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Two automatic QT algorithms compared with manual measurement in identification of long QT syndrome

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Abstract

Background: Long QT syndrome (LQTS) is an inherited disorder that increases the risk of syncope and malignant ventricular arrhythmias, which may result in sudden death.

Methods: We compared manual measurement by 4 observers (QT_{manual}) and 3 computerized measurements for QT interval accuracy in the diagnosis of LQTS:

1. QT measured from the vector magnitude calculated from the 3 averaged orthogonal leads *X*, *Y*, and *Z* (QT_{VCG}) and classified using the same predefined QTc cut-points for classification of QT prolongation as in manual measurements;
2. QT measured by a 12-lead electrocardiogram (ECG) program (QT_{ECG}) and subsequently classified using the same cut-points as in (1) above;
3. The same QT value as in (2) above, automatically classified by a 12-lead ECG program with thresholds for QT prolongation adjusted for age and sex ($QT_{interpret}$).

The population consisted of 94 genetically confirmed carriers of *KCNQ1* (LQT1) and *KCNH2* (LQT2) mutations and a combined control group of 28 genetically confirmed noncarriers and 66 unrelated healthy volunteers.

Results: QT_{VCG} provided the best combination of sensitivity (89%) and specificity (90%) in diagnosing LQTS, with 0.948 as the area under the receiver operating characteristic curve. The evaluation of QT measurement by the 4 observers revealed a high interreader variability, and only 1 of 4 observers showed acceptable level of agreement in LQTS mutation carrier identification (κ coefficient >0.75).

Conclusion: Automatic QT measurement by the Mida1000/CoroNet system (Ortivus AB, Danderyd, Sweden) is an accurate, efficient, and easily applied method for initial screening for LQTS.

Keywords: Long QT syndrome; QT interval; Automatic measurement; Vectorcardiography; Mutation analysis

Background

The long QT syndrome (LQTS) is an inherited disorder carrying an increased risk for syncope and malignant ventricular arrhythmias that may result in sudden death. The degree of QT prolongation is positively associated with the risk of a cardiac event.[1] β-Blockers are effective for decreasing this risk. It is therefore important to identify individuals with LQTS so that appropriate preventive treatment can be administered.[2] The traditional diagnostic method consists of QT measurement using a conventional 12-lead electrocardiogram (ECG).[3] However, manual measurements of QT intervals are time-consuming and error-prone because of difficulties in defining the end of the T wave.[3,4] More accurate and reproducible methods of QT interval measurement are needed. Vectorcardiography (VCG) may be superior to conventional ECG in quantifying ventricular repolarization parameters.[5] This study evaluates the ability of 4 electrocardiographic methods to diagnose LQTS: an automatic algorithm with the T-end defined from T-vector

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magnitude in a commercial VCG application (QT_{VCG}); an algorithm in a commercial 12-lead ECG equipment that computes and interprets QT (QT_{ECG} and $QT_{interpret}$, respectively); and manual QT measurement (QT_{manual}) using a 12-lead ECG. These methods were applied to patients with genetically confirmed *KCNQ1* (LQT 1) and *KCNH2* (LQT 2) mutations and to healthy individuals. DNA analysis is thus used as the reference method for identification of LQTS.

Materials and methods

Subjects

This study included 122 subjects from 16 LQTS families and 66 healthy volunteers. DNA analysis for LQTS was performed in the LQTS family members; no analysis was performed on healthy volunteers. All subjects were consecutively included from our LQTS family clinic.

The population consisted of 94 genetically confirmed carriers of *KCNQ1* (LQT1) and *KCNH2* (LQT2) mutations and a combined group of 28 genetically confirmed noncarriers and 66 unrelated healthy volunteers. Inclusion criteria for healthy volunteers were absence of known heart or lung disease, absence of medication affecting cardiac repolarization, and no history of unexplained syncope or sudden cardiac death in any first-degree relative younger than 40 years. The study was approved by the Regional Ethical Review Board at Umeå University (Umeå, Sweden). Written informed consent was obtained from all subjects or their legal guardian.

Electrocardiographic measurements

All electrocardiographic recordings were performed with the participant at rest in the supine position. A single recording was used for evaluation of QTc manually (QT_{manual}) and automatically (QT_{ECG}, $QT_{interpret}$). The vectorcardiogram for QT_{VCG} was recorded directly after the 12-lead ECG. QTc values derived from the different methods were categorized according to Goldenberg et al[3] (Table 1). "Borderline QTc" and "prolonged QTc" (Table 1) were regarded as mutation carrier for LQTS.

The sex differences of QTc tend to disappear in older age groups.[6] This was not taken into consideration in this study.

QT_{VCG}

The vectorcardiography (VCG) online automatic measurements were performed using Mida1000, software 2.74 and CoroNet (Ortivus AB, Danderyd, Sweden). The relevant technical specifications did not differ between the 2 systems.

Table 1
Cut-off QTc values for diagnosing LQTS[a]

	Children 1-15 y (ms)	Adult male (ms)	Adult female (ms)
Normal	<440	<430	<450
Borderline	440-460	430-450	450-470
Prolonged	>460	>450	>470

[a] *J Cardiovasc Electrophysiol*. 2006;17:333-6.

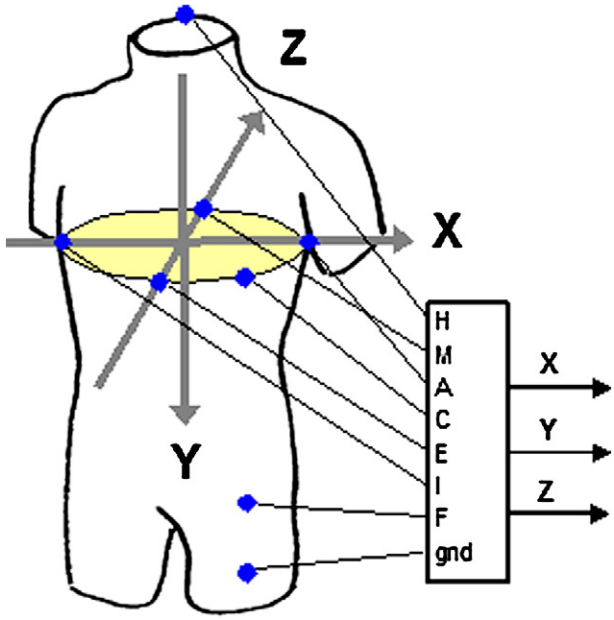

Fig. 1. Frank lead system. Frank lead system, with the 3 orthogonal leads *X*, *Y*, and *Z* recorded by 8 electrodes. $X = (0.610 \times A) + (0.171 \times C) - (0.781 \times I)$. $Y = (0.655 \times F) + (0.345 \times M) - (1.000 \times H)$. $Z = (0.133 \times A) + (0.736 \times M) - (0.264 \times I) - (0.374 \times E) - (0.231 \times C)$.

Electrodes were applied according to the Frank lead system[7] (Fig. 1). The signals from the 3 orthogonal leads *X*, *Y*, and *Z* were sampled with 500 samples per second with an amplifier bandwidth of 0.03 to 170 Hz. The isoelectric line was determined in each lead (*X*, *Y*, and *Z*) by sampling 30 milliseconds before the start of QRS. Complexes were sampled in periods of 60 seconds during 3 to 4 minutes. An averaged vector magnitude complex was computed from the 3 orthogonal leads *X*, *Y*, and *Z* (Figs. 2 and 3). The algorithms for detection of the beginning and end of QRS and end of the T wave were based on changes in the calculated derivative of the vector magnitude signal.[8–10] The proprietary algorithm starts from T peak and seeks forward to the point were the magnitude has decreased with 1/3 of T peak. From that point the algorithm seeks further forward until the slope is smaller than a predefined fixed value. Thus, a U wave beginning early in the T-wave slope will be included in the QT interval and a U wave beginning after the T wave will not be included in the QT interval. Very early U waves could be handled either way depending on the morphology of the T wave. QRS start is detected in a similar way; first the maximal slope of the complex is defined, from that point the algorithm seeks backward until the slope is significant changed and at the same time the slope is below a predefined fixed value. QT_{VCG} was computed as the interval between time points Q and F (Fig. 3). The QT interval was corrected for heart rate using Bazett's[11] formula and classified according to Table 1.

QT_{ECG} and $QT_{interpret}$

The 12-lead ECGs were recorded at paper speed 50 mm/s and amplitude gain 10 mm/mV with Mac5000 version 008B (GE Medical Systems, Information Technologies, Milwau-