QT dispersion: time for an obituary?

See page 1023 for the article to which this Editorial refers

During the past decade, studies of QT dispersion\([1]\) have become popular and numerous publications have reported some physiological and/or clinical value of QT dispersion measurement. Among others, increased QT dispersion was observed to be associated with QT interval prolongation due to drugs with known proarrhythmic properties and to be less increased on drugs with a low incidence of proarrhythmia\([2,3]\), to predict mortality in general epidemiological studies\([4,5]\); and to identify patients who are at greater risk after surviving acute myocardial infarction\([6]\). Treatment-related decrease of QT dispersion was reported to mark therapeutic efficacy in the idiopathic long QT syndrome\([7]\). More recently, however, seriously conducted studies have been published challenging the clinical usefulness of QT dispersion assessment\([8–10]\). Indeed, for most published reports, the normal values have still not been well established, the sensitivity and specificity of abnormal values are substantially overlapping. Thus, the whole area of physiological and practical clinical utility of QT dispersion assessment is controversial.

Moreover, despite different expressions of QT dispersion\([11,12]\), the measurement suffers from a poor reproducibility, both in terms of repeated measurement of the same electrocardiogram (ECG), irrespective of whether by the same or different observer, and in terms of repeated ECGs in the same subject. This might also be one of the reasons why, even in studies reporting very strong statistical results, the normal and abnormal values are substantially overlapping.

Despite the number of publications, no significant improvement in the technology has really been made since 1996 when Dr Surawicz concluded in his review\([13]\) that QT dispersion failed to pass four mandatory tests for a clinical utility. The measurement methodology has still not been standardized, the normal values have still not been well established, the sensitivity and specificity of abnormal values remain low, and the validity of the relevant background hypotheses is still being discussed.

These controversies divided cardiac researchers into strong believers and strong disbelievers of QT dispersion. A number of scientific articles start from a preamble that QT dispersion is an established technology of validated use while, at the same time, serious publications denounced it as ‘the greatest fallacy in electrocardiography in the 1990s’\([14]\).

Perhaps the believers and disbelievers represent two different poles of scientific and research attitude. Some believe that the original concept of QT dispersion is correct merely because the technology can be applied to existing ECGs, and that the results more or less frequently (irrespective of the reproducibility) statistically distinguish between clinically defined groups. Others point to the flaws of QT dispersion measurement and, based on the deep understanding of the physics involved in the ECG lead theory, argue that QT dispersion does not exist and that the published reports are based on misunderstanding and unfounded speculations.

To resolve this controversy, one should perhaps start by trying to answer the question of what is QT dispersion.

What is QT dispersion and what is not?

The group of the late Professor Campbell rekindled the concept of QT dispersion at the end of the 1980s\([1]\). Following their original suggestion, there has been speculation ever since that the increased range of QT interval measurements is caused by a regional heterogeneity of the duration of ventricular repolarization. In more detail, it has been proposed that different leads of the standard 12-lead ECG project the repolarization signals of different myocardial regions differently and that, consequently, increased dispersion is a measure of regional differences in the repolarization duration. Indeed, studies comparing QT dispersion with the dispersion (that is, the range) of the duration of monophasic action potentials found a general correlation supporting this hypothesis\([15,16]\).

However, more recent studies have shown that a similar value of QT dispersion is measured in full 12-lead ECGs and in their reconstruction from the rectangular XYZ leads, in which the separate contribution by different myocardial regions has been effectively filtered out\([17]\). It has also been shown that QT dispersion values correlate with parameters of vectorcardiographic T loop morphology\([18]\). Based on these results, it has been proposed that the different projections of the T wave vector into the different ECG leads are essential and that an increase of QT dispersion merely means an unusual projection of a more complicated T wave loop.

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Most recently, an attempt has been made to measure the ECG components independent of the vectorcardiographic T loop, speculating that such components more closely represent regional myocardial heterogeneity. While such non-dipolar components differ between different clinical different groups, their correlation with QT dispersion is almost non-existent[19].

After all, studies showing a correlation between the dispersion of monophasic action potentials and the QT dispersion measured in surface ECGs do not actually prove that both these technologies address the same entity. If an increased heterogeneity exists in the durations of monophasic action potentials, the repolarization sequence is clearly more disturbed, the vectorcardiographic T wave loop is more abnormal, the projections of the loop into the standard ECG leads are more complicated, the localization of the T wave offset in individual leads is more difficult, and an increased QT dispersion is measured.

The practical difficulty in localizing T wave offset may actually also play an important role. More abnormal T wave patterns are known to cause greater difficulties in QT interval measurement. Hence, a measurement bias cannot be excluded leading to increased QT dispersion values in ECGs where the T wave offset is less clearly defined. Since such cases are more frequent in abnormal than normal ECGs, a statistically significant difference may easily be contributed to, if not directly achieved by a bias in the measurement error.

Based on the most recent studies, it seems safe to conclude that the original concept of portraying QT dispersion as a direct measure of the regional heterogeneity of myocardial refractoriness is seriously flawed. At the same time, disproving this concept is not a good reason for stating that ‘QT dispersion does not exist’. While QT dispersion is not an expression of regional heterogeneity of myocardial refractoriness, the measurement of QT dispersion seems to be an approximate expression of repolarization abnormalities. Certainly, it is a very imprecise and imperfect expression of such abnormalities and it suffers from all the problems that were already mentioned (reproducibility, stability, etc.). However, it seems fair to say that we presently have no decent and widely available alternative to address repolarization abnormalities in 12-lead ECGs.

**What is the meaning of QT dispersion studies?**

If we accept the concept that increased QT dispersion is a primitive quantifier of what is otherwise called ‘unspecific T wave changes’, it is not unreasonable to express the measurement numerically and to subject it to statistical evaluation. True, we must not forget that the measurement of QT dispersion is usually dependent on the operator and on the quality of the analysed ECGs, that it is poorly reproducible and that the electrophysiological background is only very loosely defined. However, if we understand all this, QT dispersion is better than the verbal description of more or less expressed unspecific T wave changes. In other words, even a primitive, imprecise and imperfect approach is better than nothing.

Having this understanding in mind, we are in a clear position to interpret experimental studies that involve QT dispersion assessment. In this issue James _et al._ present an elegant study showing that psychological stress increases QT dispersion in patients with coronary artery disease but not in patients in whom coronary artery disease has not been documented[20]. If we read ‘approximate measure of repolarization abnormalities’ instead of ‘QT dispersion’, the study makes a lot of sense. Coronary artery disease is likely to make the ventricular myocardium more susceptible to various provocations and it is fully plausible that in patients with ischaemic disease, serious repolarization abnormalities can be induced by acute physiological stress. The authors of the study are right in speculating that this might be the mechanism by which psychological stress is proarrhythmic in some cardiac patients. Their observation is another important piece for the mosaic of our apprehension of the importance of repolarization abnormalities in arrhythmogenesis.

The value of the message portrayed by James _et al._ does not seem to be particularly reduced by the fact that their study used a measurement technology the electrophysiological basis of which is controversial and the precision of which is almost non-existent. True, if the study were repeated, it is highly unlikely that the same numerical values would have been observed and the same statistical significances achieved. Nevertheless, that is a problem of the presently available methodology for repolarization assessment rather than a problem of the pathophysiological observation and of its clinical relevance.

Since QT dispersion is a very crude and very imprecise method for the assessment of repolarization abnormalities, it is plausible to speculate that minute repolarization changes might be induced by acute psychological stress even in non-ischaemic hearts where the changes are too tiny to be detected by a technology as imperfect as QT dispersion. Hence, it is the difference in the response observed between patients with and without ischaemic heart disease which is the true message by James _et al._
What is the future of QT dispersion?

The slowly emerging understanding that QT dispersion is nothing more than a very crude way of expressing repolarization abnormalities has clear implications for further advances of the field of study. By relying on the localization of the end of the T wave in individual ECG leads, QT dispersion is not only imprecise, it also ignores the morphologies of the T wave. The same value of QT dispersion may easily be measured in ECGs in which the T wave patterns are normal and in cases where the T wave is grossly abnormal including inverted, notched and biphasic morphologies.

Hence, other more precise and comprehensive descriptors of abnormalities of myocardial repolarization are badly needed. QT dispersion should certainly not be taken as a gold standard for a non-invasive estimate of repolarization abnormalities suitable for judging new concepts of repolarization assessment. On the contrary, once a more focused technology for repolarization assessment is developed and once it is made widely available to the research community, the prospect of QT dispersion as a technology for repolarization assessment enabled by high quality digital ECGs, QT dispersion seems to be a small step in the correct direction.

Despite the serious difficulties with the concept of QT dispersion and despite the fact that a clear publication bias exists towards positive findings, the huge number of studies showing some meaningful results with QT dispersion measurements cannot be dismissed lightly. Repolarization is important!

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References
