

ACC POLICY STATEMENT

Standards for Analysis of Ventricular Late Potentials Using High-Resolution or Signal-Averaged Electrocardiography:

A Statement by a Task Force Committee of the European Society of Cardiology, the American Heart Association, and the American College of Cardiology

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Improved methods for detecting individual patients recovering from myocardial infarction who are at high risk for sudden cardiac death are essential for reducing mortality from ventricular arrhythmias. During the past decade, many investigators have recorded low-amplitude, high-frequency waveforms and altered frequency components in the terminal QRS complex in laboratory animals (1,2), and patients prone to sustained ventricular tachycardia (3-16). These microvolt level waveforms are termed *late potentials*. The reported prevalence of abnormal signals has ranged from 60% to 90%, depending on the method of signal processing, the definition of late potentials, and the patient groups studied (6,8,10). Conversely, the incidence of abnormal signals in normal subjects is quite low and has been reported from 0% to 7% when essentially the same recording techniques were used (17,18).

The technique for recording these abnormal signals is called *high-resolution electrocardiography*. Since the technical aspects of the available commercial systems differ considerably, standardization of recording units and the algorithm of analysis by the use of standard signals and digitized electrocardiogram (ECG) examples is strongly suggested to make results of these devices comparable. The impact of high-resolution electrocardiography on patient care will ultimately depend on its capabilities in identifying patients at high risk of ventricular tachyarrhythmias.

The purpose of this task force committee was to establish standards for data acquisition and analysis and to define the role of high-resolution electrocardiography in clinical decision making. In many areas, a consensus on standards was easily achieved. However, the committee recognizes that high-resolution electrocardiography is a new field that is under continuing investigation. Accordingly, the committee believes that recommendations in some areas are premature and additional studies are required before firm guidelines can be established.

Pathophysiological Basis of Late Potentials

Results of laboratory (19-30) and clinical (31-37) studies implicate reentrant mechanisms, at least in part, in the genesis of sustained ventricular tachycardia complicating ischemic heart disease. Abnormal ventricular conduction during sinus rhythm has been observed in regions bordering the infarct (31,32,38-43) and appears temporally related to the development of ventricular tachycardia (20-22,39-43).

Myocardial activation may be delayed because the pathway of excitation is lengthened, conduction velocity is slowed, or both. Structural features may be critical determinants of delayed activation (40,41). Clinically, most myocardial infarcts do not result in complete transmural necrosis (42). The amount of surviving myocardium is variable and may be located in subepicardial, subendocardial, and intramural regions. Islands of fibrosis create barriers that lengthen the excitation pathway. The increased separation of myocardial bundles and disruption of their parallel orientation by fibrosis distort ventricular activation (40,41). However, the action potentials of surviving myocardial cells may appear relatively normal (40). Extracellular electrograms recorded from the endocardial surface from such bundles usually have small amplitudes because of the intervening

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layers of fibrous tissue and small diameter of the muscle bundles. When individual bundles are separated by connective tissue septa, heterogeneous patterns of activation may occur and may result in fragmentation of local extracellular electrograms (40,42).

Late potentials on the body surface appear to be a manifestation of delayed activation of myocardium. They have been recorded during experimental infarction in dogs and corresponded in time with fragmented and delayed electrograms recorded from the epicardium (1,2,20,21). In patients, late potentials recorded from the body surface have been accompanied by late, fragmented electrograms recorded directly from the heart (42,44). Although fragmented electrograms can be recorded from most patients with remote infarction, including those with normal high-resolution ECGs, delayed activation is more profound and detectable at more cardiac sites from patients with sustained ventricular tachycardia, compared with those without sustained ventricular tachycardia (31,44-46).

The finding of fragmented local electrograms during direct catheter mapping or late potentials on the body surface may indicate that the substrate for reentry is present (44). Although late potentials seem to represent a fixed substrate for reentrant excitation, additional triggering mechanisms, such as one or more premature beats, as well as other modulating factors, such as the autonomic nervous system or ischemia, may also be required for spontaneous manifestation of reentry.

Technical Considerations

Electrodes and Electrocardiographic Leads

Silver-silver chloride electrodes have the lowest half-cell potential and are the electrodes of choice. The subject's skin should be thoroughly cleansed with alcohol or another solvent and abraded to decrease impedance, which generates noise. Ideally, impedance should be measured and be less than 1,000 Ω .

Most studies in the time domain have used a bipolar X, Y, and Z lead system, which the committee recognizes as a standard (6). The X lead should be positioned at the fourth intercostal space in both midaxillary lines. The Y lead should be positioned on the superior aspect of the manubrium and on either the upper left leg or left iliac crest. The Z lead should be at the fourth intercostal space (V_2 position), with the second electrode directly posterior on the left side of the vertebral column. Positive electrodes are left, inferior, and anterior.

The results of high-resolution electrocardiography are lead dependent. Accordingly, criteria and approaches established with one lead system may not be applicable to other systems. The Frank leads and modified uncorrected orthogonal leads have been used in the frequency domain (47). Additional studies are required to determine the optimum lead system.

Amplifiers and A/D Conversion

Electrocardiographic signals should be recorded with a low-noise amplifier. The American Heart Association standards concerning leakage current should be followed (48,49). The amplifiers need not be protected against damage during defibrillation since high-resolution electrocardiography is not used for arrhythmia monitoring. Notch filters for power line interference should not be used. The minimum band pass should be from 0.5 Hz to 250 Hz, and the voltage calibration should be accurate to $\pm 2\%$. The range of linearity for input signals should not be less than ± 2.5 mV.

Standard gain and calibration are also necessary for quantifying absolute differences in the magnitudes of specific frequencies and are necessary for relating changes in specific frequencies to the cardiac source when using Frank or other corrected ECG leads.

Data should be sampled at no less than 1,000 Hz and A/D converted with at least 12-bit precision. All ECG leads should be recorded and converted concurrently. Although there is no definitive evidence to support the concept that frequencies above 500 Hz contribute to the differentiation of patient groups, sampling below 1,000 Hz may preclude recovery of potential signals of interest.

Signal Averaging

The signal-averaging technique requires that a new beat first be aligned against previous beats (i.e., template) before averaging. The computer algorithm that facilitates the alignment should be capable of excluding ectopic beats or grossly noisy signals. Testing of new beats should be performed across all input leads. The input beat should be aligned by matching it against a template of averaged beats. If cross correlation is used for alignment, then correlation of at least 40 msec should be performed on the most rapidly changing part (upstroke and downstroke) of the QRS complex, and a correlation of greater than 98% should be required for acceptance. Beats immediately after a rejected beat should be rejected as well. Ideally, the input data and the template beat should be displayed as well as the proportion of the number of rejected beats. Signal averaging of all leads should be calculated in real time, and the system should be able to average at least 100 beats/min. There should be a permanent means of storage for the averaged waveforms.

High-frequency signals are attenuated during signal averaging if alignment of incoming beats is not exact (trigger jitter) (50). Trigger jitter, measured with an artificial QRS complex, should be less than 1.0 msec and ideally, 0.5 msec.

Noise Reduction

Adequate noise reduction is crucial for analysis of high-resolution ECGs (51). The extent of noise reduction primarily depends on the number of cycles averaged, the baseline level of noise at the start of the study session, and the type

of filters used. Careful preparation of the skin, patient relaxation, and warm surroundings are essential for minimizing patient-generated noise.

For time-domain analysis, the committee recommends that noise be measured in the averaged signal over an interval of at least 40 msec in the ST or TP segment with a four-pole Butterworth filter. With this approach, noise should be less than 1 μV with a 25 Hz high-pass cutoff or less than 0.7 μV with a 40 Hz high-pass cutoff as measured by the root mean square method from a vector magnitude of the X, Y, and Z leads. The segment for noise level analysis should be determined automatically. The inherent noise level of the recording should be low so that adequate noise reduction can be achieved by averaging 50–300 beats. Averaging a greater number of beats to obtain adequate noise reduction indicates that baseline noise is excessive for optimum recording.

Guidelines for noise measurements with other filters or frequency analysis have not yet been established. Ideally, background noise should first be characterized as a function of frequency. The noise level and method of determination should be stated in all studies.

Filter Characteristics

The band pass and characteristics of the filter are crucial to time-domain results since they determine the configuration and amplitude of the ECG signals to be analyzed (52). The bidirectional filter has been used in most studies in the time domain (6). This filter was designed to avoid ringing and other artifacts and was derived from a four-pole Butterworth filter (24 dB/octave). A high-pass corner frequency of 25 or 40 Hz is most commonly used. Because controversy continues over which cutoff is best, the committee recommends that the high-pass corner frequency be programmed by the user.

The committee does not want to exclude development or implementation of other filters that may improve detection of late potentials. Implementation of new filters will necessitate that normal and abnormal values be redefined since results obtained with one mode of signal processing may not be comparable to those obtained with other processing techniques.

For studies with frequency analysis, the band pass, at a minimum, should be 0.5–300 Hz. With a 1,000 Hz sampling rate, aliasing of frequencies above 500 Hz occurs. An infinite-impulse response low-pass filter of 250 Hz may distort phase below 250 Hz. No notch filters for power line interference should be incorporated into the system's hardware or software.

Ambulatory Electrocardiographic Tapes

Guidelines for deriving high-resolution electrocardiograms from Holter tapes have yet to be established, although early experience with this approach is promising (53).

Data Analysis

Time-Domain Analysis

Results of most studies have been based on analysis of a vector magnitude of the filtered leads, $\sqrt{x^2 + y^2 + z^2}$, called the *filtered QRS complex* (6). The committee recognizes the filtered QRS complex as one standard. The end of the filtered QRS complex is defined as the midpoint of a 5 msec segment in which mean voltage exceeds the mean noise level plus three times the standard deviation of the noise sample. The end point and onset of the filtered QRS complex should be verified visually, and the system should allow manual adjustment of the automatically determined end points. Analysis should include determination of 1) the filtered QRS duration (6); 2) root mean square voltage of the terminal 40 msec of the filtered QRS (6), and 3) amount of time that the filtered QRS complex remains below 40 μV (54). The definition of a late potential and the scoring of a high-resolution ECG as normal or abnormal have not yet been standardized. Representative criteria include that a late potential exists (using 40 Hz high-pass bidirectional filtering) when 1) the filtered QRS complex is greater than 114 msec, 2) there is less than 20 μV of signal in the last 40 msec of the vector magnitude complex, and 3) the terminal vector magnitude complex remains below 40 μV for more than 38 msec (55,56). Other criteria have been used, and their predictive value varies with the specific criterion applied and the prevalence of disease in the population studied. For example, a late potential was defined as the last 40 msec of the vector magnitude complex of less than 25 μV at 25 Hz and less than 16 μV at 40 Hz high-pass filtering. Each laboratory must define its own normal values.

Although the committee recognizes analysis of vector magnitude as having the largest volume of comparative publications, it is anticipated that further refinements and other approaches may improve the diagnostic power of the high-resolution ECG. The high-resolution electrocardiography system should be flexible enough to allow incorporation of new developments; these developments may include other types of filters, analysis of individual leads, alternate definitions of the end points of QRS, or of ECG intervals other than the terminal 40 msec of the filtered QRS complex. The differences in the algorithms for defining the end of QRS seem to be responsible for the discordance between various devices (57,58).

Frequency Analysis

A sequence generated by sampling a time-domain signal like the ECG can be represented in the frequency domain by taking the fast Fourier transform. Even though the informational content in time- and frequency-domain representations of a periodic waveform is equivalent, the extent to which each can depict components of interest depends on the signal being analyzed. The Fourier transform is a complete description of the ECG and contains information that

may not be seen in the output of a particular fixed-band filter. Frequency analysis offers potential advantages for identification and characterization of signals that differentiate patients with from those without sustained ventricular tachycardia. Most studies have calculated the fast Fourier transform to estimate scalar-lead spectra of the terminal QRS and ST segment of signal-averaged Frank X, Y, Z or uncorrected orthogonal leads (11-16,47,59). The results have often been expressed as indexes of the relative contributions of specific frequencies that comprise these ECG segments. A window function such as the four-term Blackman-Harris window has been used to diminish spectral leakage caused by edge discontinuities.

The development of frequency analysis of high-resolution ECGs is proceeding rapidly (14,47,59-63). Key issues that affect the spectra of ECG signals are being investigated (64). For example, the frequency content of ECG signals is spatially variable and thus lead-dependent. Indexes derived from spectra of uncorrected leads may not be comparable to end points or approaches developed using corrected leads. Analysis of multiple segments (spectrotemporal mapping) may allow better separation between noise and late potentials (14,60). The value of autoregressive models of spectral estimation (65,66) and analysis of the entire cardiac cycle with methods that obviate window functions are currently being determined (62,63). Accordingly, the committee believes it is premature to standardize this approach at present.

Beat-to-Beat Analysis

Ensemble signal averaging is predicated on the assumption that signals of interest are reproducible throughout the averaging process. Electrophysiological abnormalities may change on a beat-to-beat basis, resulting in a failure of signal-averaged recordings to identify changes related to arrhythmogenesis. Results of pilot studies have indicated the feasibility of detecting ventricular late potentials using beat-to-beat analysis of ECG signals (67,68). Adequate noise reduction remains a major challenge. Noise may be reduced by spatial averaging of data from a number of closely spaced electrode sites. This approach is limited by torso size, electrode size, and the perimeter of the chest field having similar polarity. Additional methods of signal-to-noise enhancement are required. At present, the committee believes it is premature to recommend single-beat analysis for clinical use, although the committee is optimistic about its ultimate applicability.

Potential Indications for Use in Patients

Vulnerability to Sustained Ventricular Tachycardia

Retrospective studies have demonstrated distinguishing features in the high-resolution ECG that differentiate postinfarction patients with and without sustained ventricular tachycardia (3,6-16,47,54,60,69-75). Several prospective studies in postmyocardial infarction patients have confirmed

the increased likelihood of spontaneous sustained ventricular tachycardia or sudden cardiac death in patients recovering from myocardial infarction who have an abnormal high-resolution ECG (76-83). Results of multivariate analysis have indicated that risk stratification based on the high-resolution ECG is independent of more traditional determinants of risk that include left ventricular ejection fraction or the presence and complexity of ventricular ectopy (72). Based on results of published studies, 14-29% of patients recovering from myocardial infarction with abnormal high-resolution ECGs will experience sustained ventricular tachycardia within the first year, compared with only 0.8-4.5% of those with a normal high-resolution ECG (84). Another 3.6% to 40% of patients with late potentials will die suddenly compared with 0% to 4.3% of patients without late potentials (84). Moreover, the predictive accuracy of the high-resolution ECG can be increased by combining its results with measures of left ventricular function (72,75,79,83). Thus, the high-resolution ECG is a sensitive, noninvasive method for risk stratification of patients recovering from myocardial infarction. However, the optimum time after myocardial infarction for recording the high-resolution ECG for this purpose has not been defined (85-87). Some studies suggest that recordings obtained during the second week after myocardial infarction have the highest predictive accuracy for arrhythmic events (83).

At present, sufficient data are not available for using time-domain analysis for detecting vulnerability to sustained ventricular arrhythmias among patients manifesting right or left bundle branch block patterns during sinus rhythm (83). Based on results obtained from patients with known sustained ventricular tachycardia, frequency analysis may offer promise for identifying patients at risk for sustained ventricular tachycardia regardless of the presence or absence of bundle branch block during sinus rhythm (14-16,47).

The relatively low positive predictive accuracy of the high-resolution ECG in postmyocardial infarction patients emphasizes the need for continued methodological refinements that will increase its diagnostic power. More important, improved understanding of the interaction of other factors, including autonomic tone, residual ischemia, electrolyte imbalance, and ventricular ectopy with the electrophysiological/anatomic derangements detected by analysis of the high-resolution ECG should further increase the predictive accuracy of this promising noninvasive approach.

Risk stratification of patients with remote infarction and nonsustained ventricular tachycardia appears promising. Studies have demonstrated that patients with abnormal high-resolution ECGs are more prone to inducible sustained monomorphic ventricular tachycardia (75,88-90). Prospective studies of patients with remote myocardial infarction and spontaneous nonsustained ventricular tachycardia in which the end point of follow-up is spontaneous ventricular tachycardia, ventricular fibrillation, or sudden cardiac death have recently been reported and suggest that the high-resolution ECG could be used for risk stratification and

management of patients with nonsustained ventricular tachycardia (91). The clinical value of high-resolution ECGs for the purpose of prospectively detecting patients with nonischemic cardiomyopathy, hypertrophic cardiomyopathy, or mitral valve prolapse at risk for sustained ventricular arrhythmias has not yet been established.

At present, it is the opinion of the committee that the high-resolution ECG has an established value for risk stratification after acute myocardial infarction. However, the committee wants to emphasize that management strategies for postmyocardial infarction patients who have abnormal high-resolution ECGs have not yet been defined.

Unexplained Syncope

In patients with remote infarction, sustained monomorphic ventricular tachycardia is sometimes suspected as the cause of unexplained syncope. Several prospective studies have demonstrated that patients with unexplained syncope and abnormal high-resolution ECGs are more prone to inducible sustained ventricular tachycardia during programmed ventricular stimulation (90,92-94). This should not be construed as a recommendation for requiring an abnormal high-resolution ECG before electrophysiological study since ventricular tachycardia may be inducible in certain patients in the absence of an abnormal high-resolution ECG. Furthermore, mechanisms of syncope other than ventricular tachycardia may be identified with appropriate electrophysiological studies. The extent of the clinical utility of the high-resolution ECG for this application has not yet been completely defined.

Postoperative Patients

Patients with a previously positive high-resolution ECG who have undergone surgery for recurrent ventricular tachycardia or fibrillation in whom the high-resolution ECG reverts to normal after surgery have a high likelihood (about 90%) of no recurrence of these arrhythmias (95,96). This fact may help identify postoperative patients who do not necessarily need follow-up electrophysiological studies to test for inducibility of previous ventricular arrhythmias (95,96).

Future Applications

Preliminary studies suggest that the high-resolution ECG may be helpful in detection of acute rejection of cardiac transplants (61,97), or prompt recognition of myocardial reperfusion in patients with acute myocardial infarction after treatment with thrombolytic agents (98-101).

Further refinements in the methodology may be necessary before the potential of analysis of the high-resolution ECG for these purposes is fully appreciated.

Summary

Sufficient data are available to recommend the use of the high-resolution or signal-averaged electrocardiogram in patients recovering from myocardial infarction without bundle branch block to help determine their risk for developing sustained ventricular tachyarrhythmias. However, no data are available about the extent to which pharmacological or nonpharmacological interventions in patients with late potentials have an impact on the incidence of sudden cardiac death. Therefore, controlled, prospective studies are required before this issue can be resolved. As refinements in techniques evolve, it is anticipated that the clinical value of high-resolution or signal-averaged electrocardiography will continue to increase.

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