Differentiation of arrhythmia originating from the right or left ventricular outflow tract based on the QRS morphology of premature ventricular beats and duration of repolarisation

Krzysztof Szydlo, Anna Maria Wnuk-Wojnar, Maria Trusz-Gluza, Andrzej Hoffmann, Seweryn Nowak, Iwona Woźniak-Skowierska, Jaroslaw Kolasa, Jaroslaw Chmurawa, Beata Nowak-Jeż, Anika Doruchowska

1st Chair and Department of Cardiology, Upper Silesian Medical Centre, Medical University of Silesia, Katowice, Poland

Abstract

Background: Premature ventricular beats (PVBs) and monomorphic ventricular tachycardia originating from the right ventricular outflow tract (RVOT) are the most frequent forms of idiopathic ventricular arrhythmias, but arrhythmia originating from the left ventricular outflow tract (LVOT) may be found in about 10% of these patients.

Aim: To compare electrocardiographic (ECG) patterns and duration of repolarisation after PVBs originating from the left and right superior part of the interventricular septum which were successfully treated with radiofrequency catheter ablation.

Methods: We studied 62 patients who did not receive antiarrhythmic drug treatment before ablation, including 50 patients with RVOT arrhythmia (21 males, mean age 42 ± 14 years, left ventricular ejection fraction [LVEF] 61 ± 6%) and 12 patients with LVOT arrhythmia (3 males, mean age 41 ± 17 years, LVEF 59 ± 9%). Pre-ablation 24-h Holter ECG recordings were analysed for the total number of PVBs. In addition, we evaluated ectopic beat QRS duration, prematurity index and duration of repolarisation (QT interval, JT interval and TpeakTend values uncorrected for the heart rate) based on ten random daytime PVBs during a period of stable sinus rhythm at a rate of 60–70 bpm.

Results: The study groups did not differ by age, LVEF, heart rate and the number of PVBs. RVOT arrhythmia was characterised by a lower prematurity index (0.59 ± 0.11 vs. 0.72 ± 0.09, p = 0.001) and a lower R/S ratio in leads V1–V3 (p < 0.01 for each lead). QRS duration of right-sided PVBs was shorter compared to that of left-sided PVBs (147 ± 13 vs. 166 ± 13 ms, p = 0.002). QT and JT intervals were similar (QT: 422 ± 32 vs. 429 ± 27 ms, p = 0.35; JT: 272 ± 27 vs. 266 ± 27 ms, p = 0.31), and TpeakTend was shorter in RVOT arrhythmia (100 ± 10 vs. 110 ± 6 ms, p = 0.01). Combination of R > S in lead V3 and TpeakTend-PVB > 110 ms identified LVOT arrhythmia with a sensitivity of 75% and specificity of 96%.

Conclusions: Ventricular arrhythmias originating from the left or right superior part of the interventricular septum are not only characterised by different ECG patterns of ventricular ectopic beats but also show significant differences in the repolarisation phase.

Key words: ventricular arrhythmia, right ventricular outflow tract, TpeakTend

INTRODUCTION

The most common forms of idiopathic ventricular arrhythmia are premature ventricular beats (PVBs) and ventricular tachycardias originating from the right ventricular outflow tract (RVOT). However, approximately 10% of these arrhythmias originate within the subendocardial or subepicardial layers of the left ventricular outflow tract (LVOT), as well as from the aortomitral area or the sinus of Valsalva. In many cases, QRS morphology does not allow precise differentiation between these arrhythmias, which leads to prolonged ablation time.
or even ablation failure [1, 2], particularly in case of LVOT ectopic foci located in the septal area or below the right or left coronary aortic cusp. The most common criterion used to differentiate between the RV and LV location of the ectopic focus is the ratio of the R and S waves of the PVB in the precordial leads, which indicates the location of the transition zone were R and S wave amplitudes are equal. The precordial transition zone at lead V1, suggests a LV origin of the ectopic focus, and transition at lead V6 or later (leads V6–V7) suggests a RVOT origin of the arrhythmia. However, with septal location of the ectopic focus, the electrocardiographic (ECG) pattern of PVBs is often ambiguous, making it difficult to differentiate between the LV and RV origin of the arrhythmia.

Single reports indicate a similar electrophysiologic substrate of both arrhythmias [3], with no increased repolarisation dispersion or microvolt T wave alternans [4]. However, more common postextrasystolic T and U wave changes were shown in patients with RVOT arrhythmia compared to healthy subjects [5], suggesting abnormal repolarisation in patients with idiopathic ventricular arrhythmia.

In these reports, no reference was made to the most commonly used repolarisation parameters, i.e. QT interval and its early and late phase components. It seems that different locations of the ectopic focus may affect depolarisation and repolarisation, leading to differences in QRS morphology and repolarisation duration in patients with RVOT or LVOT arrhythmia. If such differences actually exist, they might be helpful in the differentiation between these 2 types of arrhythmia and thus facilitate diagnostic work-up, patient preparation, and selection of the ablation approach.

The aim of this study was to evaluate selected ECG parameters, in particular duration of repolarisation, of sinus beats and PVBs in patients with septal ectopic foci within RVOT or LVOT. We looked for possible differences in morphological QRS parameters, prematurity index, QRS duration, and repolarisation including its late phase.

METHODS
The study population included 62 patients hospitalised in the First Department of Cardiology at the Medical University of Silesia in Katowice in 2008–2010. All patients had frequent symptomatic ventricular arrhythmia without sustained ventricular tachycardia and no structural heart disease. We included only patients who did not receive any antiarrhythmic drug therapy during the last 24 h, did not receive sotalol for at least 48 h, and did not receive amiodarone for at least 3 months. We also excluded patients with intraventricular conduction disturbances in standard surface ECG (sinus beat QRS duration of > 110 ms according to the most recent American Heart Association guidelines of 2009) [6]. In all patients, 24-h 12-lead ECG Holter recording and echocardiography were performed one day before the invasive procedure.

The initial diagnosis of LVOT or RVOT arrhythmia was based on the morphology of PVBs seen in standard ECG. The study included only those patients in whom the ectopic focus was identified correctly, as confirmed by fully successful ablation (evaluated both immediately after the procedure and during the next 3–4 days of follow-up). The present analysis includes only patients with the ectopic focus located within the septal RVOT below the pulmonic valve (50 patients) or within the septal LVOT (12 patients). We excluded patients with other locations of the ectopic focus, including supravalvular location.

24-hour ECG Holter recording
Holter monitoring was performed using Lifecard CF recorders (Del-Mar Reynolds) which allow simultaneous 12-lead ECG recording (Mason-Likar lead system) with the sampling frequency of 1024 Hz and the effective sampling rate of 128 Hz after noise filtering. The studied parameters were evaluated based on 10 PVBs and sinus beats immediately preceding these PVB occurring during the day, usually between 2 and 6 p.m., during periods of sinus rhythm at a rate of 60–70 bpm. We did not analyse tracings with frequent (bigeminy or trigeminy) or multiple PVBs. Measurements were made using an electronic caliper providing a temporal resolution of 2–4 ms. All measurements were performed twice by the same observer who had no access to the data that would allow patient identification. In leads V1–V6, the following QRS parameters were measured for both PVBs and sinus beats: QRS duration, R and S wave amplitude (in mm), and the absolute R/S ratio. Repolarisation parameters of PVBs and sinus beats were determined in lead V1 or V6 (Fig. 1). We calculated the total duration of repolarisation (QT and JT intervals) and duration of late repolarisation (time from the peak to the end of the T wave — TpeakTend). We also calculated TpeakTend/QT and TpeakTend/JT ratios for PVBs. Duration
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Differentiation of arrhythmia originating from the right or left ventricular outflow tract as described for the RV. Simultaneous display of RV and LV puncture. We performed electroanatomic mapping of the LV, mapping catheter introduced retrogradely by femoral artery in the septal area, we proceeded with LV mapping, with the site of the earliest activation of the RV was located morphologically of native PVBs. If these criteria were not met, in the surface ECG was completely concordant with the morphology, and the morphology of paced QRS complexes recorded from the tip of the mapping catheter showed a QS QRS complex by at least 30 ms, the unipolar electrogram adjacent lead ring) during PVB preceded the onset of the bipolar electrogram (recorded between the distal and an adjacent lead ring) during PVB preceded the onset of the cardiac cycle. The system visualises the lead tip within the map, allowing precise intracardiac navigation.

Under local anaesthesia, a 7 F 3.5-mm tip Navistar lead (Biosense Webster) with 2–5–2 mm spacing of the rings, cooled with normal saline and cooperating with the electroanatomic system, was placed in the RV by femoral vein puncture. During multiple single PVBs, an activation map was created based on directly recorded local bipolar electrograms. Then, pacing was initiated at the site of the earliest activation and the morphology of the paced QRS complexes was compared to that of PVBs seen in 12-lead surface ECG for both real-time and retrospective analyses. The electroanatomic system allows simultaneous recording of multiple data for a given pericardial site, such as its three-dimensional location (in relation to reference electromagnets placed under the patient body during the procedure); local electrogram voltage (bipolar and unipolar), and local activation time in relation to an a priori defined reference time point during the cardiac cycle. The system visualises the lead tip within the map, allowing precise intracardiac navigation.

Details of electrophysiologic study and ablation

Procedures were performed using the electrophysiologic system (Labsystem Pro, Bard Electrophysiology) and the electroanatomic system CARTO Merge (Biosense Webster). The electrophysiologic system allows continuous recording of intracardiac potentials and 12-lead surface ECG for both real-time and retrospective analyses. The electroanatomic system allows simultaneous recording of multiple data for a given pericardial site, such as its three-dimensional location (in relation to reference electromagnets placed under the patient body during the procedure); local electrogram voltage (bipolar and unipolar), and local activation time in relation to an a priori defined reference time point during the cardiac cycle. The system visualises the lead tip within the map, allowing precise intracardiac navigation.

Statistical analysis

Statistical analyses were performed using the Statistica 7.1 PL software with a Visual Basic macro generating receiver operating characteristic (ROC) curves that allowed evaluation of the sensitivity and specificity of the test. To evaluate measurement reproducibility, an intraobserver error (\(\sqrt{\text{SD}^2/2N}\)) was calculated and found to be equal to 1.6 ms.

We calculated mean or median values and standard deviations for all quantitative variables. Normality of the variable distribution was evaluated using the Kolmogorov-Smirnov and Lille-Lillefors test and the Shapiro-Wilk W test. Differences in normally distributed variables between the groups were tested using the Student t test for unpaired samples, and non-normally distributed variables were evaluated using nonparametric tests including the Kolmogorov-Smirnov test and the Mann-Whitney U test. Qualitative variables were compared using the \(\chi^2\) test, with the Yates’ correction for sample sizes below 5. \(P < 0.05\) was considered statistically significant.

RESULTS

The study groups did not differ by age, left ventricular ejection fraction, heart rate, and the number of PVBs during Holter monitoring (Table 1). PVBs in the RVOT arrhythmia group were characterised by a lower prematurity index (0.59 ± 0.11 vs. 0.72 ± 0.09, \(p = 0.001\)) and shorter QRS
duration (147 ± 13 vs. 166 ± 13 ms, p = 0.002). QRS complexes of the ectopic beats originating from RVOT were characterised by a lower R/S ratio in leads V₁–V₅ (Table 2). In most these patients, the transition zone was at lead V₄, while patients with LVOT arrhythmia had transition zone at lead V₃ (Table 2, Fig. 2). The R/S ratio in lead V₃ was > 1 in 10 (83%) patients with LVOT arrhythmia compared to only 14 (28%) patients with PVBs originating from RVOT (p = 0.002). This criterion had a sensitivity of 83% and a specificity of 72% for a left-sided ectopic focus.

Repolarisation parameters of sinus beats were similar in both groups (Table 3), as were QT and JT intervals of PVBs (Table 4). Duration of the late repolarisation phase (TpeakTend) after PVBs was significantly shorter in the RVOT arrhythmia group (100 ± 10 vs. 110 ± 6 ms, p = 0.01). TpeakTend/QT and TpeakTend/JT ratios for PVBs were also lower in this group but these differences did not reach statistical significance.

ROC curve analysis (Fig. 3) indicated that TpeakTend-PVB > 110 ms had a sensitivity of 58% and a specificity of 85% for a left-sided ectopic focus. For TpeakTend/JT ratio > 0.42, sensitivity was 36% and specificity was 90%.

During further analysis, we combined a morphological criterion of R > S in lead V₃ with TpeakTend-PVB > 110 ms. This combination was present in 9 patients with LVOT arrhythmia (75%) and only 2 patients with PVBs originating from RVOT (4%, p < 0.001), for a sensitivity of 75% and a specificity of 96% for a left-sided ectopic focus.

QT index was similar in both groups (1.18 ± 0.08 in the RVOT arrhythmia group vs. 1.19 ± 0.10 in the LVOT arrhythmia group, p = 0.34).
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Table 3. Duration of repolarisation after sinus beats preceding a premature ventricular beat originating from the right ventricular outflow tract (RVOT) or left ventricular outflow tract (LVOT). Values are corrected for the heart rate.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>RVOT</th>
<th>LVOT</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>QTc [ms]</td>
<td>427 ± 21</td>
<td>438 ± 21</td>
<td>0.12</td>
</tr>
<tr>
<td>TpeakTendc [ms]</td>
<td>95 ± 10</td>
<td>93 ± 14</td>
<td>0.36</td>
</tr>
<tr>
<td>JTc [ms]</td>
<td>327 ± 22</td>
<td>323 ± 24</td>
<td>0.72</td>
</tr>
</tbody>
</table>

Table 4. Duration of repolarisation after premature ventricular beats (PVB) originating from septal right ventricular outflow tract (RVOT) or left ventricular outflow tract (LVOT).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>RVOT</th>
<th>LVOT</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>QT-PVB [ms]</td>
<td>422 ± 32</td>
<td>429 ± 27</td>
<td>0.35</td>
</tr>
<tr>
<td>JT-PVB [ms]</td>
<td>272 ± 27</td>
<td>266 ± 27</td>
<td>0.31</td>
</tr>
<tr>
<td>TpeakTend-PVB [ms]</td>
<td>100 ± 10</td>
<td>110 ± 6</td>
<td>0.01</td>
</tr>
<tr>
<td>TpeakTend/QT-PVB</td>
<td>0.231 ± 0.021</td>
<td>0.248 ± 0.019</td>
<td>0.09</td>
</tr>
<tr>
<td>TpeakTend/QT-PVB</td>
<td>0.359 ± 0.038</td>
<td>0.411 ± 0.051</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Figure 3. Receiver operating characteristic for TpeakTend-premature ventricular beat. Area under curve = 0.632

DISCUSSION

Our study showed significant differences in the morphology of ventricular ectopic beats (VEB) originating from the septal LVOT or RVOT. RVOT arrhythmia was characterised by a significantly shorter late repolarisation phase. Tpeak-Tend > 110 ms was a sensitive marker of a left-sided ectopic focus, and combining a morphological criterion (R > S wave amplitude) at lead V1 with TpeakTend-PVB of > 110 ms significantly increased the ability to identify LVOT arrhythmia.

Literature data indicate the importance of evaluating standard surface ECG in the initial differentiation of RVOT and LVOT arrhythmia. The rationale of such an approach is obvious as development of an easy-to-use, noninvasive algorithm that would allow initial localisation of the arrhythmic focus might be helpful not only during patient selection for ablation but also when planning the ablation procedure itself. Previous reports highlighted the role of the R/S ratio in differentiation between right- and left-sided location of the ectopic focus. In this regard, leads V6 [8, 9] and V4 [10, 11] were indicated as having most importance for identification of the origin of ventricular arrhythmia. The transition zone (i.e. R > S wave amplitude) at lead V6 is characteristic for LVOT arrhythmia, while transition zone at lead V4 or even V3 indicates RVOT arrhythmia. Our findings are in agreement with these reports as we found significantly lower R/S ratios in case of RVOT arrhythmia. In patients with right-sided arrhythmia, the transition zone was usually at lead V4, in contrast to leads V6 and V4 in patients with a left-sided arrhythmic focus. Of note, our study group included only patients with septal location of the ectopic focus, and surface ECG-based identification of the ectopic focus has some inherent limitations, e.g. related to varying anatomic location of the heart within the chest.

Although outflow tract arrhythmia is considered potentially benign, it may lead to worsening of the LV systolic function [5]. In addition, occurrences of rapid monomorphic ventricular tachycardia, polymorphic ventricular tachycardia, and ventricular fibrillation were also reported in such patients [7, 12]. Patients with episodes of malignant ventricular arrhythmia were characterised by significantly shorter PVB coupling time and lower prematurity index. Igarashi et al. [7] introduced an interesting novel parameter known as QT index which combines the degree of PVB prematurity with duration of repolarisation determined during sinus rhythm. This index is defined as the ratio of coupling time and duration of repolarisation after a preceding sinus beat. In the study by Igarashi et al. [7], QT index was significantly lower in patients with malignant arrhythmia. In our study, both the prematurity index and the QT index values were similar to values reported elsewhere for patients with benign ventricular arrhythmia. This observation is in agreement with the clinical characteristics of our study population, as none of these patients had a history of malignant ventricular arrhythmia.

No analyses of repolarisation duration after outflow tract VEBs were reported in the available literature. Thus, our observation of a prolonged late repolarisation phase after VEBs originating from a left-sided ectopic focus is a novel finding. Of note, duration of the late repolarisation phase measured during sinus rhythm was comparable to values reported in the literature for healthy subjects [13] which seems to be closely related to the lack of structural heart disease in the study population.

Numerous studies showed that the late phase of repolarisation reflects transmural dispersion of the action potential duration [14–16]. In the study by Watanabe et al. [17], TpeakTend values were significantly lower in patients with a history of malignant ventricular arrhythmia who underwent programmed ventricular stimulation. The population evalu-
ated in that study included patients with previous myocardial infarction. In contrast, there are few data on the late repolarisation phase after both sinus and ectopic beats in patients with ventricular arrhythmia in whom no structural arrhythmic substrate was identified. Thus, we believe that despite small study sample, our findings may have an exploratory value and warrant further studies on this issue.

In our study, measurements were based on 12-lead Holter recordings which allowed selection of periods of sinus rhythm at a rate close to 60 bpm and with relatively few ectopic beats. In our opinion, this criteria allowed meaningful evaluation of repolarisation without the need for correction for the heart rate which would be difficult for PVBs and has not been referenced to in the literature.

Limitations of the study

The main limitation of our study was a relatively low number of patients, particularly with LVOT arrhythmia. This was a result of the chosen inclusion and exclusion criteria, specifically the exclusion of patients with a non-septal location of the ectopic focus. In other studies, populations of patients with this form of arrhythmia were also small. This is caused by a relatively less frequent occurrence of LVOT arrhythmia but also the fact that not all these patients undergo ablation due to a small distance between the ectopic focus and the left main coronary artery.

Another major limitation of our study was the use of only 10 VEBs for measurements. This number was set arbitrarily. QRS morphology and repolarisation duration were evaluated in only those ectopic beats which were preceded by at least 20–30 s of sinus rhythm at a rate of 60–70 bpm. In our opinion, this allowed us to omit a very problematic procedure of correcting repolarisation duration after a premature beat, increasing credibility and value of our findings. The latter were also increased due to a high reproducibility of measurements performed using an electronic caliper, estimated at 1.6 ms, and other methodologic aspects of our study including calculation of mean values from multiple measurements of individual ectopic beats.

CONCLUSIONS

Evaluation of QRS morphology and duration of transmural repolarisation dispersion (TpeakTend) after a VEB may be helpful in differentiation between ventricular arrhythmia originating from the septal LVOT or RVOT. Combination of R > S in lead V1 and TpeakTend-PVB of > 110 ms identified LVOT arrhythmia with a sensitivity of 75% and specificity of 96%.

Conflict of interest: none declared

References

Różnicowanie arytmii z części przegrodowej drogi odpływu prawej i lewej komory na podstawie morfologii pobudzeń dodatkowych i czasu trwania ich repolaryzacji

Krzysztof Szydło, Anna Maria Wnuk-Wojnar, Maria Trusz-Gluza, Andrzej Hoffmann, Seweryn Nowak, Iwona Woźniak-Skowerska, Jarosław Kolasa, Jarosław Chmurawa, Beata Nowak-Żež, Anika Doruchowska

I Katedra i Klinika Kardiologii, Samodzielny Publiczny Szpital Kliniczny Nr 7, Śląski Uniwersytet Medyczny, Katowice

**Streszczenie**

**Wstęp:** Najczęstszą formą idiopatycznej arytmii komorowej są pobudzenia przedwczesne (PVB) i częstoskurcze komorowe wywodzące się z drogi odpływu prawej komory (RVOT). Jedynie ok. 10% tych arytmii powstaje w obrębie drogi odpływu lewej komory (LVOT).

**Cel:** Celem pracy było porównanie morfologii zespołów QRS i czasu trwania repolaryzacji PVB u chorych z arytmią wywodzącą się z przegrodowej części LVOT oraz RVOT, u których za pomocą skutecznej ablacji potwierdzono lokalizację ogniska ekotopowego.

**Metody:** Badaniem objęto 62 pacjentów: grupę RVOT (50 chorych, 21 mężczyzn, 42 ± 14 lat, LVEF 61 ± 6%) oraz grupę LVOT (12 chorych, 3 mężczyzn, 41 ± 17 lat, LVEF 59 ± 9%). Analizowano 12-odprowadzeniowe EKG metodą Holtera wykonywane bezpośrednio przed zabiegiem; w tym okresie nie stosowano leków antyarytmicznych. Wybierano 10 ewolucji PVB z okresu dnia, w czasie stabilnego rytmu zatokowego o częstotliwości 60–70/min. Oceniano czas trwania QRS, amplitudę załamków R i S oraz ich iloraz (R/S) w odprowadzeniach przedsercowych, wskaźnik przedwczesności oraz czas trwania repolaryzacji (QT, JT) i jej przezściennej dyspersji (TpeakTend). Pomiarów parametrów repolaryzacji dokonywano w odprowadzeniu V₁ lub V₃.

**Wyniki:** Grupy nie różniły się pod względem wieku, LVEF, częstotliwości rytmu serca i liczby PVB. Arytmia RVOT charakteryzowała się niższym wskaźnikiem przedwczesności: 0,59 ± 0,11 vs. 0,72 ± 0,09; p = 0,001 oraz niższym wskaźnikiem R/S w V₁–V₃ (p < 0,01). W tej grupie zanotowano krótszy czas trwania zespołu QRS PVB (147 ± 13 vs. 166 ± 13 ms; p = 0,002) oraz czas trwania TpeakTend (100 ± 10 vs. 110 ± 6 ms; p = 0,01). Pozostałe wskaźniki repolaryzacji były podobne (QT: 422 ± 32 vs. 429 ± 27 ms; p = 0,35; JT: 272 ± 27 vs. 266 ± 27 ms; p = 0,31). Obecność R > S w V₃ w połączeniu z TpeakTend > 110 ms wskazuje na lewostronną lokalizację PVB z czułością 75% i swoistością 96%.

**Wnioski:** Ocena morfologii i czasu trwania przeciściennej dyspersji repolaryzacji (TpeakTend) dodatkowego pobudzenia komorowego może być przydatna w określaniu lokalizacji prawo- lub lewokomorowej arytmii komorowej z części przegrodowej drogi odpływu.

**Słowa kluczowe:** arytmia komorowa, droga odpływu prawej komory, TpeakTend

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