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Modulation of the Ectopic Focus Introduces Various Forms of Ventricular Premature Contractions

Kan Takayanagi, MD, PhD, FACC, MHRS, Shiro Nakahara, MD, PhD, FACC

Yuuichi Hori, MD, Yoshihiko Sakai, MD, PhD

From the Department of Cardiology, Dokkyo University Koshigaya Hospital, Saitama, Japan

Introduction

Frequent ventricular premature contractions (VPCs) can trigger ventricular tachyarrhythmia and occasionally induce congestive heart failure. Single VPC with short coupling interval (CI) can rarely but surely introduce fatal ventricular fibrillation. However, further detail and the essential mechanism of VPC still remain unsettled. Whether VPC can be induced by ectopic focus has not been clarified despite the progress in electrophysiological technology, including catheter ablation, which can eradicate the focus of VPCs or ventricular fibrillation. Meanwhile, today's advances in computer science can simulate clinically observed complex ventricular arrhythmias based on reentry or automaticity.

In order to quickly detect the individual feature and fundamental mechanism of the VPC including CI and intrinsic cycle length, we developed simple displays using a full-day ECG analysis based on our previously documented parasystole model¹⁻⁵. Ventricular parasystole (VP) has been known to show various CI, while most of the VPC patients

show fixed CI. We lately reported that VPC can introduce heart rate doubling by the interaction of two automaticity foci (based on anti-phasic tachycardia theory)³. By using the same displays, we analyzed cases with cyclic burst VPCs and VPCs observed in atrial fibrillation (Af). We tried to explain all of these VPCs by the modulation of ectopic focus with weak to strong degree¹⁻³.

Methods

Representative 4 cases out of 1,500 patients with frequent VPC ($\geq 3,000/\text{day}$), who went for ambulatory ECG in our institute, were reported. Patient 4 had atrial fibrillation and the rest of them had normal sinus rhythm. Their interectopic intervals including bigeminy, trigeminy and quadrigeminy were plotted against the corresponding post-extrasystolic interval (PEI) creating PEI-interectopic interval curve (PIC). PIC solely for the bigeminy intervals (PBC) corresponded to the experimentally generated phase response curve. Details of the ambulatory ECG recording and computer analysis were documented in our previous papers^{1,6,7}.

Address for correspondence: Kan Takayanagi, M.D. Department of Cardiology, Dokkyo University Koshigaya Hospital, 2-1-50 Minami Koshigaya, Koshigaya, Saitama, Japan 343-8555.

Tel: 81-489-65-1111, Fax: 81-489-60-1708; E-mail: tkyng@dokkyomed.ac.jp

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Compared with the full-day PBC, which is affected by diurnal variations of parasymp-tole cycle length, more stable 2 hour PBC was selected for analysis. Strong and weak modulation were defined by the slopes of the 2 hour PBC (≥ 0.8 or < 0.8), respectively. Degree of CI variation was expressed by coefficient of variation (CV). $CV \geq 0.14$ was used as a marker of variable CI. Catheter ablation for VPC was performed using the NavX system activation mapping.

Case presentation

Case 1: Weak modulation: VP with various CIs.

VP has been known to be associated with larger CV of VPC CI⁶. We previously reported its unique nature by simple plotting techniques^{1,2}. However, as far as we know, VP patients treated by catheter ablation are quite few. Furthermore, variation on the VP cycle length during daily activity is rarely documented. A 65-year-old man with palpitation was admitted to our hospital for VP catheter ablation. Echocardiography showed a normal ventricular ejection fraction.

The diagnosis of VP was supported by a pronounced variation of the CI and fusion beats recorded by 12-lead ECG (Figure 1). Shortest interectopic interval corresponding to bigeminy was 1,420 ms. Subsequent trigeminy interval was 2,740 ms, which was slightly shorter than the twice that of the bigeminy. Unique tachograms were obtained from the ambulatory ECG (Figure 2). In the uppermost panel, red, yellow and green dots corresponded to the bigeminy, trigeminy and quadrigeminy, respectively. The estimated least common denominator of interectopic VPC-VPC intervals (= bigeminy interval) ranges between 1,250-1,800 ms and was longer at night (1,600 to 1,800 ms). Bigeminy was observed at heart rate between 66 bpm to 95 bpm. If the heart rate was slightly slower than 75 bpm, trigeminy could also appear as shown in Figure 1. In the second panel, purple dots disclosed the VPC CIs ranging between 500 to 950 ms. Third panel shows the time course of PEI with marked variation. Fourth panel shows the VP frequency (/5min).

In Figure 3-A, interectopic intervals of bigeminy, trigeminy and so on were individually plotted against the PEI for 24 hours as

Figure 1 Case 1



Figure 1. Case 1: Twelve-leads ECG recorded from a patient with VP, which was associated with a left bundle branch block and superior axis. The shortest VPC-VPC interval corresponding to the bigeminy was 1,420 ms. VPC-VPC interval of the next trigeminy was 2,740 ms.

Figure 2 Case 1

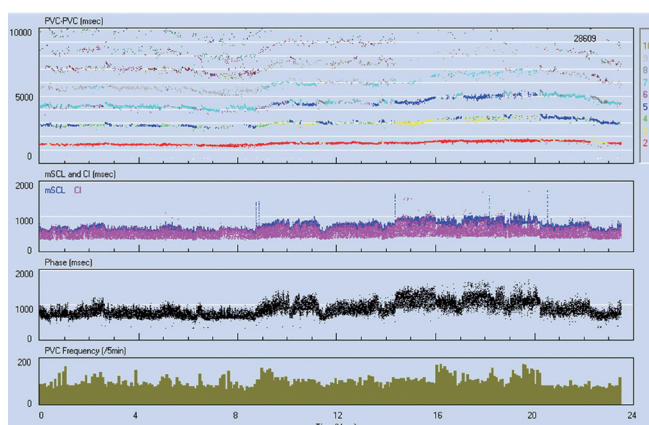


Figure 2. Case 1: VPC-VPC intervals tachogram for 24 hours obtained from Holter ECG. Red, yellow and green dots represent bigeminy trigeminy and quadrigeminy, respectively.

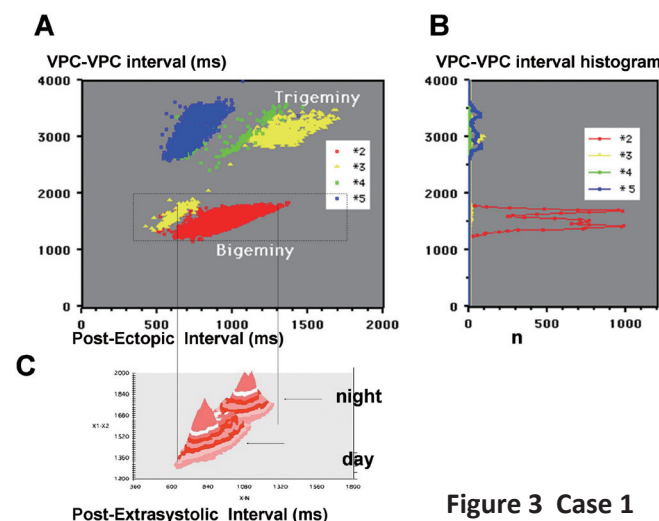


Figure 3 Case 1

Figure 3. Case 1: A. VPC-VPC interval plotted against postectopic intervals. B. Histogrammic analysis of the VPC-VPC interval. C. 3-D magnified display of the bigeminy distribution.

we reported². In Figure 3-B, histograms of interectopic intervals were individually shown. The histogram for the bigeminy was sharply separated due to the diurnal variation. This diurnal variation was magnified on 3 dimensional map in Figure 3-C. Lower left sharp peak shows PBC during daytime and upper right peak depicts PBC at night. In the lower panel in Fig. 6-A, 2 hour PBCs during daytime (red) and night (blue) were separately plotted.

Catheter ablation was performed and we could identify the earliest ventricular activation site at the mid posterior wall of the right ventricle which preceded the onset of QRS by 26ms. Good pace-mapping was obtained at this site and irrigated RF energy eliminated the VP and rendered it non-inducible.

Case 2: Strong modulation: VPC with ventricular rate doubling and fixed CIs.

In this case, we comment whether the mechanism in which repetitive interpolated ventricular bigeminy (RIVB) not requiring two circuits for tachycardia could actually exist as a counterpart of reentry³. Fig. 4 illustrated ECG and heart rate tachogram recorded in a 70 year-old man showing sudden jump up of the ventricular rate to 110 bpm associated with RIVB, which was recorded while he was sitting. The initial BI was 1,120 ms, and the preceding normal R-R interval was 1,040 ms. The initial VPC coupling interval was 456 ms and increased gradually thereafter to 512 ms. Lower tachogram shows the onset of RIVB. In this case, RIVB were observed during the daytime and none at night. ECG shows that the PQ interval immediately after the initial interpolated VPC was prolonged to 0.22 sec from 0.18 sec before the VPC. Prolonged atrio-ventricular conduction immediately after the VPC was necessary to maintain the RIVB, as shown in Fig. 4. PBC of this patient was shown in Figure 6-B.

Case 3: Strong modulation: Cyclic burst of VPCs.

Until now, the general mechanism of VPC cyclic bursts remains unsettled. Using the instantaneous heart rate tachogram obtained from ambulatory ECG monitoring, we had reported two types of VPC bursts, one corresponding to fixed CI and another to variable CI as shown in Fig. 5, both exhibiting pecu-

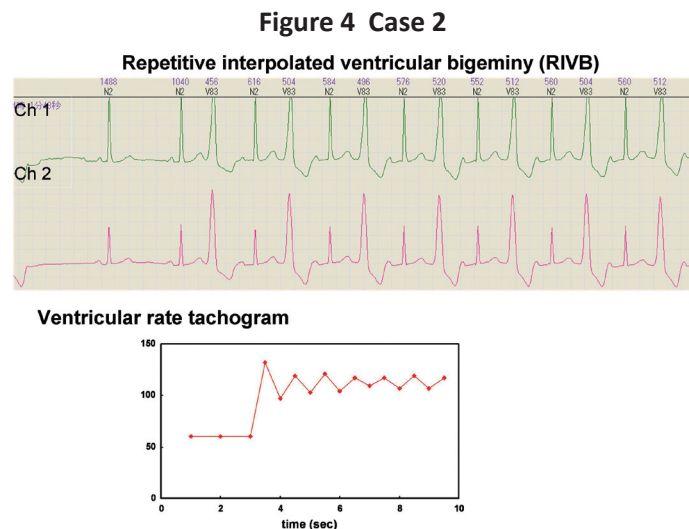


Figure 4. Case 2: Upper panel: ECG of repetitive interpolated ventricular bigeminy. Lower panel: Heart rate tachogram showing the sudden jump up of the ventricular rate to 110 bpm.

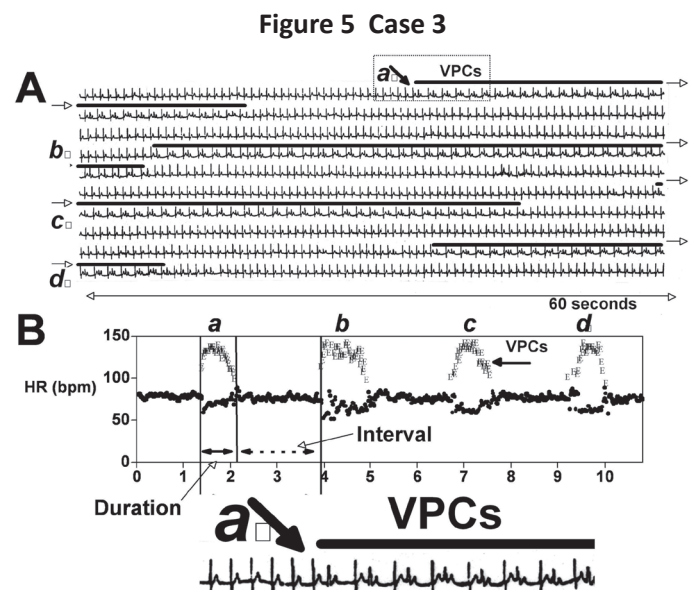


Figure 5. Case 3: A: slow speed ECG showing the four episodes of VPC cyclic bursts (a to d). B: tachogram showing the cyclic burst of VPCs with domed type CI change (gradual shortening of CI at the initial period). Corresponding PBC was shown in Figure 6-C.

liar patterns on the instantaneous heart rate tachograms⁷. In this middle aged man, 4 VPC cyclic bursts were observed during 10 minutes with gradual shortening of CI at the initial stage.

To qualitatively analyze the CI, we started to use digital measurements and introduced full-day successive CI measurement using its coefficient of variation (CV)⁶. The CV of the CI was significantly larger in VP than in fixed CI VPC as shown in Fig. 6-lowermost panel. CV of 0.140 proved to be a simple index to discriminate the VP. Analysis of the 1,500 VPC patients disclosed single peak distribution of CV

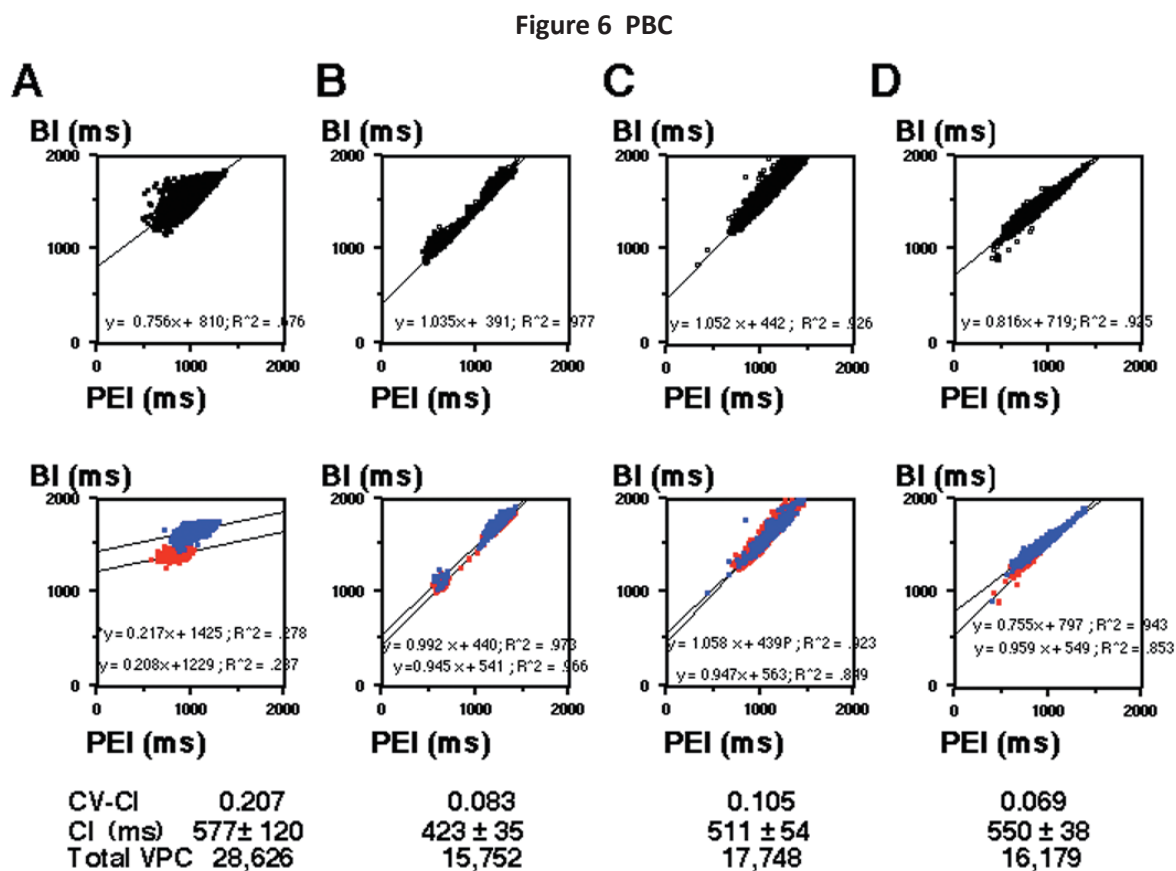


Figure 6. PBCs from the 4 cases. Upper Panel: Full-day PBCs, Lower Panel: 2 hour PBCs (red dots; day, blue dots; night). A: Case 1, B: Case 2, C: Case 3, D: Case 4. PEI: Postextrasystolic interval, BI Bigeminy interval.

skewed to the left with no clear-cut border zone in between.

Case 4: Strong and weak modulation: Ventricular parasystole associated with atrial fibrillation.

As a way to scan the post-extrasystolic interval and to estimate PRC, we could extend our analysis to VPCs associated with atrial fibrillation. Traditional VPC researchers frequently studied patients with atrial fibrillation patients. For example, the famous "rule of bigeminy" concerning the role of the preceding R-R intervals immediately before the bigeminy was found out by the analysis mainly in atrial fibrillation in 1955.

A 55y.o. man with dilated cardiomyopathy, who had atrial fibrillation and VPCs (16,788/day) was shown. Bigeminy in VPCs associated with atrial fibrillation is of value, since the randomly occurring normal QRS immediately after each VPC can fully scan the PEI compared with the normal sinus rhythm patient, in whom only interpolated QRS can scan the shorter PEI range as in case 2. Full day and 2 hour

PBCs in this case were shown in Figure 6 with linear bigeminy distribution. Slope of the bigeminy regression line was sharper during the daytime compared with the nighttime.

In the successive 170 patients associated with atrial fibrillation and frequent VPCs, significant bigeminy regression line was observed in all of them with their slope ranging between -0.20 to +1.10, which showed no difference to those with sinus rhythm. In atrial fibrillation, discrimination of interpolated VPC and compensatory VPC was not possible.

Discussion

The etiology of VPCs and VP are still controversial since the nature of the ectopic focus observed in clinical situation is hard to study in detail. Therefore, we tried to analyze their features using ambulatory ECG^{1,2} Heart rate doubling with repetitive interpolated ventricular bigeminy was infrequently observed (7/1,500) and VPCs in atrial fibrillation was not so rare (170/1,500). We could ablate both VP and VPC

with fixed CI using the earliest potential in the ventricle. From our experience, we suspect that VP originates from a weakly modulated ectopic focus, while the fixed CI VPCs derives from the more strongly modulated ectopic focus⁴. Comparison with the atrial parasystole will be of value since the foci in the four pulmonary vein, which could induce atrial fibrillation, are the good targets for catheter ablation^{8,9}. Both atrial and ventricular foci could be successfully ablated by looking for the earliest potential.

Clinical significance of modulation theory would be tested in many situations including exercise test, sleep study and atrial fibrillation. We believe the idea based on a simple experiment using Purkinje fiber can be applied widely for the analysis of VPC.

Conclusions

Direct estimation of PRC was possible from our new simple PIC and PBC. We proposed a strongly modulation hypothesis based on modulated parasystole model using a clinical ECG monitoring. Our hypothesis should be further tested by several techniques including the catheter ablation targeting the earliest excitation site of ectopic focus.

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ECG Commentary Related to the Quiz in the No.11 Issue

Yenn-Jiang Lin, MD / Shih-Ann Chen, MD

Taipei Veterans General Hospital, Taipei, Taiwan

Twelve lead ECG showed sinus rhythm with RBBB morphology. The number of QRSs (arrow) was more than the P waves, suggesting that the trigger was ventricular in origin. The morphology of the premature ventricular complex was almost similar,

but slightly different from that during sinus rhythm with aberrancy. Electroanatomic mapping revealed VT/VPCs originating near the His-bundle, and the VT was successfully ablated.



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ECG Quiz

The model commentary will be provided in the next issue No. 13

Dr. Ulhas M Pandurangi

Sr. Consultant Cardiologist & Electrophysiologist

The Madras Medical Mission

Chennai, India - 600 037

Ph: 044 26565961 2126

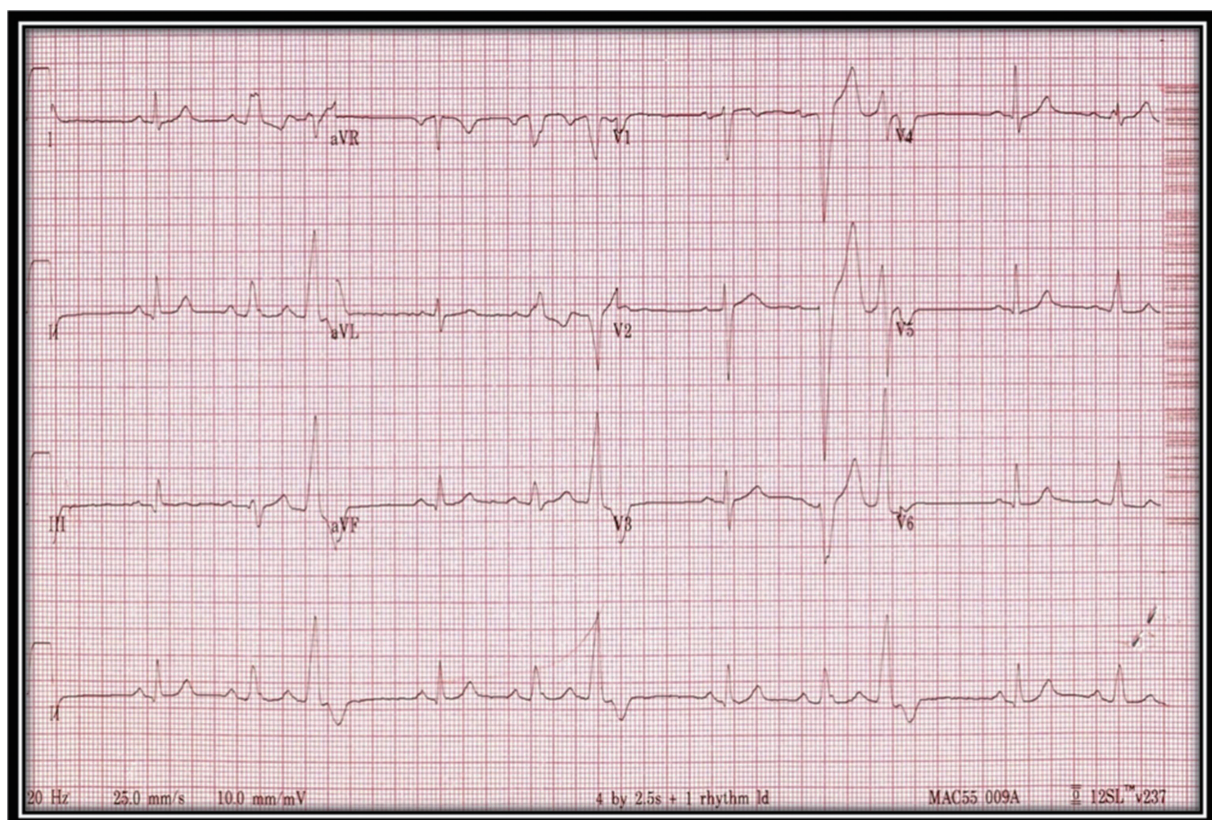
E Mail: arrhythmiaheartfailureacademy@gmail.com / epulhas@gmail.com

Question:

What is the Rhythm? Where is the origin of ectopy?

Pick the right answer from the choices below.

1. Sinus Rhythm, Ventricular ectopies in couplets of RVOT origin.
2. Sinus Rhythm, A-V conduction disease Ventricular ectopies in trigeminy of LVOT origin
3. Sinus Rhythm, A-V Wenckebach at node & Left bundle branch, No Ventricular ectopies.

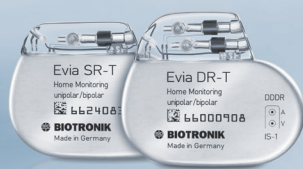


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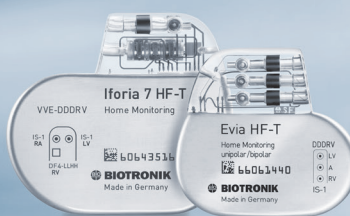
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