β₁-Adrenoceptor Blocker Aggravated Ventricular Arrhythmia

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Objectives: To assess the impact of β₁-adrenoceptor blockers (β₁-blocker) and isoprenaline on the incidence of idiopathic repetitive ventricular arrhythmia that apparently decreases with preprocedural anxiety.

Methods: From January 2010 to July 2012, six patients were identified who had idiopathic ventricular arrhythmias that apparently decreased (by greater than 90%) with preprocedural anxiety. The number of ectopic ventricular beats per hour (VPH) was calculated from Holter or telemetry monitoring to assess the ectopic burden. The mean VPH of 24 hours from Holter before admission (VPH-m) was used as baseline (100%) for normalization. β₁-Blockers, isoprenaline, and/or aminophylline were administrated successively on the ward and catheter lab to evaluate their effects on the ventricular arrhythmias.

Results: Among 97 consecutive patients with idiopathic ventricular arrhythmias, six had reduction in normalized VPHs in the hour before the scheduled procedure time from (104.6 ± 4.6%) to (2.8 ± 1.6%) possibly due to preprocedural anxiety (P < 0.05), then increased to (97.9 ± 9.7%) during β₁-blocker administration (P < 0.05), then quickly reduced to (1.6 ± 1.0%) during subsequent isoprenaline infusion. Repeated β₁-blocker quickly counteracted the inhibitory effect of isoprenaline, and VPHs increased to (120.9 ± 2.4%) from (1.6 ± 1.0%; P < 0.05). Isoprenaline and β₁-blocker showed similar effects on the arrhythmias in catheter lab.

Conclusions: In some patients with structurally normal heart and ventricular arrhythmias there is a marked reduction of arrhythmias associated with preprocedural anxiety. These patients exhibit a reproducible sequence of β₁-blocker aggravation and catecholamine inhibition of ventricular arrhythmias, including both repetitive ventricular premature beats and monomorphic ventricular tachycardia. (PACE 2013; 36:1348–1356)

monomorphic ventricular tachycardia, ventricular premature beat, isoprenaline, β₁-adrenoceptor blocker

Introduction

Idiopathic ventricular arrhythmias with normal QT interval occur in a great number of individuals, and are often considered for catheter ablation. Recently, we have noted that some patients with frequent premature ventricular contractions (PVCs) and ventricular tachycardia have a dramatic reduction of episodes just prior to catheter ablation. These patients have a slightly increased heart rate, most likely secondary to preprocedural anxiety. In such patients, who are the subject of this paper, electrophysiological stimulation, with or without isoprenaline infusion, does not induce the arrhythmia. Interestingly, in the same patients, frequent episodes are observed again just in 2–3 hours after returning to the ward. This phenomenon prompted us to develop a protocol as described later.

Isoprenaline is often used to facilitate induction of ventricular arrhythmia during catheter ablation. Conversely, β₁-adrenoceptor blockers (β₁-blockers) have long been employed for...
idiopathic and other ventricular arrhythmias.\textsuperscript{6–12} In our patients, the opposite was observed, and we hypothesized that the reduction of ventricular arrhythmias in those patients might result from increased sympathetic activity secondary to preprocedural anxiety and $\beta_1$-blockers might have inducing effect. To test the hypothesis, $\beta_1$-blockers, isoprenaline, and aminophylline were successively used to observe if they could induce ventricular arrhythmias in those patients. As yet, there is no report regarding the use of $\beta_1$-blockers for inducing and isoprenaline for suppressing idiopathic ventricular arrhythmias that marked reduce before the scheduled procedure time and with normal QT interval.\textsuperscript{12–16}

\textbf{Methods}

\textbf{Patient Enrollment}

From January 2010 to July 2012, patients with symptomatic idiopathic ventricular arrhythmia were admitted and assessed for an ablation procedure. Anxiolytic agents were not used in those patients. The level of electrolytes, including serum potassium, sodium, chloride, calcium, and magnesium, were assessed. All patients routinely had electrocardiography, chest x-ray, cardiac echocardiography, and ventricular late potential analysis.\textsuperscript{15,17} Stress testing, multislice cardiac computer tomography angiography, and/or cardiac catheterization were applied if the patient had any suggestion of ischemic heart disease. All the patients had discontinued antiarrhythmic agents over five half-life periods before admission. Holter monitors were applied before and after admission and wireless telemetry monitors were used to assess arrhythmia burden for at least 2 days after admission and throughout the inpatient period. The number of ectopic ventricular beats per hour (VPH) was recorded and calculated from the Holter before admission, from the telemetry monitoring records after admission, and from the electrophysiology recording system in catheter lab. The mean VPH from the Holter done 24 hours before admission (VPH-m) was used as baseline for normalization. All VPHs were normalized with VPH-m and expressed as relative value. The average of VPHs was used for comparison when the recording period was more than 1 hour.

The patients were enrolled in the Institutional Review Board-approved protocol to be described if the following criteria were fulfilled: (1) the number of total ectopic ventricular beats was greater than 5,000 in 24 hours; (2) the smallest normalized VPH calculated from Holter and telemetry after admission was over 15\% (except 4 hours before the scheduled procedure time); (3) the patient had no severe structural heart disease; (4) normalized VPH in 1 hour before the scheduled procedure time had a marked decrease defined as $\geq$90\% decrease from the baseline burden. Structural heart disease was defined as the presence of left ventricular ejection fraction $<40\%$, coronary artery disease $(>70\%$ stenosis of any major vessel), cardiomyopathy, moderate to severe valvular disease, or moderate to severe cardiac dilation. Cardiac magnetic resonance imaging was required for further structural evaluation in all enrolled patients.

The anxiety state of the patients was graded by self-evaluation from one to four, which indicated no, mild, moderate, and severe anxiety, respectively.

\textbf{Administration Protocol}

The enrolled patients were given drugs successively on the ward and/or in the catheter lab after written informed consent was signed.

1. In those patients who underwent ablation procedure, the administration order was esmolol, isoprenaline and repeated esmolol in the ward, and isoprenaline and esmolol in the catheter lab.

2. In those patients who declined electrophysiology study, the administration order was esmolol, isoprenaline, repeated esmolol, and aminophylline in the ward, and metoprolol at discharge. Esmolol, isoprenaline, and aminophylline were given intravenously by injection pump and metoprolol via mouth.

Isoprenaline and esmolol were administrated over 120 minutes at an interval of over 1 hour in ward, and over 30 minutes in catheter lab between doses. Normalized VPHs were calculated from 30 minutes after intravenous dosage and the third day after oral dosage. The effects of various drugs on studied arrhythmias were evaluated by telemetry monitoring or Holter examination.

1. Isoprenaline: Isoprenaline was started at a rate of 0.2 $\mu$g/kg hour ($\approx 0.1$ mg/hour) and gradually increased to achieve a target heart rate of 90–120 beats/min for 1 hour.

2. Esmolol: “Small” dose of esmolol was 0.05 mg/kg min for 1 hour, and then larger dose at a rate of 0.15 mg/kg min for another hour; repeated administration was just given with larger dose. Extra intermittent bolus injections (20–40 mg each time over 1 minute) were dosed one to eight times in the catheter lab when it was necessary. The dose was adjusted when the heart rate was less than 50 beats/min.

3. Aminophylline: Intravenous aminophylline was given continuously at a rate of 1 mg/kg hour ($\approx 0.05$ g/hour), and with two or three times of
Table I.  
The Baseline Characteristics of the Patients, the Anatomic Origin of the Ventricular Arrhythmia, and the Total Ectopic Ventricular Beats in 24 Hours on Holter before Admission

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Anatomic Origin</th>
<th>Arrhythmia Type</th>
<th>Sex</th>
<th>Age (Years)</th>
<th>Weight (kg)</th>
<th>Height (cm)</th>
<th>Total Ectopic Beats</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. 1</td>
<td>MVA</td>
<td>PVCs, NSVT, SMVT</td>
<td>M</td>
<td>35</td>
<td>61</td>
<td>164</td>
<td>42,002</td>
</tr>
<tr>
<td>No. 2</td>
<td>RVOT</td>
<td>PVCs, NSVT</td>
<td>F</td>
<td>47</td>
<td>60</td>
<td>161</td>
<td>29,064</td>
</tr>
<tr>
<td>No. 3</td>
<td>RVOT</td>
<td>PVCs, NSVT</td>
<td>F</td>
<td>59</td>
<td>64</td>
<td>162</td>
<td>36,059</td>
</tr>
<tr>
<td>No. 4</td>
<td>RVOT</td>
<td>PVCs, NSVT</td>
<td>F</td>
<td>33</td>
<td>65</td>
<td>164</td>
<td>7,968</td>
</tr>
<tr>
<td>No. 5</td>
<td>RVOT</td>
<td>PVCs, NSVT, SMVT</td>
<td>F</td>
<td>61</td>
<td>63</td>
<td>159</td>
<td>36,271</td>
</tr>
<tr>
<td>No. 6</td>
<td>RVOT</td>
<td>PVCs, NSVT</td>
<td>F</td>
<td>40</td>
<td>54</td>
<td>150</td>
<td>39,497</td>
</tr>
</tbody>
</table>

F = female; M = male; MVA = mitral valve annulus; NSVT = repetitive nonsustained ventricular tachycardia; PVCs = repetitive uniform premature ventricular contractions; RVOT = right ventricular outflow tract; SMVT = paroxysmal sustained monomorphic ventricular tachycardia.

4. Metoprolol: Oral metoprolol succinate tablets were given with 47.5–95 mg once daily.

Electrophysiological Study and Catheter Ablation

Electrophysiological study was performed with local infiltration anesthesia after written informed consent was acquired. Procaine hydrochloride (40–80 mg at final concentration of 0.5%) was used for local anesthetic and lidocaine was used if the patient was allergic to procaine. Heparin was given routinely. Multielectrode array system (Ensite, St. Jude Medical, St. Paul, MN, USA) was used if the arrhythmia originated from the right ventricle; an array electrode and a bidirectional 4-mm electrode-tip radiofrequency catheter (Safire, St. Jude Medical) were placed through a 10-French and an 8-French sheath, respectively, via the right femoral vein. NavX system was used if the arrhythmia originated from the left ventricle; a 4-mm-tip quadripolar ablation catheter (Celsius, Biosense Webster, Diamond Bar, CA, USA) was placed retrogradely through the femoral artery via an 8-French sheath; the reference electrode was placed through the left subclavian vein via a 6-French sheath.

Programmed stimulation and rapid burst pacing were performed at the right ventricular apex and outflow tract. Usually, eight ventricular stimuli at drive cycle lengths between 600 ms and 400 ms were delivered, and at twice diastolic threshold and the pulse duration of 1–2 ms. One to three ventricular extra-stimuli were delivered at baseline. Rapid burst pacing was given with 10–20 beats of stimulation at a cycle length between 500 ms and 240 ms. The above maneuver was repeated after isoprenaline infusion. Esmolol was used successively for induction as described earlier. The origin of arrhythmia and the earliest endocardial breakthrough site were mapped after three-dimensional anatomic model was constructed. Radiofrequency catheter ablation was applied at origin and breakthrough site using temperature control mode with a maximum temperature at 55°C and a maximum power of 50 Watts.

Collected Variables

The average heart rate, the total heart beats, and VPHs were collected from Holter report before admission and after discharge. VPHs were calculated by monitoring record at the first day after admission, in 1 hour before the scheduled procedure time, during various medications, and after catheter ablation. All VPHs were normalized with VPH-m as described earlier. All the data were collected, verified, and calculated by two independent investigators who were blinded to the study design.

Statistical Analysis

Continuous data were described as means ± standard deviation and as counts and percent if categorical. Student’s t-test, one-way analysis of variance, $\chi^2$ test, and Fisher’s exact test were used to compare differences across the groups. All analyses were performed using SPSS 13.0 (IBM Corp., Armonk, NY, USA). All tests were two-sided and a $P < 0.05$ was considered statistically significant.

Results

Patient Characteristics

A total of 97 patients with symptomatic idiopathic ventricular arrhythmia were admitted for a scheduled ablation procedure. All the
patients had severe palpitations and the average daily arrhythmia burden was 25.6%. Twenty-three patients had dizziness or near-syncope but none had syncope. None of the enrolled patients had positive findings in cardiac magnetic resonance and ventricular late potential analysis.

The average reduction of VPHs in 1 hour before the scheduled procedure time was 23%. Among the 97 patients, six cases (6.2%) showed a marked reduction over 90% of the VPHs in 1 hour before the scheduled procedure time (Table I). The level of plasma potassium and the results of other electrolyte analysis were within the normal range. All six patients had normal QT interval at admission. The average QT/QTc of patients was $(385 \pm 45)/(421 \pm 49)$ miniseconds. The arrhythmia originated from right ventricular outflow tract in five cases and left ventricle in one case (Table I).18,24–26 The arrhythmia could be classified as: (1) paroxysmal sustained monomorphic ventricular tachycardia (SMVT), (2) repetitive nonsustained ventricular tachycardia (NSVT), or (3) repetitive uniform PVCs. Sustained VT was defined as lasting >30 seconds, and NSVT was defined as >3 beats and <30 seconds. (Table I)

Three patients finally underwent catheter ablation. Other three patients ultimately declined electrophysiology study although they had signed the informed consent. Those three patients did agree to take the drug protocol and telemetry monitoring. The mean duration of follow-up was 7 months. All three ablated patients had no recurrence of the arrhythmia during the follow-up. The three patients who refused electrophysiology study had a similar burden of ectopic arrhythmia as that before admission.

The Baseline Characteristics of Studied Ventricular Arrhythmias

The results of Holter before their admission were analyzed. The average heart rate was $71.3 \pm 13.9$ beats/min. All normalized VPHs calculated from each hour on Holter reports in those six patients were over 15% (Fig. 1A).

Tenseness-Anxiety-Associated Decrease of Ventricular Arrhythmias

The wireless electrocardiogram telemetry monitoring showed that the average heart rate in the hour before the scheduled procedure time increased to $82.3 \pm 6.4$ beats/min with preprocedural anxiety. The anxiety state of the patients was graded by self-evaluation from one to four, which indicated no, mild, moderate, and severe anxiety, respectively. The average grade of the six enrolled patients was $3.0 \pm 0.4$ and was $1.9 \pm 0.4$ in other six randomly selected controls ($P < 0.05$). The average of VPHs in the hour before the scheduled procedure time of those six patients remarkably reduced to $(2.8 \pm 1.6\%)$ from $104.6 \pm 4.6$; $P < 0.05$; Table II).

$\beta_1$-Blocker Aggravated Ventricular Arrhythmias

The arrhythmias apparently reduced in the hour before procedure were then reinduced by $\beta_1$-blocker administration and were inhibited by isoprenaline infusion, and were again reinduced by repeated $\beta_1$-blocker administration. The changes of normalized VPHs during various medications: (1) $\beta_1$-receptor blocker-induced VPHs increased to $(97.9 \pm 9.7\%)$ from $(2.8 \pm 1.6\%; P < 0.05)$ during esmolol infusion, and $(76.9 \pm 6.4\%)$ and $(118.2 \pm 1.3\%)$ with small and large dose of esmolol, respectively (Table II, Figs. 1B–D); (2) isoprenaline-reduced VPHs decreased to $(1.6 \pm 1.0\%)$ from $(97.9 \pm 9.7\%; P < 0.05)$ Table II, Figs. 1B–D; (3) readministration of $\beta_1$-blocker: $\beta_1$-blocker readministration showed an excellent reproducibility, and VPHs increased to $(120.9 \pm 2.4\%)$ from $(1.6 \pm 1.0\%; P < 0.05)$; Table II, Figs. 1B–D; (4) aminophylline: intravenous aminophylline revealed a similar effect but less prominent than that of isoprenaline; since aminophylline had a longer metabolic half-life, it was only given after isoprenaline in patients who refused electrophysiology study; (5) metoprolol: oral metoprolol showed a significant inducing effect compared with the arrhythmia burden at the first day after admission in those three patients who declined the electrophysiology procedure.

Electrophysiological Tests and Ablation

Among the enrolled patients, three patients underwent electrophysiological testing. The episodes dramatically reduced when the patient was brought into the catheter lab. Rapid burst pacing and programmed stimulation had no inducing effect. Intravenous injection of isoprenaline further inhibited the ectopic ventricular arrhythmias, and normalized VPHs decreased to $(0.1 \pm 0.1\%)$ from $(0.4 \pm 0.1\%; P < 0.05)$. The above stimulation maneuver was repeated during isoprenaline injection and still had no inducing effects. Subsequent esmolol infusion $(0.15 \text{mg/kg min})$ markedly aggravated the arrhythmia and extra bolus injections revealed a more prominent inducing effect. Normalized VPHs increased to $111.5 \pm 3.2\%$ from $0.1 \pm 0.0\%$ during esmolol infusion $(P < 0.05$; Table III, Figs. 1E, 2A–D).

The procedure results confirmed that the arrhythmia originated from the free wall close to mitral annulus in one case and from the right ventricular outflow tract in two cases (Table I, Figs. 3A–D). All of the three cases
Figure 1. The number of ectopic ventricular beats per hour (VPH) was recorded. The mean VPH of 24 hours from Holter report before admission (VPH-m) was calculated for normalization. Normalized VPHs were used for comparison. (A) Normalized VPH was calculated from Holter report before admission; all the normalized VPH of every hour on Holter report of the six enrolled patients were over 15%. (B) As shown by the normalized VPH (mean ± standard deviation), the arrhythmias of the six enrolled patients remarkably decreased in the hour before the scheduled procedure time (Before procedure); were induced by $\beta_1$-blocker ($\beta_1$-blocker); inhibited by isoprenaline (Isoprenaline); and reinduced by repeated administration of $\beta_1$-blocker ($\beta_1$-blocker) on the ward. (C) The chart showed the normalized VPH of the six enrolled patients in every hour at the first day after admission (After admission), in 1 hour before the scheduled procedure time (Before procedure), during $\beta_1$-blocker infusion ($\beta_1$-blocker), during isoprenaline infusion (Isoprenaline), and during repeated $\beta_1$-blocker dosing (Repeated $\beta_1$-blocker). All the normalized VPHs of the six patients in every hour at the first day after admission were over 20%. (D) The chart revealed normalized VPH of the six patients at the first day after admission (After admission), in 1 hour before the scheduled procedure time (Before procedure), during $\beta_1$-blocker infusion ($\beta_1$-blocker). A large dose of $\beta_1$-blocker showed a more prominent inducing effect than a small dose of $\beta_1$-blocker on the arrhythmia. (E) The normalized VPH of the three patients who underwent electrophysiology study is shown. A similar response to $\beta_1$-blocker and isoprenaline was seen in catheter lab as on the ward. The normalized VPH was the first day after admission (After admission), during the first hour without drugs in the catheter lab (First hour in lab), during isoprenaline infusion, and during $\beta_1$-blocker infusion. *, $P < 0.05$ compared with After admission, $\beta_1$-blocker, or Repeated $\beta_1$-blocker; #, $P < 0.05$ compared with Before procedure, Isoprenaline, or First hour in lab; $\$, $P < 0.05$ compared with After admission; **, $P < 0.05$ compared with First hour in lab.
had no obvious low-voltage area and scar area during electrophysiological mapping; one or two radiofrequency ablation applications at the origin completely abolished the arrhythmia. Wireless monitoring after the procedure and Holter during follow-up showed no recurrence of the arrhythmia (Table III).

### Discussion

All six patients had a marked reduction of ventricular arrhythmia several hours before the scheduled procedure time. In those patients, isoprenaline demonstrated inhibitory effects rather than inducing effects. Traditionally, the only indication for isoprenaline for ventricular arrhythmias is Torsade de pointes, whereas none of those patients presented here had Torsade de pointes.

β1-Blockers have long been considered effective for exercise-induced ventricular arrhythmia, fascicular ventricular tachycardia, idiopathic ventricular tachycardia originating from the right

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**Table II.**

Normalized VPH† at the First Day after Admission and during Various Medications, and VPH-m‡ for Normalization

<table>
<thead>
<tr>
<th>Case</th>
<th>VPH-m Before Admission</th>
<th>VPH (%) Before Admission</th>
<th>VPH (%) After Procedure</th>
<th>VPH (%) β1-Blocker</th>
<th>VPH (%) Isoprenaline</th>
<th>VPH (%) Repeated β1-Blocker</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. 1</td>
<td>1,750 (100%)</td>
<td>104.7</td>
<td>0.2</td>
<td>120.7</td>
<td>0.0</td>
<td>118.2</td>
</tr>
<tr>
<td>No. 2</td>
<td>1,211 (100%)</td>
<td>106.6</td>
<td>0.4</td>
<td>117.3</td>
<td>0.1</td>
<td>130.1</td>
</tr>
<tr>
<td>No. 3</td>
<td>1,502 (100%)</td>
<td>108.3</td>
<td>0.2</td>
<td>65.2</td>
<td>0.8</td>
<td>117.9</td>
</tr>
<tr>
<td>No. 4</td>
<td>332 (100%)</td>
<td>95.8</td>
<td>8.7</td>
<td>116.6</td>
<td>6.3</td>
<td>125.6</td>
</tr>
<tr>
<td>No. 5</td>
<td>1,511 (100%)</td>
<td>109.9</td>
<td>0.4</td>
<td>76.9</td>
<td>0.2</td>
<td>113.7</td>
</tr>
<tr>
<td>No. 6</td>
<td>1,646 (100%)</td>
<td>102.5</td>
<td>7.0</td>
<td>90.9</td>
<td>2.3</td>
<td>120.1</td>
</tr>
<tr>
<td>Average</td>
<td>1,325 (100%)</td>
<td>104.6</td>
<td>2.8</td>
<td>97.9</td>
<td>1.6</td>
<td>120.9</td>
</tr>
</tbody>
</table>

†The number of ectopic ventricular beats (VPH) was calculated from monitoring at the first day after admission; in 1 hour before procedure; and during β1-blocker administration, isoprenaline infusion, or repeated β1-blocker administration, ‡the mean VPH of 24 hours from Holter report before admission (VPH-m) was calculated for normalization.

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**Figure 2.** The arrhythmia was induced with small dose and large dose of β1-blocker. (A) The arrhythmia completely disappeared after the patient was brought to catheter lab and isoprenaline had no inducing effect. (B and C) Continuous esmolol infusion induced the arrhythmia in trigeminy or bigeminy. (D) Larger dose of esmolol with extra bolus aggravated the arrhythmia in couplets. The name of surface leads and coronary sinus electrodes (CS) and ablation catheter (ABL) electrodes were shown in the left panel of the figure.
Figure 3. Representative charts showed the mapping results with solid arrow in one patient (No. 5, A and B) and another patient (No. 1, C and D). Three-dimensional maps were constructed by Ensite NavX System. The name of surface leads, and coronary sinus electrodes (CS) and ablation catheter (ABL) electrodes were shown in the left panel of the figure. (A) The anatomic origin of the arrhythmia was located at right ventricular outflow tract (RVOT), which was shown by solid arrow in left anterior oblique view (LAO) on the left panel and in posterior anterior view (PA) on the right panel. (B) The ablation catheter at the target site showed the earlier local activated “V” wave (denoted by solid arrow) than the surface QRS wave. (C) The anatomic origin of the arrhythmia was located at the tip of ablation catheter at the left ventricle close to the mitral valve annulus, which was shown in anterior posterior view (AP) on the left panel and in left anterior oblique view (LAO) on the right panel; solid arrow denoted the tip of ablation catheter and dotted arrow denoted the position of coronary sinus electrode. (D) The local electrogram of ablation catheter at the target site showed the earlier activated “V” wave than the surface QRS wave, which was denoted by solid arrow.

ventricular outflow tract, and certain ventricular arrhythmia associated with long-QT syndrome and mitral valve prolapse; however, we demonstrated that \( \beta_1 \)-blockers had apparent inducing effects on idiopathic ventricular arrhythmia in some patients.

It is interesting that \( \beta_1 \)-blockers markedly inhibited sinus rhythm whereas they apparently

<table>
<thead>
<tr>
<th>Case No.</th>
<th>VPH (%) after Admission</th>
<th>VPH (%) 1 Hour before Procedure</th>
<th>VPH (%) Isoprenaline</th>
<th>VPH (%) Esmolol</th>
<th>VPH (%) after Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. 1</td>
<td>1,832 (104.7%)</td>
<td>6 (0.3%)</td>
<td>0 (0.0%)</td>
<td>2,038 (116.5%)</td>
<td>0†</td>
</tr>
<tr>
<td>No. 3</td>
<td>1,626 (108.3%)</td>
<td>6 (0.4%)</td>
<td>2 (0.1%)</td>
<td>1,688 (112.4%)</td>
<td>0‡</td>
</tr>
<tr>
<td>No. 5</td>
<td>1,661 (109.9%)</td>
<td>8 (0.5%)</td>
<td>4 (0.3%)</td>
<td>1,596 (105.6%)</td>
<td>0</td>
</tr>
<tr>
<td>Average</td>
<td>1,706 (107.6%)</td>
<td>7 (0.4%)</td>
<td>2 (0.1%)</td>
<td>1,774 (111.5%)</td>
<td>0</td>
</tr>
</tbody>
</table>

† Three ectopic ventricular beats originated from other sites other than the ablation site, ‡ twelve ectopic ventricular beats originated from other sites other than the ablation site. VPH = ventricular beats per hour.
β1-BLOCKER AGGRAVATED VENTRICULAR ARYTHMIA

increased idiopathic ventricular arrhythmia at the same time. Likewise, isoprenaline also had an inverse effect on sinus rhythm and idiopathic ventricular arrhythmia. Since amino-phylline showed a similar inhibitory effect as isoprenaline, the inducing effect of β1-blocker may not be mediated by antagonizing the sympathetic system.

In summary, the data presented here demonstrated the existence of a special type of idiopathic ventricular arrhythmia, β1-blocker-aggravated and catecholamine-inhibited ventricular arrhythmias (BAVA/CIVA), which had the following characteristics: (1) there was no evidence of structural heart disease, heart failure, and ischemic heart disease; (2) both cardiac echocardiography and magnetic resonance showed no severe structural heart disease; (3) programmed electrophysiological stimulation could hardly induce the arrhythmia; (4) electro-anatomic mapping during the procedure revealed no obvious scar or low-voltage area; (5) single or several points of ablation could abolish the arrhythmia; (6) burst pacing had no apparent inducing effect; (7) both isoprenaline and aminophylline showed significant inhibitory effect. The former five aspects suggested that BAVA was not caused by reentry mechanism, whereas the latter two aspects implied that BAVA was not caused by triggered activity. In summary, the BAVA might be caused by “focal nonreentrant mechanism.”

Notably, only those patients with severe symptoms and structurally normal hearts, and who had great reduction in anxiety, were enrolled, thus the actual incidence of BAVA was likely much higher than reported here. Just as exercise can increase or decrease ventricular arrhythmias in different patients with idiopathic arrhythmias, some patients with marked arrhythmia reduction in the presence of anxiety might have no apparent response to β1-blocker and isoprenaline. In any event, this study is a preliminary report aimed to bring attention to a type of arrhythmia with a special response to β1-blockers, and to help physicians reconsider their inducing protocol during an ablation procedure and the medication strategy when encountering difficulties in certain patients.

**Study Limitations**

First, as mentioned earlier, we did not provide a full spectrum of data on all of our patients who may have BAVA. Second, the arrhythmia burden was compared by VPHs, which might have background variance between hours, making it difficult to confirm whether a decrease or an increase resulted from anxiety or from drug effects; however, the following aspects proved that our reported effects could not result from spontaneous variation: (1) normalized VPHs of every hour on Holter report before admission and telemetry monitoring after admission was 15% in all enrolled patients; (2) the reduction because of tenseness was nearly 97%; (3) further large dose of esmolol led to an increase over 100% and successively isoprenaline dosage again showed an inhibition nearly 98%; (4) repeated esmolol infusion after isoprenaline administration showed an excellent inducibility and reproducibility in all enrolled patients; (5) the arrhythmia showed a similar response to isoprenaline and esmolol in the catheter lab as that in the ward.

**References**


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