Editorial

Dispersion of Ventricular Repolarization
Reality? Illusion? Significance?

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The QT interval is considered to be a surrogate of cellular action potential duration. However, it yields a limited view of the complex electrogenesis of the ventricular repolarization (VR). Evidence of T-wave end inequality among surface ECG traces back to Wilson et al,[1] and it was recently revived by the concept of dispersion.[2] Because of its apparent simplicity, QT dispersion became fashionable, and a growing literature is now devoted to its potential prognostic interest. The study by Zabel et al[3] seems timely to temper the enthusiasm. In a prospectively collected cohort of patients, it offers evidence that avoiding technical biases of measurement, QT dispersion is not a prognostic marker. This contrasts with the confirmation that ejection fraction, heart rate variability, and simply heart rate are indeed good predictors of events. It suggests some reflections about the correct and comprehensive use of a concept that still needs to be validated.

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Technical Considerations

Measurement of QT Duration

QT interval can be measured manually or with dedicated algorithms. The performances of the 2 approaches were compared in a remarkable study conducted by the late Jos Willems.[4] The aim was to assess the diagnostic performances of computerized systems.[5] In view of the interobserver and intraobserver variability in determining wave recognition points, an elaborate reviewing scheme was devised to obtain a group estimate that should define the "truth," ultimately serving as a standard for computer measurement. Five experts defined individually the P- and QRS-wave onset and offset and the T-wave offset. The database was formed of 250 digitized (500 Hz) 12 standard leads and Frank XYZ leads, including a 25% proportion of normal hearts and a variety of ventricular hypertrophies and infarctions but no bundle-branch block or long-QT syndrome.

The interexpert variation was expressed as 2 SD of the difference between the median and the individual and final referee estimates. In the P wave, the variation was 10.2 ms for the onset and 12.7 ms for the offset. In QRS, it was 6.5 ms for the onset and 11.6 ms for the offset. Compared with these values, the variation for the T-wave offset was 30.6 ms, with an intraindividual variability of 8 ms calculated from 3 readings of 26 ECGs.

Such a discrepancy in the manual QT duration measurement is not much of a surprise. Improved homogeneity should be expected from automated systems. Comparing some 19 systems, SDs as great as 30 ms were found for the determination of the T-wave offset, compared with 6 ms for the QRS onset.[4] Thus, the approximation of QT determination is of the same order of magnitude for man and machine. In fact, the small but crucial improvement one can expect from a fully automated system is its intrinsic 100% reproducibility. The problem is not the intrasystem but the intersystem variability. At variance with human evaluation, intersystem variations are more systematic, and conceivably their discrepancies can be evaluated and compensated.

One might expect a better reproducibility in normal ECGs, but this is not so.[6] From 3-time measurements performed by 2 observers, QT dispersion is highly nonreproducible, both between subsequent recordings (25% to 35% relative error) and between observers (28% to 33%). T-wave morphology contributes greatly to the poor interobserver reproducibility. In 6 independent observers of 30 ECGs, remarkable differences in the selection between 7 morphological categories were found, with a 30% to 40% interobserver relative error in QT dispersion.[7] Thus, complex VR patterns probably explain the spectrum of values in the literature. Kautzner et al[7] conclude that "in the absence of more objective criteria for separation of the T and U waves, the measures of QT dispersion appear to be unstable and of questionable statistical properties." We share their concerns.

QT Dispersion and Body Surface Mapping

Evaluation of QT dispersion from the 12-lead ECG is a surrogate of body surface QRST integral mapping, an approach that offered somewhat overlooked although important contributions. Mirvis[8] used 150 electrodes in 50 subjects and measured QT intervals automatically. The QT dispersion, a term not yet coined at the time, was 59.4±12.9 ms. Formulating the results in terms of absolute shortest (384±40 ms) and longest (414±30 ms) QT values was, in fact, more informative to express the difference between normal subjects and patients with infarcts. In anterior infarcts (n=15), there was a significant prolongation of the longest QT intervals (476±32 ms) and no difference in the shortest. The same applied to inferior infarcts, and interestingly, the distribution of the longest QT intervals differed according to the infarct location, thus suggesting that there was indeed some information on the spatial distribution of VR.

In pathological T waves, any evaluation of their duration is further complicated by their abnormal morphology. This applies to the long-QT syndrome, in which De Ambroggi et al[9] and then Day et al[2] started observations about augmented

The opinions expressed in this editorial are not necessarily those of the editors or of the American Heart Association.

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(*Circulation.* 1998;97:2491-2493.)

QT dispersion. Sylven et al[10] had already compared normal subjects and patients with QT prolongation (>440 ms) through 120 signal-averaged torso surface leads. Using return to isoelectric line for T-wave end determination, interlead QT_c variability was 22% in normal subjects and 32% in patients ($P<0.001$). However, if a method was used that discarded the leads in which U waves could not be identified from the nadir between T and U, there was no longer any difference between groups.

Theoretical Considerations

Fundamentals of Electrocardiography: Appearance and Reality of QT Dispersion

Not only is QT dispersion difficult to measure, but its significance is also poorly understood. Some basic notions of electrocardiography and electrogenesis should be recalled. Thus, the information contained in limb leads is redundant. If any 2 of the 6 are recorded, the other 4 can be derived according to Einthoven's equation (III=II−I) and to the relationships between bipolar and unipolar leads (I=VL−VR, II=VF−VR, and III=VF−VL). This by no means implies that QT duration cannot be different in all 6 leads, for the reasons expressed below.

The entire information about the ventricular electrical activity is contained in a single image, the spatial QRS and T loops that can be characterized by their morphology, planarity, speed, etc. They can be projected on XYZ axes to form QRS-T complexes or on the frontal, sagittal, and horizontal planes to display the loops of the vectorcardiogram.

A single image like the spatial loop cannot generate any "dispersion." Any projection of the loop implies the loss of a part of the information, and looking at its dispersion in various projections may be just a way to characterize the lost information. Every time the tip of the vector progresses perpendicular to the axis or to the plane, its projection becomes nil, as if the electrical activity had disappeared. For instance, if during the last 40 ms preceding the end of VR there is a positivity in lead II and an equal negativity in lead I, according to Einthoven's equation the QT duration in III will look 40 ms shorter in this lead. Therefore, dispersion may be either an illusion or a reality, depending on the conditions of recording. It is most probably an illusion in the frontal plane, in which one cannot expect that a 2-lead recording and 4 derived leads would actually provide any information on local electrical activity. On the other hand, it probably is a reality in the horizontal plane, in which the unipolar leads V_1 through V_6 are supposed to reflect the local activity. In theory, this applies only to epicardial leads, and for QRS the intrinsic deflection defines the moment of the local depolarization. An extrapolation is admitted for precordial leads with the label "intrinsecoid" rather than intrinsic. Still, if these facts and concepts have been validated for depolarization, the same does not apply to repolarization.

VR Process: Potential Mechanisms of QT Dispersion

The timing of VR termination in a given point results from the combination of 2 factors one cannot dissociate in surface ECG: the timing of activation and the local duration of recovery. The latter can be explored by measuring the refractory periods[11] and/or recording monophasic action potentials.[12] The action potential duration tends to be shorter at the epicardium and basal regions and longer at the endocardium and apex. Conceivably, the 2 factors can compensate for each other, and a delayed activation with a shorter action potential may give the same QT interval as a normally activated zone with a prolonged action potential. Yuan et al[13] proposed to dissociate the 2 factors by combining the information obtained from QRS and the monophasic action potential.

Zabel et al[14] found a significant correlation (Pearson coefficient of 0.80) between the JT and QT dispersion and the dispersion of action potential duration at 90% repolarization and recovery time. This may suggest that the duration of recovery is the factor that predominates over the spread of activation in the genesis of QT dispersion. These authors also proposed new ECG dispersion indexes, and one would easily agree that considering 2 extremes of QT is the simplest but somewhat simplistic approach of dispersion. Our group proposed[15] to consider morphological aspects of the spatial T-wave loop to dissociate various patterns contained in the entity of QT dispersion, a possibility if one thinks of localized or diffuse VR abnormalities. Conventional QT dispersion was significantly larger than in normal subjects in 2 pathological populations, namely, patients post myocardial infarction and those with long-QT syndrome, that could not be discriminated in this regard. Spatial T-wave loops extracted from XYZ data showed a loss of planarity and an increased roundness in the 2 pathological groups. The roundness was more pronounced in the infarcted group ($P=0.02$) and the planarity more altered in the long-QT syndrome ($P=0.04$). An interesting approach of morphology was recently proposed,[16] and apparently the principal-component analysis applied to 12-lead recordings adequately quantifies the VR complexity.

QT dispersion addresses macroscopic rather than microscopic inhomogeneity. The potential interest of detecting susceptibility to arrhythmias was highlighted some time ago[8,11] by use of the concept formulated by Han and Moe.[17] These authors, however, were referring to inhomogeneity of recovery at the cellular level, and extrapolation to ECG may not be adequate. In any case, the concept of inhomogeneity and its implication in the term of dispersion can apply differently in heart diseases as different as myocardial infarction, cardiomyopathy, and long-QT syndrome. It remains to be seen whether the existence of layers of M cells, in particular, macroscopic areas,[18] may help to fill the gap between diffuse and localized electrophysiological disturbances.

Future of the Concept: Noninvasive Electrophysiology

The difficulty of measuring QT and the still not really defined significance of QT dispersion explain why we are facing contradictory conclusions concerning the prognostic value of this parameter. During the period extending from the 1960s to the present, conventional surface ECG was somewhat neglected, and priority was given to invasive electrophysiology. We think that the future of clinical electrophysiology resides in the ECG, on the condition that we use it properly. We have to merge the computer facilities now offered to the ECG and our better knowledge of electrophysiology to develop noninvasive electrophysiology.

This process started successfully for the 2 first components of the P-QRS-T complex and should continue with the third one. The P component gives access to cardiac rate, and it is unnecessary to state how heart rate and heart rate variability proved to be useful in exploring the autonomic nervous system, a major component of cardiac tachyarrhythmias. The QRS component forms the arrhythmogenic substrate, and the detection of late potentials is the noninvasive corollary of the invasive localization of earliest depolarization. Analyzing the last milliseconds of the VR is probably as important as scrutinizing the first milliseconds of depolarization. The T wave is now quantifiable, and the morphology certainly is even more important than the duration.[19] It is not really scientific to draw conclusions from a QT dispersion of >50 ms, when the precision of the measurement simply approximates the same order of magnitude. Just looking at this aspect of the problem, however, it would be inappropriate to reject a good concept because of the technical difficulties of its application.

Future of the Evaluation of VR

The evaluation of VR must be improved. Technically, only digitized recordings should be considered, a necessity that occasionally would favor prospective studies. A decisive advantage of computer techniques is a reproducible deviation from the humanly defined reference.[4,5] An adequate quantification of the QT dispersion would probably help to better understand its significance through its pathophysiological variations, on the condition that we get rid of nonrelevant information based on redundance and illusion. There is no doubt that resurgence of QRST integral mapping would be suitable, although this technique obviously suffers from practical limitations in its clinical applications.

Another development may be to extend the notion of QT dispersion to QT dynamicity, thus looking at the 2 dimensions formed by space and time. QT dynamicity is to the T wave what heart rate variability is to the P wave. QT dynamicity contains 2 important bits of information. The behavior of the cellular action potential is reflected by QT rate-dependence, and the autonomic nervous system modulates both QT duration and rate-dependence. Studying QT dynamicity presupposes selective manipulation of thousands of QRS-T complexes over 24 hours to extract relevant information. This can be achieved, and in contrast to the study of QT dispersion, the processing offers the definite advantage of measuring changes of duration rather than absolute values. Any algorithm can reliably detect changes on the order of the millisecond simply because potential deviations from reference are fixed. Our experience in the long-QT syndrome[20] shows that QT dynamicity is a reliable marker of the probability of events. If an alteration of the spatial distribution of VR indeed exists in this syndrome, a dispersion of dynamicity, ie, a different behavior of various regions, should be looked for because the underlying phenomenon should logically have time as well as space dimensions. More generally, any coincidence between different QT duration and/or QT morphology (including QT alternans and postpause changes) and/or dynamicity of VR would provide further evidence that spatial dispersion is not an illusion but a reality and that collecting, processing, and using the information properly would further validate the concept.

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KEY WORDS: Editorials ■ ventricles ■ electrophysiology