation time was  $22 \pm 6$  min. No periprocedural complications occurred.

### Cryoballoon ablation

Mean procedural and fluoroscopy times were  $67.8 \pm 14.7$  and  $13.2 \pm 7.8$  min, respectively. The 28 mm CB was used in all patients. Mean minimal temperatures were  $-49.5 \pm 8.8^\circ\text{C}$  in the left superior pulmonary vein,  $-48.7 \pm 6.1^\circ\text{C}$  in the LIPV,  $-50.6 \pm 6.5^\circ\text{C}$  in the RSPV and  $-46.4 \pm 6.7^\circ\text{C}$  in the right inferior pulmonary vein. After a mean of 2.2 applications all veins (100%) were isolated. Pulmonary vein isolation was successfully achieved in all veins without the need of additional focal catheter applications. After a first-generation CB ablation procedure, one patient (20%) experienced transient phrenic nerve palsy which completely recovered before the end of the procedure. Another patient experienced an acute pericarditis associated with fever, chest pain, diffuse ST elevation on the ECG and increased C-reactive protein a few days after a second-generation CB procedure; the patient was treated with ibuprofen and the symptoms resolved in 2 weeks.



**Figure 1** Kaplan–Meier survival curves for atrial tachyarrhythmias in patients with Brugada syndrome having undergone pulmonary vein isolation.

### Follow up

A total amount of 17 patients (73.9%) were free of AF at a mean follow-up time of  $35.0 \pm 25.4$  months (median 36 months) without AADs (Figure 1). Specifically, among five patients having undergone first-generation CB ablation, 2 of them (40%) experienced AT/AF recurrence during a mean follow-up period of  $38.4 \pm 24.4$ ; among 12 patients which underwent a second-generation CB ablation, 2 of them (17%) had an AT/AF relapse in a mean follow up of  $29.4 \pm 13.1$ . In the “RF group”, two patients (33%) experienced AT/AF recurrence after a mean follow up of  $37.5 \pm 35.3$  months. Among patients

**Table 4** Characteristics of patients presenting recurrence of tachyarrhythmias after AF ablation procedures

Pts n°	Age	Gender	Type of recurrence	Index procedures	Redo procedure	Timing of recurrence	SCN5A mutation	LVEF (%)	LA diameter (mm)	Findings
1	52	Male	Left flutter	RF	RF	2 months	No mutation	55	57.9	Roof-dep let flutter; no rec
2	66	Female	AF	RF	RF	12 months	Not performed	60	41.7	LIPV,RSPV, RIPV rec
3	37	Male	AF	CB1	RF	11 months	Not performed	55	35.6	LSPV rec
4	47	Female	AF	CB1	Not performed	17 months	Not performed	63	37.4	/
5	68	Male	AF	CB2	RF	5 months	No mutations	57.5	35.5	LIPV rec
6	60	Female	AF	CB2	Not performed	14 months	Not performed	65	44	/

AF, atrial fibrillation; LVEF, left ventricular ejection fraction; LA, left atrial diameter; RF, radiofrequency; Roof-dep left flutter, roof-dependent left atrial flutter; LIPV, left inferior pulmonary vein; RSPV, right superior pulmonary vein; RIPV, right inferior pulmonary vein; Rec, reconnection; LSPV, left superior pulmonary vein; CB1, first-generation cryoballoon; CB2, second-generation cryoballoon.

( $n = 4$ ) who had experienced inappropriate ICD interventions for AF, none of them presented neither AT/AF relapses nor further ICD shocks. Six patients (26%) had a recurrence of atrial tachyarrhythmias after a mean period of  $10.1 \pm 5.6$  months (median 11.5 months); among them, five (83%) exhibited atrial fibrillation and the remaining one (17%) showed a left atrial flutter. The latter one had underwent a PV isolation with RF technology and 2 months later a symptomatic left atrial flutter occurred; the redo procedure, performed with RF technology, highlighted a complete isolation in all PVs and showed a roof-dependent left flutter which was successfully ablated with conversion to sinus rhythm during ablation of the posterior left atrial roof. Table 4 shows the characteristics of those patients presenting recurrence of atrial tachyarrhythmias during the follow-up period. Among six patients with AT/AF recurrence, two (33%) did not undergo a repeat procedure because an alternative strategy with medical therapy was decided. Four redo procedures were performed during the follow up using RF ablation technology: among all 16 PVs, 5 (31%) showed a late PV reconnection in 3 patients (1.67 per patient), at the time of repeat ablation procedure. Overall, persistent PV isolation could be documented in 11 of 16 PVs (69%). As previously described, in only one patient could be demonstrated a persistent isolation of all PVs (25%), whereas PV reconnection could be documented in three of four patient (75%). According to the PV location, the following reconnection could be documented: one left superior PV (25%), two left inferior PVs (50%), one right superior PVs (25%), one right inferior PV (25%). After a mean follow up of  $25.7 \pm 13.2$  months (median 18 months) from the redo procedures, three out of four patients (75%) were still free from AT/AF recurrences; the remaining one experienced a recurrence of AF 15 months after the redo procedure and he was treated with anticoagulation therapy only. Therefore, considering also the repeat procedures, a total 20 out of 23 patients (86.7%) were still free from AF relapses at the last the follow-up assessment.

## Discussion

The main findings of our study are (1) the freedom from AT/AF recurrence in patients with BS and paroxysmal AF after the index PV

isolation procedure by means of RF or CB technology was 74% during a 3-year follow up and without AADs; (2) patients with inappropriate ICD interventions for AF did not present further ICD shocks after AF ablation; (3) no major complications occurred in the present study population.

To the best of our knowledge, our study analysed the largest population of patients with BS and paroxysmal AF treated by catheter ablation over a mean follow-up period of 3 years.

Our findings are similar to previously published reports on AF ablation in patients with BS.<sup>7-9</sup> Previously, Yamada et al.<sup>7</sup> reported freedom from AF after PV isolation using RF technology in 83% of patients (5/6) at 1-year follow up. Our group already showed that seven out of nine patients (67%) were free from AF without the use of antiarrhythmic drugs after a 2-year follow up after RF or CB ablation.<sup>8</sup> Recently, Kitamura et al.<sup>9</sup> reported that 92.9% of patients had freedom from AF after a mean follow up of 3.3 years in a population of 14 patients with BS having undergone catheter ablation as a primary therapy prior to antiarrhythmic drug use. The higher successful outcome in the latter one might be explained by an earlier performance of PV isolation as first-line therapy and by the follow-up electrophysiological study performed 6 months after the ablation.

It is well known that the pharmacological treatment of AF in patients with BS is challenging because the use of sodium channel blockers might expose the patients to potential pro-arrhythmic effects. Moreover, beta-blockers seem to increase the transmural dispersion of repolarization, unmasking ST-segment elevation, and the safety of amiodarone in the BS is still controversial.<sup>12</sup> As the chronic use of amiodarone is associated with important and well-known side effects, this drug does not represent the ideal choice in this young patient population. Conversely, the hydroquinidine has been demonstrated to be effective and safe in patient with BS and concomitant AF and might represent a valid alternative in this specific subgroup of patients.<sup>2</sup>

The incidence of spontaneous and induced AF in patients with BS is high.<sup>2-5,14,15</sup> Pathophysiological mechanisms leading to AF in patients with BS are not clearly elucidated and the role of PV triggering remains uncertain. The arrhythmogenic substrate described in ventricular myocardial cells of patients with BS might similarly predispose to re-entrant atrial tachyarrhythmias in the atrial tissue. In fact, the



presence of a prominent transient outward current in atria and the observation that episodes of AF are triggered by closely coupled atrial extrasystoles suggests that the development of both arrhythmias might share the same pathophysiological substrate.<sup>13,14</sup> Previous studies have demonstrated that atrial vulnerability, especially the index of intra-atrial and local atrial conduction abnormality, are enhanced in patients with BS.<sup>13–15</sup> The shorter action potential duration and the steeper restitution curve at the shorter diastolic interval observed in patients with BS might also be related to the smaller late sodium current<sup>16</sup> or greater transient outward current<sup>17</sup> at the shorter diastolic interval in these patients. The inducibility of reentrant arrhythmias to a large extent is dependent on the wave-length (conduction velocity  $\times$  refractory period) of the atrial impulse. When the wave length of a premature impulse is short—either by depressed conduction, shortened refractoriness, or both—relatively small areas of conduction block might already be able to set up reentrant circuits. For this reason, both shortening of refractoriness and conduction delay might be critical for AF induction. Therefore, similar to the pathogenesis of VF, it might also be possible that Phase 2 re-entry leads to the development of AF in BS. Furthermore, similarly to ventricular arrhythmias, the onset of AF in patients with BS is often preceded by fluctuations in the autonomic tone and generally occurs during the night.<sup>13</sup> An increased vagal tone might reduce atrial conduction velocities and shorten the effective refractory period leading to the induction of AF.

Although the pathophysiological mechanisms of AF induction and maintenance in patients with BS are deemed to be associated with channel dysfunctions in the atrial cells, results from previous studies and the present findings suggest that triggers coming from PVs might play an important role in the genesis of AF in these patients.<sup>7–9</sup> We may assume that the PV isolation might have eliminated potential significant triggers which are likely to initiate AF in a predisposed substrate such as the atrial myocardium in Brugada patients. Second, the wide antral isolation, either with CB or with RF, as performed in the present study, might hypothetically affect the periostial nervous system reducing its influence and modulating the autonomic nervous tone.

Moreover, as the clinical outcome is favorable in this patient population, one might suggest that the persistence of BS does not play any critical role in the initiation of AF and also in affecting the recurrence rate over the follow up.

Of note, ICD inappropriate interventions were completely eliminated by PV isolation in patients having previously undergone shocks for rapid AF. In fact, all four patients with inappropriate ICD therapy did not present any recurrence of AF and any further ICD inappropriate interventions following the catheter ablation during the follow-up period. The latter finding was already proven by previous studies showing that catheter ablation might be a feasible therapeutic option for treating atrial tachyarrhythmias responsible for inappropriate shocks in patients with ICD<sup>18</sup> and specifically in those with BS.<sup>8,9</sup>

Importantly, no major complications occurred. Although no CT scan was performed after ablation, no clinical signs related to PV stenosis were observed. No permanent phrenic nerve palsy was observed in patients having undergone CB ablation.

Of note, a total number of 20 out of 23 patients (86.7%) with paroxysmal AF and BS treated with catheter ablation were still free from AT/AF at the end of the follow-up period, considering also the repeat procedures.

Among four patients having undergone a repeat procedure, only one (25%) showed a complete PV isolation (Table 4); the latter one presented a roof-dependent left atrial flutter. In the remaining three cases (75%), at least one vein reconnection was observed, probably responsible of AF recurrence.

In conclusion, the present study analysed the largest consecutive series of patients with paroxysmal AF and BS treated with pulmonary vein isolation during a mean follow-up period of 3 years. The catheter ablation represents an effective therapeutic treatment for patients with BS considering the acceptable success rates, the limitations of the AADs and the safety profile of the procedure, and it should be taken into consideration especially in those patients presenting inappropriate ICD interventions secondary to AF with fast ventricular rates. Nevertheless, larger, prospective, randomized studies are needed to confirm our findings.

## Limitations

The present study is a retrospective analysis of a single-center experience without a control group. The sample size is also relatively small. Although no clinical signs related to PV stenosis were observed this complication could not be excluded as a post-procedural CT scan was not systematically performed. No loop recordings or other invasive devices were implanted in those 13 patients without ICD. Thus, we cannot exclude asymptomatic AF episodes in these patients which might have been missed during the standard ECG 24 h-holter monitoring and, consequently, freedom from AF might have been overestimated in our study. Furthermore, given the longitudinal nature of the study, the AF ablation techniques have changed over the time according to technological advances and developments.

## Conclusion

The present study sought to assess the clinical outcome on a 3 years follow-up period in a consecutive series of patients with BS having undergone PV isolation by means of RF or CB ablation. In our series, the freedom from AT/AF recurrence was 74% during a 3-year follow up after the ablation procedure and without AADs. Patients with inappropriate ICD interventions for AF did not present further ICD shocks after AF ablation. No major complications occurred in our study population. Thus, the catheter ablation might be considered a valid therapeutic choice for patients with BS considering the high success rates, the limitations of the AADs and the safety of the procedure.

**Conflicts of interest:** G. B. C. and C. d. A. receive compensation for teaching purposes and proctoring from AF solutions, Medtronic. P. B. receives research grants on behalf of the centre from Biotronik, Medtronic, St Jude Medical, Sorin, Boston Scientific and speaker's fees from Biosense-Webster, Biotronik and Medtronic. C. d. A. is consultant for Daiichi Sankyo.

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## Erratum

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