Analysis of Morphological Characteristics and Origins of Idiopathic Premature Ventricular Contractions Under a 12-Lead Electrocardiogram in Children with Structurally Normal Hearts

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Summary

Up to 40% of healthy children have premature ventricular complexes or contractions (PVCs) detected with 24-hour Holter monitoring. We aimed to investigate the morphological characteristics and origins of idiopathic PVCs under a 12-lead electrocardiogram in children with structurally normal hearts. All asymptomatic monomorphic PVC patients with structurally normal hearts under 18 years of age were included in this retrospective study. Characteristics of PVCs in lead V1 under a 12-lead electrocardiogram were classified as left bundle branch block (PVC-LBBB) or right bundle branch block (PVC-RBBB). According to limb leads, PVC-LBBB or PVC-RBBB was divided into: PVCs-LBBB type I; PVCs-LBBB type II; PVCs-RBBB type I; PVCs-RBBB type II; and PVCs-RBBB type III. Out of 178 PVC patients, 94 cases of PVCs-LBBB (PVCs-LBBB type I = 60; PVCs-LBBB type II = 34) and 84 cases of PVCs-RBBB (PVCs-RBBB type I = 3; PVCs-RBBB type II = 55; PVCs-RBBB type III = 26) were identified. The frequency of PVCs-LBBB type I increased with age and the frequency of PVCs-RBBB type II and III decreased with age. Among the children monitor tested, from 1 years old to 18 years old, PVCs originating from the left or right ventricular outflow tract gradually increased with age, while PVCs originating from the branch sources decreased with age.

Key words: Premature ventricular contractions, Origin of ventricular arrhythmia, Pediatrics

Premature ventricular complexes or contractions (PVCs) are commonly observed both in structurally normal hearts and structural heart diseases in the pediatric population. PVCs in children with structurally normal hearts are called idiopathic PVCs. Up to 40% of healthy children have PVCs detected with 24-hour Holter monitoring. Depending on the duration and type of screening, the prevalence of idiopathic PVCs is approximately 10% to 30% in children without apparent structural heart diseases. The clinical manifestations of PVCs in individuals are complex and diverse, ranging from asymptomatic syncope to death. Despite the fact that most idiopathic PVCs are generally considered benign in children, a small number of patients may develop cardiomyopathy or experience life-threatening forms of ventricular tachycardia or ventricular fibrillation. Therefore, many clinicians tend to exaggerate the prognosis of PVCs, which often causes anxiety in children and their parents, induces unnecessary treatment, and subsequently increases the economic burden on the family.

The prognosis of PVCs is correlated with its site of origin. PVCs usually originate in the right ventricular outflow tract (RVOT), tricuspid annulus, left ventricular anterior or posterior branch, mitral annulus, left ventricular outflow tract, aortic root, and epicardium. Previous studies showed that morphological characteristics under a 12-lead electrocardiogram had high diagnostic value for differentiating the origin of PVCs in the adult population. However, electrocardiographic characteristics and origin of idiopathic PVCs in children have not been fully clarified. According to the diagnostic criteria for adults, we investigated the morphological characteristics of monomorphic PVCs under the 12-lead electrocardiogram in children with structurally normal hearts in our institute, and analyzed the possible anatomical origin of PVCs based on age distribution.

Methods

Study population: This retrospective study included 178 consecutive pediatric patients (112 males and 66 females) with asymptomatic monomorphic PVCs who visited to The Second Hospital of Wenzhou Medical University from January 2009 to December 2014. Data including medical history, physical examination, blood biochemistry, chest X-ray, 12-lead electrocardiogram, 24-hour Holter monitoring, and 24-hour Holter monitoring.
monitoring, and echocardiography were collected. Patients satisfying the following criteria were included: 1) documented frequent monomorphic PVCs under the 12-lead electrocardiogram; 2) verified as having no structural heart diseases by chest X-ray and echocardiography examination; and 3) normal serum myocardial enzyme and electrolyte levels. This study was approved by the Academic Committee of The Second Affiliated Hospital of Wenzhou Medical University. Written informed consent was obtained from individual participants. All patients or guardians read and signed the consent form and agreed to participate in the study.

Classification of PVC origin: Electrocardiograms were recorded at a paper speed of 25 mm/s. All available electrocardiograms were reviewed to determine the origin of PVCs according to the following criteria:

1) PVCs with left bundle branch block (LBBB)-I: a LBBB morphology with downward main QRS wave pattern of QRS in lead V1; a large R pattern QRS in leads II, III, and aVF; and negative prominent or low R pattern of QRS in lead aVL. This type of PVC is generally considered to be of LVOT origin. Precordial R-wave transition occurring before the sinus rhythm QRS wave or wide R-wave in leads V1 and V6 is considered to be of left ventricular outflow tract (LVOT) (left coronary cusp, right coronary cusp, left and right coronary cusp junction) origin.6,14,15

2) PVCs-LBBB-II: a LBBB morphology with downward main QRS wave pattern in lead V1; no or part of large R pattern of QRS in leads II, III, and aVF (similar to the type B Wolff Parkinson-White syndrome); dominant R pattern in leads I and aVL; at least one “S” or “s” wave in the inferior leads; low amplitude of QRS wave in lead aVR. This type of PVC is generally considered to be of tricuspid annulus origin.11,16

3) PVCs-LBBB (RBBB)-I: a RBBB morphology with upward main QRS wave pattern in lead V1 and a large R pattern of QRS in leads II and III, and aVF is considered to be of LVOT origin.

4) PVCs-RBBB-II: an upward main QRS wave pattern in lead V1, and R pattern of QRS in leads II and III. This type of PVC is generally considered to be of left posterior branch origin11; while a small number of cases originate from the posterior mitral annulus or posterior mastoid muscle.

5) PVCs-RBBB-III: an upward main QRS wave in lead V1, rS pattern of QRS in leads I and aVL; dominant R pattern in leads II, III, and aVF. This type of PVC is usually considered to be of left anterior branch origin; while a small number of cases originate from the anterior mitral annulus or anterior mastoid muscle.

6) Other type of PVCs-RBBB: characteristics of PVCs do not comply with the above three types of PVCs-RBBB.

Statistical analysis: Patients were divided into 4 age groups: < 3 (infancy), 3-6 (preschool age), 6-12 (school-age), and 12-18 (adolescence) years. Frequency estimates were generated for each PVC type in each age group. Categorical data were expressed as frequencies. The difference in the constituent ratio of the PVC type (total PVCs-RBBB and total PVCs-LBBB) in each age group was determined by the chi-square tests. The correlation between the constituent ratio of the PVC type (total PVCs-RBBB and total PVCs-LBBB) and age distribution was analyzed by the chi-square test for linear trend. All statistical analyses in this study were performed using SPSS 17.0 Statistical software.

Results

Baseline characteristics: A total of 181 PVC cases were collected during the five-year study. Three cases with polymorphic PVCs were excluded. Therefore, 178 pediatric patients with PVCs were included. There were 112 (62.9%) male and 66 (37.1%) female cases, with a mean age of 6.51 ± 4.17 years (range, 1-18 years). According to morphological characteristics of the PVCs under 12-lead electrocardiograms, all patients were classified into the described PVC classifications of origin, except for four cases (PVCs-RBBB). These four cases did not belong to the typical left outflow tract origin, but were characterized as atypical left fascicular origin, manifesting as rS or RS pattern QRS wave in leads II and III or I and aVL and wider QRS waves, which were classified as PVCs-RBBB-II or PVCs-RBBB-III, separately. The representative 12-lead electrocardiograms of PVCs are presented in Figure 1 and Figure 2.

PVC classifications: Out of the 178 study patients, PVCs-LBBB and PVCs-RBBB were observed in 94 and 84 patients, respectively. Among the 94 PVCs-LBBB cases, 60 originated in the outflow tract (seven cases with precordial R-wave transition occurred earlier than sinus rhythm QRS wave) and 34 did not originate in the outflow tract (all cases had at least one “S” or “s” wave in the inferior leads). Out of the 84 patients, LVOT origin was observed in three, left anterior branch area in 55, and left posterior area in 26. The detailed age distribution of possible origin of PVCs is summarized in the Table.

Frequency of age distribution of idiopathic PVCs: The frequency of patients with PVCs-LBBB tended to increase with age, while patients with PVCs-RBBB tended to decrease with age (Figure 3A). There was an obvious increase in the frequency of patients with PVCs-LBBB (outflow tract origin) with age. However, the frequency of patients with PVCs-LBBB-II (non-outflow tract origin) did not change with age (Figure 3B). The frequency of patients with PVCs-RBBB (left anterior or posterior branch origin) tended to decrease with age (Figure 3C). Chi-square tests indicated that there was a statistical difference in the constituent ratio of the PVC type (total PVCs-RBBB and total PVCs-LBBB) in the different age groups (chi-square = 10.429, P = 0.015). A chi-square test for linear trend suggested that there was a significant linear trend in age (P = 0.002). From 1 year old to 18 years old, PVCs from the right ventricular origin increased with age, while PVCs from the left ventricular origin decreased with age.

Discussion

PVCs are a common arrhythmia in healthy children of all ages. However, studies on PVC origin and radiofre-
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Figure 1. Representative 12-lead electrocardiograms of PVCs. A: Representative electrocardiogram of PVCs-LBBB-I (RVOT origin characterized as a LBBB morphology with R-wave transition in lead V1, large R pattern in all the inferior leads). A1: RVOT origin. A2: Precedial R-wave transition occurred before the sinus rhythm QRS morphology with wide R-wave in leads V1 and V2; suggested possible LVOT origin. B: Representative electrocardiogram of PVCs-LBBB-II (tricuspid annulus origin characterized as dominant R pattern of QRS in leads I, aVL, V5, and V6 and “S” or “s” wave in the inferior leads). C: Representative electrocardiogram of PVCs-RBBB-I (LVOT origin including left coronary cusp, right coronary cusp, left and right coronary cusp junction, front wall of mitral annulus, downward left coronary cusp, mitral valve annulus anterior wall, distal great cardiac vein). D: Representative electrocardiogram of PVCs-RBBB-II (left posterior branch origin characterized as an upward QRS in lead V1, inverse QRS wave in lead II and III (rs pattern), upward QRS in lead I and aVL, and rs pattern of QRS in lead V6). E: Representative electrocardiogram of PVCs-RBBB-III (left anterior branch origin characterized as an upward QRS in lead V1, inverse QRS wave in lead I and aVL (rs pattern), upward QRS in lead II, III, and Rs pattern of QRS in lead V6). 1 mV = 10 mm, 25cm/sec.

The frequency ablation in children are very limited. The prognosis of PVCs in children depends on the origin of PVCs. Therefore, identifying PVC origin is of great importance. The main finding of this study is that idiopathic PVCs in children with structurally normal hearts mainly originated in the outflow tract (PVCs-LBBB-I) and left anterior branch (PVCs-RBBB-II). We also found that the percentage of patients with PVCs-LBBB type I increased with age and the percentage of patients with PVCs-RBBB type II and III decreased with age. However, the underlying mechanism of this age distribution remains largely unknown.

In this study, the distribution of age differed for each PVC origin. PVCs-LBBB tended to increase with age. However, if the origin of the PVCs is taken into consideration, this was only true for PVCs-LBBB-I originating in the outflow tract. The frequency of PVCs-LBBB-II originating in the non-outflow tract (PVC-LBBB) did not change with age. The percentage of PVCs arising from the left anterior branch was greater than left posterior branch origin. Both left posterior or left anterior branch origin PVCs tended to decrease with age. Consistent with our study, Gertie, et al.7) indicated that PVCs-RBBB disappeared during childhood but not for PVCs-LBBB during 3.1 years of follow-up. The percentage of PVCs in children with structurally normal hearts decreased and disappeared during a median period of 22 months of follow-up.7) Taken together, these findings indicate that follow-up for children with PVCs-LBBB-I is necessary. Our findings also support that natural history of PVCs in children with anatomically normal hearts depends on the origin of the PVCs.

With the development of electrophysiology and radiofrequency ablation, several studies9-13) have described the criteria to distinguish PVC origin according to the features of the 12-lead electrocardiogram. Site-specific crite-
ria of PVCs also have been reported in these studies. This approach provides a rapid assessment of the origin of PVCs. Specifically, children under the age of 2 years exhibit right ventricular dominance. Therefore, there may be more errors in determining the origin of PVCs on the 12-lead electrocardiogram than those in the adult population. This misclassification might come from the PVCs originating in the left or RVOT. Both the ratio of left/right ventricular thickness and position of the heart in the chest for children over the age of 3 years are similar to adults, so the diagnostic value of 12-lead electrocardiogram for determining PVC origin is similar to the adult. PVCs, particularly for those originating in the outflow tract vicinity, are affected by the right ventricular dominance.

The morphological characteristics of the QRS complexes on the 12-lead electrocardiogram are an excellent tool to identify rhythm origin. LBBB morphology with monomorphic R pattern in the inferior leads generally originates in both RVOT and LVOT (aortic root area). When there is difficulty distinguishing these two origins, Ouyang, et al. suggested that patients with a typical LBBB morphology and an inferior axis had PVCs originating in the ventricular outflow tract. The morphology of QRS in leads V1 and V2 could be used to distinguish left or RVOT origin. Amplitude of R/S wave > 0.3 or duration of R/QRS wave > 0.5 in leads V1 and V2 suggested that the PVCs originated in the LVOT. Otherwise, they originated in the RVOT. However, the above criteria for classification have limitations for categorizing some PVCs in cardiac rotation patients. Yoshida, et al. suggested that the precordial leads transitional index (transitional region in precordial leads during PVCs/VT- transitional region in precordial leads during sinus rhythm) had a higher sensitivity, specificity, and diagnostic accuracy for predicting PVCs originating in the left or RVOT. A precordial leads transitional index < 0 is considered to be the diagnostic parameter for PVCs that originate in the LVOT.

Most non-RVOT PVCs originate in the vicinity of the tricuspid annulus. The difference between tricuspid annulus and RVOT is that PVCs originated from the tricuspid annulus had at least one s or S-wave in leads II, III, and aVF. PVCs originating from branch or mitral annulus shared common RBBB morphology under the 12-lead electrocardiogram. Branch origin of PVCs exhibiting typical left anterior or posterior fascicular block in the limb leads is similar to the anterior or posterior mitral annulus. However, mitral annulus is anatomically located at the end of the left ventricle. Therefore, positive QRS wave in leads V1 through V6, which is similar to the type A Wolff Parkinson-White syndrome, and the duration of QRS wave are wider than those in branch origin. Electrocardiogram in combination with an electrophysiological investigation showed that approximately 3.5%-5% of PVCs originated in the mitral annulus. The mechanism of PVCs originating in the mitral annulus or tricuspid valve may correlate with enhanced automaticity of ectopy or some

<table>
<thead>
<tr>
<th>Classification</th>
<th>Number (%)</th>
<th>&lt;3 years</th>
<th>~6 years</th>
<th>~12 years</th>
<th>~18 years</th>
</tr>
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<tbody>
<tr>
<td>Total PVCs-LBBB</td>
<td>178 (100%)</td>
<td>53 (100%)</td>
<td>30 (100%)</td>
<td>57 (100%)</td>
<td>38 (100%)</td>
</tr>
<tr>
<td>PVCs-LBBB I</td>
<td>60 (33.7%)</td>
<td>8 (15.1%)</td>
<td>7 (12.3%)</td>
<td>7 (18.4%)</td>
<td></td>
</tr>
<tr>
<td>PVCs-LBBB II</td>
<td>34 (19.1%)</td>
<td>11 (20.8%)</td>
<td>9 (30.0%)</td>
<td>7 (2.6%)</td>
<td></td>
</tr>
<tr>
<td>Total PVCs-RBBB</td>
<td>84 (47.2%)</td>
<td>34 (64.2%)</td>
<td>14 (46.7%)</td>
<td>24 (42.1%)</td>
<td>12 (31.6%)</td>
</tr>
<tr>
<td>PVCs-RBBB I</td>
<td>3 (1.7%)</td>
<td>1 (1.9%)</td>
<td>0</td>
<td>1 (1.8%)</td>
<td>1 (2.6%)</td>
</tr>
<tr>
<td>PVCs-RBBB II</td>
<td>26 (14.6%)</td>
<td>13 (24.5%)</td>
<td>5 (16.7%)</td>
<td>3 (5.3%)</td>
<td>5 (13.2%)</td>
</tr>
<tr>
<td>PVCs-RBBB III</td>
<td>55 (30.9%)</td>
<td>20 (37.7%)</td>
<td>9 (30.0%)</td>
<td>20 (35.1%)</td>
<td>6 (15.8%)</td>
</tr>
</tbody>
</table>

PVCs indicates premature ventricular contractions; LBBB, left bundle branch block; and RBBB, right bundle branch block.
kind of the atrioventricular node in embryonic tissue. A small number of PVCs originating in the mastoid muscle has a notching of the QRS complex in the leads.

Limitations: First, this is a retrospective study based on
patients’ consequences and not from a random sample; therefore, selection bias cannot be excluded. Prospective follow-up studies with larger sample sizes are warranted. Second, we only selected asymptomatic pediatric patients with monomorphic PVCs. Patients with multiple and/or polymorphic ventricular premature beat were not included in the analysis. Third, the origins of PVCs were only determined by the morphological characteristics of a 12-lead electrocardiogram in our population. These findings need to be verified by the electrophysiological findings in future studies. Finally, electrophysiological characteristics of children, particularly in younger patients, are quite different from the adult. However, the diagnostic criteria of PVC origin in our population were made according to the criteria for adults. Therefore, misclassification of patients cannot be excluded due to the lack an agreed-upon gold standard for children.

Conclusions

This study suggests that idiopathic PVCs in children with structurally normal hearts mainly originate in the left or RVOT and left anterior branch area. Children with PVCs originating in the outflow tract appear to increase with age; PVCs originating in the left anterior or posterior branch seem to decrease with age. The prevalence of PVCs in healthy children varies with age. The mechanisms of age distribution of PVCs need to be further investigated. Moreover, the standard electrocardiogram criteria in determining origin of PVCs in children need to be established.

Disclosure

Conflict of interest: None

References

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