Prolongation of QT Interval and Ventricular Septal Hypertrophy

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SUMMARY

Long QT syndrome (LQTS) is a prime example of interplay between molecular biology, cellular physiology, and organ physiology. Both the congenital and acquired forms of LQTS are due to intrinsic and/or acquired abnormalities of the ionic currents responsible for cardiac repolarization.

We analyzed the QTc interval, QRS axes and interventricular septal thickness (IVST) in 41 patients who had a prolonged QT interval on routine electrocardiography (ECG) (5 females and 36 males, mean age 65 ± 13 years). The QRS axis of patients in the LQTS group (27 ± 49°) was significantly lower (p < 0.05) than in the control group (46 ± 26°). However, the IVST in the LQTS group (10 ± 2 mm) was significantly thicker than in the control group (9 ± 1 mm) (p < 0.05), while the WTd was not significantly different. The QTc interval in patients with ventricular septal hypertrophy (IVST ≥ 12 mm, 478.8 ± 7.9 msec) was significantly longer (p < 0.05) than in the normal group (IVST < 12 mm, 472.1 ± 17.5 msec).

In conclusion, the results of this preliminary study suggest that prolongation of the QT interval on ECG should prompt screening for electrocardiographic evidence of ventricular hypertrophy in patients with this disease. (Jpn Heart J 2000; 41: 463-469)

Key words: Long QT syndrome, Interventricular septal thickness, Echocardiography, Electrocardiography

THE long QT syndrome (LQTS) is a prime example of how the interplay between molecular biology and knowledge of ion channels, cellular physiology, and organ physiology, complement each other and provide clinical information for a new paradigm for the advancement of medical knowledge. Both the congenital and acquired forms of LQTS are due to intrinsic and/or acquired abnormalities of the ionic currents responsible for cardiac repolarization.1) Acquired LQTS develops as a result of pharmacologic interventions that prolong...
the action potential duration. Excessive action potential prolongation may lead to torsade de pointes, a potentially fatal arrhythmia.2) Congenital LQTS is caused by mutations in genes encoding ion channels that modulate the duration of the ventricular action potential.3) Recent reports have described the genetic background of acquired LQTS,4) which involves the Na⁺ / Ca²⁺ exchange current.5) However, the morphologic characterization of acquired LQTS has not been reported. Therefore, we compared patients with acquired LQTS to those with a normal QT time to determine if any echocardiographical differences could be responsible for the development of this syndrome.

SUBJECTS AND METHODS

Subjects: We studied 41 patients who had a prolonged QT interval on routine electrocardiography (ECG) (5 females and 36 males, mean age 65 ± 13 years). A long QT interval was defined as a corrected QT (QTc) ≥ 450 msec and absence of hereditary QT syndrome. We also studied 39 patients (21 females and 18 males, mean age 43 ± 19 years) with a normal QT interval defined as a QTc < 450 msec, and an ECG which was normal (Figure 1).

QT interval measurement: The 12-lead ECG was recorded at rest using a MAC VU cardiograph (Marquette Electronics, Milwaukee, WI, USA) with a sampling frequency of 150 Hz, and stored digitally. All ECGs were processed using a cardiology management system (MUSE) to obtain ECG measurements and diagnostic interpretations. The QTc interval (msec) was corrected for heart rate using Bazett's formula: QTc = QT / √ RR, where RR is the RR interval in seconds.6) The normal range of the QTc is 350-440 msec, with an upper limit of normal toward 430-450 msec. Since different ranges of normal QT are accepted by various investigators, a QTc ≥ 450 msec was considered a long QT interval for the purposes of this study. We analyzed the heart rate (HR); PR, QRS, and QTc intervals; and the P, QRS, and T axes in all subjects.

Echocardiographic studies: Echocardiography (UCG) was performed using a commercially available device (SONOS 2500, Hewlett-Packard, Andover, MA, USA) equipped with 2.5 MHz and 4.1 MHz transducers. Standard cross-sectional, M mode, and Doppler echocardiograms were conducted with the subjects in a partial left lateral decubitus position. We measured the aortic diameter (AOD), left atrial diameter (LAD), interventricular septal thickness (IVST), diastolic wall thickness (WTd), right ventricular diameter (RVD), left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), left ventricular end-sys-
tolic volume (LVESV), stroke volume (SV), ejection fraction (EF), and fractional shortening (FS).

Statistical analysis: Data are expressed as mean ± SD and were analyzed using a SPSS statistical system. A two-sided p value < 0.05 was considered statistically significant.

RESULTS

The QRS axis of patients in the LQTS group (27 ± 49°) was significantly lower (p < 0.05) than in the Normal QT group (46 ± 26°) (Figure 2). The HR, PR and QRS intervals, and the P, QRS and T axes were all similar in both groups (Table 1).

The AOD and LAD obtained on the UCG were similar in both groups. However, the IVST in the LQTS group (10 ± 2 mm) was significantly
thicker than in the Normal QT group (9 ± 1 mm) \((p < 0.05)\), while the WTd was similar (Table II, Figure 2). All other parameters, including the LVEDD, LVESD, SV, EF, and FS were not statistically significant in either group (Table II).

We also analyzed the relationship between QTc interval and IVST in patients in the LQTS group. The QTc interval in patients with ventricular septal hypertrophy (IVST \(\geq\) 12 mm, 478.8 ± 7.9 msec) was significantly longer \((p < 0.05)\) than in the Normal QT group (IVST < 12 mm, 472.1 ± 17.5 msec) (Figure 3).
DISCUSSION

The present study demonstrates that acquired LQTS is characterized by left axis deviation on ECG and ventricular septal hypertrophy on UCG. The increased septal wall thickness may induce prolongation of myocardial repolarization, resulting in prolongation of the QT interval.

LQTS is classified as either congenital or acquired. Congenital cases include the Jervell and Lange-Nielsen syndromes, the Romano-Ward syn-

<table>
<thead>
<tr>
<th>AOD (mm)</th>
<th>LAD (mm)</th>
<th>IVST (mm)</th>
<th>Wtd (mm)</th>
<th>RVD (mm)</th>
<th>LVDd (mm)</th>
<th>LVDs (mm)</th>
<th>SV (mm)</th>
<th>EF (%)</th>
<th>FS (%)</th>
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<tr>
<td>Normal QT (n)</td>
<td>28±4 (35)</td>
<td>31±5 (35)</td>
<td>9±1 (34)</td>
<td>9±2 (34)</td>
<td>15±3 (4)</td>
<td>47±4 (34)</td>
<td>30±4 (34)</td>
<td>76±20 (34)</td>
<td>0.72±0.07 (34)</td>
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<tr>
<td>Long QT (n)</td>
<td>29±5 (40)</td>
<td>33±6 (40)</td>
<td>10±2* (40)</td>
<td>10±1 (40)</td>
<td>25±15 (10)</td>
<td>46±6 (41)</td>
<td>31±5 (41)</td>
<td>71±31 (41)</td>
<td>0.70±0.09 (41)</td>
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mean ± standard deviation. AOD = aortic diameter; LAD = left atrial diameter; IVST = intraventricular septum thickness; Wtd = diastolic wall thickness; RVD = right ventricular diameter; LVD = left ventricular diastolic diameter; LVDs = left ventricular systolic diameter; LVESV = left ventricular end - systolic volume; SV = stroke volume; EF = ejection fraction; FS = fractional shortening. *p < 0.05 vs Normal QT.
Acquired cases are caused by anti-arrhythmic therapy, electrolyte abnormalities, and profound bradycardia.\cite{3, 4} LQTS is a familial disease caused by genetic abnormalities in potassium, calcium, or other channels. Prolongation of the QT interval in cases of myocardial ischemia is associated with down-regulation of K channels. We analyzed the association of the long QT with cardiac abnormalities on ECC and UCG, excluding congenital cases.

The QRS axis was significantly different in patients with a long QT interval compared to subjects with a normal QT interval. However, we did not conclude the long QT was associated with QRS deviation because the cases of left axis deviation had other variations, like left ventricular hypertrophy or cardiac infarction,\cite{9} which could explain the axial deviation of QRS. Further studies will be needed to clarify this hypothesis.

The IVST in the LQTS subjects was significantly greater than in the normal QT interval subjects. Prolongation of the QT interval has been reported in younger patients with either hypertrophic or dilated cardiomyopathies,\cite{10} suggesting that the thickness of the interventricular septum may play a role in relation to prolongation of the QT interval.

A previous report observed that left ventricular wall contraction is depressed in LQTS.\cite{11} We compared cardiac function between a control group with normal QT and patients with prolonged QT intervals. Since the SV, EF and FS, all indices of left ventricular wall contraction, were not different in our subjects with long QT intervals from the controls, the prolongation of QT may not be related with cardiac contractility by UCG. Further investigation is required to demonstrate the relationship between wall contraction and prolonged QT intervals.

No previous reports have defined a role for long QT in the progression to ventricular septal hypertrophy. Recent reports have shown that long QT is associated with modulation of K⁺ or Ca⁺² currents.\cite{12, 13, 14} Moreover, myocardial hypertrophy is associated with alterations in cardiac voltage-gated K⁺ channels.\cite{15, 16} Also, Matsubara, et al. suggested that the pathological alterations of K⁺ channel gene regulation might be involved in the occurrence of ventricular arrhythmias in hypertrophic hearts.\cite{17} Therefore, alteration of K⁺ channels may be an important role in the development of ventricular septal hypertrophy in patients with QT elongation.

QT prolongation also enhances the likelihood of ventricular extra-systoles of the R-on-T type, leading to torsade de pointes or ventricular fibrillation, which are both fatal ventricular arrhythmias.\cite{18, 19} LQTS with conduction abnormalities was noted in our subjects with septal hypertrophy. We suggest that QT interval prolongation and fatal ventricular
arrhythmias may be due to the ventricular septal hypertrophy. Prolongation of the QT interval should be promptly screened by echocardiographic evidence of ventricular hypertrophy in order to avoid a poor prognosis.

REFERENCES