QT Dispersion in Patients with Polycystic Ovary Syndrome

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SUMMARY

Cardiac risk factors are observed more frequently in patients with polycystic ovary syndrome (PCOS). On the other hand, increased QT dispersion, which is a risk factor for cardiac arrhythmias and sudden death, has not been investigated in this syndrome. In this study, we evaluated QT dispersion in PCOS patients without overt heart disease. Thirty-six consecutive women with PCOS (mean age 24±5 years) and 36 healthy women of similar ages (mean age 24±4 years) participated in this study. PCOS was diagnosed if there were polycystic ovaries by ultrasound (enlarged ovaries with ≥8 cysts 2-8 mm in diameter), oligoamenorrhea (intermenstrual interval >35 days), hirsutism (Ferriman-Gallwey score, ≥7) and elevated serum levels of testosterone (≥2.7 nmol/L). Electrocardiograms were recorded at a paper speed of 50 mm/s. QT intervals were manually measured by a cardiologist. All intervals were corrected for heart rate according to Bazett's formula: QTc interval=QT interval/square root of the RR interval. Mean values of body mass index, heart rate, and blood pressure were not significantly different between the two groups (P>0.05). No significant differences in QT intervals (maximum QT, minimum QT, QT dispersion, minimum corrected QT, maximum corrected QT, and corrected QT dispersion) were observed between the two groups (P>0.05). Our results suggest that the risk of ventricular arrhythmias or sudden cardiac death is not increased in PCOS patients. (Jpn Heart J 2002; 43: 487-493)

Key words: Electrocardiography, Polycystic ovary syndrome, QT dispersion

POLYCYSTIC ovary syndrome (PCOS) is a disorder of chronic anovulation, hyperandrogenism, hirsutism, obesity, subfertility, hyperlipidemia, and insulin resistance. Infertility is not the only important component of this syndrome, since the risks of cardiac disease and hypertension also increase in women with PCOS.1-3) Insulin resistance and hyperinsulinemia appear central to the pathophysiology of PCOS. Glucose intolerance, abnormally high fasting serum lipid concentrations, and high blood pressure are the three cardiac risk factors that have

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been associated with hyperinsulinemia in women with PCOS. The prevalence of non-insulin dependent diabetes mellitus and coronary artery disease was also found to be significantly higher in PCOS women.4)

Several aspects of cardiac disease have been previously investigated in patients with PCOS. Lean women with PCOS were found to be hyperinsulinemic and have reduced serum HDL and HDL_2 concentrations compared to women with normal ovaries.2) In this group of patients, serum insulin concentrations correlated positively with plasma glucose and blood pressure measurements. Furthermore, obese women with PCOS had higher systolic blood pressure, and higher serum triglyceride and plasma glucose concentrations than lean PCOS women and controls. Women with polycystic ovaries were reported to have more extensive coronary artery disease than women with normal ovaries.1)

Despite the presence of several well-documented risk factors, cardiac involvement in this syndrome has not been investigated thoroughly. Increased QT dispersion is believed to be a risk factor for cardiac arrhythmias and sudden death.5,6) We have searched English Medline on the internet (National Library of Medicine Gateway Search, http://gateway.nlm.nih.gov/gw/Cmd), but could not find any study regarding cardiac arrhythmias or QT interval dispersion in this syndrome. Thus, our aim in this study was to investigate QT dispersion in patients with PCOS.

**SUBJECTS AND METHODS**

**Study subjects:** Thirty-six women with PCOS (mean age, 24±5 years) and 36 healthy women of similar ages (mean age, 24±4 years) participated in this study. PCOS was diagnosed if there were polycystic ovaries by ultrasound (enlarged ovaries with ≥8 cysts 2-8 mm in diameter), oligoamenorrhea (intermenstrual interval >35 days), hirsutism (Ferriman-Gallwey score, ≥7) and elevated serum levels of testosterone (≥2.7 nmol/L).7) All subjects were apparently in good health. None of them had systemic hypertension, renal disease, chronic lung disease, or overt heart disease. The absence of overt heart disease was based on the fact that no participant had symptoms or electrocardiographic signs of cardiac disease. For at least 1 month before the study, none of the participants were taking any medication known to prolong the QT interval (erythromycine, trimethoprim-sulfamethoxazole, tricyclic antidepressants, terfenadine, etc.). Electrocardiograms were recorded before the initiation of specific therapy for PCOS.

**Analysis of the electrocardiograms:** Twelve-lead surface electrocardiograms were used to evaluate QT parameters. The electrocardiograms were recorded by a Hewlett Packard PageWriter 300pi HP M1770A Cardiograph (Hewlett Packard, Andover, Mass’ USA) at a paper speed of 50 mm/s. The QT interval was
manually measured by a cardiologist blinded to the clinical diagnosis of the subjects. The onset of a Q wave was regarded as the onset of the QT interval. The point where a T wave returned to the isoelectric TP segment was accepted as the end of the QT interval. Electrocardiograms were accepted if at least 8 leads could be analyzed. QT dispersion was calculated as the difference between maximum and minimum QT intervals. All QT intervals were corrected for heart rate according to Bazett's formula: QTc interval=QT interval/square root of the RR interval. 8) QT dispersion (QTd) was defined as the difference between maximum QT interval (QT max) and minimum QT interval (QT min). Similarly, corrected QT dispersion (QTcd) was calculated as the difference between QTc max and QTc min.

**Statistical analysis:** Data are presented as mean±SD. Mean values of QT parameters between the two groups were compared with the Student's t test. A P value <0.05 was accepted to be statistically significant. To determine the intraobserver variability of QT interval measurements, electrocardiograms of 15 randomly selected subjects were reanalyzed by the same cardiologist on a different day. These recordings were also analyzed by another cardiologist to determine the interobserver variability.

**RESULTS**

The baseline clinical and biochemical characteristics of the participants are presented in Table I. Heart rate and mean body mass index were not significantly different between the two groups (P>0.05). Resting 12-lead electrocardiograms were interpreted as normal in all subjects. The QTc max, QTc min, QTd, and QTcd were not significantly higher in patients with PCOS than the controls.

### Table I. Baseline Clinical and Biochemical Characteristics of Participants

<table>
<thead>
<tr>
<th></th>
<th>Polycystic ovary syndrome</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>36</td>
<td>36</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>24±5</td>
<td>24±4</td>
</tr>
<tr>
<td>Mean body mass index (kg/m²)</td>
<td>25±7</td>
<td>24±6</td>
</tr>
<tr>
<td>Heart rate (beats per minute)</td>
<td>77±11</td>
<td>76±13</td>
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<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>119±17</td>
<td>122±16</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>78±8</td>
<td>80±6</td>
</tr>
<tr>
<td>Smoking (yes/no)</td>
<td>8/28</td>
<td>9/27</td>
</tr>
<tr>
<td>Glucose, mg/dL</td>
<td>92±28</td>
<td>87±25</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>192±48</td>
<td>183±54</td>
</tr>
<tr>
<td>LDL cholesterol, mg/dL</td>
<td>124±19</td>
<td>116±23</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dL</td>
<td>40±9</td>
<td>42±6</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>131±118</td>
<td>120±104</td>
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</tbody>
</table>

*P*<0.05 for all of the above variables. (Mean ± SD or number of patients.)
(444±25 ms, 441±22 ms, \(P>0.05\); 399±20 ms, 396±23 ms, \(P>0.05\); 43±14, 44±22, \(P>0.05\); 48±15 ms, 47±18 ms, \(P>0.05\), respectively) (Table II). None of the subjects had overt diabetes mellitus.

Both inter- and intraobserver variabilities were \(<5\%\) for all electrocardiographic variables.

### DISCUSSION

To our knowledge, this is the first study to investigate QT intervals and QT dispersion in PCOS. The results of the present study show that QT interval prolongation or increased QT dispersion is not a part of the cardiac abnormalities in PCOS.

**QT dispersion and cardiac disease:** Increased QT dispersion reflects electrical inhomogeneity, which may occur as a result of myocardial ischemia, mitral valve prolapse, ventricular hypertrophy or dilatation, autonomic neuropathy, peripheral vascular disease, and hypertension.\(^9\)\(^\text{15}\) A recent study, which analyzed the 12-lead electrocardiograms of 1501 healthy adults and 1784 healthy children found that QTd was age and sex independent.\(^16\) Therefore, we do not think that the relatively young age of our subjects had an affect on our results. In several disease states, the use of QT interval analysis has been suggested as a screening test to determine those at high risk of arrhythmic events. In patients with vasospastic angina, it was found that QTc dispersion was increased and this was associated with ventricular arrhythmias.\(^9\) In a study of 182 patients with non-insulin dependent diabetes mellitus, QTd, QTcd, and QTc max were reported to be accurate predictors of cardiac death.\(^17\) None of our subjects had overt diabetes mellitus (Table I). This may in part be responsible for our failure to observe an increase in QTd. Compared with lean women, obese patients with PCOS were reported to have higher systolic blood pressures, plasma glucose concentrations, and serum triglyceride levels.\(^2\) However, most of our subjects were lean women. This might
have contributed to our failure to observe an increase in QTd. Recently, several studies reported that QT dispersion after exercise was a more powerful predictor of coronary artery disease than QT dispersion at rest.\textsuperscript{18,19} Koide, \textit{et al} reported that QT dispersion immediately after exercise was a clinically useful indicator of significant coronary stenosis independent of gender or the presence or absence of exercise-induced significant ST-segment depression.\textsuperscript{18} They found that QT dispersion immediately after exercise was significantly more sensitive in men and significantly more specific in women than exercise-induced significant ST-segment depression as an indicator of significant coronary stenosis. However, the mean age of their study subjects (56±9 years) was significantly higher than that of our subjects (25±5 years). The relatively young age of our subjects may explain our failure to observe a significantly higher QTd in PCOS patients. In addition, we did not intend to identify PCOS patients with coronary artery disease in this study. Instead, our aim was to evaluate QT dispersion at rest since coronary artery disease is not the only cause of increased QTd.

**Cardiac abnormalities in PCOS:** Cardiac disease is generally expected to be more prevalent among women with PCOS. In a Doppler study of uterine artery in oligomenorrheic women with polycystic ovaries, increases in the uterine artery resistance index and pulsatility index, and decreases in peak systolic and time-averaged maximum velocities in response to glyceryl trinitrate patch application were observed.\textsuperscript{20} On the other hand, this study did not report differences in the Doppler parameters for the uterine artery in women with normal cycles. The authors suggested that this finding might help to explain the pathophysiology of the higher risk of cardiovascular morbidity and mortality associated with PCOS. Non-restrictive diastolic dysfunction and left ventricular stiffness were observed in an echocardiographic study of 35 PCOS patients.\textsuperscript{21} Not only diastolic function, but also systolic function was reported to be impaired in this syndrome. In a study of 26 PCOS patients, a significant negative correlation was observed between the serum fasting insulin concentration and left ventricular systolic outflow parameters.\textsuperscript{3}

Regardless of the results of the above studies, surprising results have been published on the rates of morbidity and mortality from coronary heart disease in this syndrome.\textsuperscript{22,23} In a retrospective study, the hospital records of 786 women with PCOS in the United Kingdom were analysed.\textsuperscript{22} The patients were followed for an average of 30 years. They concluded that women with PCOS did not have markedly higher than average mortality from cardiovascular disease. In a recently published retrospective cohort study, morbidity data from 319 women with PCOS and 1060 age-matched controls were analysed.\textsuperscript{23} This study also concluded that morbidity or mortality from coronary heart disease was not as high as previously thought.
**Conclusions:** We did not observe significant prolongation of QT intervals or increased QT dispersion in PCOS patients. To our knowledge, this is the first study to investigate QT dispersion in patients with PCOS. Since QT prolongation and increased QT dispersion is a risk factor for ventricular arrhythmias and sudden cardiac death, our findings suggest that PCOS patients (without overt diabetes mellitus) do not have evidence for increased risk of ventricular arrhythmias or sudden cardiac death despite the presence of well-established risk factors for coronary artery disease. The results of the present study also suggest that not PCOS in itself, but the accompanying coronary artery disease may result in cardiac events in patients with PCOS.

**REFERENCES**