QT dispersion: an indication of arrhythmia risk in patients with long QT intervals

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Abstract

Homogeneity of recovery time protects against arrhythmias whereas dispersion of recovery time is arrhythmogenic. A single surface electrocardiographic QT interval gives no information on recovery time dispersion but the difference between the maximum and minimum body surface QT interval may be relevant. This hypothesis was tested by measuring the dispersion of the corrected QT interval (QTc) in 10 patients with an arrhythmogenic long QT interval (Romano Ward and Jervell and Lange-Nielsen syndromes or drug arrhythmogenicity) and in 14 patients without arrhythmias in whom the QT interval was prolonged by sotalol. QTc dispersion was significantly greater in the arrhythmogenic QT group than in the sotalol QT group.

In patients with prolonged QT intervals, QT dispersion distinguished between those with ventricular arrhythmias and those without. This supports the hypothesis that QT dispersion reflects spatial differences in myocardial recovery time. QT dispersion may be useful in the assessment of both arrhythmia risk and the efficacy of antiarrhythmic drugs.

The QT interval is one of the most controversial and least understood features of the surface electrocardiogram. Low T wave amplitude and U waves contribute to difficulties of QT measurement. The heart rate and the catecholamine dependence of the QT interval complicate the definition of normal values. None the less, the QT interval is clinically useful. Its prolongation has been related to an important arrhythmogenic risk in situations such as drug toxicity and in the Romano Ward and Jervell and Lange-Nielsen syndromes. Moreover, QT interval abnormalities identified high risk survivors of acute myocardial infarction.[1]

A single derived value of QT from an electrocardiogram embodies the concept of a global value for cardiac repolarisation time. Our previous work has shown that the QT interval varies from lead to lead of the surface electrocardiogram.[2] If such variation is merely a technical "artefact" caused, for example, by differences in unipolar versus bipolar leads, by differential tissue attenuation or by cancellation of vectors, then a derived average QT value from the electrocardiogram is scientifically valid.

But what if QT variation across the leads of the surface electrocardiogram reflects regional differences in repolarisation? The electrocardiogram does provide regional information about infarction and ischaemia. If the spread of QT values represents dispersion of repolarisation, this would be of great clinical importance. Increased dispersion is widely acknowledged to be an important basis for serious ventricular arrhythmias[3 4] and a decrease in dispersion probably explains the action of class III antiarrhythmic drugs.[5]

We have shown that regional differences in ventricular recovery time are expressed on the epicardial surface of the heart as reflected by monophasic action potentials measured during open heart surgery.[6] Linking this information with our observations on QT measurement from surface electrocardiogram leads,[2] we have now examined differences in the QT interval in the 12 lead electrocardiogram in two groups of patients with QT prolongation. In one group the QT prolongation was arrhythmogenic; all patients had confirmed arrhythmias caused by either the congenital long QT syndromes or by antiarrhythmic drug effects. In the other group, QT prolongation was caused by treatment with sotalol, a β blocker with class III effects; these patients had no arrhythmias.

Patients and methods

PATIENTS

We studied two groups of patients: an arrhythmogenic QT group and a group with QT prolongation caused by sotalol.

ARRHYTHMOGENIC QT

Ten patients with a history of ventricular arrhythmia and a long QT interval (nine congenital, one quinidine related) were identified either from published case reports (eight patients)[7-12] or from our own patient population (two patients). We considered nine other case reports but excluded them because the published electrocardiograms were not of adequate quality or did not show a timing reference. Selection was made before any measurement and no patient was rejected after initial selection.

SOTALOL QT

Fourteen patients were selected from a total of 41 who had received sotalol as part of a double blind randomised trial of oral sotalol one year

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Table 1   Characteristics of 10 patients with arrhythmogenic QT intervals

Patient	Sex	Age (yr)	Diagnosis	Case source
1	F	18	Romano Ward syndrome	Freeman Hospital patient
2	F	18	Romano Ward syndrome	Freeman Hospital patient
3	M	36	Romano Ward syndrome	Case 1 in reference 7
4	M	9	Romano Ward syndrome	Case 2 in reference 7
5	M	11	Romano Ward syndrome	Case 5 in reference 8
6	F	18	Romano Ward syndrome	Case 1 in reference 9
7	F	12	Jervell and Lange-Nielsen syndrome	Case 1 in reference 10
8	F	10	Jervell and Lange-Nielsen syndrome	Case 2 in reference 10
9	F	8	Jervell and Lange-Nielsen syndrome	Reference 11
10	M	50	Quinidine treatment for SVT	Reference 12

SVT, supraventricular tachycardia.

Table 2   Electrocardiographic variables (maximum QTc, QT dispersion, QTc dispersion (ms)) and number of measurable leads in 10 patients with arrhythmogenic QT (history of ventricular arrhythmias) and 14 patients with long QT caused by sotalol treatment (no history of ventricular arrhythmias)

Electrocardiographic variable	Arrhythmogenic QT group (n = 10)	Significance of difference (p)†	Sotalol QT group (n = 14)
QTc max (range)	440–750	—	530–670
QTc max (mean (SE))	645 (32)	< 0·05	572 (10)
QTc dispersion (mean (SE))	178 (18)	< 0·0001	60 (7)
QT dispersion (mean (SE))*	185 (26)	< 0·0001	60 (7)
Number of leads measurable (range)	5–10	NS	4–10

*Difference between maximum and minimum QT (QTc). QTc max, maximum corrected QT interval. †t tests performed on logarithmically transformed data.

after infarction.[13] They were all those who had a maximum corrected QT interval (QTc)[14] > 500 ms at one month. No patient treated with sotalol had symptomatic ventricular arrhythmias during one year follow up. All were in sinus rhythm. None had evidence of bundle branch block and none was taking drugs known to influence the QT interval, other than sotalol.

QT ANALYSIS

Standard 12 lead electrocardiograms were recorded in the arrhythmogenic QT group at either 25 or 50 mm/s, while those in the sotalol QT group were recorded at 50 mm/s. Electrocardiograms from the case reports were enlarged to an appropriate size for measurement. An observer used a digitiser (Calcomp 9000) to measure the QT intervals from the onset of the QRS to the end of the T wave, defined as a return to the T-P baseline. When U waves were present the QT was measured to the nadir of the curve between the T and U waves. Wherever possible, three consecutive cycles were measured in each of the 12 electrocardiogram leads and from the three values a mean QT and QTc was calculated. When the end of the T wave could not be reliably identified that lead was not included in subsequent analysis. QT dispersion was defined as the difference between the maximum and minimum QT occurring in any of the 12 electrocardiogram leads in which it could be reliably measured. QTc dispersion was also calculated.

STATISTICAL ANALYSIS

We used Student's unpaired t test to compare the group means and we calculated the confidence intervals.[15]

Results

Table 1 shows the age, sex, underlying diagnoses, and case source of the patients with arrhythmogenic QT intervals. Eight of the sotalol QT patients had suffered an anterior myocardial infarction and six an inferior infarction.

Table 2 shows the results of QT analysis. The number of measurable leads for the two groups was similar. For all three variables, QTc max, QT, and QTc dispersion, the standard deviations of the two patient groups increased with the means. To adjust for this, significance tests were performed on the data after logarithmic transformation. The QTc intervals were slightly longer in the arrhythmogenic QT group. Both QT dispersion and QTc dispersion were significantly greater in the arrhythmogenic QT group (95% confidence interval for the ratio of QTc geometric means was 2·01
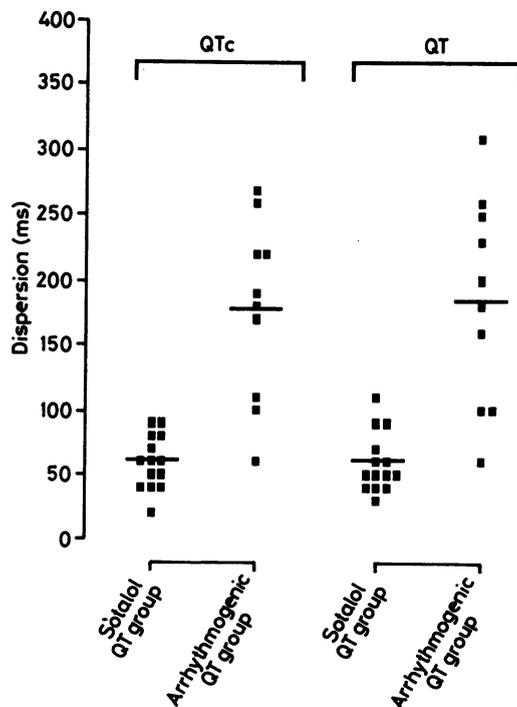
QT and QTc dispersion in 10 patients with arrhythmogenic QT (history of ventricular arrhythmias) and 14 patients with long QT due to sotalol treatment (no history of ventricular arrhythmias).

to 4·3) (see figure). No patient in the sotalol group had a QTc dispersion > 100 ms while only one patient in the arrhymogenic group had a QTc dispersion < 100 ms.

Discussion

Our results of QT measurement in arrhythmogenic and non-arrhythmogenic patients support the concept that QT variability on the surface electrocardiogram is not a technical artefact but rather reflects regional myocardial electrical recovery. Our results challenge the concept of a single global value for the QT interval. Such a value has been reported to be clinically useful but usually only when markedly abnormal or when monitored for change. Our results suggest that much more information is available on the surface electrocardiogram regarding repolarisation than is reflected by a single QT value. But are the results reliable? The measurement methods have been painstakingly validated.[2] Surface electrocardiogram QT measurements can never be wholly accurate but we have previously shown that variation in interlead measurements far outweighs inaccuracies introduced by any other factor.

The maximum QTc was significantly greater in the arrhythmogenic group than in the sotalol group but there was considerable overlap between the groups. A QTc dispersion of 100 ms was better at separating the two groups than any single value of maximum QTc.

The concept that body surface QT variation reflects dispersion of repolarisation is supported by other work. Studies in patients with the long QT syndromes have shown large spatial differences in myocardial recovery time as shown both by the duration of monophasic action potentials in different parts of the ventricle[16] and by body surface mapping.[17] Moreover, bretylium, a class III as well as a class II antiarrhythmic agent, reduced temporal dispersion of effective refractory periods in dogs and this effect correlated with an increase in the ventricular fibrillation threshold.[5]

Our results do not prove that QT variability on the surface electrocardiogram reflects dispersion of repolarisation but they do support that hypothesis. The conventional 12 lead electrocardiogram remains in clinical practice more for historical than for scientific reasons. For the purpose of this research, different lead positions and consistent lead configurations (unipolar) have many attractions. We used the standard 12 lead electrocardiogram both because rare patient data (long QT syndromes) were available in this format and because, if the results of our study are accepted, a beguilingly simple and accessible clinical method could be used and tested by others. The proof of the concept must come from intraoperative studies in which epicardial monophasic action potentials are correlated with body surface electrocardiogram features. Such work is technically difficult but is in progress. Reliable, non-invasive access to dispersion of repolarisation could radically alter our approach to arrhythmias, our concepts and prediction of arrhythmogenesis, and the precision of prognosis.

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