Electrocardiographic findings and global coronary risk assessment

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In patients with overt clinical heart disease, the prevalence as well as the prognostic value of several kinds of electrocardiographical (ECG) changes are well documented and accounted for. Furthermore, in daily clinical practice or during routine examinations and health check-ups, physicians often deal with ‘non-specific’ ECG changes in asymptomatic individuals without any suggestion or symptoms of disease. These ‘minor’ abnormalities are often discarded as clinically meaningless receiving no further attention. Despite the cumulating evidence from numerous epidemiological studies that subclinical forms of heart disease are highly predictive regarding further development or complications, ECG changes that may be markers of an asymptomatic stage of the disease, rarely yield attention with respect to preventive measures.

One of the major problems in combining evidence from large-scale population based studies, is the comparability of study methods. This is particularly true for epidemiological studies with the resting electrocardiogram as the screening method. Differences in registration (e.g. number of leads), inaccurate readings and observer bias, inconsistencies in interpretation and classification of findings, and the nature of the underlying population and exclusion criteria, all compromise the comparability of large-scale ECG studies to a major extent. Despite these differentiating characteristics inherent to ECG studies, nearly all have in common that abnormalities observed on the resting electrocardiogram, either isolated or concomitantly, emerge as very powerful predictors for future cardiac events, independent of conventional cardiovascular risk factors [1–4].

In the current issue, Larsen and colleagues publish their findings obtained from their follow-up of the original cohort of the Copenhagen City Heart Study [5]. Based on Minnesota Coding criteria, they report on the association between ST depression, negative T waves, and left ventricular hypertrophy defined using voltage criteria only (ECG-left ventricular hypertrophy), and subsequent cardiac events in a large population-based cohort of Danish adults. They provide compelling evidence that these ECG items are associated with elevated risk and particularly that the joint occurrence of ECG-left ventricular hypertrophy in combination with ST-T changes carries the highest prognostic importance in both men and women.
In contrast to what is commonly accepted, the prevalence of clinically meaningful ECG findings in the general population is far from negligible. In their sample of persons with no history of coronary heart disease, no Rose angina and no antihypertensive treatment, the prevalence of T-wave inversion, shown to carry a highly elevated risk for ischaemic heart disease whether or not in conjunction with ST depression or ECG diagnosis of left ventricular hypertrophy, is about 9% in both sexes. This ECG finding proves more prevalent than diabetes. This brings us, in our opinion, to their most important finding, that the risk associated with their ECG criteria is comparable, if not greater, than the risk associated with conventional risk factors. This is completely in line with our own observations from the BIRNH study, that in an apparently healthy population, so-called major ECG changes on the baseline ECG, prevalent in, respectively, 6% and 4% of adult men and women, are of greatest importance for later cardiovascular disease and coronary heart disease mortality, with an independent predictive value exceeding that of hypertension, diabetes, smoking, hyperlipidaemia, obesity, and even sex, only being overruled by the effect of age.

Moreover, the true importance of abnormalities detected by classical resting ECG recording is very likely to be under-estimated as most electrocardiographical diagnoses are made by inference and are therefore subject to error. Imprecision in the classification of ECG traces through the limited discriminating capacities of the reader’s eye, has a diluting effect on the estimated size of the intrinsic association with subsequent events. However, with the increasing use of computers in medical sciences, many software programs have been developed, such as the MEANS (Modular ECG Analysis System) computer program for analysis of ECG wave forms, to overcome the problem of high inter- and intra-observer variability. New computer techniques, such as expert systems and artificial neural network technology, have been proposed or are currently under evaluation.

Computerized methods have the additional advantage that quantitative features of the ECG are being analysed rather than qualitative aspects alone. In a recent study, Prineas et al. report using data from the Multiple Risk Factor Intervention Trial, that a significant change in continuous ECG-left ventricular hypertrophy criteria was a stronger independent predictor of future cardiovascular disease mortality than was the use of a conventional dichotomous classification of the same criteria. In the Zutphen study, a similar conclusion was made regarding the predictive value of normal variations in repolarization characteristics. In a very recent publication, Okin et al. shows that computerized ST depression substantially improves the prediction of cardiovascular mortality.

It is well documented that some ECG findings, such as ST-T changes, are of a transient nature. Using data from the Chicago Western Electric Study, Daviglus et al. found that persistent or recurrent non-specific minor ST-T abnormalities are associated with further increases in risk and concluded that this was the result of the gradual impact of the frequency of the occurrence of minor ST-T changes on long-term mortality. Therefore, the high predictive value associated with ECG abnormalities obtained at a single examination, such as in the current paper from the Copenhagen Heart Study, is even more striking and again reflects an under-estimation of the true association between certain ECG findings and subsequent events. This diluting effect may be particularly evident in observations from cohort studies with long-term follow-up, as the authors point out in their discussion.

Regarding their huge impact on future disease and death, independent of and in comparison with classical risk factors, in addition to practical considerations such as the non-invasive character of ECG methodology, the low costs involved, the ready availability of an ECG recorder in most physicians’ offices, we think it very worthwhile adding ECG information to the conventional risk profile in order to improve the identification of subjects at elevated risk for the development of future disease. Therefore, we support the need for a formal evaluation of certain ECG findings to be taken into consideration in the calculation of risk assessment, as was done for instance in the Framingham prediction functions published in 1991. These included an electrocardiographic diagnosis of left ventricular hypertrophy besides the other conventional risk factors of age, sex, smoking, blood pressure, total and HDL cholesterol. The power of using computer software programs in combination with a policy of obtaining serial ECGs on a regular basis, can contribute to an improved electrocardiographic diagnosis of subclinical disease, by its accuracy and consistency. This would increase the positive predictive value of a risk prediction model, including specific ECG items, or including a more general ECG score with various gradual levels of risk.

The question of whether ECG findings, rather than risk factors, are to be treated in the capacity of risk indicators as markers of pre-existing subclinical disease, may be irrelevant in this context. As the ECG signal arises from changes in potential at the cellular level, it may capture functional alterations and detect
abnormalities well in advance of any morphological expression or defect. Moreover, the observation made in several studies that statistical adjustment for conventional risk factors do not change the magnitude of the observed association between ECG changes under study and subsequent events, suggests that conventional risk factors do not act as strong confounders or play an intermediate role in this association. Hence, in an asymptomatic population ECG findings should be treated on an equal footing to classical risk factors and can be involved in risk assessment along with them.

Although there is no convincing direct evidence available that pharmacological and/or lifestyle interventions are capable of influencing prognosis in the early electrocardiographically detected of a subclinical manifestation of heart disease, the identification of a subgroup based upon a prediction formula including certain ECG findings or an ECG score, should result in even more intensified intervention strategies for the management of established controllable risk factors in a particular group with a priori high risk.

Measures of coronary calcium by computerized tomography, measures of carotid intimal–medial wall thickness by B-mode sonography, and the ankle/brachial blood pressure index are among other non-invasive measures of subclinical coronary heart disease documented to have predictive power. However, the prognostic utility of these methods and their incremental value over and above conventional risk factor measurements have not been fully validated in large population-based samples to the same extent as the ECG. According to a recent report by the American Heart Association, these more advanced measures of atherosclerotic burden should be used for high-risk assessment alone, on medical office information including ECG findings.

Despite the high relative risks associated with the resting ECG, in order to fully consider its value in the refinement of risk assessment, the question remains whether the ECG contributes to the individuals’ absolute risk well above that of established risk factors. Regarding the scarce documentation from the literature on this important issue until now, we call upon authors of previously published papers dealing with the impact of certain ECG findings on future heart disease, to prospectively examine in their own longitudinal databases to see to what extent an ECG enhanced model provides incremental predictive power over the conventional risk profile. Not before these results become available can health economists evaluate the estimated economic benefit in terms of cost-effectiveness.

In the meantime, studies are needed to define a set of ECG findings, which are known to be fairly frequent and highly prognostic for future heart disease in the general population. The current report from the Copenhagen City Heart Study published in this issue certainly merits much attention in this respect.

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References


