Published in final edited form as:

J Am Geriatr Soc. 2008 November ; 56(11): 2089–2092. doi:10.1111/j.1532-5415.2008.01949.x.

Centenarian Offspring: Start Healthier and Stay Healthier

Emily R. Adams, BA[‡], Vikki G. Nolan, MPH^{*}, Stacy L. Andersen, BS[†], Thomas T. Perls, MD, MPH[†], and Dellara F. Terry, MD, MPH[†]

[‡]School of Medicine, Boston University and Boston Medical Center, Boston, Massachusetts

^{*}Department of Epidemiology, School of Public Health, Boston University, Boston, Massachusetts

[†]New England Centenarian Study, Geriatrics Section, Department of Medicine, Boston University and Boston Medical Center, Boston, Massachusetts

Abstract

OBJECTIVES—To assess the relative incidence of age-related diseases in a group of centenarian offspring who have thus far been considered to be predisposed to “healthy” aging.

DESIGN—Longitudinal study.

SETTING—Nationwide sample.

PARTICIPANTS—Four hundred forty centenarian offspring and 192 referent cohort subjects who met inclusion criteria of having initial and follow-up health questionnaire data available. Median age of both cohorts was 72 at the initial health questionnaire.

MEASUREMENTS—Initial health questionnaires were collected from 1997 to 2006. Follow-up questionnaires were collected from 2004 to 2007. The mean period of follow-up was 3.5 ± 1.7 years for the centenarian offspring and 3.9 ± 2.2 years for the referent cohort.

RESULTS—During the follow-up period, centenarian offspring had a 78% lower risk of myocardial infarction ($P < .04$), 83% lower risk of stroke ($P < .004$), and 86% lower risk of developing diabetes mellitus ($P < .005$) than the referent cohort. There were no significant differences in new onset of other age-related diseases. Additionally, centenarian offspring were 81% less likely to die ($P < .01$) than the referent cohort during the follow-up.

CONCLUSION—These findings suggest that centenarian offspring retain some important cardiovascular advantages over time over similarly aged referent cohort subjects. These findings reinforce the notion that there may be physiological reasons that longevity runs in families and that centenarian offspring are more likely to age in better cardiovascular health and with a lower mortality than their peers.

Keywords

centenarian; longevity; morbidity; familial

Previous studies have shown that the offspring of centenarians (centenarian offspring) demonstrate a delayed age of onset of a number of age-related morbidities, particularly

cardiovascular disease (coronary heart disease and myocardial infarction) and cardiovascular disease risk factors (diabetes mellitus and hypertension).¹ They also exhibit lower cardiovascular and all-cause mortality than referent cohort subjects.² Centenarian offspring have also been noted, like their centenarian parent(s), to have genetic and functional advantages associated with lower cardiovascular disease risk.^{3–5} These findings support the hypothesis that centenarian offspring are predisposed to healthy aging and longer survival.

Over the past 10 years, the New England Centenarian Study (NECS) has enrolled and followed centenarian offspring and members of a similarly aged referent cohort whose parents died at average life expectancy. Initial and follow-up health questionnaires were administered to assess incidence of age-related diseases and mortality. To the authors' knowledge, this is the first study to assess the health of centenarian offspring over time, providing longitudinal depth to reports that centenarian offspring develop fewer age-related morbidities than similarly aged controls. The specific goal of this longitudinal analysis was to discern whether the differences in the presence of age-related diseases between centenarian offspring and control subjects persist over time or whether the differences disappear as the two groups get older. It was hypothesized that, over time, centenarian offspring would demonstrate less incidence of newly diagnosed age-related diseases and lower mortality than the referent cohort.

METHODS

Study Population

The NECS is a cross-sectional, nationwide study of individuals aged 97 and older (referred to as centenarians) and their family members. Attempts are made to recruit and enroll all living centenarian offspring enrolled in the NECS by letter or telephone. A full description of the recruitment and demographics of centenarian offspring and the referent cohort in the NECS was provided in an earlier report.⁶ Detailed health, physical function (as assessed according to the Older Americans Resources and Services (OARS) Multidimensional Functional Assessment Questionnaire), and demographic information were collected for 516 centenarian offspring (48.1% were unrelated offspring; 51.9% were siblings) whose parents were concurrently enrolled in the NECS.

Two types of referent cohort subjects were used: spouses of centenarian offspring ($n = 200$) and individuals with at least one parent born at approximately the same time as the centenarians but who died at the average life expectancy for that birth cohort (73 years for the 1900 birth cohort, $n = 43$). The latter group was identified through obituary notices of their parent(s); attempts were made to contact all children mentioned in the obituary notice, as has been previously described.⁶ Detailed health, physical function, and demographic information was collected for 243 referent cohort subjects (82.3% were unrelated; 17.7% were siblings).

Inclusion criteria consisted of completion of the initial questionnaires and completion of at least one follow-up health status questionnaire; 440 (85%) of the centenarian offspring and 192 (79%) of the referent cohort subjects met the inclusion criteria. Of those who met the inclusion criteria, 370 (72%) of the centenarian offspring and 140 (58%) of the referent cohort subjects completed the initial and at least one follow-up physical function questionnaire. The median age of the centenarian offspring and the referent cohort at the time of the initial health questionnaire was 72. Follow-up questionnaires were sent to all of the participants. The period of follow-up ranged from 1 to 8 years, with means of 3.5 years for the centenarian offspring and 3.9 years for the referent cohort. The wide range in the follow-up period was attributed to two factors; there was a significant delay between the study initiation in 1997 and the first follow-up examination in 2004, and in some cases, participant relocation extended the time interval between study contacts.

Measurement Tools

The health questionnaire is a self-report questionnaire of sociodemographic factors; history of diabetes mellitus, coronary artery disease, heart attack, cardiac arrhythmia, heart failure, stroke, cancer, dementia, high blood pressure, cataracts, glaucoma, macular degeneration, osteoporosis, depression, Parkinson's disease, thyroid condition, emphysema, or chronic obstructive pulmonary disease; hip, wrist, and spine fractures; current medications; reproductive history; alcohol consumption; smoking history; and exercise. The rationale for the selection of the above conditions was to capture major age-related diseases that contribute to morbidity and mortality and are accurately self-reported. Additionally, the participant's physician filled out a physical examination questionnaire for height, weight, blood pressure, and temperature at a routine examination. The final part of the health questionnaire, the OARS Multidimensional Functional Assessment Questionnaire,⁷ is based on a 14-point scale (with 14 representing the highest functioning) that has been validated in older populations.

Statistical Methods

Descriptive statistics were generated for centenarian offspring and the referent cohort. The total number of subjects who developed each health condition and the respective ages of onset were determined. The proportion of subjects that developed each condition was compared using chi-square tests, or for those with expected cell counts of less than 5, the Fisher exact test was used. Age of onset was compared using analysis of variance (ANOVA).

After crude analysis, adjusted analyses were performed. Multiple logistic regression was used to compare categorical traits, and multiple linear regression was used for age-of-onset analyses. All analyses were adjusted for potential confounders, including sex and age, and for results for which the measure differed from the crude by more than 10%, the adjusted results were reported. In this study, sex was the only variable that confounded the relationship between offspring status and age of disease onset; therefore, all analyses were sex-adjusted. Some of the study subjects had shared environments (spousal controls) or were blood related (centenarian offspring siblings); therefore, all analyses were repeated using generalized estimating equations (GEEs) to account for correlations between individuals.

All analyses were performed using SAS version 9 (SAS Institute, Inc., Cary, NC).

RESULTS

Table 1 provides the number of incident cases of various age-related diseases for centenarian offspring and referent cohort subjects. The mean period of follow-up was 3.5 ± 1.7 years for centenarian offspring and 3.9 ± 2.2 years for the referent cohort. Centenarian offspring were 78% less likely than the similarly aged referent cohort (mean age at enrollment was 72 years for both groups) to have a myocardial infarction ($P < .04$), 83% less likely to have stroke ($P < .01$), and 86% less likely to develop diabetes mellitus ($P < .01$). There was no significant difference between the two groups for the incidence of hypertension, arrhythmia, dementia, cancer, depression, fracture, glaucoma, macular degeneration, osteoporosis, or thyroid disease.

Centenarian offspring were less likely to die during the period of follow-up evaluation than were equivalent referent cohort subjects. During follow-up, 1.1% ($n = 5/440$) of centenarian offspring died, compared with 5.2% ($n = 10/192$) of the referent cohort. Overall, the centenarian offspring had a 81% lower odds of mortality ($P < .01$) during the period from the health questionnaire to follow-up.

Centenarian offspring and the referent cohort had similar levels of functional decline based on decrease in OARS Multidimensional Functional Assessment Questionnaire score over the period subjects were followed ($P = .14$): centenarian offspring declined on average 0.16 points

and the referent cohort declined a mean of 0.36 points on the OARS Multidimensional Functional Assessment Questionnaire score between initial screening and follow-up (out of a total possible score of 14).

As stated earlier, some of the study subjects had shared environments or were blood-related; therefore, all analyses were repeated using GEEs to account for correlations between individuals. Because few subjects develop an age-related condition during the follow-up, and most often, there was no familial correlation between those who developed disease, the results of GEE analyses were virtually identical to those obtained through multiple logistic regression.

DISCUSSION

Over an average follow-up period of 3 to 4 years during their 70s, centenarian offspring were less likely to be diagnosed with new cases of myocardial infarction, stroke, and diabetes mellitus than the similarly aged referent cohort. In addition, centenarian offspring had 81% lower all-cause mortality during the period examined.

Previous studies^{1,6} have shown that, at similar ages, centenarian offspring have a lower prevalence of cardiovascular disease than sex-matched referent cohort subjects and that centenarian offspring tend to be older when they acquire the same cardiovascular morbidities. Published results from the original health questionnaire demonstrate that the centenarian offspring and the referent cohort had different initial health profiles. This study demonstrates that, centenarian offspring, as a group, retain their initial advantages, especially in terms of better vascular health than the comparison group. The differences originally found between the offspring and referent group are preserved and possibly accentuated over time, suggesting that the two groups have different patterns of aging. In other words, almost 4 years after initial evaluation the centenarian offspring were still demonstrating a relative compression of morbidity and their odds of mortality were substantially lower than those of the referent group.

For centenarians to achieve their exceptional longevity, they must consistently avoid or somehow survive acute and chronic conditions that can lead to mortality. It has previously been noted that approximately 32% of centenarians survive longer than 15 years with an age-related disease and that the remainder delay or escape the conditions that cause earlier mortality in others of their birth cohort.⁸ The current findings suggest that centenarian offspring are following in their parent's footsteps, avoiding some of the vascular morbidities afflicting their peers and, more importantly, being less likely to die over time.

Although one might expect that the more-frequent onset of acute disease such as myocardial infarction or stroke would be associated with decline in physical function, this study demonstrated that centenarian offspring and the referent cohort had similar levels of decline, as measured according to the OARS Multidimensional Functional Assessment, in the time between the original health questionnaire and follow-up questionnaire. The lack of observed difference may be a function of the low prevalence of many age-related diseases (partially due to the population's still relatively young age). In addition, although the list of age-related diseases on the health questionnaire is extensive, it is not exhaustive and misses conditions such as osteoarthritis that may lead to functional decline. Finally, the OARS Multidimensional Functional Assessment, which is heavily dependent upon preserved cognitive function, may not have been adequately sensitive to differences in the decline of physical function between the groups.

The current study examines the change in disease incidence of centenarian offspring and the referent cohort from the initial data collection to the first (and in a few cases second) follow-up survey. In years to come, continued follow-up of centenarian offspring and the referent cohort will allow whether differences will emerge in the incidence of other age-related diseases.

and whether the lower rates of onset of diabetes mellitus, myocardial infarction, and stroke are sustained to be observed. Furthermore, future serial measurements of health variables such as blood pressure and cholesterol values will allow whether there are differences in physiological measures to be determined. Ultimately, ongoing investigation of this unique population will explore the role, nature, and extent of familial contribution to exceptional longevity.

This study had several potential limitations that need to be acknowledged. The initial health questionnaire and follow-up questionnaires relied on self-report, although these data have been validated through medical record review, and therefore this is unlikely to be a significant source of bias. Another possible limitation was the varying lengths of time that elapsed between the initial and follow-up health data, because the questionnaires are administered through the mail. This may result in higher rates of disease onset reported by those with more time between questionnaires. Although statistically different (3.5 years in offspring vs 3.9 years in the referent cohort), the difference in follow-up was, on average, approximately 4.8 months, which should not result in considerable overreporting of disease by the referent cohort. Another limitation was that more siblings were enrolled in the centenarian group than in the referent group. Although the study attempted to contact all siblings of the referent group whose parents died at average life expectancy, siblings from the second referent group (spousal controls) were not enrolled. Because there are so few instances in which siblings develop the same condition over follow-up, it is unlikely that this was a significant source of bias. Finally, selection bias due to differential participation rate in the follow-up questionnaire may be of some concern. Although there was a higher rate of participation in the follow-up questionnaire among the centenarian offspring (85%, vs 79% in referent cohort subjects), participants who did not follow up did not significantly differ from those who did according to sex, education, age, or baseline prevalence of heart attack, hypertension, diabetes mellitus, or stroke. Furthermore, there were no significant differences in the baseline characteristics listed above between the centenarian offspring and referent cohort that did not participate in follow-up.

CONCLUSION

By examining the onset of new disease over time, this study takes the original health data from the centenarian offspring and extends it to compare how they age with how the referent cohort ages. Studies have consistently shown that centenarian offspring have a lower prevalence of cardiovascular disease.⁶ The most recent results suggest that centenarian offspring retain many of their vascular advantages as they age, further reinforcing the importance of cardiovascular health in achieving exceptional old age as well as the familial nature of longevity.

Acknowledgments

Conflict of Interest: Dellara F. Terry: National Institute on Aging (NIA) Grants K08AG22785, K23 AG026754—Paul Beeson Physician Faculty Scholar in Aging Awards. Thomas T. Perls: NIA Grant K24 AG025727. Emily R. Adams: The American Federation for Aging Research provided funding through the Medical Student Training in Aging Research Program. Vikki G. Nolan: National Heart, Lung, and Blood Institute Grant T32 HL007501. Stacy L. Andersen: NIA Grant U01 AG023755.

Sponsor's Role None.

REFERENCES

1. Terry DF, Wilcox MA, McCormick MA, et al. Cardiovascular disease delay in centenarian offspring. *J Gerontol A Biol Sci Med Sci* 2004;59A:M385–M389.
2. Terry DF, Wilcox MA, McCormick MA, et al. Lower all-cause, cardiovascular, and cancer mortality in centenarians' offspring. *J Am Geriatr Soc* 2004;52:2074–2076. [PubMed: 15571545]
3. Barzilai N, Gabriely I, Gabriely M, et al. Offspring of centenarians have a favorable lipid profile. *J Am Geriatr Soc* 2001;49:76–79. [PubMed: 11207846]

4. Atzmon G, Rincon M, Schechter CB, et al. Lipoprotein genotype and conserved pathway for exceptional longevity in humans. *PLoS Biol* 2006;4:e113. [PubMed: 16602826]
5. Barzilai N, Atzmon G, Schechter C, et al. Unique lipoprotein phenotype and genotype in humans with exceptional longevity. *JAMA* 2003;290:2030–2040. [PubMed: 14559957]
6. Terry DF, Wilcox MA, McCormick MA, et al. Cardiovascular advantages among the offspring of centenarians. *J Gerontol A Biol Sci Med Sci* 2003;58A:M425–M431. [PubMed: 12730251]
7. Fillenbaum GG. Screening the elderly. A brief instrumental activities of daily living measure. *J Am Geriatr Soc* 1985;33:698–706. [PubMed: 4045087]
8. Terry DF, Sebastiani P, Andersen SL, et al. Disentangling the roles of disability and morbidity in survival to exceptional old age. *Arch Intern Med* 2008;168:277–283. [PubMed: 18268168]

Table 1
Changes over Time in Disease Incidence: Centenarian Offspring Versus Reference Cohort

Disease or Condition	n*	Centenarian Offspring with New Onset of Disease, n (%)	n*	Reference Cohort Subjects with New Onset of Disease, n (%)	Prevalence Odds Ratio (95% Confidence Interval)	P-Value
Myocardial Infarction	404	3 (0.7)	172	6 (3.5)	0.22 (0.05–0.92)	.04
Diabetes mellitus	395	3 (0.8)	166	9 (5.4)	0.14 (0.04–0.55)	.005
Stroke	413	4 (1.0)	179	11 (6.1)	0.17 (0.05–0.57)	.004
Hypertension	300	53 (17.7)	105	26 (24.8)	0.65 (0.38–1.13)	.13
Dementia	419	2 (0.5)	184	5 (2.7)	0.21 (0.04–1.14)	.07
Cancer	297	32 (10.8)	118	18 (15.3)	0.82 (0.43–1.56)	.54
Arrhythmia	350	19 (5.4)	142	15 (10.6)	0.51 (0.25–1.06)	.07
Depression	350	13 (3.7)	143	9 (6.3)	0.62 (0.25–1.53)	.30
Fracture	346	15 (4.3)	149	10 (6.7)	0.59 (0.25–1.38)	.22
Glaucoma	353	9 (2.5)	148	5 (3.4)	0.92 (0.30–2.88)	.89
Macular degeneration	355	10 (2.8)	149	5 (3.4)	0.75 (0.24–2.29)	.61
Osteoporosis	338	40 (11.8)	145	15 (10.3)	0.86 (0.45–1.66)	.66
Thyroid disease	314	17 (5.4)	145	11 (7.6)	0.58 (0.26–1.29)	.18

Note: All analyses were sex adjusted.

* Total sample size from each cohort who were free of the condition or disease at beginning of study and had follow-up data available.