Effect of Exceptional Parental Longevity and Lifestyle Factors on Prevalence of Cardiovascular Disease in Offspring

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Offspring of parents with exceptional longevity (OPEL) manifest lower prevalence of cardiovascular disease (CVD), but the role of lifestyle factors in this unique cohort is not known. Our study tested whether OPEL have lesser prevalence of CVD independent of lifestyle factors. Prevalence of CVD and CVD risk factors was assessed in a population of community-dwelling Ashkenazi Jewish adults aged 65 to 94 years. Participants included OPEL (n = 395), defined as having at least 1 parent living past the age of 95 years, and offspring of parents with usual survival (OPUS, n = 450), defined as having neither parent survive to 95 years. Medical and lifestyle information was obtained using standardized questionnaires. Socioeconomic status was defined based on validated classification scores. Dietary intake was evaluated with the Block Brief Food Frequency Questionnaire (2000) in a subgroup of the study population (n = 234). Our study found no significant differences in the prevalence of obesity, smoking, alcohol use, physical activity, social strata scores, and dietary intake between the 2 groups. After adjustment for age and gender, the OPEL demonstrated 29% lower odds of having hypertension (95% confidence interval [CI] 0.53 to 0.95), 65% lower odds of having had a stroke (95% CI 0.14 to 0.88), and 35% lower odds of having CVD (95% CI 0.43 to 0.98), compared with OPUS. In conclusion, exceptional parental longevity is associated with lower prevalence of CVD independent of lifestyle, socioeconomic status, and nutrition, thus highlighting the potential role of genetics in disease-free survival among individuals with exceptional parental longevity. **(Am J Cardiol 2017;120:2170–2175)**

Individuals with exceptional longevity demonstrate a marked delay in the onset of age-related diseases and in many cases are spared from developing diseases altogether.[1–3] Thus, this group of individuals has served as a model of healthy aging, with many scientific efforts devoted to elucidating the mechanisms that allow these unique subjects to stay well as they age.[4] In humans, life span is at least in part heritable, but the inheritance appears to be stronger for exceptional longevity, with several longevity-associated genes and genetic signatures identified.[5–8] A number of studies have demonstrated that the offspring of parents with exceptional longevity (OPEL) have lower incidence of cardiovascular disease (CVD) and lower prevalence of heart disease, stroke, and cancer compared with offspring of parents without exceptional longevity.[8–11] These observations suggest that the offspring are probably inheriting genetic factors from their parents that protect them from the effects of aging and diseases. Although exceptional longevity has been associated with reduced CVD risk, numerous studies conducted in the general population have also demonstrated that physical activity, healthy dietary patterns, higher socioeconomic status, and higher education are consistently related to better cardiovascular health.[12–14] However, to our knowledge, no studies have been conducted to date that compare the lifestyle factors of the OPEL with the offspring of parents without exceptional longevity. Thus, the present study tests the hypothesis that exceptional parental longevity is associated with lesser CVD prevalence independent of lifestyle factors, which if confirmed, would highlight the probable role of genetics on life span and health span.

Methods

The subjects are participants of the LonGenity study, an ongoing longitudinal study conducted at Albert Einstein College of Medicine, Bronx, New York since 2008. LonGenity focuses on identifying factors that contribute to protection from age-related diseases and extension of life span. All

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study participants are of Ashkenazi Jewish background, defined by all 4 grandparents being Ashkenazi Jewish, recruited from the Northeastern United States. This ensures relative genetic homogeneity of study subjects, thereby resulting in greater power to discover relevant genetic factors.[15] Two groups of participants were recruited based on the maximum life span achieved by their parents. The OPEL were defined as subjects with at least 1 parent living past the age of 95 years, about 20 years longer than the average life expectancy for the 1900 birth cohort.[2] These subjects are presumed to be enriched with longevity genotypes that they inherited from their parent with exceptional longevity. Offspring of parents with usual survival (OPUS) were defined as subjects whose both parents died before the age of 95 years. Both OPEL and OPUS were recruited through systematic searches of publicly available voter registration lists, contacts at synagogues and community organizations, and advertisements in Jewish newspapers.[16] A subset of eligible subjects (n = 85) were recruited from the Einstein Aging Study and were cross-enrolled. Potential participants were contacted by mail and then by telephone to assess interest and eligibility. Eligible participants were adults aged 65 to 94 years without baseline dementia, defined as a BLESSED score >8 and a score of >2 on the Eight-item Informant Interview to Differentiate Aging and Dementia at the initial screening interview, who were also free of severe visual or hearing impairments and who did not have a sibling already enrolled in the study.

At enrollment and at yearly follow-up visits, medical, lifestyle, and socioeconomic information was obtained using detailed standardized questionnaires. Cardiovascular-related diseases and outcomes included hypertension (HTN), diabetes mellitus (DM), myocardial infarction (MI), congestive heart failure (CHF), percutaneous coronary interventions (PCI), coronary artery bypass graft surgery (CABG), and stroke. A composite outcome of CVD included a self-reported history of any one of the following conditions: MI, PCI, CABG, or stroke. Data on antihypertensive medication use were also collected. Lifestyle assessments included a history of past or current tobacco use, alcohol use, and habitual physical activity. A physical performance questionnaire assessed self-reported walking endurance, number of blocks walked daily, number of stairs climbed daily, number of times strenuous physical activity undertaken weekly, and one's physical activity in the past year compared with people of similar age and gender. The nutritional information was obtained from a subgroup of the study population using the Block Brief Food Frequency Questionnaire (FFQ 2000) and the nutrient data were extracted from the questionnaires by NutritionQuest, Berkeley, California. This validated questionnaire was developed based on a modified food frequency questionnaire by Block et al.[17] Socioeconomic factors included education and social strata score that was calculated based on the classification described by Hollingshead.[18] Physical assessments performed at baseline included measurements of height, weight, and waist circumference. Body mass index (BMI) was calculated as weight in kilograms/height in meters^2 and obesity was defined as a BMI of ≥30 kg/m^2. Abdominal obesity was defined as waist circumference of ≥102 cm and ≥88 cm for men and women, respectively. A written informed consent was obtained from all the participants. The study was approved by the Institutional Review Board at the Albert Einstein College of Medicine.

Baseline data collected at enrollment were analyzed for this study. Descriptive statistics were used to compare prevalence of medical conditions, lifestyle factors, socioeconomic factors, and dietary intake between OPEL and OPUS. Continuous normally distributed data and nonparametric data were analyzed with parametric and nonparametric tests, respectively. Normality was assessed by visual inspection. The chi-square test was used for analysis of categorical variables, with Fisher exact test employed when appropriate. Odds ratios (OR) for disease prevalence were adjusted for age and gender in all models. Additional analyses were adjusted for tobacco use, social strata score, weekly strenuous activity, and BMI. Weekly strenuous activity was dichotomized as none weekly versus ≥1 times per week. Testing for interactions between OPEL or OPUS status and tobacco use, social strata score and weekly strenuous activity was performed in logistic models, with CVD as the outcome of interest. Stratified analysis was also conducted in those considered to be at high risk and low risk for CVD. High-risk subjects were defined as having diabetes mellitus or at least 2 of the following: obesity, HTN, or history of tobacco use. Those subjects who did not meet the above criteria were classified as low risk. About 20% (n = 176) of the study subjects were married couples, with 77 OPUS-OPEL pairs and 11 OPUS-OPUS pairs. There were no statistically significant differences in smoking rates ($p = 0.15$), weekly physical activity ($p = 0.19$), or education ($p = 0.33$) between couples and noncouples; thus, we pooled all subjects together and did not distinguish between coupled and noncoupled individuals in our final analysis. A p value of <0.05 was considered to be statistically significant. Data analysis was performed using SPSS version 12.0 (SPSS Inc., Chicago, Illinois) and STATA software, version 12 (StataCorp LP, College Station, Texas).

Results

The demographics, lifestyle and socioeconomic factors of the study population are presented in Table 1. The study included 845 participants, with 47% being OPEL. There were no significant differences in any of the lifestyle or socioeconomic factors between OPEL and OPUS. Despite having similar physical activity rates, the OPEL demonstrated greater walking endurance compared with OPUS. Physical characteristics and disease prevalence for the 2 groups are depicted in Table 2. There were no significant differences in BMI, blood pressure, or obesity between the 2 groups; however, OPUS were more likely to use antihypertensive medication than OPEL ($p < 0.01$). In models adjusted for age and gender, OPEL were found to be 29% less likely to have been hypertensive, 65% less likely to have had a stroke, and 35% less likely to manifest CVD overall, compared with OPUS. Although OPEL were also less likely to have had DM, MI, CHF, PCI, or CABG than OPUS, these differences did not persist after adjustment. Additional adjustment for BMI did not change the results. Age- and gender-adjusted logistic regression analysis, stratified on CVD risk, did not identify significant differences in the odds of CVD between OPEL and OPUS who were at low risk for CVD (n = 498) (OR 0.87 [0.49 to 1.54], $p = 0.63$). However, among the subjects at high risk