Radiofrequency Ablation vs. Antiarrhythmic Medication for Treatment of Ventricular Premature Beats from the Right Ventricular Outflow Tract: A Prospective Randomized Study

Running title: Ling et al.; Catheter ablation vs AADs in RVOT VPBs treatment

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Abstract:

Background - The purpose of this study was to compare the efficacy of radiofrequency catheter ablation (RFCA) versus antiarrhythmic drugs (AADs) for treatment of patients with frequent ventricular premature beats (VPBs) originating from the right ventricular outflow tract (RVOT).

Methods and Results - 330 eligible patients were included in the study, and were randomly assigned to RFCA or AADs group. The absolute number and the burden of VPBs on 12-lead Holter monitors were measured at baseline, and 1st, 3rd, 6th and 12th months after randomization. Left ventricular eject fraction (LVEF) was evaluated by transthoracic echocardiogram at baseline and at 3 and 6 months following randomization. During the 1-year follow-up period, VPB recurrence was significantly lower in patients randomized to RFCA group (32 patients, 19.4%), versus AADs group (146 patients, 88.6%; P<0.001, log-rank test). In a Poisson generalized estimating equations (GEE) regression model, RFCA was associated a greater decrease in the burden of VPBs (RR 0.105; 95%CI: 0.104-0.105; P<0.001) compared to AADs. In a liner GEE model, the LVEF had a tendency to increase after the treatment in both groups (coefficient 0.584; 95%CI: 0.467-0.702; p<0.001). In a cox proportional model, the QS morphology in lead I was the only predictor of VPB recurrence free for catheter ablation (HR 0.154; 95% CI: 0.044 –0.543; p = 0.004).

Conclusions - Catheter ablation is more efficacious than AADs for preventing VPB recurrence in patients with frequent VPBs originating from the RVOT. QS morphology in lead I was associated with better outcome after ablation.

Key words: premature ventricular contraction arrhythmia, catheter ablation, antiarrhythmic drug, radiofrequency catheter ablation
Introduction

Ventricular premature beats (VPBs) are the most common arrhythmia in clinical practice. The right ventricular outflow tract (RVOT) myocardium is frequently the source of VPBs or idiopathic ventricular tachycardia (VT)\(^1\text{–}^3\). Patients with frequent RVOT VPBs often have no structural heart disease and have a benign outcome. If symptomatic or associated with left ventricular (LV) dysfunction, the VPBs can be treated conservatively with antiarrhythmic drugs (AADs)\(^4\text{–}^5\), however, drug therapy may predispose to recurrence and is associated with risks including pro-arrhythmia. Catheter ablation has been reported to be efficacious at VPBs suppression\(^6\text{–}^{10}\), and to improve cardiac function in patients with high VPB burden\(^8\text{–}^{10}\). Few reports, however, have compared the effects of AADs and radiofrequency catheter ablation (RFCA). This randomized prospective study was designed to compare the efficacy of radiofrequency catheter ablation versus AADs for suppression of frequent VPBs from the RVOT.

Methods

Study population

From May 2004 through December 2012, 513 consecutive patients who were referred to the Second Affiliated Hospital of Chongqing Medical University for treatment of RVOT VPBs were screened for enrollment in the study. Patients underwent review of history, physical examination, conventional 12-lead electrocardiography (ECG), 24-hour 12-lead Holter monitor, exercise stress test, transthoracic echocardiography, chest X-ray, as well as electrolyte, thyroid, hepatic and...
renal function tests prior to enrollment. Magnetic resonance imaging (MRI) was also performed in patients with suspected arrhythmogenic right ventricular cardiomyopathy (ARVC). The inclusion criteria were 1) frequent symptomatic VPBs from the RVOT documented by 12-lead ECG to have inferior axis and left bundle branch block (LBBB) QRS morphology, and 2) greater than 6000 VPBs per 24 hours on Holter monitoring. The exclusion criteria included 1) the presence of non-RVOT origin for VPBs indicated by an S wave in lead I; R wave duration index in \( V_1 \) and \( V_2 \geq 0.5 \), and R/S wave amplitude index in \( V_1 \) and \( V_2 \geq 0.3 \); 2) prior AADs therapy; 3) evidence of any structural heart disease; 4) hyperthyroidism or electrolyte disturbance; 5) drug toxicity; 6) diabetes; 7) blood pressure greater than 165/100 mmHg; 8) significant impairment of renal function; 9) QT interval \( >450 \) ms in the absence of bundle-branch block; and 10) significant atrioventricular conduction disease and left or right bundle-branch block. Of all patients screened, 330 patients were eligible for the study and provided written informed consent for participation. Figure 1 shows, schematically, the flow chart of participants in the study. The Ethics Committee of the second affiliated hospital of Chongqing Medical University approved the study protocol.

**Study protocol**

A computer-generated list of random numbers was used for randomization. After the medical evaluation and diagnosis of idiopathic VPBs from the RVOT, patients were randomly assigned 1:1 to ablation or antiarrhythmic drug group based on the computerized random numbers. Allocation concealment was safeguarded by ensuring that allocation was obtained by computer
output after the patients had consented. AADs were administered in 165 patients and the other 165 patients underwent RFCA. Crossovers were only permitted following 1-year follow-up, or occurrence of the clinical endpoint. The AADs included metoprolol and propafenone, and were provided in an open-label fashion. Selection of metoprolol or propafenone was not randomized. If the patient had a higher VPB burden during daytime hours, then metoprolol was used. Otherwise, propafenone was selected. Initial doses of 12.5 mg bid for metoprolol and 100 mg tid for propafenone were recommended. Dosages of AADs were titrated up to the maximum based upon clinical response and/or occurrence of side effects. Doses were reduced or discontinued if intolerable adverse reactions occurred.

**Echocardiography**

All patients underwent echocardiography to assess LV ejection fraction (LVEF) and dimension. The echocardiograms were digitized and analyzed off-line by an expert analyst who was blinded to patient status. LVEF was calculated using the Simpson biplane method\(^{12}\).

**Radiofrequency catheter ablation**

In the presence of clinical VPBs, activation mapping was performed using a 4-mm tip ablation catheter. Pace mapping was performed in addition to activation mapping to identify the VPB focus during sinus rhythm. In patients without spontaneous VPBs, programmed ventricular stimulation was performed from the right ventricular (RV) apex and RVOT at two drive cycle lengths with up to three extra stimuli and incremental burst pacing at a cycle length up to 250ms. In 3 patients, a three-dimensional electroanatomic mapping system was used for activation
mapping (CartoXP, Biosense Inc., Diamond Bar, CA). Radiofrequency energy was delivered with a 4-mm-tip irrigated ablation catheter (Biosense Inc., Diamond Bar, CA) in temperature-controlled mode with a target temperature of 45°C at a power of 30W. If the VPBs were abolished within 20 seconds, the energy application was continued for 60-90 seconds followed by a second 60-second application. If VPBs were still present after 25-30 seconds, the energy application was terminated, and mapping was continued to find an optimal target site. Once the optimal target site was identified, it was documented on two orthogonal fluoroscopic views. After ablation programmed ventricular stimulation and burst pacing on and off isoproterenol infusion were utilized to confirm the effectiveness of RFCA in all patients. Acute success was defined as the absence of VPBs with similar morphology during a 30 minutes observation period.

**Follow up**

All patients were followed in the outpatient department within 2 weeks, and thereafter at monthly intervals, during which physical examination and 12-lead ECG were conducted. Routine 12-lead Holter monitoring was performed at the 1st, 3rd, 6th, and 12th months and echocardiography was performed at the 3rd and 6th months. When patients reported symptoms of palpitations, dizziness, or syncope during follow-up, they were advised to contact their doctors immediately for evaluation of vital signs, 12-lead ECG, and 12 lead 24 hour Holter monitoring. MRI was also recommended if worsening of LVEF or LV dimension were noted during the follow up period. A 14-day blanking period was allowed for uptitration of medications prior to
inclusion of events as clinical endpoints. The patients assigned to the RFCA group were AADs free after successful ablative procedures.

**Study endpoint**

The primary endpoint was recurrence of RVOT VPBs at a rate of $\geq 300$ beats per day documented by 24h Holter monitoring. The secondary variables of interest including the number of VPBs, the burden of VPBs (the number of VPBs/ total QRS complexes $\times 100$) and LVEF at each follow-up time point were collected.

**Statistical analysis**

All analyses were performed using the intention-to-treat principle. Continuous variables were presented as mean $\pm$ standard deviation or median (IQR: $25^{th}$ percentile, $75^{th}$ percentile) depending on normality of distribution and categorical values as frequency (%). The Kaplan-Meier method was used to estimate time dependent freedom from VPB recurrence among the study groups. Differences in VPB recurrence were assessed by the log-rank test. The Cox proportional hazards model was used to examine the association between treatment groups and VPB recurrence, the clinical characteristics including age, gender, VPB burden, duration of VPB symptoms, body mass index (BMI), LVEF, systolic blood pressure and left atrial diameter (LAD) were included in the model to correct the potential imbalance between the two groups. The VPB burden was analyzed using a Poisson generalized estimating equations GEE model with the VPB numbers as the outcome variable, the heart beat numbers as an offset, visit time and treatment allocation as predictor variables. A linear GEE model was used to analyze the
differences of LVEF during the follow up visit. The interaction term between the predictor variables were examined in both GEE model. Cox proportional hazards regression analysis was used to identify independent predictors for VPB recurrence free in patients assigned to RFCA group. One-way ANOVA was used to test the differences of mean target focus activation times in QRS morphology subgroups of patients received RFCA treatment. We also used a linear GEE model to analyze the association between LVEF and VPB burden with LVEF as outcome, randomization group and VPB burden as predictors. A two-sided P<0.05 was considered to indicate statistical significance. Statistical analysis was performed using STATA version 10.0 (STATA Corp, TX, USA)

**Results**

The baseline characteristics of patients have been summarized in Table 1. Of 165 patients assigned to AADs, 50 patients received metoprolol, and 115 patients received propafenone. After the blanking period, the average doses of metoprolol and propafenone were 48.16±3.18mg and 518.34±51.56mg per day, respectively. At the end of the study, the average doses were 46.8±3.78mg per day for metoprolol and 557.6±54.74mg per day for propafenone, respectively.

**Primary endpoint**

Of 5 patients that were lost to follow-up, 1 was in the RFCA group, and 4 were in the AADs group. The primary endpoint was reached in 32 patients assigned to RFCA, and 146 patients assigned to AADs therapy. As shown in Figure 2, the Kaplan–Meier survival analysis...
demonstrated a significant reduction in VPB recurrence in the RFCA group when compared to AADs therapy (P<0.001, log-rank test). The 1 year recurrence rate calculated with the KM estimate is 19.4% (95% CI, 13.9%-26.5%) in RFCA group and 88.6% (95%CI, 82.5%-92.8%) in AADs, respectively. Compared with the AADs group, the relative risk reduction of VPB recurrence is 78.1% in RFCA group. Cox proportional hazards model analyzing showed catheter ablation was associated with decreased VPB recurrence, both in models with (HR 0.088; 95%CI: 0.058–0.131; P<0.0001) and without (HR 0.094; 95% CI: 0.062-0.139; P<0.001) adjusting for age, gender, VPB burden, duration of VPB symptoms, BMI, LVEF, systolic blood pressure and LAD.

Secondary Endpoints

The secondary endpoints including the burden of VPBs and LVEF at each follow-up visit for both groups have been summarized in Table 2. In a Poisson GEE regression model, RFCA group was associated a greater decrease in the burden of VPBs (RR 0.105; 95%CI: 0.104-0.105; P<0.001) during the follow up period (Table 2, Figure 3). Results from the linear GEE model suggested that LVEF had a tendency to increase after the treatment in both groups (coefficient 0.584; 95%CI: 0.467-0.702; p<0.001), and this effect was not associated with group allocation (coefficient, -0.880, 95%CI:-0.283-2.044; p=0.138). In a linear GEE model, the VPB burden was negative associated with LVEF (Coefficient -0.192; 95%CI: -0.23--0.153; p<0.001).

The effect of VPB morphology on the primary endpoint in the ablation group

All patients met the ECG inclusion criteria and lacked exclusion criteria as specified in the
methods section. There were 58 patients with QS morphology, 56 with rsr’/rsR’ and 51 with qR/R/Rs in lead I, respectively. The mean procedural time was 82±35 minutes and the mean fluoroscopy time was 13.5 ± 9.8 minutes. The anatomic distribution of successful ablation targets for the three different QRS morphologies in lead I has been summarized in Supplemental table 1. The mean target focus activation time relative to surface QRS onset was more presystolic in the QS subgroup compared to the rsr’/rsR’ and qR/R/Rs subgroups (44±5ms vs 36±5ms vs 34±4ms, p<0.001). The primary endpoint was reached in 3 patients (5.2%) assigned to the QS subgroup, 14 (24.1%) assigned to rsr’/rsR’ subgroup, 15 (25.8%) assigned to qR/R/Rs subgroup. As shown in Figure 4, the Kaplan–Meier survival analysis demonstrated a significant reduction of VPB recurrence in the QS morphology subgroup (P=0.005, log-rank test) when compared with other two subgroups. In a Cox proportional hazards regression model, QS morphology in lead I was the only significant independent predictor of VPB recurrence free (HR 0.154; 95% CI: 0.044–0.543; p = 0.004) (Supplemental table 2)

Complications

In RFCA group, 1 patient required cardioversion out of short-coupled triggered ectopy induced ventricular fibrillation (VF) during ablation in the RVOT septum. One arteriovenous fistula and 2 hematoma complications occurred after the procedure. All patients with complications recovered without residual symptoms before discharge.

In the AADs group, drug related adverse effects were found in 17 patients. Three patients in the metoprolol subgroup and 4 patients in the propafenone subgroup developed symptomatic
sinus bradycardia with heart rate <50 beats per minute, and 1 patient in the metoprolol subgroup and 2 patients in the propafenone subgroup developed symptomatic hypotension with blood pressure <90/60 mmHg. Other adverse effects included 2 patients with mild fatigue and 1 with a cold extremity (with intact perfusion) in the metoprolol subgroup, and 3 patients with recurrent headaches and 1 with lower extremity edema in the propafenone subgroup.

Discussion

Main findings

This is the first prospective study to perform a head-to-head comparison of the clinical efficacy between RF ablation and AADs in patients with frequent VPBs from the RVOT. The results of this study revealed that the efficacy of radiofrequency catheter ablation was superior to antiarrhythmic drugs for prevention of VPB recurrence. RFCA had a better effect on the VPB burden decrease. The efficacy of ablation in patients with QS morphology in lead I was higher than those with rsr'/rsR' and qR/R/Rs morphology.

VPB and LV dysfunction

The relationship between frequent ventricular arrhythmias and LV dysfunction has been demonstrated in prior reports. Bogun et al confirmed in a large population of patients that frequent VPBs may be associated with LV enlargement and systolic dysfunction. This study demonstrated that the LVEF was inversely associated with VPB burden. A causal relationship between frequent ventricular ectopy and reduced EF was suggested only when Duffee et al
demonstrated an improvement in LV function in association with suppression of ventricular ectopy by AADS therapy. Furthermore, several studies demonstrated that enlarged LV dimensions decreased after successful ablation of frequent predominantly RV ectopy9-10,14-15. Yarlagadda et al10 showed that frequent ectopy originating from the RVOT can cause a reversible form of cardiomyopathy. In agreement with prior studies, we found that the LVEF had a tendency to increase after the treatment in both groups. In this study, there were 35.8% of our patients had a VPB burden>20% at baseline, the burden of VPBs decreased after treatment in both groups, this might be the reason of LVEF increase during follow up. Our findings confirm that treatment is warranted in patients with VPB burden >25% and LV dysfunction, and strongly supports the notion that frequent VPBs result in a reversible form of cardiomyopathy. The potential mechanism by which frequent VPBs result in LV dysfunction is unclear. The mechanism may involve ventricular dyssynchrony or increased oxygen consumption due to LV diastolic dysfunction and mitral regurgitation, as demonstrated previously by other investigators16-18.

QRS morphology of VPBs in lead I and RF ablation outcomes

Our data shows that 87.9% of QS, 80.3% of rsr’/rsR’, and 88.2% of qR/R/Rs morphology VPBs originate in the RV septum, anterior/posterior wall, and RV free wall, respectively. Additionally, the QRS morphology in lead I is strongly associated with outcome after ablation. Therefore, the QRS morphology in lead I can be used as a tool to predict the ablation outcome. In this study, we demonstrated that patients with QS morphology of VPBs in lead I had a better RFCA outcome.
than those with rsr’/rsR’ and qR/R/Rs PVC morphologies. Krittayaphong et al 16 demonstrated that monophasic R-wave in lead I was the only ECG predictor for unsuccessful RF ablation outcome. We presume that ablation outcome in patients with VPBs originating from the free wall of the RVOT is related to structural abnormalities, or proximity of the source to vascular structures that limit RFCA delivery and efficacy. Although there is no direct evidence to document structural abnormalities in patients with VPBs from RVOT, several studies have shown that structural abnormalities such as localized wall bulging, wall thinning, fatty infiltration, and fibrosis, that may be detected by MRI exist in the RVOT, not only in patients with ARVC19, 20 but also in patients with RVOT tachycardia.21

**Antiarrhythmic drugs and idiopathic VPBs**

The majority of monomorphic ventricular ectopic activity is probably benign, especially in patients without obvious structural disorders. Treatment is often unnecessary. When the ectopic activity is symptomatic, the symptoms can be addressed by allaying the patient's anxiety with reassurance. If this is not successful, the frequency of the ectopic beats may be reduced by administration of AADs.5 According to the ACC/AHA/ESC guidelines5, Class III AADs are not optimal as first-line AADs for the treatment of symptomatic VT arising from the RV in patients with structurally normal hearts. Currently, sotalol and amiodarone are the only class III AADs choices in China. Considering the potential side effects associated with long-term use of class III AADs, we opted not to use these medications in the study.

We adopted strict criteria for the judgment of success in the RFCA group. In order to be
consistent, we used the same primary endpoint criteria both the RFCA and AADs groups. Due to these strict criteria some patients (equal proportion in both groups) met the primary outcome despite having subjective improvement in symptoms. In this study, although both metoprolol and propafenone partly relieve symptom and reduce the burden of VPBs, the recurrence of VPBs was higher than RFCA. Therefore, class I and II AADs appear to be mildly effective, at best, for RVOT VPB suppression. Additionally, the side effects caused by long-term use of AADs should not be overlooked. Although no drug related pro-arrhythmic effect was documented in this group of patients, the potential hazards were noted in other studies.\textsuperscript{22–23}

\textbf{VPBs and lethal arrhythmias}

Patient prognosis in the setting of VPBs from the RVOT is excellent in the absence of structural heart disease. However, lethal arrhythmias such as spontaneous VF and polymorphic VT can occur with short–coupled VPBs\textsuperscript{24}. No lethal arrhythmias were observed in this group of patients; however, the phenomenon has been noted by other investigators\textsuperscript{25-26}. In this setting, RFCA has been shown to be effective in eliminating VPBs and reducing the incidence of further VF recurrences. If short–coupled VPB or VPB triggered lethal arrhythmias are noted, RFCA might be the best choice.

\textbf{Study limitations}

Several limitations may have influenced our results. First, although periodic 12-lead ECG and 24 hour Holter were performed during the follow-up period, episodes of asymptomatic VPBs or more serious arrhythmias might have been missed in some patients. Additionally, the study
sample size and follow-up duration may have been insufficient to fully characterize the incidence of lethal arrhythmias among study groups. Second, other more potent AADs, albeit with greater side effects, were not utilized in this study. Third, a 1-year follow-up period may be insufficient to judge the long-term efficacy of either treatment modality.

Conclusions

The results of this study suggest that the efficacy of catheter ablation is superior to antiarrhythmic drugs for preventing VPB recurrence in patients with VPBs originating from the RVOT. QS morphology in lead I was associated with better outcome after ablation.

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Conflict of Interest Disclosures: Dr. Nazarian is a scientific advisor to Biosense-Webster Inc. Dr. Nazarian receives research funding from the US National Institutes of Health and from Biosense-Webster. The other authors declare no conflicts of interest.

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**Table 1:** Baseline Characteristics* of study patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>AADs group (n=165)</th>
<th>RFCA group (n=165)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>50.54±11.52</td>
<td>52.68±10.37</td>
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<tr>
<td>Female n (%)</td>
<td>125(75.8%)</td>
<td>118(71.5%)</td>
</tr>
<tr>
<td>VPB burden (%)</td>
<td>14(IQR:12,21)</td>
<td>14(IQR:12,21)</td>
</tr>
<tr>
<td>VPB numbers</td>
<td>13823(IQR:11948,19892)</td>
<td>14049(IQR:11882,19535)</td>
</tr>
<tr>
<td>Hypertension(n)</td>
<td>11(165)</td>
<td>10(165)</td>
</tr>
<tr>
<td>LAD(mm)</td>
<td>34.39±2.65</td>
<td>34.78±2.76</td>
</tr>
<tr>
<td>LVEF(%)</td>
<td>64.48±4.89</td>
<td>64.07±5.21</td>
</tr>
<tr>
<td>BMI (Kg/m^2)</td>
<td>24.38±2.53</td>
<td>23.89±2.36</td>
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<tr>
<td>Systolic BP(mmHg)</td>
<td>130.58±7.52</td>
<td>128.15±7.23</td>
</tr>
<tr>
<td>Diastolic BP(mmHg)</td>
<td>80.4/±7.61</td>
<td>77.84 ±5.56</td>
</tr>
</tbody>
</table>

*Continuous variables are expressed as mean±SD if normally distributed or as median (IQR; 25th percentile, 75th percentile) if not normally distributed, categorical variables are expressed as number (percentage).

AADs indicates antiarrhythmic drugs; RFCA, radiofrequency catheter ablation; VPB, ventricular premature beats; LAD, left atrial diameter; LVEF, left ventricular ejection fraction; BMI, body mass index; BP, Blood pressure.

**Table 2:** VPB burden and LVEF at baseline and each follow up point

<table>
<thead>
<tr>
<th>Variables</th>
<th>VPB burden (%)</th>
<th>LVEF (%)</th>
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<tr>
<td></td>
<td>RFCA group</td>
<td>AADs group</td>
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<tr>
<td>Baseline</td>
<td>14(IQR:12, 21)</td>
<td>14(IQR:12, 21)</td>
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<tr>
<td>1 month</td>
<td>0.18 (IQR:0.07,0.25)</td>
<td>6 (IQR: 5.8,9)</td>
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<td>3 months</td>
<td>0.14(IQR:0.07,0.22)</td>
<td>6 (IQR:5,8)</td>
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<tr>
<td>6 months</td>
<td>0.1(IQR:0.05,0.21)</td>
<td>6(IQR:5,7)</td>
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<tr>
<td>12 months</td>
<td>0.11(IQR:0.05,0.20)</td>
<td>7(IQR:6,9)</td>
</tr>
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</table>

Variables are expressed as mean ± SD or median (IQR: 25th percentile, 75th percentile).

VPBs indicates ventricular premature beats; LVEF, left ventricular ejection fraction; RFCA, radiofrequency catheter ablation; AADs, antiarrhythmic drugs; IQR, Inter Quartile Range.
Figure Legends:

Figure 1. Flow chart of study participants

Figure 2. Kaplan–Meier estimates of VPB recurrence-free survival after randomization

Figure 3. The burden of VPBs at each follow-up visit

Boxes span the 25th and 75th percentiles, horizontal lines in each box indicate median values, whiskers indicate values within 1.5 IQR of the nearest quartile, and circles indicate values outside this range.

Figure 4. Kaplan–Meier estimates of VPB recurrence-free survival in patients with different VPB morphologies.
513 Patients Screened

Exclusion, n=183
- Structural heart disease, n=25
- ARVC, n=5
- Hyperthyroidism, n=11
- Electrolyte disturbance, n=6
- Drug poisoning, n=3
- Refuse to participate, n=112
- Patients who had taken an AADs, n=21

Clinically eligible, n=330

Randomization

Drug group, n=165
- Side effect, n=17
  - Symptomatic sinus bradycardia, n=7
  - Symptomatic hypotension, n=3
  - Fatigue, n=2
  - Cold extremity, n=1
  - Headaches, n=3
  - Lower limbs edema, n=1

Included analysis, n=165

RF group, n=165
- Complications, n=4
  - Ventricular fibrillation, n=1
  - Arteriovenous fistula, n=1
  - Hematoma, n=2

Included analysis, n=165
Ventricular premature beat (VPB) recurrence free survival

- QS in lead I
- rsr'/rsR' in lead I
- qR/R/Rs in lead I

Follow-up (days)

Number at risk

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<tbody>
<tr>
<td>QS in lead I</td>
<td></td>
<td>56</td>
<td>55</td>
<td>55</td>
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<tr>
<td>rsr'/rsR' in lead I</td>
<td></td>
<td>44</td>
<td>43</td>
<td>42</td>
<td>42</td>
<td>42</td>
</tr>
<tr>
<td>qR/R/Rs in lead I</td>
<td>50</td>
<td>39</td>
<td>37</td>
<td>36</td>
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p = 0.005, Log-rank test
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**Supplemental Material**

Supplemental table 1: Anatomic distribution of three different VPB QRS morphologies

<table>
<thead>
<tr>
<th>QRS morphology in lead I</th>
<th>Right ventricular septum</th>
<th>Anterior/posterior free wall</th>
<th>Right ventricular free wall</th>
<th>Left Coronary Aortic Sinus / left ventricular septum</th>
</tr>
</thead>
<tbody>
<tr>
<td>QS (n=58)</td>
<td>51</td>
<td>5</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>rs'r/rsR' (n=56)</td>
<td>8</td>
<td>45</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>qR/R/Rs (n=51)</td>
<td>0</td>
<td>6</td>
<td>45</td>
<td>0</td>
</tr>
</tbody>
</table>

VPB indicates ventricular premature beat.
Supplemental table 2: Cox proportional hazards model for analyzing the predictors of VPB recurrence after RFCA

<table>
<thead>
<tr>
<th>Variables</th>
<th>Hazard Ratio</th>
<th>P value</th>
<th>95% Confidential Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.034</td>
<td>0.085</td>
<td>0.995 - 1.074</td>
</tr>
<tr>
<td>Female gender</td>
<td>0.483</td>
<td>0.068</td>
<td>0.221 - 1.054</td>
</tr>
<tr>
<td>VPB burden</td>
<td>1.035</td>
<td>0.328</td>
<td>0.966 - 1.110</td>
</tr>
<tr>
<td>VPB duration</td>
<td>0.878</td>
<td>0.438</td>
<td>0.632 - 1.220</td>
</tr>
<tr>
<td>BMI</td>
<td>0.893</td>
<td>0.123</td>
<td>0.774 - 1.031</td>
</tr>
<tr>
<td>LVEF</td>
<td>1.055</td>
<td>0.227</td>
<td>0.967 - 1.151</td>
</tr>
<tr>
<td>SBP</td>
<td>0.988</td>
<td>0.644</td>
<td>0.940 - 1.039</td>
</tr>
<tr>
<td>LAD</td>
<td>1.002</td>
<td>0.978</td>
<td>0.877 - 1.145</td>
</tr>
<tr>
<td>QS in lead I</td>
<td>0.154</td>
<td>0.004</td>
<td>0.044 - 0.543</td>
</tr>
<tr>
<td>rsr'/rsR' in lead I</td>
<td>0.833</td>
<td>0.636</td>
<td>0.391 - 1.776</td>
</tr>
</tbody>
</table>

VPB indicates ventricular premature beat; BMI, body mass index; LVEF, left ventricular eject fraction; SBP, systolic blood pressure; LAD, left atrial dimension.