The ischemic electrocardiogram: A harbinger for ischemic heart disease independent of the blood pressure level. The Copenhagen City Heart Study

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Abstract. Information is limited on the co-existence and prognostic association of the ischemic electrocardiogram (ECG) and blood pressure. Prospectively collected data sets from 28,118 examinations in the Copenhagen City Heart Study were analyzed for cardiac morbidity and mortality for a 5.9-year follow-up. The prognosis of the ECG, independently of blood pressure, was examined. The Cox proportional hazard model was employed to evaluate the prognostic implications of ECG findings and relative risk was adjusted for age and multivariately adjusted for traditional cardiovascular risk factors. End-points were (1) fatal and non-fatal ischemic heart disease (IHD) events and (2) cardiovascular disease (CVD) mortality. During a total follow-up period of 166,471 person years (mean: 5.9 years) 1.481 IHD events were recorded and 1.051 CVD deaths. The relative risk of an ischemic ECG was independent of the blood pressure level. The multivariately adjusted relative risk for fatal and non-fatal IHD for the ischemic ECG was 1.70 (95\% CI: 1.39–2.09, \(p < 0.001\)) in women, and 1.96 (95\% CI: 1.67–2.30, \(p < 0.001\)) in men, and for CVD mortality 1.71 (95\% CI: 1.34–2.17, \(p < 0.001\)) in women and 2.08 (95\% CI: 1.74–2.49, \(p < 0.001\)) in men. An ECG with left ventricular hypertrophy (LVH) and ST-depression was the finding with the highest risk for future events. LVH by ECG voltage-only was associated with no statistically increased risk, except for men treated for arterial hypertension.

Key words: Blood pressure, Electrocardiogram, Epidemiology, Hypertension, Prognosis, ST depression

Abbreviations: CVD = cardiovascular disease; ECG = electrocardiogram; IHD = ischemic heart disease; LVH = left ventricular hypertrophy; ST/T = ST depression with negative T-wave

Introduction

The resting electrocardiogram (ECG) is a simple, non-invasive tool useful both for diagnosing heart disease and as a predictor. In the evaluation of subjects with elevated blood pressure a resting 12-lead ECG is a standard procedure, even among those without symptoms of heart disease [1]. The presence of ST-depression and negative T-waves occurs with myocardial ischemia and infarction, cardiomyopathy, acute pulmonary embolism, electrolyte abnormalities and drugs, including digitalis [2]. The presence of electrocardiographic ST-depression and negative T-waves is also documented to be associated with future risk of sudden death [3] and a predictor of coronary heart events [4–7]. Isolated minor T-wave findings, minor ST-segment depression, or a combination of minor ST-segment and T-wave findings are each associated with increased mortality risk [8]. Electrocardiographic manifestations of left ventricular hypertrophy (LVH) include an increase in QRS amplitude and are often seen in association with repolarization abnormalities including ST-depression and flat or negative T-wave, sometimes called LVH strain pattern. Data from the Framingham Study and many others have documented that LVH with ST/T findings is a harbinger of impending cardiovascular events [6, 7, 9, 10]. However information on the prognostic significance of ischemic ECG changes in relation to blood pressure level is limited.

None of the previous studies have examined the coexistence and prognostic association of ischemic ECG and the blood pressure level in the general population and in those treated for arterial hypertension. It is of great importance to evaluate whether ischemic ECG findings are associated with risk in different blood pressure groups.

The purpose of the present study was to evaluate whether ECG changes such as voltage-only LVH, isolated negative T-waves, ST-depression and
negative T-waves (ST/T), LVH with negative T-waves and LVH with ST/T findings have the same prognostic information for developing ischemic heart disease (IHD) and cardiovascular disease (CVD) mortality in different blood pressure groups among a general population outside hospital.

Methods

Subjects

The Copenhagen City Heart Study is a prospective cardiovascular population study. The original population sample of nearly 20,000 subjects was randomly drawn in 1976 from a background population of 90,000 inhabitants who were 20 years or older and who were listed in the Copenhagen Population Register in a district of Copenhagen, Denmark. The first examination took place in the period 1976–1978. A total of 14,223 subjects were examined (response rate 74%). The original cohort was re-invited together with a new sample of 500 subjects in the age group 20–25 years and examined between 1981 and 1983. A total of 12,698 subjects were examined (response rate 70%). Finally, a third examination of the cohort with an additional sample of 3000 subjects 20–49 years of age was performed between 1991 and 1994. A total of 10,135 participated in this examination (response rate 61%). Less than 2% of the population was of non-Caucasian origin, and socio-economically the majority was middle class. Details of the selection procedure, a description of the eligible non-participants and the complete examination program, and the examination program and information on the subjects have been presented elsewhere [11]. To evaluate the independent prognostic influence of ECG changes, we excluded subjects with a self-reported previous history of IHD and/or discharged from a hospital with a diagnosis of IHD with International Classification of Diseases (ICD) 8: 410–414). The Rose Questionnaire was used to evaluate previous history of IHD [12].

In the evaluation of the prognostic information of ECG findings we restricted the age range to 35–74 years of age, due to a very low number of events in the youngest age group. Subjects with ECG major Q waves, second and third degree A–V block, Wolff–Parkinson–White syndrome, right and left bundle branch block, supraventricular and ventricular tachycardia and atrial fibrillation were excluded from the present analysis, as these ECG findings itself influences the prognosis. The Minnesota codes IV₁–₃ describing ST-depression has an optional code V describing the T-waves. Subjects with isolated ST-depression, code IV₁₄ were excluded, as were subjects with code V₄ describing non-specific T-waves findings. Information on the use of diuretics/antihypertensive medication was available.

Data from all three examinations are analyzed in the present study. The number of data sets that were excluded due to exclusion criteria were 2531, 2800 and 3599 from the first, second and third examination respectively. The present analysis comprises the data sets from 11,692 subjects from the first examination, and from 9898 to 6528 subjects from the second and third examination respectively. Thus in total the study group comprises 28,118 data sets from 15,204 subjects. Of the 15,204 subjects 5,912 participated in only one of the three examinations. The number of subjects who participated in two or in all three examinations was 5670 and 3622 respectively.

Follow-up

The National Patient Register provides information on all hospital admissions in Denmark, and the discharge diagnoses are registered after the World Health Organization’s ICD8 to the end of 1992, and ICD10 from 1993. End-point was defined as hospitalization and/or death due, fatal and non-fatal IHD events (ICD8: 410–414 and ICD10: 120–125), and CVD mortality (ICD8: 390–458 and ICD10: 100–199 and G45). The follow-up period was 7 years, and information about end-points during follow-up was obtained from the Register of Causes of Death and the National Patient Register. Subjects with a new examination within the 7-year follow-up period participated in the data analysis in the period from the start of the first examination and then got censured at the start of the second examination. The ethics committee for the City of Copenhagen approved the study, and all participants provided oral informed consent.

Electrocardiogram

A resting supine 12-lead ECG was recorded in each subject. ECGs were evaluated according to the Minnesota Code [12] by two independent technicians, and in case of disagreement a third person settled the disagreement. The ECG findings were divided in six mutually exclusive groups. Voltage-only LVH as code III₁–₃, negative T-waves as code V₁–₃, ST/T changes as code IV₁–₃, LVH with negative T-waves as code III₁–₃, and code V₁–₃, and LVH with ST/T changes as code III₁–₃, code IV₁–₃, and code V₁–₃. ECGs were classified as normal in the absence of major Q waves, LVH, ST segment depression, Negative/flat T-waves, second and third degree A–V block, Wolff–Parkinson–White syndrome, PQ < 0.12 sec, left bundle branch block, right bundle branch block, QRS duration > 0.12 sec, ventricular tachycardia, atrial fibrillation, supraventricular tachycardia, Idioventricular rhythm, and A–V nodal rhythm.