Racial Differences in Heart Age and Impact on Mortality

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Abstract: Background: Heart age is an estimate of the age of a person's cardiovascular system given their cardiovascular disease (CVD) risk factors. The difference between a person's chronological age and heart age (excess heart age) represents their added CVD risk.

Objective: To examine racial differences in excess heart age and whether race impacts the association between excess heart age and CVD mortality.

Methods: This analysis included 5110 participants (2449 non-Hispanic white, 1287 non-Hispanic black, and 1374 Mexican-American) from the NHANES III who were free of CVD. Heart age was calculated using the sex-specific non-laboratory-based Framingham risk prediction functions. Multivariable Cox proportional-hazards regression models were used to evaluate the relationship (overall and by race) between excess heart age and CVD mortality.

Results: Mean excess heart age was greatest in non-Hispanic blacks (13.0 years), followed by Mexican-Americans (10.5 years), and non-Hispanic whites (8.5 years); $p < 0.001$ for pairwise differences. Over a mean follow-up of 13.0 years, 394 CVD deaths occurred. Each 10 years of excess heart age was associated with 65% increased risk of CVD mortality (HR, 95% CI: 1.65, 1.53–1.78). This association was stronger in non-Hispanic whites (1.83, 1.63–2.02) compared to non-Hispanic blacks (1.50, 1.29–1.72) and Mexican American (1.60, 1.33–1.87), interaction $p = 0.065$.

Conclusions: Compared to non-Hispanic whites, non-Hispanic blacks and Mexican Americans have more excess heart age, but the risk of CVD death for the same level of excess heart age appears more pronounced in non-Hispanic whites. Further investigation is needed to show the usefulness of these findings in directing future efforts and resource allocation for reduction of health disparities between ethnic groups.

Keywords: Heart age■Mortality■Race

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INTRODUCTION

"Heart age" represents the predicted age of a person's cardiovascular system given certain cardiovascular disease (CVD) risk factors, including age, gender, and medical history of hypertension, hyperlipidemia, diabetes, and smoking.[1] Previous studies have investigated the comparison of heart age with chronological age as a method of expressing cardiovascular health.[2–5] Excess heart age (i.e., the difference between heart age and chronological age) represents the CVD risk added by risk factor burden. In the United States, racial differences in CVD risk and mortality have been largely attributed to increased risk factor burden among blacks and Hispanics as compared with whites.[6–8] To date, excess heart age has yet to be investigated as a method for quantifying the effect of collective risk factor burden on CVD mortality. Therefore, we sought to examine racial differences in excess heart age and whether race modifies the association between excess heart age and cardiovascular mortality using data from the Third National Health and Nutrition Examination Survey (NHANES III).

MATERIALS AND METHODS

The NHANES is a periodic survey of a representative sample of the civilian non-institutionalized United States population. The survey aims to determine estimates of disease prevalence and health status of the United States population. NHANES III baseline data were collected during an in-home interview and subsequent visit to a mobile examination center between 1988 and 1994. Data collected during the in-home interview included demographics, past medical history, and medication usage. Age, sex, race/ethnicity, and history of dyslipidemia and smoking were self-reported. Medication history including use of antihypertensive and lipid-lowering agents was also self-reported. Blood pressure data were averaged from three in-home measurements and three mobile center measurements. Hypertension was defined as any of the following: systolic blood pressure $\geq$140 mmHg, diastolic blood pressure $\geq$90 mmHg, and/or use of antihypertensive medications. Height and weight measurements made at the mobile examination center were used to calculate body mass index (BMI) as the weight in kilograms divided by the square of the height in meters. Obesity was defined as BMI $\geq$30 kg/m^2. Blood samples were obtained at mobile centers and basic laboratory values were recorded for each participant, including plasma glucose, total cholesterol, and high-density lipoprotein (HDL) cholesterol. Diabetes

was defined as any of fasting plasma glucose ≥126 mg/dl, a non-fasting plasma glucose ≥200 mg/dl, a glycosylated hemoglobin A1c value ≥ 6.5%, or a history of diabetic medication use.

Mortality data for NHANES III participants were available through December 31, 2006.[9] A probabilistic matching algorithm based on 12 identifiers, including social security number, gender, and date of birth, was used to link participants with death information captured in the National Death Index. The follow-up period was defined as the interval between the NHANES III examination and whichever of the following came first: date of death, date of censoring, or December 31, 2006. Participants who were unable to be matched with a death record were considered to be alive through the entire follow-up period. The cause of death was determined using the underlying cause listed on the death certificates. CVD mortality endpoints were examined and analyzed using data from the NHANES III Linked Mortality File. *International Classification of Diseases, Tenth Revision* codes were used to identify each endpoint. CVD mortality was defined by codes 100−178.

The present analysis included 5110 participants without baseline CVD and with complete baseline demographic, laboratory, medication, and mortality data available. Participants were excluded if determined to have baseline CVD based on self-reported history of heart attack and/or stroke, or electrocardiographic evidence of myocardial infarction by Minnesota Electrocardiogram Classification.[10] Participants aged 75 years and older were excluded from analysis per the recommended age range for heart age calculation.[1] We also excluded races other than non-Hispanic white, non-Hispanic black, and Mexican-American.

Heart age data were calculated with the sex-specific non-laboratory-based Framingham risk prediction function, which estimated the risk of developing cardiovascular disease over a 10-year period.[1] These analyses incorporated participant age, gender, BMI, systolic blood pressure, use of antihypertensive medications, and smoking (e.g., current smoker) and diabetes status. Heart age was then estimated by finding the age of a person of the same gender with the same estimated 10-year CVD risk but optimal risk factors (i.e., BMI of 22 kg/m^2, non-treated systolic blood pressure of 125 mmHg, non-smoker, and non-diabetic). Predicted heart age values were reset at a maximum of 100 years to control the effect of outliers in 348 (6.8%) participants. Excess heart age was calculated as the difference in years between participant self-reported age and calculated heart age.

Racial differences in the mean (±standard deviation) of the heart age and excess heart age were tabulated and compared across races using the nonparametric Kruskal−Wallis analysis of variance (ANOVA). Bonferroni corrected pairwise comparisons of the means were also conducted for significant ANOVA tests. Cox proportional-hazards regression was used to examine the association between excess heart age and cardiovascular mortality, both overall and by racial stratification. Two models were constructed: unadjusted (Model 1) and adjusted for sex, race, hypertension, diabetes, obesity, smoking, and dyslipidemia (Model 2). Excess heart age was used in models as a continuous variable (per 10 years increase) and as a binary variable (higher vs. lower than median in the overall sample which was 8 years), separately. Interaction p-value by race was calculated in model 2. Statistical significance was defined as $p < 0.05$ for the main analysis and $p < 0.10$ for interaction analysis. Data were analyzed using SAS Version 9.4 (SAS Institute Inc., Cary, North Carolina).

The National Centers for Health Statistics of the Center for Disease Control and Prevention institutional review board approved the protocol for NHANES III. All participants gave written informed consent at the time of study enrollment.

RESULTS & DISCUSSION

Across the 5110 participants examined, mean chronological age was 55.0 years, with ages ranging from 40 to 74 years. The study population was 52.5% female with 19.9% obesity, 31.4% hypertension, 23.7% dyslipidemia, and 9.8% diabetes. Baseline characteristics for study participants stratified by race are shown in Table 1. Whites had the highest chronological age, followed by Hispanics and blacks. Mexican-Americans were more likely to be obese and diabetic as compared with blacks and whites. The prevalence of smoking and hypertension was greatest in blacks, with whites more frequently hypertensive than Mexican-Americans and near-equal rates of smoking. Whites had higher rates of dyslipidemia compared with blacks and Mexican-Americans.

For the total study population, the mean heart age and excess heart age was 65.1 and 10.1 years, respectively. Blacks had the highest mean heart age (66.3 years), followed by whites (64.9 years) and Mexicans-Americans (64.3 years). Excess heart age was greatest in blacks (13.0 years), followed by Mexican-Americans (10.5 years) and whites (8.5 years). Pairwise differences in excess heart age between races were significant for all comparisons. Excess heart age in whites was 4.49 years lower than in blacks and 2.03 years lower than in Mexican-Americans. Mexican-Americans carried 2.46 fewer years of excess heart age than blacks, placing Mexican-Americans in an intermediate category (Figure 1).