Electrocardiogram abnormalities and risk of cardiovascular mortality and all-cause mortality in old age: The Kahrizak Elderly Study (KES)

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ABSTRACT

Resting electrocardiographic (ECG) abnormalities might be value for mortality prediction. The aim of this study is to evaluate whether ECG abnormalities are associated with increased mortality in older residents of Kahrizak Charity Foundation (KCF). A total of 247 participants >60-years of KES were enrolled in this study. Adjudicated all cause mortality was collected over 3 years between 2006 and 2009. The subjects were classified as having major, minor or no ECG abnormalities according to the Minnesota Code. The addition of ECG to risk factors were examined to predict cardiovascular diseases (CVD) and all-cause mortality by using Cox proportional hazards regression models. At baseline, 104(42.1%) had major ECG abnormalities and 73(29.6%) had minor abnormalities. During a median follow-up of 3.2 years, 73 participants died from all-cause mortality and 31 deaths from CVD. Major ECG abnormalities were associated with an increased risk of CVD mortality in all models. The associations between minor ECG abnormalities at baseline and CVD mortality were not statistically significant. After adjustment for age and sex, Body mass index (BMI), smoking, diabetes, hypertension (HTN), hyperlipidemia and history of CVD, the participants with the major ECG abnormalities had higher risks of CVD mortality (HR: 3.12(95% CI, 1.02-9.57)) and all-cause mortality (HR: 2.45(95% CI, 1.23–4.85) compared with those with normal ECG.

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1. Introduction

The determination of predicting factors for mortality in older people is essential, because it can help make better clinical decision and assign priorities in health intervention (Sharifi et al., 2012; Tuomilehto et al., 1999).

Previous studies have found several factors for prediction of mortality (Allard et al., 2004; Cohen-Mansfield, Marx, Lipson, & Werner, 1999; Dong et al., 2008). CVD has been known as the leading cause of mortality and morbidity worldwide (Edejer, 2000). In older adults, traditional risk factors are less accurate for predicting CVD than among middle-aged adults (D’Agostino, Grundy, Sullivan, & Wilson, 2001).

Resting ECG abnormalities have been shown to be associated with incident coronary heart disease (CHD) and CVD events independent of traditional risk factor (Auer et al., 2012). ECG is an available, low cost and safe tool to consider for risk stratification of asymptomatic participants (Denes, Larson, Lloyd-Jones, Paine, & Greenland, 2007). However, performing a routine ECG is not recommended for screening asymptomatic adults, but risk prediction incorporating ECG might be useful in population of older adults given their higher prevalence of both CVD events and ECG abnormalities (Chou et al., 2011).

Although previous studies have examined the association between ECG data and CHD outcome (Auer et al., 2012), there are limited data on the prevalence of ECG abnormalities and their association with longitudinal cardiovascular outcomes and all-cause mortality in the elderly (Denes et al., 2007).

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The aim of this study was to assess the prevalence of significant ECG abnormalities and evaluate their association with subsequent cardiovascular mortality and all-cause mortality in older residents of KCF.

2. Materials and methods

The participants of this study were selected by simple-random cluster sampling and the units of the clusters were the wards of KCF (21 wards). The KCF is the largest center providing aged care facilities in Iran. The most common admission reason is social vulnerability. The participants were selected randomly based on medical record numbers which were unique. The sample size in individual ward was weighted to the number of people who lived there (about 27%). The total number of the participants was 302 individuals, the data of 49 subjects were not considered for analyzing because of incomplete data. Six participants were censored because left the KCF and we could not follow up their outcomes. There was no difference regarding age, sex and past medical history between 247 subjects who were considered for analyzing vs. those not.

Inclusion criteria included: age >60 years, admission time at least more than 6 months prior to the study. Exclusion criteria were end-stage diseases such as patients with terminal cancer, chronic renal failure (Cr > 2.5 mg/dl), hepatic failure and recent acute myocardial infarction (during 3 months prior to the study).

Our subjects were followed up for about 39 months from September 2006 until December 2009. The ethics committee of Endocrinology and Metabolism Research Institute approved the study protocol. Each subject gave written informed consent before entry into the trial.

Demographic information (age and sex) was collected from the KCF computerized database bank. Medical information (history of disease, surgery, medication use and smoking behavior) was extracted from KCF medical records and also obtained by completing a questionnaire that was approved by two geriatricians. The questionnaire was carried out by a trained nurse.

 Anthropometric measurements were carried out using standard protocols and techniques. Weight and height were measured in light clothing without shoes and with light clothing. BMI was calculated as weight (kg) divided by height squared (m²). Waist circumference (WC) was measured midway between the lower border of the rib margin and the iliac crest at the end of normal expiration. WC and height were measured using a non-elastic tape. The measurements of systolic and diastolic blood pressure were performed using a standardized mercury sphygmomanometer (calibrated by Iranian Institute of Standards and Industrial Researches) on the right arm after a 15 min rest in a sitting position; the first and fifth Korotkoff sounds were recorded as systolic and diastolic blood pressure, respectively.

Standard 12-lead ECGs were recorded at baseline in the resting supine position according to the standard recording protocol developed by the School of Public Health, the University of Minnesota, using a PC-ECG 1200 machine. Two qualified physicians coded the ECGs in parallel according to the Minnesota codes using a measuring loop, specially manufactured by the University of Minnesota (Primeas, Harland, Janzon, & Kannell, 1982). For assurance of quality and resolving any discrepancy between them, a third qualified physician who was a cardiologist, re-evaluated and finally approved the ECG codes.

To determine biochemical values, 12-h overnight fasting blood samples were collected. Serum specimens were stored at −70 °C until laboratory assays were carried out. Serum lipid profiles (triglyceride, total cholesterol, high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C), and fasting blood glucose (FBG) were measured by an enzymatic colorimetric technique on a Hitachi 902 Analyzer (Roche, Basel, Switzerland).

2.1. Definition of terms

Diabetes mellitus was defined as fasting plasma glucose ≥126 mg/dl and/or current use of pharmacological treatment. Smoking included current or past users of cigarettes. In KCF, for each participant, the standardized questionnaire was asked about the history of CVD which included questions on present and past cardiovascular disorders, including myocardial infarction, angina pectoris, arrhythmias, stroke, peripheral arterial disease and heart failure. When any or a combination of these disorders was proved, subjects were considered to have a history of CVD.

HTN was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg or current use of antihypertensive medication. Subjects with total cholesterol ≥240 mg/dl or triglycerides≥200 mg/dl or those using anti- lipid drugs were named as hyperlipidemia.

Criteria for major ECG abnormalities were any of the following: Q-QS wave abnormalities (MC 1-1 to 1-2-8); left ventricular hypertrophy (MC 3-1); Wolff–Parkinson–White syndrome (MC 6-4-1 or 6-4-2); complete bundle branch block or intraventricular block (MC 7-1-1, 7-2-1, 7-4, or 7-8); atrial fibrillation or atrial flutter (MC 8-3); or major ST-T changes (MC 4-1, 4-2, 5-1, and 5-2). Criteria for minor ECG abnormalities were minor ST-T changes (MC 4-3, 4-4, 5-3, and 5-4). Participants with both major and minor abnormalities were classified as having major abnormalities. Participants without minor or major ECG abnormalities were classified as having no abnormalities and their ECG was considered normal.

2.2. Outcome measurements

During the study, cause and time of the participants’ mortality were recorded daily based on a national death certificate, which was completed by a responsible physician. In addition, duration of life of subjects in KCF and medical problems around their time of death were recorded. All cause mortality is assigned according to the International Statistical Classification of Diseases and Related Health Problems criteria, 10th Revision (ICD-10). CVD mortality is specified as a composite measure of CHD death, stroke and cerebrovascular death.

Follow-up time was defined by the time of the baseline visit until the day of death or was censored at the last contact date (for those participants who did not have any event or were lost to follow-up).

2.3. Statistical analyses

Mean (standard deviation: SD) values for continuous and frequencies (%) for categorical variables of the baseline characteristics variables were compared between ECG group using student’s t-test and χ² test, respectively.

To evaluate outcome occurrence, results are presented with the number of events, the percentage of total participants in the event, the rate per 1000 people per year, and a 95% confidence interval (CI) for the rate. Kaplan–Meier survival curves were estimated and compared between ECG groups by using the log-rank test. A crude relative risk was estimated from the event rates. Adjusted hazard ratios (HRs) for the association between outcome occurrences and ECG abnormalities were modeled with Cox proportional hazards regression models. The proportional hazards assumption was checked by modeling each outcome (CVD mortality and all-cause mortality) by a time by baseline ECG status interaction term in a proportional hazards model along with the baseline ECG main
effects term. This was not significant for events (interaction \( P = 0.08 \)), indicating that the proportional hazards assumption was satisfied.

\( P \)-values \( \leq 0.05 \) were considered statistically significant. All data analyses were carried out using SPSS 18 PASW version.

3. Results
At baseline, mean (SD) age was 76.7 ± 8.5 years, and 41.3% were men. Of the 247 participants, 104(42.1%) had major ECG abnormalities and 73(29.6%) had minor ECG abnormalities. During a median follow-up of 3.2 years, 73 participants died from all-cause mortality and 31 deaths from CVD. Subjects in the group with minor or major ECG abnormalities were older than group with normal ECG (Table 1).

The Kaplan–Meier estimates of all-cause mortality cumulative hazard over time for those participants without ECG abnormalities vs. any ECG abnormalities (Fig. 1) and for those participants without ECG abnormalities vs. major and minor ECG abnormalities (Fig. 2) were calculated.

Table 2 shows the HR for CVD mortality and all-cause mortality, according to minor and major ECG abnormalities. Major ECG abnormalities were associated with an increased risk of CVD mortality in all models. The associations between minor ECG abnormalities at baseline and CVD mortality were not statistically significant.

Table 3 shows the HR for CVD mortality and all-cause mortality, according to any ECG abnormalities. Any ECG abnormalities were associated with an increased risk of all-cause mortality in the model (multivariate adjusted HR: 2.27(95% CI, 1.18–4.39).

4. Discussion
This present study showed that in elderly people, ECG abnormalities were associated with cardiovascular mortality and all-cause mortality and significantly improved the prediction of mortality independent of other cardiovascular risk factors. Although, history of CVD is a strong predictor of mortality, but
Table 2
HR for CVD mortality and all-Cause mortality in elderly, according to minor and major ECG abnormalities.

<table>
<thead>
<tr>
<th>CVD mortality</th>
<th>All cause mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate per 1000 person-years (95% CI)</td>
<td></td>
</tr>
<tr>
<td>No ECG abnormality</td>
<td>18.7 (5.1–47.2)</td>
</tr>
<tr>
<td>Minor ECG abnormality</td>
<td>52.6 (25.3–94.6)</td>
</tr>
<tr>
<td>Major ECG abnormality</td>
<td>60.5 (35.6–95.1)</td>
</tr>
<tr>
<td>Crude HR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>No ECG abnormality</td>
<td>1</td>
</tr>
<tr>
<td>Minor ECG abnormality</td>
<td>2.72 (0.85–8.66)</td>
</tr>
<tr>
<td>Major ECG abnormality</td>
<td>3.31 (1.12–9.90)</td>
</tr>
<tr>
<td>Multivariate analysis; HR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>No ECG abnormality</td>
<td>1</td>
</tr>
<tr>
<td>Minor ECG abnormality</td>
<td>1.64 (0.46–5.87)</td>
</tr>
<tr>
<td>Major ECG abnormality</td>
<td>3.12 (1.02–9.57)</td>
</tr>
<tr>
<td>Age</td>
<td>1.05 (1.01–1.10)</td>
</tr>
<tr>
<td>Sex</td>
<td>0.99 (0.44–2.26)</td>
</tr>
<tr>
<td>Body mass index</td>
<td>0.97 (0.10–1.05)</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.94 (0.35–2.53)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.03 (0.64–1.64)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.83 (0.38–1.81)</td>
</tr>
<tr>
<td>Hypo磷iriaphasia</td>
<td>0.62 (0.08–4.86)</td>
</tr>
<tr>
<td>History of CVD</td>
<td>2.35 (1.03–5.33)</td>
</tr>
</tbody>
</table>

* P < 0.05.

Our study showed that a routine ECG adds to the prognostic information on risk of mortality in older people.

Some studies have shown that preventive measures against the cause of mortality are often missing in elderly (Ramsay et al., 2006; Tran, Laupacis, Mandani, & Tu, 2004). For mortality risk management in older people, it is essential that a complete search would be done through the medical records for any history of cardiovascular risk factors (Mitka, 2006). Previous studies confirmed earlier observations that preventive medication is underused in older people. Also, risk prediction with traditional risk factors are less accurate in older people compared with middle-aged adults (D’Agostino et al., 2001). Given the safety and the low cost of electrocardiography in the older people, ECG data might be useful to improve risk prediction and help identify persons who would benefit from interventions to reduce risk factors (Denes et al., 2007).

Previous studies have described the value of one specific abnormality of ECG, mainly either myocardial infarction or atrial fibrillation and not all anomalies as in the present study (Lloyd-Jones et al., 2004; Nadelmann et al., 1990).

The increases in all-cause and cardiovascular mortality have been observed in earlier studies in populations of older patients with prior MI (Sheifer et al., 2000; Nadelmann et al., 1990). In the Framingham cohort, a comparable increase in all-cause mortality risk was observed in people who developed AF (Lloyd-Jones et al., 2004).

Several previous studies reported an association between ECG abnormalities and CHD outcomes (De Ruijter et al., 2007; Denes et al., 2007). In postmenopausal women aged 55–79 years, Denes et al. (2007) found that baseline major and minor as well as incident ECG abnormalities were associated with significantly increased risks for CHD events, independent of established risk factors and hormone treatment. In a recent population-based study of older adults, Auer et al. (2012) showed that major and minor ECG abnormalities were associated with future CHD events, but did not predict all-cause mortality.

The benefit of our study is the evaluation of the specific effect of ECG findings on cardiovascular mortality and all-cause mortality. In this context, Daviglius et al. (1999) focused on only minor ST–T abnormalities and found these findings were associated with increased risk of mortality due to CVD and all causes in men aged 40–55 years. We assessed the association between both minor and major ECG abnormalities and CVD and all cause mortality among men and women older adults (mean age 76.7 ± 8.5 years). We also compared these findings with those with no ECG abnormalities.

Another study evaluated the association between the presence of major ECG abnormalities (myocardial infarction or atrial fibrillation) and mortality and CVD morbidity, in strata depending on history of CVD (De Ruijter, Assendelft, Macfarlane, Westendorp, & Gussekloo, 2008). Like other studies, our results showed that although the traditional risk factors are important predictors of CVD and all-cause mortality but the value of ECG abnormalities is more powerful than well-established risk factors (De Bacquer, De Backer, Kornitzer, & Blackburn, 1998; De Bacquer, De Backer, Kornitzer, Myny, et al., 1998).

The present cohort study has several strengths. Precise measurements of ECG abnormalities, clear definition of cardiovascular risk factors, formally adjudicated cardiovascular mortality and all cause mortality, and near completeness of follow-up data, are the strengths of our study.

However, some limitations must be considered. The effect of ethnicity on our data could not be adequately evaluated because most of whom were of one ethnicity. Our study findings need to be confirmed in a larger population with longer follow-up. The most important limitation of our study was that its sampling was institution-based and could not be a precise representative of community dwelling aged adults.

5. Conclusions

Our findings have important clinical and research implications. Although some older adults are recognized as having higher cardiovascular risk, these data allow further risk stratification. Major or minor ECG abnormalities may be identified as a particularly high risk for future cardiovascular events and all cause mortality, thereby allowing focused interventions that target known cardiovascular risk reduction. Whether ECG should be added in screening of older population, should be evaluated in clinical trials.

Conflict of interest statement

None.

Acknowledgments

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