Heart Rate Variability in Patients with Ventricular Arrhythmia from Right Ventricular Outflow Tract

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Abstract
Background: Sympathetic tone may be an underlying mechanism in the occurrence of ventricular arrhythmia from right ventricular outflow tract (RVOT).

Objectives: To assess the difference in heart rate variability (HRV) in patients with ventricular arrhythmia from RVOT compared to control group.

Methods: We studied HRV from ambulatory monitoring in patients with ventricular arrhythmia from right ventricular outflow tract and control group who were requested for ambulatory monitoring during the same study period. Ventricular arrhythmia from right ventricular outflow tract must be more than 1000 PVC in 24 hours to be enrolled in the study. Parameters for autonomic tone acquired from ambulatory monitoring were average heart rate, standard deviation of all normal RR intervals (SDNN), standard deviation of average of normal RR intervals every 5 minute (SDANN).

Results: A total of 62 patients with ventricular arrhythmia from right ventricular outflow tract and 101 controls were studied. Females are predominant (71%). Average age was 53 years. There were no significant differences in baseline characteristics between the 2 groups except for more frequent symptoms in patients with ventricular arrhythmia from right ventricular outflow tract and markedly different in the amount of ventricular arrhythmia from right ventricular outflow tract by enrollment criteria. There were no significant differences in average heart rate, SDANN and SDNN between the 2 groups.

Conclusion: Markers of autonomic tone were not different between patients with ventricular arrhythmia from right ventricular outflow tract and controls. Sympathetic tone may not be the major underlying mechanism of ventricular arrhythmia from right ventricular outflow tract.

Introduction
Ventricular arrhythmia from right ventricular outflow tract is a common form of ventricular arrhythmia in clinical practice. Patients may be asymptomatic or symptomatic. Symptoms of ventricular arrhythmia from right ventricular outflow tract include palpitation, presyncope or syncope. Most patients have no evidence of structural heart disease and have a good prognosis. The pathogenesis of ventricular arrhythmia from right ventricular outflow tract has not been clearly understood. Recent studies suggested that defects in cAMP signalling may be involved. Sympathetic activity may play an important role in the occurrence of this form of ventricular arrhythmia and this arrhythmia may be triggered by exertion in a certain number of patients. Symptomatic patients may be treated by medication or radiofrequency ablation at the site of origin identified during electrophysiologic study. Beta blocker is one of the commonly used medications for this condition since it had very few serious adverse effects. Its efficacy for the treatment of this form of ventricular arrhythmia has been reported to be around 25-50%.

Heart rate variability (HRV) is the measurement that reflects autonomic modulation. Decreased HRV has been reported to be a good predictor of mortality in patients after myocardial infarction, heart failure, and even in community-based populations. Measurements of HRV can be performed by time-domain or frequency-domain analysis. Results from each type of analysis indicate autonomic modulation.
The objective of this study was to determine the difference in sympathovagal balance assessed by heart rate variability in patients with ventricular arrhythmia from right ventricular outflow tract compared to control group.

Methods
Study population: We performed retrospective analysis on Holter monitoring data from patients who were referred for ambulatory ECG monitoring due to palpitation, presyncope, syncope or arrhythmia detection. Patients with total count of PVC from right ventricular outflow tract defined as left bundle branch block and inferior axis morphology more than 1000 per 24 hour ECG monitoring were classified as patients with ventricular arrhythmia from RVOT. Patients with normal beats at least 99% of total QRS complexes from 24-hour ambulatory ECG monitoring and have total PVC count less than 10 beats per 24 hour were defined as control group. Ventricular tachycardia was defined as tachycardia with more than 3 consecutive beats of PVC. All patients and controls had no evidence of structural heart disease from history and clinical examination.

Ambulatory ECG monitoring: A 3-channel ECG monitoring was performed in each patient for 24 hour period. A Zymed digital recorder was used to obtain the ECG data. Electrodes were attached at 5 different positions for the standard EASI lead system (14). All patients were free of effect of medication during ambulatory ECG monitoring. Patients were instructed to press the event button if they have symptoms such as palpitation, chest pain, fainting so that the ECG playback would automatically display the ECG at that time. All patients kept a detailed diary recording the time of each episode of symptom.

Tapes were analysed with the Zymed system (Camarillo, California, USA). The sampled ECG data were transformed from the Zymed scanner to a microcomputer for processing HRV. The ECG data were scanned and all QRS complexes were classified under the computer program. The accuracy of QRS complex detection and the label of QRS complexes were reviewed and manually edited by an experienced cardiologist. The QRS complexes were carefully classified into sinus beats, supraventricular or ventricular ectopic beats or artifacts or unclassified. The frequency histogram of the normal RR interval was displayed and the ECG of the intervals in both tails of the normal RR distribution was reviewed. Time domain variables and average heart rate were obtained from the 24 hour ECG data. Time domain variables included standard deviation of all normal RR intervals (SDNN), standard deviation of average of normal RR intervals every 5 minute (SDANN). Average heart rate was also calculated. The software handles noise and ectopic beats by filling up the gaps in the time series with linear interpolation.

Statistical analysis
Test for normal distribution of data was performed by Kolmogorov-Smirnov test. Continuous variables were described as mean standard deviation for parametric data or median and interquartile range (IQR) for non-parametric data and frequencies and percentages for categorical variables. A comparison of continuous variables was made by the unpaired t-test for parametric continuous data, Mann-Whitney U test for non-parametric continuous data and Chi-square or Fisher exact test for categorical data. In all tests, the criterion for statistical significance was two-sided p 0.05.

Results
One-hundred sixty-three subjects were studied. There were a total of 47 males (29%) and 116 females (71%) at an average age of 52.8 ± 16.9 years. Sixty-two cases (38%) were in patient group and 101 cases (62%) were controls. Presenting symptoms were as follows: palpitation in 138 (85%), presyncope in 23 (14%), syncope in 27 (17%), dizziness in 9 (6%), dyspnea in 16 patients (10%). Symptoms were aggravated by exertion in 16 (10%). Baseline characteristics of both groups are shown in Table 1. Symptoms were more frequent in patients compared to controls. Ventricular tachycardia was demonstrated in 6 patients (9.7%) in patient group and none in controls.

Results of ambulatory ECG monitoring
Median PVC count in patient group was 5360 (IQR 1674, 10389). Details of both groups are shown in Table 1. Average heart rate, SDANN and SDNN were not significantly different between the 2 groups.
Discussion

Main results of this study demonstrated that there were no significant differences in indicators of sympathovagal balance between patients with ventricular arrhythmia from right ventricular outflow tract and control group.

Previous reports suggested that sympathetic tone may have influence in the occurrence of ventricular arrhythmia from right ventricular outflow tract. A significant proportion of patients with ventricular arrhythmia from right ventricular outflow tract reported that the symptoms related to tachycardia were aggravated by exertion (3) and occurred at daytime more than nighttime (15). The tachycardia may also be induced by exercise test. However, the characteristic that indicates sympathetic influence may not explain the whole group of ventricular arrhythmia from right ventricular outflow tract. It has been reported that 24% of patients with ventricular arrhythmia from right ventricular outflow tract are bradycardia dependent (17). In our study, symptoms were aggravated by exertion in 13% of patients and were not different from control group. Previous reported showed that certain group of patients with ventricular arrhythmia from right ventricular outflow tract had symptoms mainly at night (18), had no clinical response to beta-blocker or worsening with beta-blocker (19). Increased vagal tone has been postulated to the underlying mechanism of the arrhythmia in this group.

Table 1. Baseline characteristics and Holter monitoring findings in patients with ventricular arrhythmia from right ventricular outflow tract and controls

<table>
<thead>
<tr>
<th>Baseline Parameters</th>
<th>RVOTN = 62</th>
<th>Controls N = 101</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (%)</td>
<td>16 (25.8)</td>
<td>31 (30.7)</td>
<td>0.504</td>
</tr>
<tr>
<td>Age (years)</td>
<td>52.3 ± 16.1</td>
<td>53.1 ± 17.4</td>
<td>0.767</td>
</tr>
<tr>
<td>Frequency of attack (attacks/month)</td>
<td>25 (3.30)</td>
<td>3 (2.29)</td>
<td>0.007</td>
</tr>
<tr>
<td>Onset of symptom (months)</td>
<td>6 (2.24)</td>
<td>4.5 (1.12)</td>
<td>0.453</td>
</tr>
<tr>
<td>Symptom - Palpitation (%)</td>
<td>53 (85.5)</td>
<td>85 (84.2)</td>
<td>0.820</td>
</tr>
<tr>
<td>- Presyncope (%)</td>
<td>8 (12.9)</td>
<td>15 (14.9)</td>
<td>0.729</td>
</tr>
<tr>
<td>- Syncope (%)</td>
<td>6 (9.7)</td>
<td>21 (20.8)</td>
<td>0.064</td>
</tr>
<tr>
<td>- Dyspnea (%)</td>
<td>7 (11.3)</td>
<td>9 (8.9)</td>
<td>0.620</td>
</tr>
<tr>
<td>- Dizziness (%)</td>
<td>5 (8.1)</td>
<td>4 (4)</td>
<td>0.265</td>
</tr>
<tr>
<td>Symptoms aggravated by exercise (%)</td>
<td>8 (12.9)</td>
<td>8 (7.9)</td>
<td>0.299</td>
</tr>
<tr>
<td>Holter monitoring</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- PVC count (per 24 hours)</td>
<td>5360 (1674,10389)</td>
<td>0 (0.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>- Couplet (per 24 hours)</td>
<td>247 (1177)</td>
<td>0</td>
<td>0.036</td>
</tr>
<tr>
<td>- Triplet (per 24 hours)</td>
<td>16 (65)</td>
<td>0</td>
<td>0.015</td>
</tr>
<tr>
<td>- VT (per 24 hours)</td>
<td>20 (113)</td>
<td>0</td>
<td>0.070</td>
</tr>
<tr>
<td>- Average heart rate (bpm)</td>
<td>73.1 (11.5)</td>
<td>73.6 (10.7)</td>
<td>0.770</td>
</tr>
<tr>
<td>- SDANN (ms)</td>
<td>111 (83,149)</td>
<td>116 (86,145)</td>
<td>0.925</td>
</tr>
<tr>
<td>-SDNN (ms)</td>
<td>138 (105,188)</td>
<td>127 (97,153)</td>
<td>0.115</td>
</tr>
</tbody>
</table>

* Non-parametric data are presented as median (IQR)

Some patients developed tachycardia after exercise was terminated. Frequency domain HRV analysis demonstrated an increase in sympathetic tone before the occurrence of tachycardia episodes (2). Heart rate may accelerate before the occurrence of ventricular arrhythmia from right ventricular outflow tract which indicates parasympathetic withdrawal (16).

Therefore, beta-blocker should not be used in this group. There are certain parameters from ambulatory monitoring that can guide us for the possibility of sympathetic influence on the occurrence of the arrhythmia. Besides HRV parameters such as SDNN and SDANN used in this study, other parameters include average heart rate, daytime or nighttime predominance of the arrhythmia and...
evidence of heart rate surge before the onset of the tachycardia. If there is evidence of sympathetic influence, beta-blocker may be effective. However, results in our study for the whole group of ventricular arrhythmia from right ventricular outflow tract indicate that there was no difference in markers of sympathetic tone between patients and control. This finding may be due to a study in a mixed group of population with ventricular arrhythmia from RVOT which contain some patients with tachycardia dependent, some with bradycardia dependent and some who may not be related to autonomic tone. This finding may explain why response rate of beta-blocker is on the average of no more than half of patients with ventricular arrhythmia from right ventricular outflow tract (4, 5).

In conclusion, patients with ventricular arrhythmia from right ventricular outflow tract had no difference in HRV compared to controls. This finding indicates that sympathetic tone may not be the major underlying mechanism of ventricular arrhythmia from right ventricular outflow tract.

References
Heart Rate Variability ในผู้ป่วยที่เป็น Right Ventricular Outflow Tract Tachycardia

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บทคัดย่อ
ที่มาของการศึกษา: ดังนี้ไม่มีข้อมูลเชิงลึกเกี่ยวกับระบบประสาทอัตโนมัติในผู้ป่วยหรือไม่ในการทำให้เกิด right ventricular outflow tract (RVOT) tachycardia

วัตถุประสงค์ของการศึกษา: เพื่อศึกษาความแตกต่างในของ heart rate variability (HRV) ของผู้ป่วย ventricular arrhythmia from right ventricular outflow tract เกี่ยวกับกลุ่มควบคุม

วิธีการศึกษา: ผู้เชี่ยวชาญ HRV จาก ambulatory monitoring ของผู้ป่วยที่มี ventricular arrhythmia from right ventricular outflow tract (ไม่ premature ventricular contraction กิน 1,000 คือ 24 ชั่วโมง) เรียกกลุ่มควบคุม โดยวิเคราะห์ด้วยสรุปผลที่ได้จาก heart rate เลือก standard deviation ของ RR interval ทั่วถึง (SDNN) และของ RR interval ที่เกิดขึ้นทุก 5 นาที (SDANN)

ผลการศึกษา: ผู้อยู่ใน ventricular arrhythmia from right ventricular outflow tract 62 คน และควบคุม 101 คน สรุปได้ว่าเป็นหญิง (71%) อายุจาก 53 ปี ไม่เกิดความแตกต่างกันของปัจจัยพื้นฐานระหว่าง 2 กลุ่ม ยกเว้นผู้อยู่ใน ventricular arrhythmia from right ventricular outflow tract มีอาการรุนแรงกว่า ไม่เกิดความแตกต่างของ heart rate เลือก รวมถึง SDNN และ SDANN ระหว่าง 2 กลุ่ม

สรุปผลการศึกษา: ตัวแปรที่น่าสนใจ autoonomic tone ไม่ต่างกันระหว่างผู้อยู่ใน ventricular arrhythmia from right ventricular outflow tract และควบคุม แสดงว่า autoonomic tone อาจไม่ได้เป็นปัจจัยหลักในการทำให้เกิด ventricular arrhythmia from right ventricular outflow tract