Positive QRS Complex in Lead I as a Malignant Sign in Right Ventricular Outflow Tract Tachycardia
– Comparison Between Polymorphic and Monomorphic Ventricular Tachycardia –

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Background: Idiopathic ventricular fibrillation (VF) or polymorphic ventricular tachycardia (PVT) arising from the right ventricular outflow tract (RVOT) is occasionally observed. The difference in the initial ventricular premature contraction (VPC) between VF/PVT and monomorphic VT (MVT) from the RVOT, however, has not yet been fully investigated.

Methods and Results: The electrocardiogram findings and the clinical characteristics were compared between 14 patients with PVT and 77 with MVT. The episodes of syncope were more frequent in the VF and/or PVT group (57%) than in the MVT group (10%). An initial VPC with a positive QRS complex in lead I was observed in 10 (71%) of 14 patients with VF/PVT, and in 27 (35%) of 77 patients with MVT (P<0.05). Although radiofrequency (RF) catheter ablation targeting the trigger VPC often produced a morphological change, VF/PVT was eliminated in 13 (93%) of 14 patients after additional RF applications.

Conclusions: Malignant arrhythmias from the RVOT, although rare, should be considered when the patient has a syncopal episode and VPC with a positive QRS complex in lead I. (Circ J 2013; 77: 968–974)

Key Words: Outflow tract; Polymorphic ventricular tachycardia; QRS morphology; Radiofrequency catheter ablation; Ventricular fibrillation
Malignant VPCs From RVOT

Despite the programmed electrical stimulation in the EP laboratory, i.v. infusion of isoproterenol (0.5–2.0 μg/min) and/or a single injection of phenylephrine (250 μg) were given to evoke the VAs. RF energy was delivered under the guidance of activation mapping and pace mapping. If the VPC morphology changed during the procedure, additional RF applications were given to eliminate the VPCs completely.

In RFCA, we used a 7-Fr quadripolar catheter with a non-irrigated 4-mm or 8-mm tip distal electrode, embedded thermistor, interspacing of 2–5–2 mm, and deflectable tip (EP Technologies, San Jose, CA, USA; Biosense-Webster, Diamond Bar, CA, USA; or Japan Lifeline, Tokyo, Japan).

Successful ablation was defined as the elimination of all VT and VPCs without any anti-arrhythmic drugs. Partial success was defined as the elimination of the VT with residual isolated VPCs from the RVOT. A failed ablation was defined as the inability to suppress the VAs.

Statistics Analysis
Continuous variables are expressed as mean±SD, and were compared using Student’s t-test. The categorical variables were compared using chi-square analysis. P<0.05 was considered statistically significant.

Analysis of 12-Lead ECG
We confirmed that the first VPC initiating the VF/PVT was identical to the frequent isolated VPCs (Figure 1) and analyzed the VPC morphology in each of the 12 leads. In addition, we measured the essential ECG parameters, such as the coupling interval of the first VPC initiating VA and the shortest R-R interval during the VA. A positive QRS complex was defined as a positive deflection exceeding the negative component by >0.1 mV in amplitude.

Mapping and RFCA
After anti-arrhythmic agents had been withdrawn for >5 half-lives, electrophysiological study (EPS) and RFCA were carried out. The electroanatomical voltage mapping was performed in 29 (32%) of 91 patients. To induce VA, programmed ventricular stimulation using up to 3 extrastimuli and incremental burst pacing at a cycle length of up to 2:1 ventricular or atrial capture were repeatedly performed from the right atrium and right ventricular apex. In patients without VPCs despite the programmed electrical stimulation in the EP laboratory, i.v. infusion of isoproterenol (0.5–2.0 μg/min) and/or a single injection of phenylephrine (250 μg) were given to evoke the VAs. RF energy was delivered under the guidance of activation mapping and pace mapping. If the VPC morphology changed during the procedure, additional RF applications were given to eliminate the VPCs completely.

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QRS duration (range, 62–96 ms) without right bundle branch block during sinus rhythm. The mean coupling interval of the initial VPC was 440 ± 73 ms (range, 350–640 ms). The mean of the shortest coupling interval during the PVT was 224 ± 34 ms (range, 180–280 ms). The total VPCs in the 24-h Holter monitoring ranged from 2,221 to 38,953 beats (18,788 ± 12,228 beats/day). Comparisons of the clinical characteristics between the VF/PVT and MVT groups are given in Table 2. There was no difference in the age, gender or total number of VPCs in a 24-h period. Prior syncopal episodes were observed more often in the VF/PVT group than in the MVT group (P<0.001). A family history of sudden cardiac death was noted in 1 patient in the MVT group. No significant difference was observed in the time from VPC detection by medical checkup to the clinical onset of VA between the 2 groups.

ECG Characteristics of the First VPC Initiating VF/PVT
The VPC waveforms in leads I and II initiating VF/PVT in all 14 patients are shown in Figure 2. Before RFCA, 10 (71%) of 14 patients in the VF/PVT group had spontaneous VPCs with a positive deflection of the QRS complex in lead I (patients 1–3, 5, 8, 10–13, and 14). Comparisons of the ECG characteristics between the VF/PVT and MVT groups are given in Table 2. A positive QRS complex in lead I was more frequent in the VF/PVT group than in the MVT group (P<0.05). The positive QRS complex in lead I predicted the occurrence of VF/PVT with a sensitivity of 71%, specificity of 65%, positive predictive accuracy of 27%, and negative predictive accuracy of 93%. We also compared the following parameters: (1) amplitude of the R wave in the inferior leads; (2) duration and amplitude of the R wave in V1 and V2; (3) presence of QRS notching in the inferior leads; (4) precordial transition zone; (5) R/S ratio in lead V2; and (6) Q wave ratio of aVr/aVL. No other significant difference, however, was detected in the QRS waveform during VPCs between the 2 groups. The positive QRS complex in lead I with the syncopal episodes predicted the occurrence of VF/PVT with a sensitivity of 43%, specificity of 99%, positive predictive accuracy of 86%, and negative

### Results

#### Patient Clinical Characteristics

The clinical characteristics of the patients with VF/PVT are listed in Table 1. Twelve (86%) of 14 patients were female. Eight (57%) of the 14 patients had prior repeated episodes of syncope at rest. Including presyncope, 11 (79%) of the 14 patients experienced some symptoms associated with a cerebral circulatory disturbance. In 4 (29%) of the 14 patients, spontaneous VFs were recorded, and implantable cardioverter-defibrillators were implanted. All patients had a normal intrinsic
predictive accuracy of 90%. The coupling interval of the initial VPC was also unchanged between the 2 groups. The shortest R-R interval during VT was significantly shorter in the VF/PVT group than in the MVT group (P<0.0001).

Mapping and RFCA
The results of EPS and RFCA are given in Table 3. The documented VT was repeatedly inducible in 13 (17%) of 77 patients in the MVT group. In contrast, no VA was inducible during EPS in the VF/PVT groups. In 5 (36%) of 14 patients with VF/PVT, however, the documented polymorphic QRS waves were reproduced by burst pacing at the successful ablation sites. A change in the spontaneous VPC morphology after several RF applications was observed in more than half of the patients in both the VF/PVT (71%) and MVT groups (52%). At the start of the RFCA, 4 of 14 patients (patients 4, 6, 7, and 9) in the VF/PVT group had spontaneous VPCs with an isoelectric or negative QRS complex in lead I, but 2 of these patients (patients 4 and 6) with non-positive QRS complexes in lead I acquired a positive QRS after several RF energy applications (Figure 3). Such a morphological change was also observed in 7 (14%) of 50 patients in the MVT group with isoelectric or negative QRS complexes in lead I. Including the QRS morphological change of the VPC, a positive QRS complex in lead I was observed in 12 (86%) of 14 patients in the VF/PVT group and in 34 (44%) of 77 patients in the MVT group. As shown in Figure 4, in the VF/PVT group, the VPCs were finally eliminated at the posterior attachment of the free wall in 7 patients, at the posterior attachment of the septum in 2,

Table 3. EPS and RFCA Findings vs. Type of VT

<table>
<thead>
<tr>
<th></th>
<th>VF/PVT (n=14)</th>
<th>MVT (n=77)</th>
<th>P-value</th>
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<tbody>
<tr>
<td><strong>EPS</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>ERP of RVA (ms)</td>
<td>234±21</td>
<td>248±22</td>
<td>NS</td>
</tr>
<tr>
<td>Inducibility of documented VT</td>
<td>0</td>
<td>13 (17)</td>
<td>&lt;0.05</td>
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<tr>
<td><strong>RFCA</strong></td>
<td></td>
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<td></td>
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<tr>
<td>Any morphological change during RFCA</td>
<td>10 (71)</td>
<td>40 (52)</td>
<td>NS</td>
</tr>
<tr>
<td>Morphological change from an iso/neg to positive QRS in lead I</td>
<td>2 (14)</td>
<td>7 (9)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Short-term results</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Success</td>
<td>13 (93)</td>
<td>65 (84)</td>
<td>NS</td>
</tr>
<tr>
<td>Partial success</td>
<td>1 (7)</td>
<td>10 (13)</td>
<td>NS</td>
</tr>
<tr>
<td>Failure</td>
<td>0</td>
<td>2 (3)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Long-term results</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Follow-up period (months)</td>
<td>68±23</td>
<td>71±36</td>
<td>NS</td>
</tr>
<tr>
<td>VF/VT recurrence</td>
<td>0</td>
<td>2 (3)</td>
<td>NS</td>
</tr>
<tr>
<td>Syncope</td>
<td>0</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>0</td>
<td>NS</td>
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</table>

Data given as mean±SD or n (%). EPS, electrophysiological study; ERP, effective refractory period; iso, isoelectric; neg, negative; RFCA, radiofrequency catheter ablation; RVA, right ventricular apex. Other abbreviations as in Tables 1,2.
midway between the anterior and posterior attachment of the septum in 1, and at the anterior attachment of the septum in 4. The final successful ablation site for the VPCs was above the pulmonary valve in 2 patients (14%) in the VF/PVT group and in 7 patients (9%) in the MVT group. In all 9 patients with VPC originating above the pulmonary valve, a sharp potential preceding the QRS onset and a subsequent dull potential were recorded during the VPCs from the ablation catheter (Figure 5). The sharp potential was also eliminated after successful RF energy application. After a mean follow-up period of 71±34 months, successful RFCA was achieved in 13 patients (93%) in the VF/PVT group and in 65 (84%) in the MVT group. Partial success (elimination of the VT with residual isolated VPCs from the RVOT) was obtained in 1 (7%) and 10 (13%) patients in the VF/PVT and MVT groups, respectively.

**Figure 3.** Representative case of QRS morphological change after radiofrequency (RF) energy application. Patient 6. (A) 12-lead electrocardiogram (ECG) before and after the initial RF energy application in the right ventricular outflow tract (RVOT). (B) Radiograms (right anterior oblique projection [RAO] 35° and left anterior oblique projection [LAO] 45°) at (Left) the initial ablation site and (Right) final ablation site in the RVOT. In this case, the earliest ventricular activation site was initially located on the anterior attachment side of the septum. A ventricular premature contraction (VPC) with a positive QRS complex, however, appeared after the RF application at that site. Finally, an RF application at the posterior attachment side of the free wall in the RVOT successfully eliminated the residual VPC. ABL, ablation catheter; RV, right ventricle.

**Figure 4.** Distribution of the final successful ablation sites in 14 patients with ventricular fibrillation/polymorphic ventricular tachycardia (VF/PVT): coronal section image of the ventriculopulmonary junction. In 9 of 14 patients, the successful ablation sites were located on the posterior attachment of the right ventricular outflow tract (RVOT). AC, anterior cusp of pulmonary valve; ant, anterior attachment; FW, free wall; LC, left cusp; PA, pulmonary artery; post, posterior attachment; PV, level of pulmonary valve; RC, right cusp; SEP, septum.

**Discussion**

**Major Findings**

The major findings are as follows: (1) a positive QRS complex of the initial VPC in lead I was observed in the majority of cases of VF/PVT; (2) syncopal episodes were more often observed in the VF/PVT group than in the MVT group; (3) no difference was observed in the coupling interval of the initial VPC between the 2 groups; and (4) the effect of RFCA for several years was favorable in the 2 groups.

These results indicate that idiopathic VF/PVT from the
Malignant VPCs From RVOT

Same individual were almost constant with or without subsequent VF/PVT. In addition, no significant difference was observed in the QRS morphology between the isolated VPC and trigger VPC of VF/PVT, and the coupling interval of trigger VPCs was similar to that of the RVOT-VPC in other common benign cases. We could not understand how the slight difference in the coupling interval as shown in Figure 1 is related to polymorphic QRS complex formation.

In this study, a morphological change in the targeted VPC was frequently observed during the RFCA sessions in the VF/PVT group. Noda et al also reported that the alterations of QRS morphology were detected in the initial VPC of VF/PVT. As previously reported, the QRS morphological change during RFCA was considered to be a result of the shift of the activation pathways between the tachycardia focus and the exit point of the targeted VPC.

Tada et al noted that morphological changes during RFCA were often observed in patients with VA arising from the pulmonary artery, and asserted that this phenomenon may be associated with the structure and distribution of the pulmonary myocardial extensions.

A previous study using autopsy hearts found that only 17% of subjects with no association with arrhythmic events had a ventricular RVOT, although rare, should be considered when a patient has a syncopal episode and RVOT-VPC with a positive deflection of the QRS complex in lead I. Six (86%) of 7 patients with syncope plus positive QRS in lead I had a malignant VA. The RF applications targeting the trigger VPC frequently caused a change in the QRS morphology, but the VF/PVT had been eliminated by additional ablation applications for residual VPCs.

**ECG Characteristics of the First VPC Initiating the PVT**

Although there are several case reports of RVOT-PVT, no report referred to the QRS morphology of the trigger VPC. In these reports, all of the first VPCs initiating the PVT had a positive deflection in lead I. In the present study, 10 of 14 patients with VF/PVT had a positive QRS complex in lead I before RFCA. The RVOT-VPCs with a positive QRS wave in lead I usually arise from the posterior attachment side of the septum or free wall. As shown in Figure 4, in 9 of 14 patients, the final successful ablation sites in the present study were also on the posterior attachment of the RVOT.

As shown in Figure 1, the coupling interval between the single VPC and the first VPC initiating PVT in patient 2 was not identical, but the coupling intervals of each VPC in the same individual were almost constant with or without subsequent VF/PVT. In addition, no significant difference was observed in the QRS morphology between the isolated VPC and trigger VPC of VF/PVT, and the coupling interval of trigger VPCs was similar to that of the RVOT-VPC in other common benign cases. We could not understand how the slight difference in the coupling interval as shown in Figure 1 is related to polymorphic QRS complex formation.

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myocardial extension into the pulmonary artery beyond the ventriculo-arterial junction. In addition, the pulmonary myocardial extensions are widely distributed in the basal region of the pulmonary valve and taper at the distal pulmonary artery. RF applications at the basal region of the pulmonary valve result in changes in the tachycardia exit, and as a result, the morphology of the VPC may be changed during RF ablation. In the present study, 2 of 4 patients with VF had a tachycardia focus above the pulmonary valve. The pulmonary artery, especially at the posterior attachment site, might be a commonly affected site of VF.

Possible Mechanism of VF/PVT
The mechanism of benign idiopathic MVT from the RVOT is considered to be triggered activity; that of RVOT-VF/PVT is still unclear because it is difficult to induce VF/PVT by any ventricular burst pacing or ventricular programmed stimulation with or without catecholamines in the EP laboratory. Furthermore, even if the VF/PVT is inducible by ventricular stimulation, EPS during tachycardia is difficult due to its hemodynamic instability.

At baseline, no patients had any negative T waves in the precordial leads or late potentials in the SAECG. During mapping of the RVOT in sinus rhythm, neither any low-voltage area nor delayed potentials were recognized in any of the patients. No patients had any fibro-fatty changes in the RV on cardiac CT or MRI. The diagnosis of ARVC, however, can be difficult in the absence of any overt clinical abnormalities. Therefore, patients with early-phase ARVC might have been included.

In cases of VF/PVT reported previously, the QRS complex demonstrated a polymorphism during rapid ventricular pacing from the RV. In addition, burst pacing from the earliest activation site could reproduce several initial QRS complexes identical to the documented PVT. This reproducibility suggested that the PVT from the RVOT occurred from a single focus by triggered activity or micro-reentry with multiple myocardial exits to the RV and the development of polymorphic QRS waves.

All 14 patients with VF/PVT were previously diagnosed with isolated VPCs. The average period from VPC detection to clinical onset of VA was 120±118 months. This indicates that VF/PVT developed at some point after an asymptomatic period of several years.

Study Limitations
The number of patients in the RVOT-VF/PVT group was small. In the 14 patients with VF/PVT, the QT prolongation and/or T wave alteration by isoproterenol was not observed during EPS and RFCA. It might be possible, however, that the latent T wave alteration by isoproterenol was not observed during rapid ventricular pacing or ventricular programmed stimulation with or without catecholamines in the EP laboratory. In addition, burst pacing from the earliest activation site could reproduce several initial QRS complexes identical to the documented PVT. Therefore, it is not known whether the malignant form of VPCs is frequent in female patients or not.

A positive QRS complex in lead I itself was common in the patients with isolated VPCs or MVT arising from the RVOT. A total of 27 of 77 patients in the MVT group also had a positive QRS in lead I in the present study. Many other individuals who did not undergo RFCA consisted of asymptomatic patients with isolated RVOT-VPCs. It is important to distinguish malignant VPCs from benign VPCs in many asymptomatic patients with isolated RVOT-VPCs, but it remains unknown how many patients with isolated VPCs with a possible malignant form will develop VF/PVT in the future.

Conclusion
Malignant VAs from the RVOT are rare. We should pay attention, however, to any syncopal episodes and VPCs with a positive deflection of the QRS complex in lead I.

Acknowledgments
Conflict of Interest: None.

Disclosures
No author has a real or perceived conflict of interest.

References