Distribution of spectral energy on the body surface: a physiological road map to improve identification of patients vulnerable to sustained ventricular arrhythmias

See page 1126 for the article to which this Editorial refers

Reduction in the incidence of death from ventricular arrhythmias in patients convalescing from myocardial infarction requires accurate detection of the fingerprint of the electrophysiological abnormalities induced in response to injury that increase susceptibility to sustained ventricular tachycardia and effective antiarrhythmic therapies. Recent landmark studies have convincingly demonstrated the superiority of implantable cardioverter defibrillators over antiarrhythmic drugs in reducing death from ventricular arrhythmias. These results underscore the need to accelerate efforts to evolve methods of identifying patients likely to benefit from implantable cardioverter defibrillators prophylaxis. Non-invasive, cost-effective methods of risk stratification are attractive techniques for screening large numbers of patients. Several, including signal-averaged electrocardiography, heart rate variability, QT dispersion, and T-wave alternans have been tested clinically. Approaches that evolve by bridging human biology and electrical engineering, and take advantage of the increasing understanding of the pathophysiological basis of ventricular tachycardia in humans are likely to have a favourable impact on patient outcomes.

Since its inception, investigators in the field of high-resolution electrocardiography have spearheaded purposeful change in methods of analysis to overcome the limitations of the low (17–29%) positive-predictive accuracy of the signal-averaged electrocardiogram that was recognized over 15 years ago when analysis focused only on the detection of microvolt-level late potentials in the terminal QRS complex. Late potentials have been shown to correspond temporally to delayed activation of the ventricles and were thought to be generated by tissue critical to arrhythmogenesis. Refinements of analysis of the signal averaged ECG have followed three strategies: (1) characterization of late potentials using time- and frequency-domain techniques and their combination; (2) combination of the signal averaged ECG with other non-invasive methods of risk stratification; and (3) reexamination of whether the terminal QRS complex is the optimal ECG interval for interrogation to detect signals generated by the tissue responsible for ventricular tachycardia. This last strategy stems from analyses of computer-assisted, three-dimensional, intra-operative maps of ventricular activation during normal sinus rhythm and during ventricular tachycardia in patients with ischaemic heart disease. Data acquired indicate that current methods of high-resolution electrocardiography fail to completely detect the electrophysiological abnormalities induced during infarct healing that increase susceptibility to ventricular tachycardia. Recent findings demonstrate: (1) ventricular tachycardia initiates at infarct border zones by intramural reentry and focal mechanisms; (2) tissue generating non-sustained ventricular tachycardia is not a surrogate for sustained ventricular tachycardia; (3) analysis limited to the terminal QRS complex of signal averaged ECGs excludes detection of >95% of the signals generated by myocardium critical for patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. Lancet 1998; 351: 1755–62.

ventricular tachycardia; and (4) late potentials originate from surviving epicardium overlying the infarct, which is spatially and temporally remote from the tissue critical to ventricular tachycardia. These findings provided an impetus to expand the ECG interval analysed. Subsequent interrogation of the entire cardiac cycle demonstrated previously unrecognized features in the magnitude, phase, and group-delay spectra of signal averaged ECGs that further identify patients with sustained ventricular tachycardia[4].

Signals generated by myocardium responsible for ventricular tachycardia are spatially distributed over the body torso. Accordingly, orthogonal ECGs may not be the optimal lead system for detecting signals of interest. Magnitudes of specific frequencies can be plotted as isoharmonic maps constructed directly from body surface maps or estimated from Frank leads with the use of forward-problem solutions to Poisson’s equation. It has recently been discovered that spatial information augments the ability of spectral analysis of ECGs to identify patients prone to ventricular tachycardia. Comparison of magnitude spectra of spatially-selected ECGs at sites of the maximum and minimum of the spectral energy defined at the 1–7 Hz band of each individual’s body surface isoharmonic map estimated from Frank leads demonstrated a significantly broadened band width that further differentiated patients with from those without ventricular tachycardia compared with the results achieved with Frank ECGs along[5]. Frank ECGs differentiated patients over the band from 11 to 84 Hz (mean P =0.0094), while ECGs at the maximum of the 1–7 Hz isoharmonic map separated patients over the band from 8 to 111 Hz (mean P =0.0062). ECGs at isoharmonic map minima extended the low-frequency end of the band of separation, which covered 1 to 69 Hz (mean P =0.0039).

Subgroup analysis verified that results were independent of QRS duration.

In this issue, Meeder and colleagues investigate the extent to which spectral analysis of spatially-selected ECGs measured directly on the body surface improves the identification of patients with healed myocardial infarction who developed sustained ventricular tachycardia[6]. Results confirm that analysis of spatially-selected ECGs is superior to Frank ECGs; and further strengthen the concept that low-frequency signals are more important that high-frequency signals for this purpose. Strengths of their study include: (1) inclusion of age- and sex-matched patient groups; (2) systematic analysis of predetermined ECG intervals as well as of the entire cardiac cycle; (3) reliance on direct, and not estimated, ECGs from 117 body-surface sites; (4) analysis using windowed and non-windowed data; and (5) a training set-test set design. The results of this study independently confirm the added value of analysing spatially-selected ECGs in individual patients. This confirmation is important and validates the opportunity to improve current techniques of high-resolution electrocardiography. The authors are to be congratulated for a well-performed study, and should be encouraged to prospectively test the approach developed.

The studies by K avesh and M eeder establish proof-of-concept that physiologically-selected ECGs are diagnostically superior to orthogonal leads and augment detection of features in ECGs indicative of risk of sustained ventricular arrhythmias. The results reported underscore the likelihood that analysis of ECGs at sites as close as possible to the myocardial tissue responsible for ventricular tachycardia will facilitate the detection of the fingerprint of the electrophysiological abnormalities that increase vulnerability to sustained ventricular arrhythmias. Driven by these findings, a likely next step for improving risk stratification is to focus on analysis of those bioelectrical signals generated by myocardium enveloping arrhythmogenic tissue. This non-invasive approach requires that the spatial distributions of bioelectrical signals on the epicardium be inferred from body surface measurements using individualized heart-torso geometry models. The formidable difficulties that previously limited the feasibility of acquiring ECGs for this purpose have recently been overcome with the development and implementation of a procedure for simultaneously obtaining geometric and electrical data from the body surface and the heart[7]. Measurements of individual torso shape and of the location of body-surface mapping electrodes, as well as measurements of heart size and its location can be achieved without the need for computerized tomographic or magnetic resonance scans. Analysis of inferred epicardial ECGs subserving arrhythmogenic tissue should permit more definitive identification of the frequency bands that distinguish patients with from those without ventricular tachycardia as well as the specific ECG interval(s) that should be analysed to maximize their detection. The incremental evolution in methods of analysing high-resolution electrocardiograms continues to offer promise as a non-invasive, cost-effective, and clinically useful approach for identifying patients prone to the development of life-threatening ventricular arrhythmias.

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The incidence and epidemiology of myocarditis

Inflammatory cardiomyopathy, i.e. myocarditis in association with cardiac dysfunction\cite{1}, in adolescents and adults may have disparate clinical presentations, including (a) acute onset of symptoms mimicking those of myocardial infarction\cite{2-3}; (b) cardiac insufficiency of acute or insidious onset that may develop into dilated cardiomyopathy\cite{4}, and (c) sudden unexpected cardiac death\cite{5}. A rhythmia may be a feature in (a) and (b) and is the usual cause of (c). The severity of symptoms is highly variable and subclinical myocarditis is common.

Although several non-infectious causes are known, the majority of myocarditis instances are considered to have an infectious origin\cite{6-7}. There is solid evidence to suggest that the microbial pathogenesis may be complex\cite{6}. One very recent contribution to this intriguing field of research is the finding of a link between Chlamydia spp. and heart disease through antigenic mimicry\cite{8}. It is commonly recognised that myocarditis may develop as a complication of an infection elsewhere, most often an upper respiratory tract or gastrointestinal infection, where general symptoms such as fever and myalgia predominate for some microorganisms. In such cases, several days or even weeks may elapse until cardiac involvement occurs, which may or may not be linked to clinical symptoms\cite{6-7}. One study encompassing 12 747 unselected routine autopsies performed over a 10-year period in a defined geographical area in Sweden showed a frequency of histopathological myocarditis fulfilling the Dallas criteria of 1.06\%\cite{10}. However, the true incidence of myocarditis, whether clinical or subclinical, across various age segments of the general population remains unknown.

To carry out prospective clinical studies to establish the incidence and epidemiology of myocarditis associated with cardiac symptoms and of its various aetiologies in a defined population is a formidable undertaking for sundry reasons. For instance, the relative infrequency of the disease requires a large study population and, in acute myocarditis, the patient will have to be examined during the early course of the disease so that a reasonably certain clinical diagnosis is feasible\cite{11-12}. Furthermore, to establish a microbial aetiology, an early blood sample is required for comparison with subsequently obtained samples in serological tests. This is because ‘paired sera’ is mandatory for organisms for which specific IgM methods are not available.

The article by Karjalainen and Heikkilä in this issue\cite{13} represents a solid contribution to the field of myocarditis epidemiology. One merit of this publication is that it is an extremely large-scale study that included 672 672 Finnish military conscripts with a mean age of 20 years. The sample is representative of healthy, young Finnish men, of whom 85\% eventually serve in the Armed Forces. A second merit is that, at the beginning of the study, special effort within the Finnish Armed Forces health care system was