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The value of the electrocardiogram in risk assessment in primary prevention: Experience from the West of Scotland Coronary Prevention Study

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Abstract Electrocardiograms (ECGs) were recorded at baseline, annually thereafter, and at run-out in the West of Scotland Coronary Prevention Study to which 6595 men aged from 45 to 65 years on entry were recruited. The baseline ECGs were analyzed with respect to (*a*) the primary end point of the study, namely, fatal or nonfatal myocardial infarction (MI) and (*b*) all-cause mortality. In addition, incident MIs were reviewed to determine those detected by ECG only. Heart rate, indexed left ventricular mass, frontal T axis, and T amplitude in lead I were all significantly predictive with respect to the primary end point in a multivariate analysis. With respect to all-cause mortality, minor ST-T changes, 10-second heart rate variability, and frontal T axis were similarly predictive. Of 355 incident MIs, 47.3% were silent or unrecognized and detected by ECG only. A simple ECG-based risk prediction equation for fatal and nonfatal MI is introduced.

Keywords: Electrocardiogram; WOSCOPS; Statins; Primary prevention

Introduction

The electrocardiogram (ECG) has been of major interest in many epidemiological and clinical trials[1-6] in which the prognostic value of ECG abnormalities has been assessed, often with respect to classification of the ECG based on the Minnesota Code.[7] In most of such studies, the Minnesota Coding has been undertaken manually.

There have been both primary and secondary intervention trials aimed at reducing the risk of fatal or nonfatal myocardial infarction (MI) in patients with raised lipids, notably the LIPID Research Clinic Trial,[2] the Helsinki Heart Study,[3] and the 4S Trial.[4] Electrocardiographic data from these studies are limited, and after the completion of the West of Scotland Coronary Prevention Study (WOSCOPS),[5] the opportunity has arisen to review the electrocardiographic data, particularly with a view to studying the ECG as a risk factor and to assessing the benefits of intervention with respect to baseline electrocardiographic findings.

In addition, on account of the fully automated techniques of ECG recording and measurement used during WOSCOPS, there was a further unique opportunity to consider relatively recently developed measures of interest, such as QT dispersion, in the setting of primary prevention.

In the WOSCOPS, 6595 men with moderate hyperlipidemia and no previous history of MI were randomized to treatment either by placebo or pravastatin 40 mg nocte. Subjects were followed up for a mean of 4.9 years, and all events, cardiovascular or otherwise, were recorded over the period of the trial. Full details of the study are available elsewhere.[5,8] The principal finding was a 31% reduction in risk of definite coronary heart disease (CHD), death, or nonfatal MI, that is, the primary end point, in the treated group compared with the placebo group.

Twelve-lead electrocardiography was used throughout the study, and this article reviews the methodology, presents

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the ECG findings in the study, and assesses the value of ECG recording in primary prevention. Some preliminary observations have already been reported in this journal.[9]

Methods

Twelve-lead ECGs were recorded using a computer-assisted electrocardiograph, that is, the SICARD 440, in which the Glasgow ECG interpretation program resided.[10] The ECGs were collected initially in more than 45 screening centers in the West of Scotland and, latterly, in more than 20 trial centers and transmitted in digital form by telephone to the ECG Core Laboratory in the former Department of Medical Cardiology in the Glasgow Royal Infirmary. A 12-lead interpretation was provided at the screening or trial center and in the core laboratory, Minnesota Codes were automatically added to the interpretation.

Electrocardiograms were recorded at screening before entry into the study and also annually throughout the duration of the trial. At the end of the study during the run-out period, ECGs were recorded from all individuals who could be contacted, and a few ECGs were obtained in paper form from subjects who, for example, had emigrated. The ECGs were compared with baseline ECGs using automated techniques based on Minnesota Code rules for serial comparison.[11] Full details of the techniques used can be found elsewhere.[12]

All interpretations and codings were overread in the core laboratory. Copies of edited reports were returned to the screening and trial centers and made available to general practitioners if desired. Screening ECGs were used to exclude patients from the study if a previous MI (Minnesota Code 1), atrial fibrillation or flutter (Minnesota Code 8-3-1 or 8-3-2), Wolff-Parkinson-White pattern (code 6-4-1), left bundle-branch block (Minnesota Code 7-1-1), or evidence of marked ischemic changes (Minnesota Code 4-1 or 5-1) was detected.

If new ischemic changes were detected during the trial, a request was made for further clinical details to be obtained. Such changes included new Q waves (Minnesota Code 1) or new ST-T changes (Minnesota Codes 4-1, 4-2, 5-1, 5-2). In this way, end points could be determined based on electrocardiographic findings. The definitions of the electrocardiographic end points are provided in the Appendix. Essentially, the ECG was classified as diagnostic or equivocal and, in combination with other clinical data, was used in the classification of outcomes.

Myocardial infarction was classified as "definite" or "suspect," but within these categories, further subdivisions of recognized, unrecognized, and silent were made. Truly silent MI was diagnosed based on definite ECG changes (new Minnesota Code 1) without any supporting clinical history; unrecognized MI was diagnosed based on electrocardiographic changes accompanied by symptoms, which, in retrospect, were consistent with acute MI but which had not been recognized as such at the time by either the patient or his general practitioner. The diagnosis of recognized MI was based on clinical data with or without accompanying electrocardiographic abnormalities.

ECG classification

Minor ECG changes

The presence of Minnesota Codes 4-2, 4-3, 5-2, and 5-3 either singly or in combination was regarded as constituting minor ECG changes.

Left ventricular hypertrophy

Probable left ventricular hypertrophy (LVH) according to Minnesota Code was a combination of 3-1 or 3-3 plus any of 4-2, 4-3, 5-2, or 5-3 at baseline. Possible LVH was defined as 3-1 or 3-3 without minor ST-T changes, as defined above.

Indexed left ventricular (LV) mass was estimated in 2 ways. The first was based on the equation of Rautaharju et al,[13] namely, for males:

$$\begin{aligned}\text{Indexed LV mass}\left(\text{g/m}^2\right) = &-36.4 + 0.01\ (\text{RV}_5)\\ &+ 0.02\ (\text{SV}_1) + 0.028\ (\text{SIII})\\ &+ 0.0182\ (\text{T}-\text{V}_6)\\ &- 0.148\ (\text{T}+\text{III})\\ &+ 1.049\ (\text{QRSd})\end{aligned}$$

The second was based on equations developed locally,[14] namely, for males:

$$\begin{aligned}\text{Indexed LV mass}\left(\text{g/m}^2\right) = &\ 99.66 + 0.034\ (\text{SV}_5)\\ &+ 0.101(\text{T}+\text{V}_1)\\ &- 0.4231(\text{T}-\text{V}_1)\\ &- 0.127(\text{T}-\text{V}_6)\end{aligned}$$

In both cases, corresponding equations for females were available but were of no relevance in this study.

QT interval

The QT interval was measured in a global fashion, taking the difference between the earliest QRS onset and the latest T-end over all 12 leads. The corrected QT interval (QTc) was based on the formula of Hodges et al[15] namely,

$$\text{QTc} = \text{QT} + 1.75(\text{Rate} - 60)$$

The PR interval, measured as the global QRS onset minus the global P onset, was also studied, as was the QRS duration determined from all 12 leads.

QT dispersion

QT dispersion was determined based on the maximum minus the minimum QT interval across all 12 leads. Further details of this particular technique can be found elsewhere.[16] It should be noted that a corrected QT dispersion is identical to an uncorrected QT dispersion when the linear rate correction formula of Hodges et al[15] above is used to correct for rate.

Heart rate

Baseline heart rate was taken from the resting ECG, which was, on average, recorded approximately 15 minutes after screening visit 3 commenced. A second rate was available, as measured by the nurse earlier in the screening process.