Association of electrocardiogram abnormalities and incident heart failure events

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Background Unless effective preventive strategies are implemented, aging of the population will result in a significant worsening of the heart failure (HF) epidemic. Few data exist on whether baseline electrocardiographic (ECG) abnormalities can refine risk prediction for HF.

Methods We examined a prospective cohort of 2,915 participants aged 70 to 79 years without preexisting HF, enrolled between April 1997 and June 1998 in the Health, Aging, and Body Composition (Health ABC) study. Minnesota Code was used to define major and minor ECG abnormalities at baseline and at year 4 follow-up. Using Cox models, we assessed (1) the association between ECG abnormalities and incident HF and (2) the incremental value of adding ECG to the Health ABC HF Risk Score using the net reclassification index.

Results At baseline, 380 participants (13.0%) had minor, and 620 (21.3%) had major ECG abnormalities. During a median follow-up of 11.4 years, 485 participants (16.6%) developed incident HF. After adjusting for the Health ABC HF Risk Score variables, the hazard ratio (HR) was 1.27 (95% CI 0.96-1.68) for minor and 1.99 (95% CI 1.61-2.44) for major ECG abnormalities. At year 4, 263 participants developed new and 549 had persistent abnormalities; both were associated with increased subsequent HF risk (HR 1.94, 95% CI 1.38-2.72 for new and HR 2.35, 95% CI 1.82-3.02 for persistent ECG abnormalities). Baseline ECG correctly reclassified 10.5% of patients with HF events, 0.8% of those without HF events, and 1.4% of the overall population. The net reclassification index across the Health ABC HF risk categories was 0.11 (95% CI 0.03-0.19).

Conclusions Among older adults, baseline and new ECG abnormalities are independently associated with increased risk of HF. The contribution of ECG screening for targeted prevention of HF should be evaluated in clinical trials. (Am Heart J 2014;167:869-875.e3.)

The prevalence of heart failure (HF) is rising, especially in older adults,[1] and remains one of the most frequent causes of hospitalization in persons older than 65 years.[2-4] Most HF research focuses on treatment of patients with manifest HF, but few studies have assessed the prediction of incident HF hospitalization in primary prevention.[5,6] The guidelines emphasize the importance of identifying subjects at risk for HF at an early stage and controlling risk factors such as hypertension, diabetes, metabolic syndrome, and atherosclerotic disease.[7,8] Subclinical changes in cardiac structure and function often precede clinical manifestations of HF and may alter the morphology of electrocardiographic (ECG) recording.[9]

Although it remains controversial whether screening ECG should be routinely done in clinical practice,[10] we[11] and others[12,13] have shown that resting ECG abnormalities are (1) common among older individuals, (2) associated with incident coronary heart disease (CHD), and (3) improve the prediction of CHD events beyond traditional risk factors.[11] In contrast, few studies have examined the association between ECG abnormalities

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and incident HF,[14-17] and no study has specifically assessed (1) the impact of ECG changes on HF risk in older adults, (2) the association between dynamic ECG changes and HF risk over time, and (3) the impact of ECG on net reclassification of HF risk beyond traditional risk factors.[5] In this study, we sought to assess the association between baseline major and minor ECG abnormalities and the risk of incident HF among older adults in the Health, Aging, and Body Composition Study ABC (Health ABC) as well as the risks associated with dynamic ECG changes over time. We also evaluated the impact of ECG on reclassification in the Health ABC HF Risk Score.[5]

Methods

Study design and population

We analyzed data from the Health ABC study, a prospective cohort study of 3,075 community-dwelling men and women aged 70 to 79 years enrolled between April 1997 and June 1998 and who were without overt physical disability at enrollment. Participants were identified from a sample of white and black Medicare-eligible adults living in designated zip coded areas surrounding Pittsburgh, PA, and Memphis, TN. Details of eligibility and exclusion criteria have been previously described.[18] All participants gave written informed consent, and the local institutional review boards approved the protocol. We excluded participants with preexisting HF (97 participants), those with missing baseline HF data (43 participants), those with a pacemaker (19 participants), and those with missing baseline ECG data (1 participant). The final sample consisted of 2,915 participants.

Electrocardiographic classification

As previously described,[11] standardized procedures were used at all clinical centers for the recording of the 12-lead resting ECGs at baseline and at the year 4 follow-up visit. Briefly, 2 trained coders read ECG records, and cases with discrepancies were resolved by a third senior coder. All ECGs were assessed according to the Minnesota Code, as in previous large prospective cohorts.[11,13,19-22] Electrocardiographic abnormalities were classified into minor and major abnormalities, as previously described.[11-13,21] Minor baseline ECG abnormalities were defined as any minor ST-segment or T-wave abnormalities. Criteria for major baseline ECG abnormalities were any of the following: (1) Q-QS wave abnormalities, (2) major ST-T abnormalities, (3) left ventricular hypertrophy (LVH), (4) atrial fibrillation or atrial flutter, (5) Wolff-Parkinson-White, (6) complete bundle-branch block or intraventricular block (online Appendix Supplementary Table I). Participants with both minor and major abnormalities were classified as having major ECG abnormalities. A random sample of 5% of baseline ECG underwent the same coding process to assess reproducibility of the readings. κ Values for the categorization described above were 0.90 for major, 0.81 for minor, and 0.82 for no abnormalities. At year 4, we analyzed repeat ECG data among 2,300 participants. From the baseline sample of 2,915 participants, 212 died within the first 4 years of non-HF causes. In addition, we excluded 59 participants who had interim HF events and 396 participants who had no available data on ECG.

Incident HF

All participants were contacted every 6 months to report any cardiovascular events.[18] *Incident HF* was defined as any overnight hospitalization related to HF among participants without HF at baseline. The presence of clinical HF at baseline was based on self-reported history, use of selected drugs, and 5-year review of Medicare data.[23] The HF criteria required at least a diagnosis of HF from a physician and treatment for HF, including current prescription for a diuretic agent and either digitalis or vasodilator or β-blocker. Clinicians at each center adjudicated HF events based on symptoms, clinical signs, chest x-ray, and echocardiographic findings, using criteria similar to those used in the Cardiovascular Health Study.[24] The available data on left ventricular ejection fraction (LVEF), as assessed by echocardiography or left ventriculography, were abstracted from medical records during the index hospitalization for HF events. *Follow-up time* was defined as the time from baseline ECG to the first HF event, death, or last contact date.

Covariates definition

The Health ABC HF Risk Score was developed in the Health ABC[5] Study and validated in the Cardiovascular Health Study to assess the 5-year risk of HF among older adults.[25] The model had a C-statistic of 0.73 in the derivation data set, 0.72 by internal validation, and 0.74 in the external validation data set. The Health ABC Risk Score classifies patients into 4 groups of 5-year HF risk (<5%, 5%-10%, 10%-20%, >20%) and includes the following variables: age, smoking, systolic blood pressure, CHD at baseline, heart rate, fasting glucose, LVH, serum albumin, and creatinine.

Statistical analysis

Differences in proportions and mean of covariates across participants with and without incident HF events during follow-up were assessed using χ^2 and analysis of variance statistics, respectively. For covariates that were not normally distributed, median values with interquartile ranges were reported and compared with the use of Mann-Whitney *U* statistics. We used Cox proportional hazards models to assess the association between ECG abnormalities and HF events in multivariate analyses. We examined the proportionality of hazards using graphical