Journal of the American College of Cardiology
© 2000 by the American College of Cardiology
Published by Elsevier Science Inc.

Vol. 36, No. 6, 2000
ISSN 0735-1097/00/$20.00
PII S0735-1097(00)00962-1

Measurement, Interpretation and Clinical Potential of QT Dispersion

Marek Malik, PHD, MD, FACC, Velislav N. Batchvarov, MD, PHD
London, United Kingdom

QT dispersion was originally proposed to measure spatial dispersion of ventricular recovery times. Later, it was shown that QT dispersion does not directly reflect the dispersion of recovery times and that it results mainly from variations in the T loop morphology and the error of QT measurement. The reliability of both automatic and manual measurement of QT dispersion is low and significantly lower than that of the QT interval. The measurement error is of the order of the differences between different patient groups. The agreement between automatic and manual measurement is poor. There is little to choose between various QT dispersion indices, as well as between different lead systems for their measurement. Reported values of QT dispersion vary widely, e.g., normal values from 10 to 71 ms. Although QT dispersion is increased in cardiac patients compared with healthy subjects and prognostic value of QT dispersion has been reported, values are largely overlapping, both between healthy subjects and cardiac patients and between patients with and without adverse outcome. In reality, QT dispersion is a crude and approximate measure of abnormality of the complete course of repolarization. Probably only grossly abnormal values (e.g. ≥100 ms), outside the range of measurement error may potentially have practical value by pointing to a grossly abnormal repolarization. Efforts should be directed toward established as well as new methods for assessment and quantification of repolarization abnormalities, such as principal component analysis of the T wave, T loop descriptors, and T wave morphology and wavefront direction descriptors. (J Am Coll Cardiol 2000;36:1749–66) © 2000 by the American College of Cardiology

Attempts to characterize the abnormalities of ventricular repolarization from the surface electrocardiogram (ECG) have a long history. Precise mathematical approaches can be traced back to the 1960s (1). For clinical purposes, however, the ECG based assessment of ventricular repolarization has traditionally been limited to the measurement of the QT interval and to the description of the polarity and shape of the T wave often using vague terms such as "nonspecific ST segment and T wave changes."

In 1990, a report by the group of the late Professor Campbell revived an old idea of the interlead differences in the QT interval duration. The range of the durations, termed "QT dispersion," was proposed as an index of the spatial dispersion of the ventricular recovery times (2). It was proposed that the different ECG leads magnify the ECG signal of different myocardial regions and that, consequently, QT dispersion is an almost direct measure of the heterogeneity of myocardial repolarization. The cardiological community welcomed the idea. The methodological simplicity and the promise of solving the old and much debated problem of regional information within the standard ECG were appealing.

Since the first publication, the cardiological literature has been flooded by articles reporting QT dispersion in practically every cardiac as well as many noncardiac syndromes and diseases. However, voices of concern about the validity of the concept and the methodology of the measurement were raised repeatedly. Today, after a decade of the "QT dispersion era," some conclusions may be drawn from the wide spectrum of opinions ranging from sheer enthusiastic approval to verdicts of 'the greatest fallacy in electrocardiography in the 1990s (3).

PATHOPHYSIOLOGY OF QT DISPERSION

The initial concept of QT dispersion seemed to be based on a sound logic. The link between the dispersion of ventricular recovery times and arrhythmias had been demonstrated repeatedly (4–6). It was also believed that the standard surface ECG contains regional information. Therefore, finding increased QT dispersion in patient groups in whom the heterogeneity of the ventricular recovery times was previously established, it was assumed that QT dispersion is a reflection of the dispersion of ventricular recovery times. The validity of the concept seemed to be further consolidated by studies correlating intracardiac monophasic action potentials (MAPs) with various QT dispersion indices.

Higham et al. (7) recorded epicardial MAPs during cardiac surgery and measured directly the dispersion of recovery times as well as surface QT dispersion during sinus rhythm and during ventricular pacing. They found a high positive correlation between the MAPs and ECG dispersion indices. Later, using a custom-built rabbit heart setup with simultaneous recording of MAP and 12-lead ECGs, Zabel et al. (8) showed that the dispersions of the QT and JT intervals were significantly correlated with the dispersion of 90% duration of the action potential duration (ADP_{90})

From the Department of Cardiological Sciences, St. George's Hospital Medical School, London, United Kingdom. Supported in part by a Travelling Research Fellowship by the Wellcome Trust, London, United Kingdom.

Manuscript received May 3, 2000; revised manuscript received June 15, 2000, accepted July 25, 2000.

JACC Vol. 36, No. 6, 2000
November 15, 2000:1749–66

Abbreviations and Acronyms

APD = action potential duration
CI = confidence interval
DCM = dilated cardiomyopathy
ECG = electrocardiogram
HCM = hypertrophic cardiomyopathy
LVH = left ventricular hypertrophy
MAP = monophasic action potential
MI = myocardial infarction
QTc = heart-rate-corrected QT interval

and with the dispersion of recovery times. The same authors also confirmed this in patients with 12-lead ECGs recorded within 24 h of the MAPs (9). These studies were generally interpreted as a proof of QT dispersion representing regional variations in the duration of the ventricular action potentials.

Serious arguments against this concept originated from the electrocardiographic lead theory. If the majority of the information about the ventricular electrical activity is contained in the spatial QRS and T loops, the major reason for the differences between separate leads has to be the loss of information from the projection of the loop into the separate leads (10). Two original studies published in 1998 supported this idea.

Macfarlane et al. (11) and Lee et al. (12) showed independently that QT dispersion can also be found in the so-called derived 12-lead ECGs, i.e., ECGs reconstructed from the XYZ leads, which naturally contain no regional information. In both studies the QT dispersion in the originally recorded and in the "derived" 12-leads was surprisingly similar (29.1 ± 10.2 vs. 27.5 ± 10.8 ms and 41 ± 18 vs. 40 ± 20 ms, respectively).

Kors et al. (13) further contributed to the understanding of the interlead differences. They found that QT dispersion was significantly different between patients with narrow (54.2 ± 27.1 ms) and wide T loops (69.5 ± 33.5 ms, $p < 0.001$). They also showed that in each of the six limb as well as the six precordial leads, the difference between the QT interval in a lead and the maximum QT interval was dependent on the angle between the axis of the lead and the axis of the terminal part of the T loop.

Punske et al. (14) compared the spatial distribution of the QT intervals from high-resolution maps on (a) human body surface, (b) the surface of a tank containing an isolated canine heart, and (c) the surface of exposed canine hearts, with the potential distributions on cardiac and body surfaces, and with recovery times on cardiac surfaces. They showed that on the body and tank surface, as well as on the epicardium, the "zero potential line" (no potential difference relative to a reference electrode) stabilizes for 10 to 30 ms at the end of repolarization. This stabilization of the zero line in a given location leads to isoelectric terminal portions of the T wave for leads in the vicinity. Regions of shortest QT intervals always coincided with the location of the zero line. In addition, there were no consistent regions of earliest recovery times on the cardiac surface that coincided with the location of the zero potential line or shortest QT intervals. These studies showed convincingly that the interlead differences of the QT intervals are a reflection of (and could be quantified from) the morphology of the T wave loop.

Most recently, Malik et al. (15) proposed a new ECG processing technique to distinguish the T wave signals representing the three-dimensional movement of the ECG dipole from the nondipolar components likely to be related to regional heterogeneity of myocardial repolarization. Although the nondipolar components differed among the clinical groups, there was very little correlation between the relative amount of the nondipolar components and QT dispersion measured in the same ECGs ($r = -0.046$, 0.2805, −0.1531, and 0.0771, in normal subjects, HCM patients, DCM patients, and survivors of acute MI, respectively, $p = 0.03$ for HCM, others NS).

Hence, it is reasonable to conclude that the dispersions of ventricular recovery times measured with MAPs and QT dispersion are direct and indirect expressions of repolarization abnormalities that are likely to correlate even without any mechanistic link. General abnormalities of ventricular repolarization, not only those leading to regional dispersion of recovery times, modify the spatial T wave loop. As a result of any abnormality, projections of the loop into the individual ECG leads may become less normal and the terminal points of the T wave in the ECG tracings become more difficult to be localized. The effect of local dispersion of repolarization on the morphology of the T wave loop explains the (indirect) link between MAP recordings and QT dispersion. Thus, T wave loop dynamics and the variable projections of the loop into individual ECG leads seem to be the true mechanistic background of QT dispersion.

The studies of the link between the T loop morphology and QT dispersion also confirmed what was empirically known long ago: the more abnormal the T wave morphology in separate leads, the more difficult and unreliable the localization of the T wave offset in each lead and, consequently, the greater the likelihood of an increased QT dispersion. As Kors et al. (13) demonstrated, variations of the T loop morphology lead to variations in the practically unmeasurable final part of the T wave, i.e., the proportion of the signal falling within the noise band (Fig. 1). Thus, variations of the T loop morphology may lead to both true variations in the length of the projections of the T loop onto the separate leads and to an increased measurement error (Fig. 2).

It is now clear that QT dispersion is merely a crude and indirect measure of general repolarization abnormalities. Thus, the original hypothesis linking QT interval duration in separate ECG leads to repolarization duration in separate myocardial regions was ill founded. At the same time, disproving this hypothesis is not a good reason for stating that "QT dispersion does not exist." QT dispersion is clearly

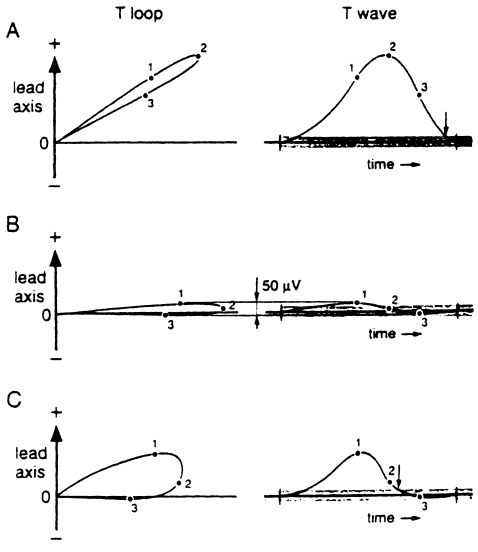

Figure 1. Effect of the shape of the T loop on the QT interval measurement in a hypothetical lead. Projections of T loops with different shapes and at different angles to the axis of the lead result in T waves with different amplitude and morphology. Only an insignificant proportion of the final part of a T wave with high amplitude may be unmeasurable because of falling into the noise band **(A)**; T waves with smaller amplitude as a result of wider T loop **(C)** or elongated loop at different angle **(B)**, have a greater proportion of their final parts falling into the noise band. Thus, the measurable QT interval can almost coincide with the real end of repolarization **(A)**, or be significantly smaller **(B,C)**. Points 1, 2 and 3 indicate three time instants of the T loop and of the T wave. (Reproduced with permission from Kors et al. QT dispersion as an attribute of T-Loop morphology. Circulation 1999;99:458–63.)

only a very approximate and rather simplistic expression of repolarization abnormalities that suffers from a poor pathophysiologic concept as well as, as shown in the next section, from methodological difficulties. However, regardless of the crudeness of the expression, abnormalities of the repolarization are of significant importance (16,17). Even very indirect and very approximate measures of T wave loop abnormalities may still have some, though restricted, informative value. Consequently, it would not be appropriate to dismiss all the numerous observations made with QT dispersion just because the original pathophysiological concept was flawed. Rather, all the previous observations should be reevaluated with an insight into the limitations of the concept and the shortcomings of the technique.

MEASUREMENT OF QT DISPERSION

It has been known for decades that manual determination of the T wave offset is very unreliable (18). Unfortunately, available automatic methods have not proven their superiority. The main sources of error, both for human observers and computers, are low T wave amplitude (19,20) and merges of T waves with U and/or P waves. The morphology of the T wave also strongly influences QT interval measurement.

Several basic algorithms for automatic determination of the T wave end are available (Fig. 3). The threshold methods localize the T offset as an intercept of the T wave or of its derivative with a threshold above the isoelectric line, usually expressed as a percentage of the T wave amplitude. The slope methods determine the T offset as an intercept between the slope of the descending part of the T wave and the isoelectric line, or a threshold line above it. The slope can be the steepest tangent computed by various line fitting algorithms or a straight line through the inflex point and the peak of the T wave. Obviously, the measured values of the QT interval depend on the shape of the descending part of the T wave (Fig. 4). The amplitude of the T wave strongly influences the reliability of both automatic (19,21) and manual (20) measurement.

U wave. The origin of the U wave remains disputed. The theories that attributed the U wave to the delayed repolarization of the His-Purkinje fibers (22) or to mechanoelectrical mechanism (23) were superseded by the M-cell theory by Antzelevich et al. (24). However, later experiments by the same group showed that what is often interpreted as a "pathologically augmented U wave" or "T-U complex" is in fact a prolonged biphasic T wave with an interrupted ascending or descending limb (25). Manual measurement is even less reliable for certain T-U patterns, e.g., when the T wave is flat or inverted and the U wave augmented. Repolarization patterns of complex morphology are frequently classified differently by different observers, leading to substantial variability of the measurement (26).

Probably, electrophysiological mechanisms responsible for usual "physiologic" U wave are different from those leading to abnormal gross U waves, for instance those seen in congenital and acquired long-QT syndrome. In our view,

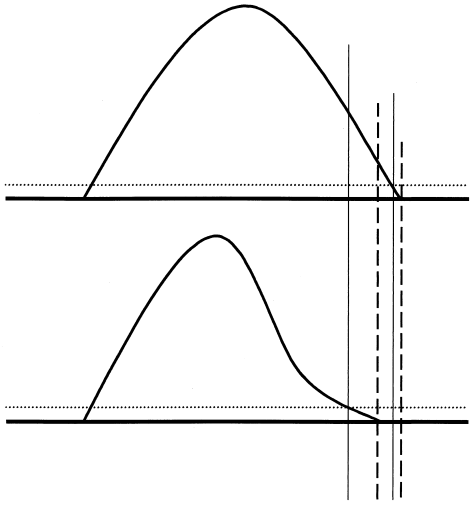

Figure 2. QT dispersion as a result of both different real duration and different measurable duration of QT intervals. Two hypothetical T waves of the same amplitude have different offset **(dashed lines)** when the heart vector becomes perpendicular to the axis of one of the leads. This results in "real" dispersion of the QT intervals **(vertical dashed lines)**. In addition, different proportion of the final part of the two T waves is below the threshold level (e.g., with an automatic threshold method). This leads to the measured dispersion of the QT intervals **(vertical solid line)**, which is different from the real dispersion.

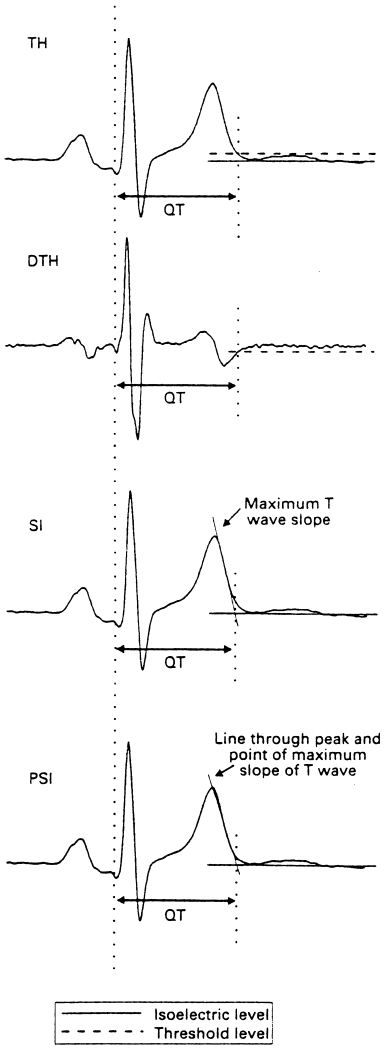

Figure 3. Main automatic QT measurement techniques. From top to bottom: threshold method applied to the original T wave (TH), or to its differential (DTH), tangent method with a tangent to the steepest point of the descending limb of the T wave (SI), tangent method with a line through the T wave peak and the maximum slope point (PSI). (Reproduced with permission from McLaughlin NB, et al. Comparison of automatic QT measurement techniques in the normal 12 lead electrocardiogram. Br Heart J 1995;74:84–89).

all repolarization signals originating from repolarization of ventricular myocardium should belong to the T wave. In this sense, we agree that the concept of biphasic and other unusually shaped T waves is more appropriate than a distinction between the T wave and an augmented U wave which may lead to serious underestimation of QT interval.

A pattern resembling a U wave may also originate from slow afterdepolarization of ventricular myocytes. Distinction of such a pattern from bizarre T waves may be very difficult. At the same time, in practical QT interval measurements (e.g., for the assessment of acquired long-QT syndrome) signs of afterdepolarizations indicate the same proarrhythmic danger as bizarre T wave shapes and prolonged QT interval.

Thus, in all cases that are difficult to reconcile, augmented

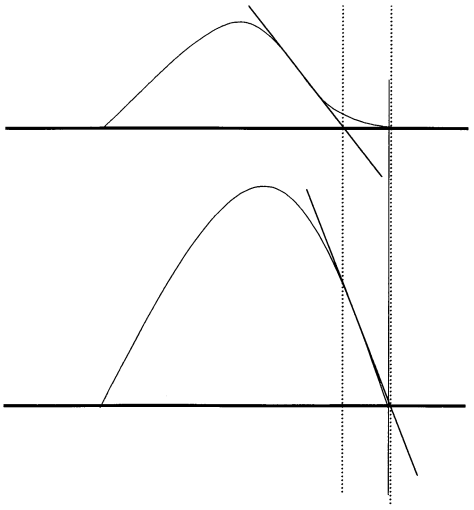

Figure 4. Effect of the shape of the descending part of the T wave on the QT interval measured with a tangent method. The two hypothetical T waves have a common offset **(vertical dashed line)**, but significantly different shape of the descending part. As a result, a tangent to the steepest point may significantly underestimate **(top panel)** or overestimate **(bottom panel)** the T wave offset.

U waves should be preferably included into the T wave. Only distinction between T wave and clearly physiologic U waves of small amplitude should be attempted when measuring QT interval.

Already in 1952, Lepeschkin and Surawicz (27) described and classified various patterns of T and U wave merging and suggested methods for determining the end of the T wave when "buried" within the U wave. They showed that, depending on the pattern of T-U wave merging, either the intersection of the tangent to the downslope steepest point with the isoelectric line, or the nadir between the T and the U wave is closer to the "real" T wave end. This article is clearly more often quoted than read. The tangent method was proposed merely as ". . . an attempt to determine the true end of the T wave in cases of partial merging of T and U . . ." (27), rather than as a universal method for determining of the end of the T wave.

In a recently published extensive review, Surawicz (28) summarized the available knowledge that could help distinguish normal or abnormal U wave merging with a T wave. It is remarkable that the author adds nothing to the method proposed in 1952 for exact determining of the T end in case of merging of the T wave and the U wave.

JT dispersion. In experimental and clinical studies, Zabel et al. (8,9) showed that the QT dispersion values reflect better the dispersion of the recovery times than the action potential duration. On the other hand, the JT dispersion reflected better the dispersion of action potential duration $(APD)_{90}$. Consequently, some authors suggested the QT and JT dispersions to be used as separate entities rather than mutual surrogates (29,30). However, neither the QT dispersion nor the JT dispersion reflect directly the dispersion of the ventricular recovery time or of the action potential duration. As already discussed, the dispersion of various

repolarization duration intervals is merely an indirect measure of general repolarization abnormalities. It is therefore questionable whether JT dispersion offers any real complement to the QT dispersion, except possibly in cases of conduction abnormalities such as bundle branch block.

The Q wave dispersion, although significantly smaller than the T wave offset dispersion, may also influence QT dispersion (31,32). Traditional manual measurement, as well as some computer algorithms, assesses the Q wave onset separately in each lead (33), whereas other computer algorithms use a common, lead-independent Q onset (34,35). This may account for part of the variability between different algorithms.

Measurement features. Theoretically, an accurate assessment of QT dispersion requires all 12 leads of the ECG to be recorded simultaneously in order to avoid the effect of QT dynamicity due to heart rate changes. Therefore, simultaneous 12-lead recordings have been proposed as a "gold standard" for QT dispersion measurement. On the other hand, it is possible that the slow dynamicity of the QT interval (36) renders QT dispersion measurements based on simultaneous recording of six or even only three recordings during ectopic-free sinus rhythm acceptable for practical purposes. This approach, however, has never been properly validated.

Influence of heart rate. Many studies, including large prospective evaluations (37,38) used the so-called corrected QT dispersion, i.e., the dispersion of the QT intervals corrected for heart rate by some formula. Although the application of additive formulae for heart-rate correction, such as those proposed by Hodges et al. (39) and in the Framingham Study (40) renders identical values for QT dispersion and QTc dispersion, this is not true for the multiplicative formulae, which include the Bazett correction. Although experimental and clinical data show that the rate, the rhythmicity and the site of impulse origin can influence the dispersion of the ventricular recovery times (41–43), this has never been shown for QT dispersion. Clinical (44) and experimental (45) studies failed to find correlation between heart rate and the dispersion of ventricular recovery times measured with MAPs or QT dispersion.

The exact relation between the heart rate and the dispersion of recovery times is still an unresolved issue. It is certain, however, that QT dispersion measured in the standard 12-lead ECG does not depend on (and therefore should not be corrected for) the heart period in the same way as the QT interval. Even more importantly, it has been demonstrated that the dispersion of the corrected QT intervals may differ between different clinically defined groups simply from the application of Bazett formula in the presence of different heart rates (46).

Meanwhile, many studies, including large prospective ones such as the Rotterdam (37) and the Strong Heart Study (38) continue to report statistically significant and physiologically meaningful differences in the "corrected" QT dispersion between different clinical groups, somewhat contributing to the credit of this parameter. The gross inappropriateness of such approaches should clearly be recognized, especially because the observation of these studies that increased QT dispersion (i.e., repolarization abnormality) predicts adverse outcome in a general population seems to be independent of the heart rate correction.

Generally, it is incorrect to apply any heart-rate correction formula to a parameter, the dependence of which on heart rate, let alone a mathematical model of such dependence, has never been demonstrated.

Influence of the number of ECG leads and of the ECG lead system. In addition to the original expression of QT dispersion as the range of QT interval duration in all measurable ECG leads, many other measurement possibilities have been proposed. To mitigate the effect of outliers in the QT interval data, standard deviation of the QT interval duration in all leads (47) or coefficient of variation (SD of QT/QT average $\times 100$, the so-called relative QT dispersion [48]) have been used. However, the range and standard deviation values have been shown to correlate very closely (47,49).

The number of measurable leads in the standard ECG also influences the range of QT interval durations. Some researchers proposed a correction factor dividing QT interval range by the square root of the number of measurable ECG leads, leading to the so-called adjusted QT dispersion (50). Hnatkova et al. (47) showed that this formula results in a reasonable correction of mean values of QT dispersion in normal ECGs. However, they also showed that the individual errors caused by omitting separate leads are very substantial. Consequently, it is not appropriate to compare results based on QT interval values measured in ECGs of very different number of measurable leads.

Many clinical studies have measured QT dispersion only in the six precordial leads. In addition, other lead combinations, such as the orthogonal XYZ or "quasiorthogonal" I, aVF or V2 leads, have also been studied. It was reported that although, as one would expect, QT dispersion is decreased when a smaller number of leads is used for QT measurement, QT dispersion differences between different patient groups can still be detected with the three leads (aVF, V1, V4) that are most likely to contribute to QT dispersion (51): the limb leads (52), the orthogonal (X,Y,Z) (53,54) or the quasi-orthogonal leads aVF and V2 (51–53). Clearly, practically any lead combination may detect abnormalities in the morphology of the T loop and translate them into increased values of QT dispersion. On the other hand, the more projections of the T loop into different leads with different axes are used, the more sensitive the measurement becomes. Unfortunately, as already mentioned, none of this directly translates into an increased regional heterogeneity of recovery times. Therefore there is little point in continuing the quest for the "perfect lead combination" for QT dispersion measurement.

Reliability of QT dispersion assessment. Many studies have shown high inter- and intraobserver variability of

manually measured QT dispersion. The errors reach the order of the differences between normal subjects and cardiac patients. Relative errors of 25–40% of interobserver and intraobserver variability of manual measurement of QT dispersion have been reported (27,55), and opposed to relative errors <6% for manual measurement of the QT interval (55). Occasionally, substantially better reproducibility of manual measurement of QT dispersion has also been reported, with interobserver variability of 13–18% (56) and even <5% (57). Explanations of these discrepancies can only be very speculative. Because a majority consensus clearly agrees on poor reproducibility of QT dispersion measurement, a wishful bias was likely involved in some reports presenting very low measurement errors.

In addition to the differences in the investigated populations, the variations of the results can be attributed to differences in the measurement method (manual measurement with calliper or ruler (58), application of a digitizing board with or without magnification, on screen measurement with electronic callipers, etc.), the noise level, and the paper speed at which the ECGs were recorded (20). In a technical study, Malik and Bradford (59) showed that even the "gold standard" manual measurement using the digitizing board, can produce intraobserver variations corresponding to purely error-related QT dispersion >40 ms and >60 ms, in 20% and 10% of observers, respectively.

The available automatic methods for QT measurement have not shown a superior reproducibility. For example, Yi et al. (60) reported that the immediate reproducibility (in sequentially recorded ECGs) of various QT dispersion indices measured with a downslope tangent method in healthy volunteers varied between 16% and 44%. Variations of computer algorithms for T wave offset determination (61) include signal processing options, the way in which the tangent is characterized, the definition of the isoelectric line, the threshold level, etc. Some software packages offer a great variety of parameter settings. For instance, one of the versions of the QT Guard software package by GE Marquette (34) offers >100 programmable options for the T wave end localization.

Many studies tried to validate automatic algorithms against manual measurement by experienced ECG readers. The results were disappointing showing large difference (21,62–64). Savelieva et al. (63) investigated the agreement between automatic (downslope tangent) and manual QT measurement in normal subjects and patients with HCM. The agreement between the two methods of QT interval measurement was poor and lower in normal subjects (r^2 = 0.10 to 0.25 in the separate leads) than in HCM patients (r^2 = 0.46 to 0.67). The agreement between automatic and manual measurement of QT dispersion was even much worse (r^2 = 0.06 in HCM patients and r^2 = 0.00 in normal subjects, Fig. 5).

Relatively few studies compared different algorithms for automatic QT measurement. McLaughlin et al. (61) compared two threshold and two slope-based techniques, and a validated manual measurement. The results of the mean measurements with different algorithms varied up to 62 ms, which was greater than the manual interobserver variability. The threshold algorithm demonstrated the largest variability and its results depended on filtering and algorithm parameters. In another study (65) the same authors showed that the variability of automatic QT measurement in cardiac patients was twice that in normal subjects and that it was significantly increased with the decrease of the T wave amplitude. In a study only part of which was published, Batchvarov et al. (66) evaluated the multiple parameter options in the QT Guard package. The differences between the downslope tangent method using different numbers of samples around the inflex point used for the tangent computation and the modifications of the threshold method were substantial. Changes in the permissible range of the settings of the package led to differences of up to 60 ms in normal subjects and up to 70 ms in HCM patients. Hence, only comparison of results obtained with the same automatic methods and with the same parameter setting is appropriate.

Unfortunately, no systematic experience exists that would allow an optimum algorithmic setting to be selected. Moreover, it seems reasonable to speculate that all present algorithmic approaches to QT interval measurement are too simplistic and superficial and that a truly successful algorithm for automatic QT interval measurement will eventually need to be based on a completely different mathematical approach reflecting a deep electrocardiographic knowledge.

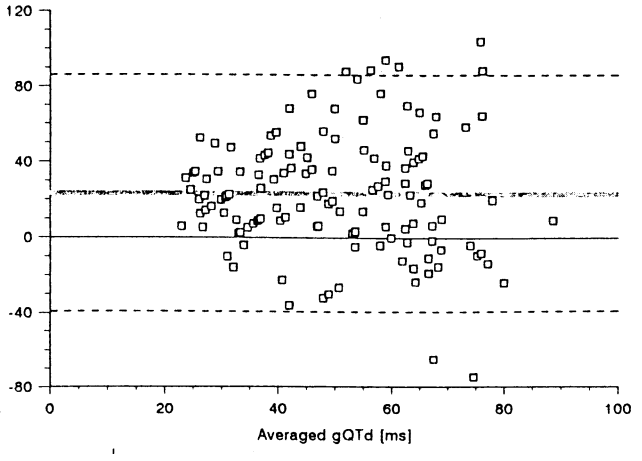

Figure 5. Agreement between automatic and manual measurement of QT dispersion in patients with hypertrophic cardiomyopathy. The differences between the measurements are plotted against the mean value from the two measurements. Most of the differences are within 2 SD from the mean differences **(dashed line)**, which is approximately ±60 ms, obviously an unacceptably high measurement error. There is also no correlation between the two sets of measurements (r_2 = 0.00). (Reproduced with permission from Savelieva I, et al. Agreement and reproducibility of automatic versus manual measurement of QT interval and QT dispersion. Am J Cardiol 1998;81:471–7).

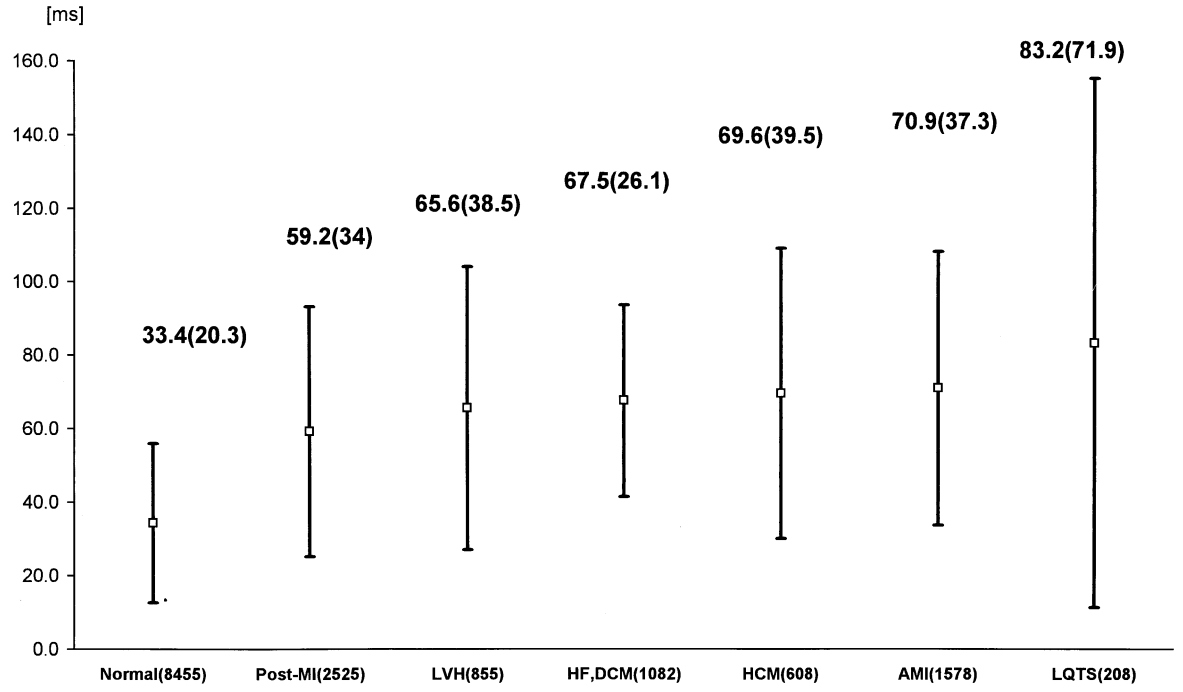

Figure 6. Weighted mean ± SD values of QT dispersion (in milliseconds) from reviewed studies in normal subjects, patients with chronic myocardial infarction (chr.MI), left ventricular hypertrophy (LVH) of various etiology except hypertrophic cardiomyopathy, in heart failure and dilated cardiomyopathy (HF,DCM), in hypertrophic cardiomyopathy (HCM), in acute myocardial infarction (acute MI), and in long-QT syndrome (LQTS). See text for details.

CLINICAL STUDIES

A review of the extreme abundance of studies on QT dispersion published over the past decade reveals an amazingly wide range of QT dispersion values in both "positive" and "negative" studies, and a complete lack of any tendency towards establishing reference values. For example, large studies (67) or literature reviews (68) suggesting QT dispersion of 65 ms as an upper normal limit in healthy subjects were published alongside reports claiming QT dispersion >40 ms to have 88% sensitivity and 57% specificity for prediction of inducibility of sustained ventricular tachycardia during an electrophysiology study (69). Many of the studies with positive results published QT dispersion data well within the demonstrated measurement error of both manual and automatic measurement.

QT dispersion in normal subjects and in the general population. Literature reviews found the QT dispersion to vary mostly between 30 and 60 ms in normal subjects (70,71), although average values around 70 ms were also reported. In 51 studies (40 published during the past three years) in which QT dispersion was measured in 56 groups with a total of 8,455 healthy subjects of various ages (including three large studies of healthy children [72–74]), we found mean QT dispersion values (QT maximum–QT minimum) to range from 10.5 ± 10.0 ms (75) to 71 ± 7 ms (76). The weighted mean ± SD from all these studies is 33.4 ± 20.3 ms (Fig. 6), while the median is 37 ms. Moreover, most researchers reported a wide overlap of values between normal individuals and different patient groups (Figs. 6 and 7). Thus, all values proposed for upper normal limit in healthy subjects are unreliable.

Published reports show either no statistically significant difference in QT dispersion between the genders (11,73) or marginally greater values in men (77,78). Age-related differences <10 ms were reported and appeared to be statistically significant in some studies (79,80) but not in others (72,73). For example, in the study by Savelieva et al. (81) on more than 1,000 healthy subjects, QT dispersion was 29.1 ± 17.8 ms in the age group of 17 to 29 years and 21.7 ± 13.3 ms in the age group of 50 to 80 years ($p < 0.0001$). However, in another large study, Macfarlane et al. (11) found no significant age differences (QT dispersion of 23.6 ±7.7 ms, 24.8 ± 8.2 ms, 24.8 ± 8.5 ms and 24.5 ± 9.8 ms in the age groups of <30, 30–40, 40–50 and >50 years, respectively). In this study, no age differences of QT dispersion were found in 1,784 neonates, infants and children divided in 16 age groups from <24 h to >15 years of age.

Several large prospective studies published recently assessed the predictive value of QT dispersion for cardiac and all-cause mortality in the general population. In the Rotterdam study (37) QT dispersion was found to predict cardiac mortality in a general population of 5,812 adults of 55 years or older, followed up for 3 to 6.5 (mean 4) years.

In the Strong Heart Study (38) the predictive value of the "corrected" QTc dispersion was assessed in 1,839 American Indians followed up for 3.7 ± 0.9 years. Heart rate corrected QT interval assessed as a continuous variable remained a significant and independent predictor of cardiovascular

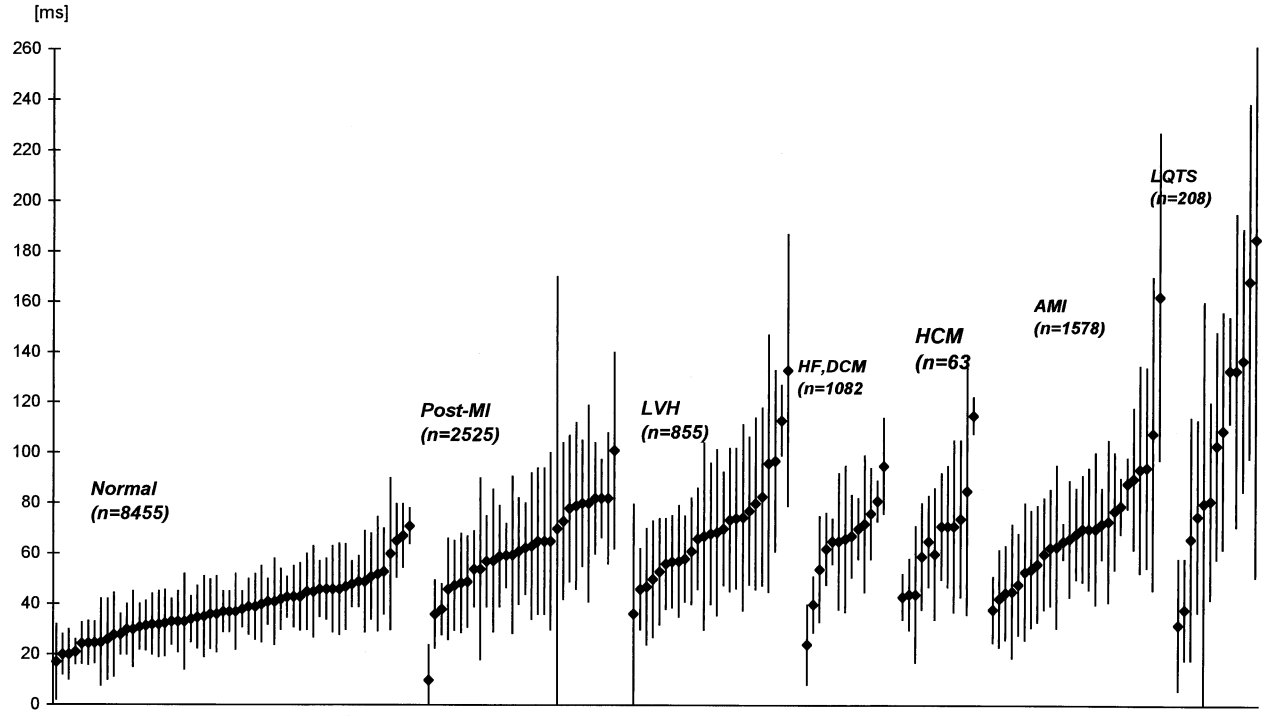

Figure 7. Mean±SD of QT dispersion (in milliseconds) from the reviewed studies of normal subjects, and patients with chronic myocardial infarction, left ventricular hypertrophy, heart failure and dilated cardiomyopathy, hypertrophic cardiomyopathy, acute myocardial infarction, and long QT syndrome. Abbreviations as in Figure 6. See text for details.

mortality in both univariate and multivariate Cox Proportional Hazard Models, with 34% increase of cardiovascular mortality for each 17 ms increase in QTc dispersion in multivariate analysis. In multivariate analysis QTc dispersion >58 ms (the upper 95th percentile in a separate population of normal subjects) was associated with a 3.2-fold increased risk of cardiovascular mortality (95% confidence interval [CI] 1.8–5.7). Unfortunately, no values for the uncorrected QT dispersion or the simple resting heart rate were provided. Thus, the possibility of the strong predictive power being maintained by the differences in heart rate cannot be excluded.

The West of Scotland Coronary Prevention Study (WOSCOPS) (82) included 6,595 middle-aged men with moderately raised cholesterol but no previous MI. In a multivariate analysis, an increment of 10 ms in QT dispersion increased risk for death of coronary heart disease or nonfatal MI by 13% (95% CI 4% to 22%, p = 0.0041). QT dispersion >44 ms carried an increased risk of 36% (95% CI 2% to 81%, p = 0.034) compared with QT dispersion <44 ms. On the other hand, this cutoff level of 44 ms had a sensitivity of only 8.8% with a specificity of 93.8%. The area under the receiver operator characteristic curve was only 54%, indicating an almost complete lack of predictive power of QT dispersion.

QT dispersion in cardiac disease. A majority of studies have shown increased QT dispersion in various cardiac diseases. We have pooled data from 18 studies with a total of 2,525 post-MI patients; 16 studies with 855 patients with LVH of various origin, excluding HCM; 8 studies with 1,082 patients with heart failure, including idiopathic DCM; 11 studies with 635 patients with HCM; 16 studies with a total of 1,578 patients with acute MI; and 10 studies with 208 patients with long-QT syndrome of various genotype (Fig. 6).

There is a clear tendency towards increase of QT dispersion in various cardiac diseases, with highest mean values reported in long-QT syndrome, "the pure global repolarization disease" (Figs. 6 and 7). On the other hand, the overlap of values between patients with different cardiac diseases, between patients and normal subjects, and the wide variation of values within each cardiac disease render any attempt at establishing reference values fruitless. However, patients with various clinical symptoms, with and without arrhythmias, and on various medications have been included in these pooled studies, which probably accounts for part of the variation.

Generally, QT dispersion is increased in acute MI, although mean values from 40 ± 18 (75) to 162.3 ± 64.8 ms (83) have been reported. Although QT dispersion is increased in the chronic phase of MI and in other chronic forms of ischemic artery disease, there seems to be a trend towards lower values compared with the acute phase of MI, possibly due to the spontaneous dynamicity or to revascularization procedures. Some authors did not find significant differences in QT dispersion between patients with chronic MI or other forms of chronic CAD and normal subjects (84,85).

Compared with healthy controls, an increased QT dispersion has been reported in heart failure and left ventricular dysfunction of various etiology (86–89) including highly trained athletes (90–92), in LVH of various origin (93–97), in patients with arterial hypertension irrespective of the presence or absence of hypertrophy (98), in HCM patients compared with healthy controls (99–101), in long-QT syndrome (102–104) and in many other cardiac and even noncardiac diseases. However, some studies have found QT dispersion values not significantly different between healthy subjects and patients with heart failure (105), patients with LVH as a result of physical training (106–108), or between patients with and without LVH (109).

Many studies tried to correlate QT dispersion with the extent or the localization of the pathological process of various diseases. Some studies have shown greater QT dispersion in anterior compared to inferior MI (110–112); correlation between QT dispersion in MI and indirect measures of infarct size, such as ejection fraction (113); or the amount of viable myocardium in the infarct region (114). Similarly, significant correlation between QT dispersion and left ventricular mass index in hypertensive patients with LVH was found in some studies (115,116), but not in others (117).

Changes of QT dispersion have been shown to follow the spontaneous or induced dynamicity of the pathological process in some cardiac diseases. For instance, QT dispersion seems to undergo dynamic changes during the first day (118), as well as during the following days (119,120), of acute MI. It increases significantly during ischemia induced by balloon inflation during angioplasty (121–123), by exercise stress testing (124) or atrial pacing (125), or during reperfusion following angioplasty (126). It has also been shown to correlate with improvement of left ventricular contractility on the echocardiogram after infarction (127) and with the degree of improvement of left ventricular function after revascularization (128,129).

Treatment has been shown to decrease QT dispersion, e.g., after successful reperfusion after thrombolysis (130,131), revascularization with angioplasty (132–134) or coronary artery bypass grafting (129). Treatment of patients with heart failure with losartan (135), successful antihypertensive treatment of patients who had hypertension with LVH (136–139), or successful beta-blocker treatment of patients with long-QT syndrome (140) have also been shown to decrease QT dispersion.

Prognostic value of QT dispersion. Many studies have been aimed at investigating the value of QT dispersion for the prediction of ventricular arrhythmias or other adverse events in various cardiac diseases. The results are again controversial.

We have pooled data from 23 studies on patients with and without serious ventricular arrhythmias in various cardiac diseases, most of them with ischemic heart disease. Altogether, 490 patients with and 1,341 patients without serious ventricular arrhythmias were included. Although most studies show significantly greater QT dispersion in patients with arrhythmias, the values largely overlap (Fig. 8).

Several studies, most of them retrospective, have found that patients with acute (141,142) or chronic MI (143–145) with ventricular arrhythmias have significantly higher QT dispersion than patients without arrhythmias. However, the first prospectively analyzed study in post-MI patients reported by Zabel et al. (146) showed that none of the 26 ventricular dispersion indices that were tested had any predictive value for an adverse outcome in 280 consecutive MI survivors followed up for 32 $\pm$ 10 months. Newer studies (147,148) provided controversial findings. The main prospective studies on QT dispersion are summarized in Table 1.

Some studies showed that QT dispersion could predict inducibility of ventricular arrhythmias during electrophysiology study (149–151), whereas others failed to observe this (152–154).

Several studies (155–157) showed significant correlation between QT dispersion and outcome in patients with heart failure. Analysis (158) from the ELITE heart failure study, in which heart failure patients treated with the angiotensin-II antagonist losartan had reduction of sudden cardiac death compared with those treated with captopril (159), showed that captopril but not losartan increased QT dispersion. However, the results of ELITE were not confirmed by the much larger double-blind, randomized controlled ELITE-II trial (160), in which patients treated with losartan showed no significant differences in all-cause mortality, sudden death or resuscitated cardiac arrest compared with those treated with captopril. The analysis of the ECG data of ELITE-II will shed additional light on the value of repolarization assessment in patients with heart failure.

Substudies of the DAMOND-CHF Study (161), the UK-HEART study (162) as well as other large prospective studies (163) failed to show any power of QT dispersion for predicting outcome in heart failure patients. Available studies also failed to show independent predictive value of QT dispersion for sudden cardiac death and cardiac mortality in patients with LVH (164).

Several authors reported significantly higher QT dispersion in HCM patients with ventricular arrhythmias compared with those without arrhythmias (165–167). Larger studies, however, did not confirm these findings (168,169).

In long-QT syndrome, the diagnostic value of increased QT dispersion seems undisputed. On the other hand, although Priori et al. (170) reported that patients not responding to beta-blockers had a significantly higher QT dispersion than responders (137 $\pm$ 52 vs. 75 $\pm$ 38 ms, $p < 0.05$), no other presently available data suggest that QT dispersion has any prognostic value in patients with long-QT syndrome.

Generally, the positive results of small retrospective studies conducted in the years of initial enthusiasm were later confirmed only in some very large prospective studies.

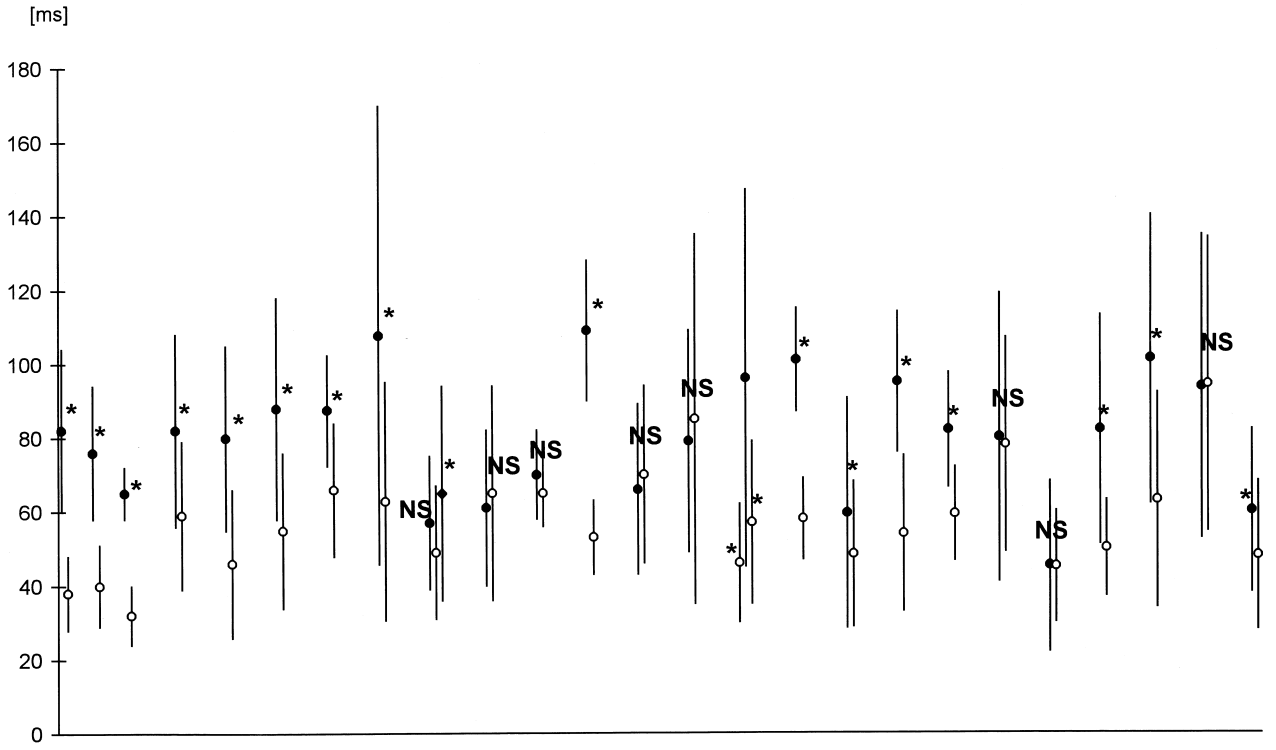

Figure 8. Mean and standard deviations of QT dispersion in patients with **(closed circles)** and without **(open circles)** serious ventricular arrhythmias. In one study patients with ventricular fibrillation **(closed diamond)** and sustained monomorphic ventricular tachycardias **(closed circle)** were compared separately with patients without sustained ventricular arrhythmias. *$p < 0.05$ between groups with and without serious ventricular arrhythmias; NS: statistically nonsignificant difference between groups with and without serious ventricular arrhythmias.

However, even in the large studies, patient groups with adverse outcomes often had QT dispersion values well within both the measurement error and the range of values in healthy subjects reported in other studies. Thus, as phrased by Surawicz (171), the positive results can be interpreted as indicating an "indifferent" QT dispersion. This does not necessarily signify lack of clinical importance. In the majority of the cases, the abnormality was already visible from abnormal T wave morphology and/or increased QT interval. At present, this does not necessitate a specific therapeutic action and, in practice, does not help in the risk stratification of individual patients.

Effect of drugs on QT dispersion and the risk of torsades de pointes tachycardia. The limitations of both the presence and the degree of QT interval prolongation for prediction of torsades de pointes are well known (172). Consequently, the potential role of QT dispersion for the prediction of drug-induced torsades de pointes has been addressed in several studies.

Quinidine increases QT dispersion (173,174) and, unlike the corrected QTc interval, increased QT dispersion seems to have some predictive value for development of torsades de pointes during quinidine therapy (173,174). Sotalol has been shown to decrease (175) or not to change (176) QT dispersion in patients with ischemic heart disease. However, Dancey et al. (177) observed increased QT dispersion in 4 cases of torsades de pointes caused by low dose sotalol in patients with renal failure.

In clinical studies, amiodarone has been reported to decrease (176,178) or not to change (173,179,180) QT dispersion. It is known that amiodarone can be administered relatively safely in patients who had experienced torsades de pointes during antiarrhythmic therapy with other drugs (181) and this effect is paralleled by a decrease of QT dispersion (173). However, cases of an excessive increase of QT dispersion and induction of torsades de pointes by amiodarone have also been reported (182). On the other hand, it has been demonstrated that increase of QTc and QT dispersion during chronic amiodarone treatment does not affect survival and is independent of the decrease in arrhythmia risk (183).

Propafenone (184), disopyramide (185) and almokalant (blocker of the rapid component of the delayed rectifier, I_{Kr}) (186) has been shown to increase QT dispersion, whereas in one study dofetilide infusion did not produce increase of the dispersion of repolarization between two right ventricular endocardial sites (187). A decrease of QT dispersion after treatment with azimilide (188) and magnesium has also been reported (189).

In addition to long-QT syndrome (140), beta-blockers have been shown to decrease QT dispersion in patients with syndrome X (190) and heart failure (191), but not in HCM (168).

Table 1. Prospective Studies on QT Dispersion

Author (reference)	Cardiac Disease	End Points	Follow-up	No (+) Group	No (−) Group	QTd (+) Group	QTd (−) Group	p Value	Comments
Zabel et al, 1998 (146)	Post-MI	Total mortality, sustained VT, resuscitated VF	32 ± 10 months	30	250	61 ± 21	65 ± 29	NS	
Okin et al, 2000 (38)	General population, 45–74 years	All-cause, cardiac mortality	3.7 ± 0.9 years	188* 55†	1651	26 ± 22* 33 ± 31†	21 ± 16	<0.001 <0.001	Only QTcd; QTcd >58 has ≈twofold increased risk
de Bruyne et al, 1998 (37)	General population, ≥55 years	All-cause, cardiac mortality, SCD	3–6.5 years (mean 4 years)	568* 166† 73§	5244	Subject with QTd in the highest tertile >60 (66)‡ had a 1.4 (1.3) increased risk for total mortality compared to those in the lower tertiles, only QTcd was studied			
Brooksby et al, 1999 (162)	Chronic heart failure	All-cause mortality, SCD, death due to heart failure	471 ± 168 days	71*	424	79 ± 32	89 ± 33	0.03	QTcd, no independent predictive value in multivariate analysis
Fu et al, 1997 (155)	Ischemic and idiopathic dilated cardiomyopathy	SCD, sustained VT	26 ± 15 months			109 ± 23	57 ± 20‖ 55 ± 20¶		JTcd was the most important multivariate predictor of SCD/VT
Anastasiou-Nana et al, 2000 (157)	Congestive heart failure (EF <35%)	Sudden and nonsudden cardiac death	average 20 months	23	81	95 ± 48†	78 ± 31	≤0.03	QTd>90 carried 2.8 (CI 1.2–64) risk for cardiac death
Brendorp et al. (161)	Left ventricular dysfunction	Total mortality	1 year	188	302	QTd risk ratio 1.0 (CI 0.996–1.004)			
Macfarlane et al, 1998 (82)	Normal adults 45–56 years with moderate hyperlipidemia	Coronary artery disease death or nonfatal MI			1,501	96% percentile range of 12–44 ms			In multivariate analysis QTd >44 ms increased risk by 13%, but with only 9% sensitivity and 94% specificity. and ROC area of 0.54

*All-cause mortality; †cardiac deaths; ‡in 8 independent (in 12) leads: §sudden cardiac deaths; ‖survivors; ¶died from pump failure or acute myocardial infarction.

QTd = QT dispersion; MI = myocardial infarction; QTcd = dispersion of QTc interval; JTd = JT dispersion; ROC = receiver-operator characteristic; VT = ventricular tachycardia; VF = ventricular fibrillation; SCD = sudden cardiac death; CI = confidence interval.

JACC Vol. 36, No. 6, 2000
November 15, 2000:1749–66

It seems that ECG monitoring of the effect of drugs that prolong ventricular repolarization is the only area in which QT dispersion preserved (some) immediate clinical significance. Grossly abnormal values (e.g., ≥100 ms, unlikely to be due to measurement error) during treatment with drugs effecting repolarization signify "bad QT dispersion" (171), which probably should prompt urgent assessment of the drug effect. On the other hand, lack of abnormal QT dispersion value is by no means a reassuring sign of therapeutic safety. Generally, the ECG detection of increased risk of torsades de pointes during treatment with repolarization-active drugs is still an unresolved issue, and most probably QT dispersion will have only some supportive value even in this area.

CONCLUSIONS

QT dispersion after 10 years. Contrary to the initial expectations, QT dispersion did not evolve into a useful clinical tool. Although this simple ECG parameter is probably not (only) a result of measurement error, it does not reflect directly and in a quantifiable way the dispersion and the heterogeneity of the ventricular recovery times. The standard 12-lead ECG contains information about regional electrical phenomena, but this information cannot be extracted by such a simple technique as QT dispersion assessment.

In addition, not only the magnitude of dispersion of recovery times, but the distance over which they are dispersed is important for arrhythmogenesis. In a similar way as we distinguish, though arbitrarily, "micro reentry" from "macro reentry," it seems logical to distinguish dispersion of recovery times of adjacent areas (local dispersion) from dispersion over large areas (global dispersion) and, possibly, from dispersion between both ventricles (interventricular dispersion). Such a scale is clearly beyond the resolution of the standard surface ECG. Local dispersion of recovery times created by MI is no more visible on the standard surface ECG than the delayed conduction caused by the same infarct.

The very idea of detecting and quantifying only the dispersion of the end of repolarization, i.e., the dispersion of the complete recovery times, also seems questionable. Action potentials of different duration usually have very different shape, particularly during phase 3. Such a "phase 3 dispersion," i.e., the dispersion of the partial recovery times, has direct relation to arrhythmogenesis. Although it is reflected in the shape of the T wave, it does not contribute to the dispersion of the ends of the MAPs, let alone the dispersion of the QT intervals.

In a recently published experimental study Shimizu et al. (192) showed that the T wave alternans induced by rapid pacing were a result of alterations in the APD of the M-cells, leading to exaggeration of transmural dispersion of repolarization during alternate beats, and thus to the potential for development of torsades de pointes. The result of the study clearly emphasized that spatial dispersion of the recovery times cannot be estimated without the analysis of the morphology of the T wave, as well as without taking into account its dynamicity.

"State of the art" of QT dispersion. Despite all limitations, the decade of investigation of QT dispersion emphasized the clinical importance of the repolarization abnormalities. We have to understand that QT dispersion is nothing more (and nothing less) than an approximate and simplistic expression of repolarization abnormality. The concept of QT dispersion seems to be a correct step, although a small step, in the correct direction. In the absence of other widespread possibility of quantifying repolarization abnormality in 12-lead ECGs it is probably not that unreasonable to use QT dispersion in approximate pilot studies. Because it seems reasonable to speculate that there is a monotonic relationship between measured values of QT dispersion and the degree of repolarization abnormality (i.e., that greater values of QT dispersion indicate greater repolarization pathology), it is not even very unreasonable to subject the numerical measurements of QT dispersion to statistical tests.

At the same time, the technology clearly suffers from serious methodological problems, from the lack of any direct link to a pathophysiological background, and from complete absence of any reference values. At present, the role of QT dispersion (if any) should therefore be restricted purely to preliminary pilot investigations when testing hypotheses of whether changes in myocardial repolarization are involved in a given pathology, condition or clinical prognosis. When such pilot studies are attempted, all limitations of the technology must be recognized and accounted for. Strictly blinded evaluation of measured ECGs is essential because difficulties of QT interval measurement in tracings with abnormal T waves are likely to contribute to increased QT dispersion. Because the measurement is also poorly reproducible, all ECGs of any study must be read by two or perhaps even more independent experienced electrocardiologists.

The technological limitations and methodological problems also impose serious restrictions on the interpretation of the results of any study, including those already published. The poor reproducibility and substantial dependence of the measurement on the operator make the results of different studies not easily comparable. Group differences of only few milliseconds even when statistically significant, should always be interpreted with caution and skepticism because they are unlikely to be reproducible. Similarly, the lack of a difference in QT dispersion values does not prove the absence of the involvement of myocardial repolarization. The technology is clearly too crude to depict minor repolarization changes.

When evaluating clinical studies, "approximate repolarization characteristics" should always be read in place of QT dispersion. Hence, the clinical studies reviewed in the previous section show that disturbed ventricular repolariza-

tion is linked to poor prognosis in a general population, is present in survivors of acute MI, etc. At the same time, the particular numerical values of QT dispersion reported in individual studies are of little consequence.

In clinical practice concerning individual patients, only grossly abnormal values of QT dispersion that are clearly outside the possible measurement error, e.g., ≥100 ms, may have a significance by signaling that the repolarization is abnormal. It seems, therefore, that the potential clinical use will be limited to diseases and syndromes in which such values may be encountered, e.g., drug-induced torsades de pointes. Of course, one can wonder about the likelihood of finding such extreme values in ECGs with normal T wave morphology and how likely is QT dispersion to offer any additional information beyond the traditional verbal diagnosis of substantial T wave abnormality. Even in long-QT syndrome, i.e., in the case of the pure global repolarization disease, QT dispersion failed to add substantial additional information to that provided by the general observation of abnormal TU complexes.

The major technical problem of QT dispersion is the imprecision of T wave end localization. Further purifications of technology of QT dispersion, such as optimum lead selection, replacement of the simple computation of the range of QT interval durations, various correction factors, etc., are clearly unable to overcome this principal shortcoming of the concept of QT dispersion and should therefore be discouraged. We should also discourage evaluations of QT dispersion in studies of a small number of ECGs because they are unlikely to contribute to our understanding of physiological and clinical correlates of repolarization changes. Perhaps QT dispersion may only have a role in evaluating very large collections of ECGs when the simplicity and speed with which QT dispersion can be measured may have some practical appeal. In such cases, all the limitations and restrictions of the technology and concept of QT dispersion must always be remembered. Actually, many would probably second the view that the most "state-of-the-art" approach to QT dispersion assessment is not to perform it at all.

Where Do We Go From Here?

As Abildskov et al. (193) wrote 13 years ago , the regional information continues to be a part of "The Unidentified Information Content of the Electrocardiogram."

Classification and quantification of the regional information in the 12-lead ECG remains a challenging problem. Despite initial hopes, it is now obvious that it has not been addressed by QT dispersion, which is more about global than localized repolarization abnormality.

Older concepts of quantification of repolarization abnormalities, as well as newer ideas, deserve more attention than parameters based on duration of repolarization intervals. Principal component analysis has been used for decades in the analysis of ECG signals from body surface potential mapping for reduction of redundancy of the data (194). Recently, principal component analysis has also been implemented to assess the complexity of the T wave from standard 12-lead ECG and from 12-lead digital Holter recordings. The method has been shown to differentiate between normal subjects and patients with long-QT syndrome from 12-lead Holter ECGs (195) and in patients with HCM (196) and arrhythmogenic right ventricular dysplasia (197). In general (1,194), the method defines the principal, nonredundant spatial components (or "factors") into which the T wave is decomposed and that contribute (in descending order of significance) to the morphology of the T wave. The significance of each component is measured by its eigenvalue. When the repolarization is uniform, i.e., the T wave is smooth, without notches, most of the information about its morphology is contained in the first, main principal component. When the T wave becomes more complex, the relative value of the next, smaller components of the T wave increases (i.e., their eigenvalues increase). Although principal component analysis has already been included in some commercially available programs for automatic repolarization analysis, its clinical role is still not well defined.

Frontal and horizontal T wave axis has also been demonstrated to be predictive of cardiac mortality (198). Most probably, other wavefront direction parameters based on measurement of vector time integrals (i.e., QRST areas) will also be studied in the near future.

Most recently, a concept of measuring the T wave "morphology dispersion" in surface ECGs has been proposed by Acar et al. (199). Based on single-value decomposition of simultaneously recorded 12-lead ECGs and on the computation of the eigenvalues of the signal, they proposed several indices characterizing the sequence of repolarization changes through the ventricular myocardium, including parameters describing the dissimilarities of the shape of the T wave in individual ECG leads. Comparison of normal and abnormal ECG of HCM patients showed that indices of T wave morphology separated these two groups more powerfully than both QT dispersion and rate-corrected QT interval duration. The concept was subsequently applied to the ECGs database of the first prospective study on QT dispersion in survivors of MI by Zabel et al. (146). They showed that unlike QT dispersion, selected indices of T wave morphology characteristics obtained from single-beat resting 12-lead ECGs are powerful and independent predictors of adverse events during follow-up (17).

Only after more experience has accumulated with these and other descriptors of repolarization morphology will it be possible to address their relationship to the expressions of repolarization dynamicity, such as T wave alternans or QT/RR relationship and adaptation. The present approaches to the assessment of repolarization dynamics are also rather simplistic and in need of further improvement. Studies of the dynamics of repolarization morphology are an obvious step forward. It is therefore reasonable to expect

that the distinction between "static" and "dynamic" repolarization assessment will gradually be suppressed and that a "comprehensive" spectrum of repolarization characteristics will eventually appear.

Future efforts should concentrate on more focused and more detailed technologies for repolarization assessment. The available technologies (e.g., principal component analysis, T wave loop descriptors, T wave morphology dispersion) should be subjected to evaluation in existing ECG databases and in ECG collections of new studies. At the same time, special effort should be devoted to the development of new ECG processing concepts addressing detailed aspects of repolarization characteristics and repolarization changes.

Reprint requests and correspondence: Dr. Marek Malik, Department of Cardiological Sciences, St. George's Hospital Medical School, London SW17 0RE, United Kingdom. E-mail: m.malik@sghms.ac.uk.

REFERENCES

1. Horan LG, Flowers NC, Brody DA. Principal factor waveforms of the thoracic QRS complex. Circ Res 1964;XV:131–45.
2. Day CP, McComb LM, Campbell RWF. QT dispersion: an indication of arrhythmia risk in patients with long QT intervals. Br Heart J 1990;63:342–4.
3. Rautaharju PM. QT and dispersion of ventricular repolarization: the greatest fallacy in electrocardiography in the 1990s. Circulation 1999;18:2477–8.
4. Han J, Moe GK. Nonuniform recovery of excitability in ventricular muscle. Circ Res 1964;14:44.
5. Allessie MA, Bonke FIM, Schopman FJG. Circus movement in rabbit atrial muscle as a mechanism of tachycardia. II: the role of nonuniform recovery of excitability in the occurrence of unidirectional block, as studied with multiple microelectrodes. Circ Res 1976;39:168–77.
6. Kuo C-S, Munakata K, Reddy P, Surawicz B. Characteristics and possible mechanism of ventricular arrhythmia dependent on the dispersion of action potential durations. Circulation 1983;67:1356–67.
7. Higham PD, Hilton CJ, Aitcheson JD, Furniss SS, Bourke JP, Campbell RWF. Does QT dispersion reflect dispersion of ventricular recovery? (abstr). Circulation 1992;86 Suppl I:392.
8. Zabel M, Portnoy S, Franz MR. Electrocardiographic indexes of dispersion of ventricular repolarization: an isolated heart validation study. J Am Coll Cardiol 1995;25:746–52.
9. Zabel M, Lichtlen PR, Haverich A, Franz MR. Comparison of ECG variables of dispersion of ventricular repolarization with direct myocardial repolarization measurements in the human heart. J Cardiovasc Electrophysiol 1998;9:1279–84.
10. Coumel P, Maison-Blanche P, Badilini F. Dispersion of ventricular repolarization. Reality? Illusion? Significance? Circulation 1998;97:2491–3.
11. Macfarlane PW, McLaughlin SC, Rodger C. Influence of lead selection and population on automated measurement of QT dispersion. Circulation 1998;98:2160–7.
12. Lee KW, Kligfield P, Okin PM, Dower GE. Determinants of precordial QT dispersion in normal subjects. J Electrocardiol 1998;31 Suppl:128–33.
13. Kors JA, van Herpen G, van Bemmel JH. QT dispersion as an attribute of T-loop morphology. Circulation 1999;99:1458–63.
14. Punske BB, Lux RL, MacLeod RS, et al. Mechanisms of the spatial distribution of QT intervals on the epicardial and body surfaces. J Cardiovasc Electrophysiol 1999;10:1605–18.
15. Malik M, Acar B, Yap Y-G, Yi G, Hnatkova K, Camm AJ. QT dispersion does not represent electrocardiographic interlead heterogeneity of ventricular repolarization. J Cardiovasc Electrophysiol 2000;11:835–43.
16. Kors JA, de Bruyne MC, Hoes AW, et al. T axis as an indicator of risk of cardiac events in elderly people. Lancet 1998;352:601–4.
17. Zabel M, Acar B, Klingenheben T, Franz MR, Hohnloser SH, Malik M. Analysis of twelve-lead t wave morphology for risk stratification after myocardial infarction. Circulation 2000;102:1252–7.
18. Taran L, Szilagyi N. The measurement of the Q-T interval in acute heart disease. Bull St. Francis Sanatorium 1951;8:13.
19. McLaughlin NB, Campbell RWF, Murray A. Influence of T wave amplitude on automatic QT measurement. In: Computers in Cardiology 1995, IEEE Computer Society Press, 1995;777–80.
20. Murray A, McLaughlin NB, Bourke JP, Doig JC, Furniss SS, Campbell RWF. Errors in manual measurement of QT intervals. Br Heart J 1994;71:386–90.
21. Kors JA, van Herpen G. Measurement error as a source of QT dispersion: a computerised analysis. Heart 1998;80:453–8.
22. Watanabe Y. Purkinje repolarization as a possible cause of the U wave in the electrocardiogram. Circulation 1975;51:1030–7.
23. Lepeschkin E. Physiologic basis of the U wave. In: Schlant RC, Hurst JW, editors. Advances in Electrocardiography. New York and London: Grune and Stratton, 1972, 431–47.
24. Anzelevich C, Nesterenko VV, Yan GX. The role of M cells in acquired long QT syndrome, U waves and torsade de pointes. J Electrocardiol 1996;28 Suppl:131–8.
25. Yan G-Y, Antzelevich C. Cellular basis for the normal T wave and the electrocardiographic manifestations of the long-QT syndrome. Circulation 1998;98:1928–36.
26. Kautzner J, Yi G, Kishore R, et al. Interobserver reproducibility of QT interval measurement and QT dispersion in patients after acute myocardial infarction. Ann Noninvas Electrocardiol 1996;1:363–74.
27. Lepeschkin E, Surawicz B. The measurement of the Q-T interval of the electrocardiogram. Circulation 1952;VI:378–88.
28. Surawicz B. U wave: facts, hypotheses, misconceptions, and misnomers. J Cardiovasc Electrophysiol 1998;9:1117–28.
29. Spodick DH. Reduction of QT-interval imprecision and variance by measuring the JT interval. (editorial). Am J Cardiol 1992;72:103.
30. Zhou SH, Wong S, Rautaharju PM, et al. Should the JT rather than the QT interval be used to detect prolongation of ventricular repolarization? An assessment in normal conduction and in ventricular conduction defects. J Electricardiol 1992;25 Suppl:131–6.
31. Cowan JC, Yusoff K, Moore M, Amos PA, Gold AE, Bourke J. Importance of lead selection in QT interval measurement. Am J Cardiol 1988;61:83–7.
32. Mirvis DM. Spatial variation of QT intervals on normal persons and patients with acute myocardial infarction. J Am Coll Cardiol 1985;5:625–31.
33. Macfarlane PW, Devine B, Latif S, McLaughlin S, Shoat DB, Watts MP. Methodology of QRS interpretation in the Glasgow program. Methods Inf Med 1990;29:354–61.
34. Xue Q, Reddy S. New algorithms for QT dispersion analysis. Proceedings of the Marquette 14th ECG Analysis Seminar 1996;20–3.
35. Van Bemmel JH, Kors JA, Van Herpen G. Methodology of the modular ECG analysis system MEANS. Methods Inf Med 1990;29:346–53.
36. Lau CP, Freedman AR, Fleming S, Malik M, Camm AJ, Ward DE. Hysteresis of the ventricular paced QT interval in response to abrupt changes in pacing rate. Cardiovasc Res 1987;22:67–72.
37. de Bruyne MC, Hoes AW, Kors JA, Hofman A, van Bemmel JH, Grobbee DE. QTc dispersion predicts cardiac mortality in the elderly. The Rotterdam study. Circulation 1998;97:467–72.
38. Okin PM, Devereux RB, Howard BV, Fabsitz RR, Lee ET, Welty TK. Assessment of QT interval and QT dispersion for prediction of all-cause and cardiovascular mortality in American Indians. The Strong Heart Study. Circulation 2000;101:61–6.
39. Hodges M. Rate correction of the QT interval. Cardiac Electrophysiol Rev 1997;3:360–3.
40. Sagie A, Larson MG, Goldberg RJ, Bengtson JR, Levy D. An improved method for adjusting the QT interval for heart rate (The Framingham Heart Study). Am J Cardiol 1992;70:797–801.
41. Han J, Millet D, Chizzonitti B, Moe GK. Temporal dispersion of

recovery of excitability in atrium and ventricle as a function of heart rate. Am Heart J 1966;71:481–7.
42. Mitchell LB, Wyse DG, Duff HJ. Programmed electrical stimulation for ventricular tachycardia induction in humans. I. The role of ventricular functional refractoriness in tachycardia induction. J Am Coll Cardiol 1986;8:567–75.
43. Morgan JM, Cunningham D, Rowland E. Dispersion of monophasic action potential duration: demonstrable in humans after premature ventricular extrastimulation but not in steady state. J Am Coll Cardiol 1992;19:1244–53.
44. Maarouf N, Aytemir K, Gallagher M, Yap YG, Camm AJ, Malik M. Is QT dispersion heart rate dependent? What are the values of correction formulas for QT interval? (abstr). J Am Coll Cardiol 1999;33 Suppl A:113A–114A.
45. Zabel M, Woosley RL, Franz MR. Is dispersion of ventricular repolarization rate dependent? PACE 1997;20:2405–11.
46. Malik M, Camm AJ. Mystery of QTc interval dispersion. Am J Cardiol 1997;79:785–7.
47. Hnatkova K, Malik M, Yi G, Camm AJ. Adjustment of QT dispersion assessed from 12 lead electrocardiograms for different number of analysed electrocardiographic leads: comparison of stability of different methods. Br Heart J 1994;72:390–6.
48. Hailer B, Van Leeuwen P, Lange S, Pilath M, Wehr M. Coronary artery disease may alter the spatial dispersion of the QT interval at rest. Ann Noninvas Electrocardiol 1999;4:267–73.
49. Yi G, Guo X-H, Crook R, Hnatkova K, Camm AJ, Malik M. Computerised measurements of QT dispersion in healthy subjects. Heart 1998;80:459–66.
50. Day CP, McComb JM, Mathews J, Campbell RW. Reduction of QT dispersion by sotalol following myocardial infarction. Eur Heart J 1991;12:423–7.
51. Glancy JM, Garratt CJ, Woods KL, De Bono DP. Three-lead measurement of QTc dispersion. J Cardiovasc Electrophysiol 1995; 6:987–92.
52. Zareba W, Moss A. Dispersion of repolarization evaluated in three orthogonal-type electrocardiographic leads: L1, aVF, V2 (abstr). PACE 1995;18:895.
53. Saint Beuve C, Badilini F, Maison-Blanche P, Kedra A, Coumel P. QT dispersion: comparison of orthogonal, quasi-orthogonal, and 12-lead configurations. Ann Noninvas Electrocardiol 1999;4:167–75.
54. Macfarlane PW, McLaughlin SC, Rodger C. Influence of lead selection and population on automated measurement of QT dispersion. Circulation 1998;98:2160–7.
55. Kautzner J, Yi G, Camm AJ, Malik M. Short- and long-term reproducibility of QT, QTc, and QT dispersion measurement in healthy subjects. PACE 1994;17:928–37.
56. Perkiömäkki JS, Kiostinen MJ, Yli-Mäyry S, Huikuri HV. Dispersion of the QT interval in patients with and without susceptibility to ventricular tachyarrhythmias after previous myocardial infarction. J Am Coll Cardiol 1995;26:174–9.
57. Halle M, Huonker M, Hohnloser SH, Alivertis M, Berg A, Keul J. QT dispersion in exercise-induced myocardial hypertrophy. Am Heart J 1999;138:309–12.
58. Tran HT, Fan C, Tu WQ, et al. QT Measurement: a comparison of three simple methods. Ann Noninvas Electrocardiol 1998;3:228–31.
59. Malik M. Bradford A. Human precision of operating a digitizing board: implications for electrocardiogram measurement. PACE 1998;21:1656–62.
60. Yi G, Guo X-H, Crook R, Hnatkova K, Camm AJ, Malik M. Computerised measurements of QT dispersion in healthy subjects. Heart 1998;80:459–66.
61. McLaughlin NB, Campbell RWF, Murray A. Comparison of automatic QT measurement techniques in the normal 12 lead electrocardiogram. Br Heart J 1995;74:84–9.
62. Murray A, McLaughlin NB, Campbell RWF. Measuring QT dispersion: man versus machine. Heart 1997;77:539–42.
63. Savelieva I, Yi G, Guo X-H, Hnatkova K, Malik M. Agreement and reproducibility of automatic versus manual measurement of QT interval and QT dispersion. Am J Cardiol 1998;81:471–7.
64. Vloka ME, Babaev A, Ehlert FA, Narula DD, Steinberg JS. Poor correlation of automated and manual QT dispersion measurements in patients and normal subjects (abstr). J Am Coll Cardiol 1999;33 Suppl A:350A.
65. McLaughlin NB, Campbell RWF, Murray A. Accuracy of four automatic QT measurement techniques in cardiac patients and healthy subjects. Heart 1996;76:422–6.
66. Batchvarov V, Yi G, Guo X-H, Savelieva I, Camm AJ, Malik M. QT interval and QT dispersion measured with the threshold method depend on threshold level. PACE 1998;21:2372–5.
67. Zaidi M, Robert A, Fesler R, Derwael C, Brohet C. Dispersion of ventricular repolarization: a marker of ventricular arrhythmias in patients with previous myocardial infarction. Heart 1997;78:371–5.
68. Surawicz B. Will QT dispersion play a role in clinical decision-making? J Cardiovasc Electrophysiol 1996;7:777–84.
69. Goldner B, Brandspiegel HZ, Horwitz L, Jadonath R, Cohen T. Utility of QT dispersion combined with the signal-averaged electrocardiogram in detecting patients susceptible to ventricular tachyarrhythmia. Am J Cardiol 1995;76:1192–4.
70. Kautzner J, Malik M. QT dispersion and its clinical utility. PACE 1997;20:2625–40.
71. Statters DJ, Malik M, Ward DE, Camm AJ. QT dispersion: problems of methodology and clinical significance. J Cardiovasc Electrophysiol 1994;5:672–85.
72. Berul CI, Sweeten TL, Hill SL, Vetter VL. Provocative tests in children with suspect congenital long QT syndrome. Ann Noninvas Electrocardiol 1998;3:3–11.
73. Tutar H, Ocal B, Imamoglu A, Atalay S. Dispersion of QT and QTc interval in healthy children, and effects of sinus arrhythmia on QT dispersion. Heart 1998;80:77–9.
74. Macfarlane PW, McLaughlin SC, Devine B, Yang TF. Effects of age, sex, and race on ECG interval measurements. J Electrocardiol 1994;27:14–9.
75. Shah CP, Thakur RK, Reisdorff EJ, Lane E, Aufderheide TP, Hayes OW. QT dispersion may be a useful adjunct for detection of myocardial infarction in the chest pain center. Am Heart J 1998;136: 496–8.
76. Davey PP, Bateman J, Mulligan IP, Forfar C, Barlow C, Hart G. QT interval dispersion in chronic heart failure and left ventricular hypertrophy: relation to autonomic nervous system and Holter tape abnormalities. Br Heart J 1994;71:268–73.
77. Challapalli S, Lingamneni R, Horvath G, Parker M, Goldberger JJ, Kadish A. Twelve-lead QT dispersion is smaller in women than in men. Ann Noninvas Electrocardiol 1998;3:25–31.
78. Savelieva I, Camm AJ, Malik M. Gender-specific differences on QT dispersion measured in 1100 healthy subjects (abstr). PACE 1999; 22:885.
79. Savelieva I, Camm AJ, Malik M. QT dispersion should be adjusted for age: observations from 1096 normal subjects (abstr). J Am Coll Cardiol 1993;33 Suppl A:129A.
80. Zhang N, Ho TF, Yip WCL. QT dispersion in healthy Chinese children and adolescents. Ann Noninvas Electrocardiol 1999;4: 281–5.
81. Savelieva I, Camm AJ, Malik M. Do we need age-adjustment of QT dispersion? Observations from 1096 normal subjects (abstr). Heart 1999;81 Suppl 1:P47.
82. Macfarlane PW, on behalf of the WOSCOPS. QT dispersion—lack of discriminating power (abstr). Circulation 1998;98 Suppl:I-81.
83. Glancy JM, Garrat CJ, de Bono DP. Dynamics of QT dispersion during myocardial infarction and ischemia. Int J Cardiol 1996;57:55–60.
84. Ashikaga T, Nishizaki M, Arita M, et al. Effect of dipyridamole on QT dispersion in vasospastic angina pectoris. Am J Cardiol 1999;84: 807–10.
85. Sporton SC, Taggart P, Sutton PM, Walker JM, Hardman SM. Acute ischemia: a dynamic influence on QT dispersion. Lancet 1997;349:306–9.
86. Fei L, Goldman JH, Prasad K, et al. QT dispersion and RR variations on 12-lead ECGs in patients with congestive heart failure secondary to idiopathic dilated cardiomyopathy. Eur Heart J 1996; 17:258–63.
87. Pye M, Quinn AC, Cobbe SM. QT interval dispersion: a non-invasive marker of susceptibility to arrhythmia in patients with sustained ventricular arrhythmias? Br Heart J 1994;71:511–4.
88. Zaidi M, Robert A, Fesler R, Derwael C, Brohet C. Dispersion of ventricular repolarization in dilated cardiomyopathy. Eur Heart J 1997;18:1129–34.
89. Bonnar CE, Davie AP, Caruana L, et al. QT dispersion in patients

with chronic heart failure: beta-blockers are associated with a reduction in QT dispersion. Heart 1999;81:297–302.
90. Muir DF, Love MWA, MacGregor GD, McCann GP, Hillis WS. Athletic left ventricular hypertrophy is associated with increased QT dispersion: an observational study (abstr). J Am Coll Cardiol 1999;33 Suppl A:510A.
91. Mandecki T, Szulc A, Kastelik J, Mizia-Stec K, Szymanski L. The observation of the QT dispersion in left ventricular hypertrophy in weight lifters. Ann Noninvas Electrocardiol 1998;3:S18(abstr).
92. Simoncelli U, Rusconi C, Nicosia F, Drago F, Marchetti A. QT dispersion in endurance athletes. Int J Sports Cardiol 1998;7:63–7.
93. Davey PP, Bateman J, Mulligan IP, Forfar C, Barlow C, Hart G. QT interval dispersion in chronic heart failure and left ventricular hypertrophy: relation to autonomic nervous system and Holter tape abnormalities. Br Heart J 1994;71:268–73.
94. Ichkhan K, Molnar J, Somberg J. Relation of left ventricular mass and QT dispersion in patients with systemic hypertension. Am J Cardiol 1997;79:508–11.
95. Perkiömäki JS, Ikäheimo MJ, Pikkujämsä SM, et al. Dispersion of the QT interval and autonomic modulation of heart rate in hypertensive men with and without left ventricular hypertrophy. Hypertension 1996;28:16–21.
96. Maheshwari VD, Girish MP. QT dispersion as a marker of left ventricular mass in essential hypertension. Ind Heart J 1998;50: 414–7.
97. Tomiyama H, Doba N, Fu Y, et al. Left ventricular geometric patterns and QT dispersion in borderline and mild hypertension: their evolution and regression. Am J Hypertens 1998;11:286–92.
98. Özerkan F, Zoghi M, Gürgün C, Yavuzgil O, Kaylikçioglu, Önder R. QT dispersion in hypertensive patients who had normal coronary angiogram with or without left ventricular hypertrophy (abstr). Eur Heart J 1999;20 Suppl:85.
99. Yi G, Elliott P, McKenna WJ, et al. QT dispersion and risk factors for sudden cardiac death in patients with hypertrophic cardiomyopathy. Am J Cardiol 1998;82:1514–9.
100. Dritsas A, Sbarouni E, Gilligan D, Nihoyannopoulos P, Oakley CM. QT-interval abnormalities in hypertrophic cardiomyopathy. Clin Cardiol 1992;15:739–42.
101. Zaidi M, Robert A, Fesler R, Derwael C, Brohet C. Dispersion of ventricular repolarization in hypertrophic cardiomyopathy. J Electrocardiol 1996;29 Suppl:89–94.
102. Priori SG, Napolitano C, Diehl L, Schwartz PJ. Dispersion of the QT interval. A marker of therapeutic efficacy in the idiopathic long QT syndrome. Circulation 1994;89:1681–9.
103. Gavrilescu S, Luca C. Right ventricular monophasic action potentials in patients with long QT syndrome. Br Heart J 1978;40:1014–8.
104. Bonatti V, Rolli A, Botti G. Recording of monophasic action potentials of the right ventricle in long QT syndromes complicated by severe ventricular arrhythmias. Eur Heart J 1983;4:168–79.
105. Yap YG, Yi G, Aytemir K, Guo X-H, Camm AJ, Malik M. Comprehensive assessment of QT dispersion in various at risk groups including acute myocardial infarction, unstable angina, hypertrophic cardiomyopathy, idiopathic dilated cardiomyopathy, and healthy controls. PACE 1999;22:A38(abstr).
106. Zoghi M, Gürgün C, Ercan E, et al. QT dispersion in patients with different aetiology of left ventricular hypertrophy (abstr). Eur Heart J 1999;20 Suppl:335.
107. Halle M, Huonker M, Hohnloser SH, Alivertis M, Berg A, Keul J. QT dispersion in exercise-induced myocardial hypertrophy. Am Heart J 1999;138:309–12.
108. Mayet J, Kanagaratnam P, Shahi M, et al. QT dispersion in athletic left ventricular hypertrophy. Am Heart J 1999;137:678–81.
109. Bugra Z, Koylan N, Vural A, et al. Left ventricular geometric patterns and QT dispersion in untreated essential hypertension. Am J Hypertens 1998;11:1164–70.
110. Yap YG, Yi G, Guo X-H, Aytemir K, Camm AJ, Malik M. Dynamic changes of QT dispersion and its relationship with clinical variables and arrhythmic events after myocardial infarction (abstr). J Am Coll Cardiol 1999;33 Suppl A:107A.
111. Bennemeier H, Hartmann F, Giannitsis E, et al. Effects of primary angioplasty on the course of QT dispersion after myocardial infarction and its association with infarct size. PACE 1999;22:A19(abstr).
112. Paventi S, Bevilacqua U, Parafati MA, Di Luzio E, Rossi F, Pelliccioni PR. QT dispersion and early arrhythmic risk during acute myocardial infarction. Angiology 1999;50:209–15.
113. Puljevic D, Smalcelj A, Durakovic Z, Goldner V. Effects of post-myocardial infarction scar size, cardiac function, and severity of coronary artery disease on QT interval dispersion as a risk factor for complex ventriculararrhythmia. PACE 1998;21:1508–16.
114. Schneider CA, Voth E, Baer FM, Horst M, Wagner R, Sechtem U. QT dispersion is determined by the extent of viable myocardium in patients with chronic Q-wave myocardial infarction. Circulation 1997;96:3913–20.
115. Clarkson PBM, Naas AAO, McMahon A, MacLeod C, Struthers AD, MacDonald TM. QT dispersion in essential hypertension. QJM 1995;88:327–32.
116. Kohno I, Takusagawa M, Yin D, et al. QT dispersion in dipper- and nondipper-type hypertension. Am J Hypertens 1998;11:280–5.
117. Bugra Z, Koylan N, Vural A, et al. Left ventricular geometric patterns and QT dispersion in untreated essential hypertension. Am J Hypertens 1998;11:1164–70.
118. Higham PD, Furniss SS, Campbell RWF. QT dispersion and components of the QT interval in ischemia and infarction. Br Heart J 1995;73:32–6.
119. Yap YG, Yi G, Guo X-H, Aytemir K, Camm AJ, Malik M. Dynamic changes of QT dispersion and its relationship with clinical variables and arrhythmic events after myocardial infarction (abstr). J Am Coll Cardiol 1999;33 Suppl A:107A.
120. Glancy JM, Garrat CJ, de Bono DP. Dynamics of QT dispersion during myocardial infarction and ischemia. Int J Cardiol 1996;57:55–60.
121. Aytemir K, Bavafa V, Ozer N, Aksoyek S, Oto A, Ozmen F. Effect of balloon inflation-induced acute ischemia on QT dispersion during percutaneous transluminal coronary angioplasty. Clin Cardiol 1999; 22:21–4.
122. Okishige K, Yamashita K, Yoshinaga H, et al. Electrophysiological effects of ischemic preconditioning on QT dispersion during coronary angioplasty. J Am Coll Cardiol 1996;28:70–3.
123. Tarabey R, Sukenik D, Milnar J, Somberg JC. Effect of intracoronary balloon inflation at percutaneous transluminal coronary angioplasty on QT dispersion. Am Heart J 1998;135:519–22.
124. Yi G, Crook R, Guo H, Staunton A, Camm AJ, Malik M. Exercise-induced changes in the QT interval duration and dispersion in patients with sudden cardiac death after myocardial infarction. Int J Cardiol 1998;63:271–9.
125. Sporton SC, Taggart P, Sutton PM, Walker JM, Hardman SM. Acute ischemia: a dynamic influence on QT dispersion. Lancet 1997;349:306–9.
126. Michelucci A, Padeletti L, Frati M, et al. Effects of ischemia and reperfusion on QT dispersion during coronary angioplasty. PACE 1996;19:1905–8.
127. Gabrielli F, Balzotti L, Bandiera A. QT dispersion variability and myocardial viability in acute myocardial infarction. Int J Cardiol 1997;61:61–7.
128. Nakajima T, Fujimoto S, Uemura S, et al. Does increased QT dispersion in the acute phase of anterior myocardial infarction predict recovery of left ventricular wall motion? J Electrocardiol 1998;31:1–8.
129. Schneider CA, Voth E, Baer FM, Horst M, Wagner R, Sechtem U. QT dispersion is determined by the extent of viable myocardium in patients with chronic Q-wave myocardial infarction. Circulation 1997;96:3913–20.
130. Moreno FL, Villanueva T, Karagounis LA, Anderson JL. Reduction of QT interval dispersion by successful thrombolytic therapy in acute myocardial infarction. TEAM-2 study investigators. Circulation 1994;90:94–100.
131. Karagounis LA, Anderson JL, Moreno FL, Sorensen SG, for the TEAM-3 Investigators. Multivariate associates of QT dispersion in patients with acute myocardial infarction: primacy of patency status of the infarct-related artery. Am Heart J 1998;135:1027–35.
132. Kelly RF, Parillo JE, Hollenberg SM. Effect of coronary angioplasty on QT dispersion. Am Heart J 1997;134:399–405.
133. Szydlo K, Trusz-Gluza M, Drzewiecki J, Wozniak-Skowerska I, Szczogiel J. Correlation of heart rate variability parameters and QT interval in patients after PTCA of infarct related coronary artery as an indicator of improved autonomic regulation. PACE 1998;21:2407–10.
134. Choi K-J, Lee C-W, Kang D-H, et al. Change of QT dispersion

after PTCA in angina patients. Ann Noninvas Electrocardiol 1999; 4:195–9.
135. Brooksby P, Robinson PJ, Segal R, Klinger G, Pitt B, Cowley AJC, on behalf of the ELITE study group. Effects of losartan and captopril on QT dispersion in elderly patients with heart failure. Lancet 1999;534:395–6.
136. Mayet J, Shahi M, McGrath K, et al. Left ventricular hypertrophy and QT dispersion in hypertension. Hypertension 1996;28:791–6.
137. Lim PO, Nys M, Naas AAO, Struthers AD, Osbakken M, MacDonald T. Irbesartan reduces QT dispersion in hypertensive individuals. Hypertension 1999;33:713–8.
138. Karpanou EA, Vyssoulis GP, Psichogios A, et al. Regression of left ventricular hypertrophy results in improvement of QT dispersion in patients with hypertension. Am Heart J 1998;136:765–8.
139. Gonzalez-Juanatey JR, Garcia-Acuna JM, Pose A, et al. Reduction of QT and QTc dispersion during long-term treatment of systemic hypertension with enalapril. Am J Cardiol 1998;81:170–4.
140. Priori SG, Napolitano C, Diehl L, Schwartz PJ. Dispersion of the QT interval. A marker of therapeutic efficacy in the idiopathic long QT syndrome.Circulation 1994;89:1681–9.
141. Zaputovic L, Mavric Z, Zaninovic-Jurjevic T, Matana A, Bradic N. Relationship between QT dispersion and the incidence of early ventricular arrhythmias in patients with acute myocardial infarction. Int J Cardiol 1997;62:211–6.
142. Papandonakis E, Tsoukas A, Christakos S. QT dispersion as a noninvasive arrhythmogenic marker in acute myocardial infarction. Ann Noninvas Electrocardiol 1999;4:35–8.
143. Zareba W, Moss AJ, le Cessie S. Dispersion of ventricular repolarization and arrhythmic cardiac death in corornary artery disease. Am J Cardiol 1994;74:550–3.
144. Pye M, Quinn AC, Cobbe SM. QT interval dispersion: a noninvasive marker of susceptibility to arrhythmia in patients with sustained ventricular arrhythmias? Br Heart J 1994;71:511–4.
145. Shulan Z, Yin'an S, Huixian H. Prediction value of ventricular arrhythmia of patients with acute myocardial infarction by QT dispersion. J Xi'An Med Univ 1998;19:616–7.
146. Zabel M, Klingenheben T, Franz MR, Hohnloser SH. Assessment of QT dispersion for prediction of mortality or arrhythmic events after myocardial infarction. Circulation 1998;97:2543–50.
147. Tavernier R, Jordaens L. Repolarization characteristics and sudden death after myocardial infarction: a case control study (abstr). J Am Coll Cardiol 1999;33 Suppl A:146A.
148. Moenning G, Haverkamp W, Schulte H, et al. Prognostic value of QT-interval and -dispersion in apparently healthy individuals. Results from the Münster heart study (PROCAM) (abstr). J Am Coll Cardiol 1999;33 Suppl A:333A.
149. Lee KW, Okin PM, Kligfield P, Stein KM, Lerman BB. Precordial QT dispersion and inducible ventricular tachycardia. Am Heart J 1997;134:1005–13.
150. Gillis AM, Trabousli M, Hii JTY, et al. Antiarrhythmic drug effects on QT interval dispersion in patients undergoing electropharmacologic testing for ventricular tachycardia and fibrillation. Am J Cardiol 1998;81:588–93.
151. Berul CI, Michaud GF, Lee VC, Hill SL, Estes M III, Wang PJ. A comparison of T-wave alternans and QT dispersion as noninvasive predictors of ventricular arrhythmias. Ann Noninvas Electrocardiol 1999;4:274–80.
152. Zabel M, Klingenheben T, Sticherling C, Franz MR, Hohnloser SH. QT-dispersion does not predict inducibility or adequate device treatment in patients with malignant ventricular tachyarrhythmias (abstr). Eur Heart J 1998;19 Suppl:600.
153. Armoundas AA, Osaka M, Mela T, et al. T-Wave alternans and dispersion of the QT interval as risk stratification markers in patients susceptible to sustained ventricular arrhythmias. Am J Cardiol 1998; 82:1127–9.
154. De Sutter J, Tavernier R, van de Wiele C, et al. QT dispersion is not related to infarct size or inducibility in patients with coronary artery disease and life threatening ventricular arrhythmias. Heart 1999;81: 533–8.
155. Fu G-S, Meissner A, Simon R. Repolarization dispersion and sudden cardiac death in patients with impaired left ventricular function. Eur Heart J 1997;18:281–9.
156. Galinier M, Vialette J-C, Fourcade J, et al. QT interval dispersion as a predictor of arrhythmic events in congestive heart failure. Importance of aetiology. Eur Heart J 1998;19:1054–62.
157. Anastasiou-Nana MI, Nanas JN, Karagounis LA, et al. Dispersion of QRS and QT in patients with advanced congestive heart failure: relation to cardiac and sudden cardiac death mortality (abstr). Eur Heart J 1999;20 Suppl:117.
158. Brooksby P, Robinson PJ, Segal R, Klinger G, Pitt B, Cowley AJC, on behalf of the ELITE study group. Effects of losartan and captopril on QT dispersion in elderly patients with heart failure. Lancet 1999;534:395–6.
159. Pitt B, Segal R, Martinez FA, et al. Randomised trial of losartan versus captopril in patients over 65 with heart failure. Lancet 1997;349:747–52.
160. Pitt B, Poole-Wilson PA, Segal R, et al., on behalf of the ELITE II investigators. Effect of losartan compared with captopril on mortality in patients with symptomatic heart failure: randomised trial—the Losartan Heart Failure Survival Study ELITE II. Lancet 2000;355: 1582–7.
161. Brendorp B, Elming H, Køber L, Malik M, Jun L, Torp-Pedersen C, for the Diamond Study Group. Prognostic implications of QT interval and dispersion in patients with congestive heart failure (abstr). Eur Heart J 1999;20 Suppl:89.
162. Brooksby P, Batin PD, Nolan J, et al. The relationship between QT intervals and mortality in ambulant patients with chronic heart failure. The United Kingdom Heart Failure Evaluation and Assessment of Risk Trial (UK-HEART). Eur Heart J 1999;20:1335–41.
163. Radmanabhan S, Amin J, Silvet H, Pai RG. QT dispersion has no impact on mortality in patients with moderate and severe left ventricular dysfunction: results from a cohort of 2263 patients (abstr). J Am Coll Cardiol 1999;33 Suppl A:107A.
164. Galinier M, Balanescu S, Fourcade J, et al. Prognostic value of arrhythmogenic markers in systemic hypertension. Eur Heart J 1997;18:1484–91.
165. Buja G, Miorelli M, Turrini P, Melacini P, Nava A. Comparison of QT dispersion in hypertrophic cardiomyopathy between patients with and without ventricular arrhythmias and sudden death. Am J Cardiol 1993;72:973–6.
166. Miorelli M, Buja G, Melacini P, Fasoli G, Nava A. QT-interval variability in hypertrophic cardiomyopathy patients with cardiac arrest. Int J Cardiol 1994;45:121–7.
167. Baranowski R, Malecka L, Poplawska W, et al. Analysis of QT dispersion in patients with hypertrophic cardiomyopathy—correlation with clinical data and survival (abstr). Eur Heart J 1998;19 Suppl:428.
168. Yi G, Elliott P, McKenna WJ, et al. QT dispersion and risk factors for sudden cardiac death in patients with hypertrophic cardiomyopathy. Am J Cardiol 1998;82:1514–9.
169. Maron BJ, Leyhe MJ, Gohman TE, Casey SA, Crow RS, Hodges M. QT dispersion is not a predictor of sudden cardiac death in hypertrophic cardiomyopathy as assessed in an unselected patient population (abstr). J Am Coll Cardiol 1999;33 Suppl A:128A.
170. Priori SG, Napolitano C, Diehl L, Schwartz PJ. Dispersion of the QT interval. A marker of therapeutic efficacy in the idiopathic long QT syndrome. Circulation 1994;89:1681–9.
171. Surawicz B. Long QT: good, bad, indifferent and fascinating. ACC Current J Rev 1999;19–21.
172. Moss AJ. Drugs that prolong the QT interval: regulatory and QT measurement issues from the United States and European perspectives. Ann Noninvas Electrocardiol 1999;4:255–6.
173. Hii JTY, Wyse DG, Gillis AM, Duff HJ, Solylo MA, Mitchell LB. Precordial QT interval dispersion as a marker of Torsade de Pointes. Disparate effects of class Ia antiarrhythmic drugs and amiodarone. Circulation 1992;86:1376–82.
174. Hohnloser SH, van de Loo A, Baedeker F. Efficacy and proarrhythmic hazards of pharmacologic cardioversion of atrial fibrillation: prospective comparison of sotalol versus quinidine. J Am Coll Cardiol 1995;26:852–8.
175. Day CP, McComb JM, Mathews J, Campbell RWF. Reduction in QT dispersion by sotalol following myocardial infarction. Eur Heart J 1991;12:423–7.
176. Cui G, Sen L, Sager P, Uppal P, Singh BN. Effects of amiodarone, sematilide, and sotalol on QT dispersion. Am J Cardiol 1994;74: 896–900.
177. Hohnloser SH, van de Loo A, Kalusche D, Arendts W, Quart B.

Does sotalol-induced alteration of QT-dispersion predict drug effectiveness or proarrhythmic hazards? (abstr). Circulation 1993;88 Suppl I:397.
178. Dritsas A, Gilligan D, Nihoyannopoulos P, Oakley CM. Amiodazrone reduces QT dispersion in patients with hypertrophic cardiomyopathy. Int J Cardiol 1992;36:345–9.
179. Meierhenrich R, Helguera ME, Kidwell GA, Tebbe U. Influence of amiodarone on QT dispersion in patients with life-threatening ventricular arrhythmias and clinical outcome. Int J Cardiol 1997;60: 289–94.
180. Grimm W, Steder U, Menz V, Hoffmann J, Maisch B. Effect of amiodarone on QT dispersion in the 12-lead standard electrocardiogram and its significance for subsequent arrhythmic events. Clin Cardiol 1997;20:107–10.
181. Van de Loo A, Klingenheben T, Hohnloser SH. Amiodarone therapy after sotalol-induced torsade de pointes: prolonged QT interval and QT dispersion in differentiation of pro-arrhythmic effects. Z Kardiol 1994;83:887–90.
182. Tran HT, Chow MS, Kluger J. Amiodarone induced torsades de pointes with excessive QT dispersion following quinidine induced polymorphic ventricular tachycardia. PACE 1997;20:2275–8.
183. Yadav A, Paquette M, Newman D, Connolly SJ, Dorian P. Amiodarone is associated with increased QT dispersion but low mortality in a CIDS cohort. PACE 1999;22:896(abstr).
184. Faber TS, Zehender M, Krahnfeld O, Daisenberger K, Meinetz T, Just H. Propafenone during acute myocardial ischemia in patients: a double-blind, randomized, placebo-controlled study. J Am Coll Cardiol 1997;29:561–7.
185. Trusz-Gluza M, Świderska E, Śmieja-Jaroczynska B, Wozniak-Skowerska I, Filipecki A. Factors influencing dispersion of repolarization under antiarrhythmic treatment. Ann Noninvas Electrocardiol 1998;3:S18(abstr).
186. Houltz B, Darpö B, Edvardsson N, et al. Electrocardiographic and clinical predictors of torsades de pointes induced by almokalant infusion in patients with chronic atrial fibrillation of flutter: a prospective study. PACE 1998;21:1044–57.
187. Sedwick ML, Rasmussen HS, Cobbe SM. Effects of the class III antiarrhythmic drug dofetilide on ventricular monophasic action potential duration and the QT interval dispersion in stable angina pectoris. Am J Cardiol 1992;70:1432–7.
188. Brum J, Alkhalidi H, Karam R, Marcello S. Effects of Azimilide, an IKs/IKr blocking anti arrhythmic on QT and QTc dispersion, in patients with ventricular tachycardia (VT). PACE 1999;22: A13(abstr).
189. Parikka H, Toivonen L, Naukkarinen V, et al. Decreases by magnesium of QT dispersion and ventricular arrhythmias in patients with acute myocardial infarction. Eur Heart J 1999;20:111–20.
190. Leonardo F, Fragasso G, Rosano GMC, Pagnotta P, Chierchia SL. Effect of atenolol on QT Interval and dispersion in patients with Syndrome X. Am J Cardiol 1997;80:789–90.
191. Bonnar CE, Davie AP, Caruana L, et al. QT dispersion in patients with chronic heart failure: beta-blockers are associated with a reduction in QT dispersion. Heart 1999;81:297–302.
192. Shimizu W, Antzelevitch C. Cellular and ionic basis for T-Wave alternans under long-QT conditions. Circulation 1999;99:1499–1507.
193. Abildskov JA, Burgess MJ, Urie PM, Lux RL, Wyatt RF. The unidentified information content of the electrocardiogram. Circ Res 1977;40:3–7.
194. Horan LG, Flowers NC, Brody DA. Principal factor waveforms of the thoracic QRS complex. Circ Res 1964;XV:131–45.
195. Priori SG, Mortara DW, Napolitano C, et al. Evaluation of the spatial aspects of T-wave complexity in the long-QT syndrome. Circulation 1997;96:3006–12.
196. Yi G, Prasad K, Elliott P, Sharma S, Guo X, McKenna WJ, Malik M. T wave complexity in patients with hypertrophic cardiomyopathy. PACE 1998;21:2382–6.
197. De Ambroggi LD, Aime E, Ceriotti C, Rovida M, Negroni S. Mapping of ventricular repolarization potentials in patients with arrhythmogenic right ventricular dysplasia. Principal component analysis of the ST-T waves. Circulation 1997;96:4314–8.
198. Kors JA, de Bruyne MC, Hoes AW, et al. T axis as an indicator of risk of cardiac events in elderly people. Lancet 1998;352:601–4.
199. Acar B, Yi G, Hnatkova K, Malik M. Spatial, temporal and wavefront direction characteristics of 12-Lead T wave morphology. Med Biol Eng Comput 1999;37:574–84.