The Unidentified Information Content of the Electrocardiogram

J.A. Abildskov, Mary Jo Burgess, Paul M. Urie, Robert L. Lux, and Roland F. Wyatt

DEVELOPMENT of practical recording methods for the human electrocardiogram was rapidly followed by important medical applications. Electrocardiography was established as the major means of classifying disturbances of cardiac rhythm and an important aid in the recognition of myocardial disease including infarction. Applications have been sufficiently significant to result in widespread use of the method and there have been continuing technological improvements and extensions of the method's utility. At the present time and as presently used, electrocardiography is one of the major medical diagnostic methods.

Despite considerable utility, it is unlikely that the full medical significance of electrocardiographic examination has been achieved. A variety of theoretic considerations together with supporting experimental and clinical observations suggest that the record may contain information of equal or even greater medical significance than that now obtained. This communication will review some of these considerations and observations. Material will be presented under the headings of regional cardiac examination, prognostic utility, and extended diagnostic applications. None of these represent totally new objectives for electrocardiographic examination but each offers substantial possibilities for improved use of the technique. The material reviewed does not include all areas in which improvements of electrocardiography are likely and should be viewed only as selected examples. Much of the material is necessarily speculative although some theoretic and/or clinical and experimental support for the speculations in each area will be furnished.

Regional Cardiac Examination

For most clinical purposes, the electrocardiographic system has been considered to consist of a single fixed location dipole and a homogeneous conductive medium usually assumed to have a simple geometric form. Such conceptions underlie not only vectorcardiography in the sense of a particular display method, but vector-based interpretations of scalar leads including those of the usual 12-lead examination. These representations of the electrocardiographic system have had great clinical utility despite many obvious defects. Simple representations of the system have permitted rational interpretation of some body surface leads and systematic classification of findings in the leads. They have provided a basis for widespread and reasonably uniform clinical use of the electrocardiogram with the important consequence of accumulating sufficient data for correlation with various clinical states. The considerable utility of simple representations of the electrocardiographic system should not however, obscure their defects. In particular, efforts to further improve the already important technique of electrocardiography should not be limited by excessively simplified models.

Development of an electrocardiographic examination of specific cardiac regions is excluded by any approaches in which the heart is represented as a single fixed location dipole. In effect, such approaches assume the heart to have no volume, and selective evaluation of particular cardiac areas is not possible using these approaches. This conclusion is not contradicted by the fact that myocardial infarcts can often be successfully localized as anterior, lateral, etc., using present electrocardiographic methods. The electrocardiographic classification of infarcts in terms of cardiac location is achieved by different effects of variously located lesions on the direction and magnitude of vectors representing the heart as a dipole source. It is not accomplished by leads with selective sensitivity to particular cardiac areas and does not constitute regional cardiac examination.

The identification of specific leads, each having predominant and specified sensitivity to a particular cardiac region, would be the most direct method of regional cardiac examination. Practical means to achieve such leads are not evident, however. An alternate approach is the use of extensive arrays of electrodes. Electrocardiograms from a large number of body surface sites undoubtedly contain redundant information but also include whatever information from various local cardiac regions is present on the body surface.

There is no doubt that some local cardiac information appears on the body surface. Multiple potential maxima or minima appear in both normal and abnormal body surface potential maps obtained from a sufficient number of electrodes. Whether information is provided by these multiple maxima or minima is excluded by all single-vector
analyses of the electrocardiogram, since, by definition, the vector represents a single potential maximum and minimum. Whether nondipolar electrocardiographic information from the body surface has medical value and how to recognize and use such information are complex questions. Available studies provide evidence of more precise recognition of hypertrophy, some congenital cardiac lesions, and the location of anomalous conduction paths in the Wolff-Parkinson-White (WPW) syndrome than is achieved with less extensive electrocardiographic examination.\textsuperscript{6-18} Possible approaches to the interpretation of extensive electrocardiographic examinations range from the evaluation of individual leads to qualitative and quantitative analyses of isopotential maps. Other possibilities are interpretation in terms of multiple fixed cardiac sources or a moving cardiac source.\textsuperscript{19-24} Whatever display and analytic methods prove most appropriate and useful, many technical advances, experimental findings, and clinical correlative studies will be necessary to develop a practical electrocardiographic examination of individual cardiac regions. If such an examination can be achieved, the clinical merit seems obvious. Possibilities such as recognition and localization of regional hypertrophy, localization of repolarization abnormalities, and others including definition of the size and severity of ischemic lesions are among those offered by such examination.

Prognostic Utility

With limited exceptions, clinical use of the electrocardiogram has been restricted to diagnosis. It is likely, however, that the record also contains prognostic information particularly with respect to cardiac rhythm. A variety of cardiac states in which vulnerability to arrhythmias is high are characterized by greater than normal disparity of recovery times.\textsuperscript{25-29} The degree of inequality of ventricular repolarization, determined both by the activation sequence and by differences in the duration of intracellular action potentials in different portions of the myocardium, is also one of the determinants of ST-T waveform. It therefore seems plausible that states of increased susceptibility to arrhythmia may be recognizable from electrocardiographic waveform. Some clinical observations supporting this possibility have been made. Relations between mortality as well as ventricular dysrhythmias and the magnitude of S-T segment displacement associated with acute myocardial infarction have been reported.\textsuperscript{30-31} High peaked T waves in the electrocardiogram are frequent in the early stages of acute myocardial infarction when the incidence of ventricular fibrillation is greatest.\textsuperscript{32} These considerations and observations suggest the possibility of useful relations between electrocardiographic waveform and cardiac conditions in which the heart is susceptible to arrhythmias.

It is unlikely that a broadly useful index of susceptibility to arrhythmia can be based on a single electrocardiographic feature or a small number of electrocardiographic leads. The established relation between vulnerability to arrhythmia and disparate ventricular recovery time concerns recovery in localized cardiac areas. Detection of locally disparate recovery by electrocardiography is described in the preceding section. An appropriate measure of local recovery based on electrocardiographic waveform also will be required. The exact nature of such an index has not been established but several considerations suggest that the QRST area is a promising measurement for this purpose. That quantity was proposed by Wilson et al.\textsuperscript{33} under the title of the “ventricular gradient” as one which would be independent of ventricular activation sequence if ventricular recovery properties remained constant. Although there is some conflict in reported findings it now appears that QRST area is not quantitatively independent of activation sequence.\textsuperscript{34-35} There is also evidence that recovery properties are not constant with varied activation sequences. The probable mechanism of altered recovery properties is that of different electrotonic interactions with varied activation orders.\textsuperscript{36-38}

The rationale for considering QRST area as an index of inequalities of ventricular recovery time and of vulnerability to arrhythmia can be illustrated by a hypothetical situation. If two unipolar local leads showed identical QRS complexes but different T waves, these differences would reflect differences of repolarization in the cardiac areas sampled by the leads. The QRST areas in the leads would differ and, in the situation described, differences would be due to repolarization only. If QRS complexes in the leads differed, T waves could differ as a result of both differences of activation orders and differences of repolarization in the areas sampled. Electrotonic or other influences affecting repolarization differently in the two cardiac areas would be among the factors contributing to differences of the QRST area in the two local leads. It is actual differences in repolarization, including those due to different electrotonic effects, which are likely to be related to vulnerability to arrhythmia.

At present it is not certain whether body surface electrocardiographic leads contain sufficiently local cardiac information to provide a useful index of disparate recovery related to susceptibility to arrhythmia. The most appropriate electrocardiographic index of vulnerability also is uncertain although, as described, QRST area has promise for this purpose. Figure 1 shows records which illustrate this promise. The records shown are maps of QRST area from 192 simultaneously recorded electrocardiographic leads from the torso of a dog. QRST areas were determined by computer processing in which potentials sampled at 1-msec intervals were algebraically summed. Body surface points at which QRST area is equal are joined by the “isoarea” contours shown. Panel A shows the iso-area map during atrial drive with a cycle length of 400 msec. Panels B and C, respectively, show maps during ventricular drive at the same cycle length from the left and right ventricles via catheter-mounted stimulating electrodes. Despite the different activation orders which resulted in expectedly different QRS and T waveforms, the QRST iso-area maps are grossly similar. In comparison to the map during supraventricular activation, peak areas are displaced slightly toward the stimulating electrodes during ventricular drive. This effect is compatible with electrotonic effects during ventricular repolarization. Excitation near the stimulus site occurs early in the cardiac cycle and the obligatory
FIGURE 1 QRST iso-area maps obtained from 192 electrodes symmetrically distributed on the torso of a closed-chest dog. Maps are displayed with the chest represented as an unrolled cylinder. The top and left edges of each map correspond to electrode columns nearest the posterior midline, and a vertical axis at the center of each map would correspond to the midsternal line. Electrocardiograms from the 192 electrodes were recorded simultaneously and data in each map are from a single QRST complex. Each contour line joins points with equal QRST area, and contours are plotted at a scale of 10 mV msec. Panel A shows the QRST iso-area map during atrial drive at a cycle length of 400 msec. Panels B and C, respectively, show QRST iso-area maps during drive at the same cycle length from electrodes in the left and right ventricular cavities. Major features of the maps are similar although the form of QRS and T waves from which maps were computed differed markedly. There are systematic differences in the details of the three maps of which the most evident is displacement of the peak area toward the ventricular stimulus sites in records B and C in comparison to the supraventricular record shown in A.

recovery times in the surrounding tissue by electrotonic interaction. If this condition were reflected in body surface electrocardiograms it would be expected to shift the positive pole of the QRST area map toward the stimulus site. The fact that such a shift occurs, as illustrated in Figure 1, itself suggests that local cardiac information concerning inequalities of recovery can be detected by electrocardiographic examination.

Evidence that electrocardiographic manifestations of locally unequal recovery may be useful in recognizing states in which the heart is susceptible to arrhythmia is shown in Figure 2. The figure shows QRST area maps during premature beats elicited from the right ventricular stimulus site used to obtain the QRST iso-area map shown in panel C of Figure 1. Both QRST iso-area maps shown in Figure 2 were obtained from premature beats initiated during a regular drive at 400-msec cycle lengths. The map shown in panel A of Figure 2 is that of a premature beat late in the cardiac cycle, and that in panel B is from an early premature beat which is the second of a pair of premature beats. This condition has been demonstrated to enhance vulnerability to arrhythmia. The late premature beat illustrated in panel A differs in details from that obtained during regular drive but retains the major characteristics of single positive and negative poles with approximately the same body surface locations. The map during the early premature beat shows multiple poles which are explicable on the basis of local inequalities of repolarization.

The maps shown in Figures 1 and 2 are intended only to illustrate the possible utility of electrocardiographic waveform as an index of disparate ventricular repolarization and susceptibility to arrhythmia. A clinically useful index of such susceptibility would require systematic studies of the QRST area and other electrocardiographic parameters in a variety of arrhythmia prone states. It also will be necessary to devise quantitative descriptors which differentiate normal states and those of enhanced susceptibility to arrhythmia. In particular, it will be necessary to take account of the already established fact that cardiac events may be manifest by single positive and negative body surface poles despite their origin from multiple cardiac regions. With respect to local inequalities of ventricular repolarization, this means that not all states associated with vulnerability to arrhythmia are likely to be evidenced by multipolar QRST iso-area maps. The identification of...
means to separate dipolar body surface maps of cardiac potentials due to multiple cardiac areas from those due to events in single areas is a major problem for the development of a regional cardiac examination in general as well as for the specific purpose of recognizing vulnerability to arrhythmia.

**Extended Diagnostic Applications**

One significant recent advance in this area is the use of intracardiac electrograms for detection of specialized tissue potentials. These are already in active clinical use and will not be reviewed here. There are also other substantial possibilities for improved electrocardiographic diagnosis and one of these will be summarized.

At present, diagnostic interpretation of electrocardiographic waveform makes use of the cardiac excitation sequence which exists in a particular patient. In most cases, the ventricular activation sequence is "supraventricular," and diagnostic conclusions based on QRS waveform involve comparison with the waveform of normal subjects. The development of practical means of artificial pacing from ventricular sites makes it reasonable to consider deliberate use of the technique and the resulting ectopic QRS waveform for diagnostic purposes. The usefulness of such a procedure has not been established nor its indications defined but some examples suggesting its possible utility exist.

The best known example is that of septal infarction in the presence of complete left bundle branch block. Such infarction may not be clearly manifest when the conduction defect is absent but is sometimes recognizable by Q waves in leads I, AVL, V5, and V6 when left bundle branch block is present. In contrast, electrocardiographic recognition of infarcts in other locations in the presence of left bundle branch block is well known to be difficult. These conditions provide evidence that significant cardiac lesions which are not apparent by electrocardiographic findings with a particular activation sequence may be recognizable during a different activation order.

Another example of the possible utility of electrocardiographic waveform during altered activation patterns is provided by the ST-T deflection. Prolongation of the QT interval in a particular lead has been demonstrated to occur with some agencies which reduce ventricular recovery time. Such paradoxical behavior of the QT interval associated with ventricular pacing is longer than that during supraventricular activation by an amount which cannot be accounted for by the differences of QRS duration. These findings establish that electrocardiographic information which is not evident with a particular activation order and recovery sequence can be exposed by another activation sequence.

The examples given seem sufficient to suggest serious consideration of studies designed to examine the diagnostic utility of the electrocardiographic waveform during induced alterations of cardiac activation sequence.

**Conclusions**

Some of the areas in which improved clinical use of electrocardiography seem likely are the development of regional cardiac examination, prognostic applications, and expanded diagnostic uses by controlled activation orders. Regional cardiac examination is being developed using extensive mapping of body surface potentials and by identification of lead systems which minimize redundant information. It is likely that the electrocardiogram has prognostic utility with respect to identifying cardiac states of greater than normal vulnerability to arrhythmia. Deliberate alteration of ventricular activation sequence by ventricular pacing offers the possibility of exposing electrical events from cardiac areas which do not affect electrocardiographic waveform during normal excitation. These and other approaches can be expected to increase substantially the already considerable clinical utility of electrocardiography.

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