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Parents' Attained Age and Biomarkers of Aging in Their Children

Barbara E. K. Klein, MD, MPH, Michael D. Knudtson, MS, Kristine E. Lee, MS, and Ronald Klein, MD, MPH

Department of Ophthalmology and Visual Sciences, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin

Abstract

Purpose—To examine levels of biomarkers of aging in offspring by the attained age of their parents.

Methods—Current age or age at death of parents of participants in the Beaver Dam Eye Study was obtained in 1988–2000 (baseline examination). Biomarkers of aging (i.e., hand grip strength, chair stand, gait time, peak expiratory flow rate, visual acuity, and contrast sensitivity) were measured 10 and 15 years later (second and third follow-up examination).

Main Findings—Gait time, peak expiratory flow rate, visual acuity, and contrast sensitivity were significantly positively associated with increased parental age. Lower scores on an index combining poor measures of biomarker measures were highly associated with increased parental age.

Conclusions—Greater attained parental age is associated with better functional status of adult children as reflected in levels of biomarkers of aging.

Keywords

Biomarkers of aging; parents' age and function in adult children; frailty and parents' age

1. INTRODUCTION

Longevity is a familial trait (Perls et al., 1998; Willcox et al., 2006; Schoenmaker et al., 2006). Survival advantage to children of longer-lived parents is not confined to children whose parents live to be 100 years of age or older. Pearl and Pearl (Pearl and Pearl 1934) and Abbott and colleagues (Abbott et al., 1978) demonstrated a survival benefit to children of 90 year olds, and the Framingham study extended that to 85 year old parents (Terry et al., 2007). Others have found a salutary effect on children of parents age extending to parents in their 8th decade of life (Kerber et al., 2001; Klein et al., 2007). Terry et al. (Terry et al., 2007) have found that cardiovascular risk factor levels are lower in children of older parents. We hypothesized that there would likely be functional benefits as opposed to simply absence of specific disease or low risk factor levels for specific diseases that would accrue to children of longer-lived parents and that this would manifest itself as better scores on measures of general functional ability. In this report, we describe the effect of parents' attained age on the presence and severity of biomarkers of aging as measures of functional ability in their children.

Correspondence to: Barbara Eden Kobrin Klein, MD, MPH University of Wisconsin Madison Department of Ophthalmology and Visual Sciences 610 N. Walnut Street, 4th Floor WARF Madison, Wisconsin 53726 USA 608/263-0276 608/263-0279 fax kleinb@epi.ophth.wisc.edu.

CONFLICT OF INTEREST

None of the authors has a conflict of interest with this paper.

2. EXPERIMENTAL/MATERIALS AND METHODS

All persons 43-84 years of age living in Beaver Dam, Wisconsin, in 1987 identified by a private census were requested to participate in a study of age-related eye disease. Tenets of the Declaration of Helsinki were followed, institutional review board at the University of Wisconsin – Madison granted approval, and informed consent was obtained from each subject (Klein et al., 1991). Of the 5924 persons in the target age range, 4926 participated in a baseline evaluation that included history of whether their parents were alive or not and attained age or age at death of the parents. A medical history was obtained and an eye and abbreviated medical examination were performed at baseline and at each follow-up examination. The medical history included questions about cardiovascular disease. Diabetes was diagnosed by history and glycosylated hemoglobin (Klein et al., 1992). Hypertension was diagnosed based on blood pressures taken by protocol (Hypertension Detection and Follow-up Program Cooperative Group 1976) (systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg or use of anti-hypertensive medication). Next, we summarize only those other methods pertinent to this paper. Distance visual acuity was measured according to a modification of the Early Treatment Diabetic Retinopathy Study (ETDRS) protocol (Early Treatment Diabetic Retinopathy Study (ETDRS) 1985; Klein et al., 1991) for each eye and was denoted as best-corrected visual acuity. Results were given as the number of letters read (Klein et al., 1991). Contrast sensitivity was measured using the Pelli-Robson charts (Pelli et al., 1988). Examinations were conducted at 5-year intervals with few additions to the study evaluations at specific examinations. Aside from parents' attained age, the data for this paper are from measurements taken at the second (10-year) follow-up examination because some of the biomarkers were first measured at that examination.

Ambulatory participants were instructed to walk a measured course at their usual pace. The time was recorded (gait-time) (Guralnik et al., 1994). The peak expiratory flow rate was measured using the mini-Wright meter (Klein and Klein 1999). The participant was asked to stand and was instructed to take as deep a breath as possible and to blow as hard and fast as s/he was able. This was repeated two more times, and the best value (greatest flow rate) was used in the analysis. Dynamometry (hand grip strength) was performed in each hand two times. The mean of two measures for the dominant hand was used in these analyses (Evans 1995). The participant was then seated in a standard chair (seat 19 1/2 inches from the floor) which was against the wall. The participants who felt that it was safe for them to stand up without help were asked to do so without using her/his hands. If unable to rise without using hands, the participant was instructed to stand up using hands. The method (with or without hands) was recorded.

Preliminary analyses were performed for each eye. There were no systematic differences between the eyes. We used data for responses in the better eye for visual acuity and contrast sensitivity based on the assumption that performance is a function of vision in the better eye.

2.1 Statistical Methods

Analytical techniques including computation of means, standard deviations, proportions, and regression models were performed using version 9.1 of SAS (Cary, NC) (SAS Institute Inc. 2004).

Maximum parental age was considered to be the attained age irrespective of survival reported by their children at the baseline examination of the cohort (e.g., for parents where the mother is alive and age 83 years, and the father was deceased at age 76 years, the maximum parental age was 83 years). The parent with the highest attained age was still alive at baseline in 1122 of the 2649 participants with complete data. Survival status of parents was not determined at follow-up examinations. The majority of outcomes were continuous variables (e.g., number of

letters identified in the log MAR vision test). Multivariate regression was used to model these outcomes. Ability to rise from the chair in one attempt without using arms was modeled with logistic regression.

For purposes of analysis, we categorized the aging biomarkers as follows: best corrected visual acuity was categorized into 20/20 or better, 20/25-20/32, and 20/40 or poorer in better seeing eye (because analyses using visual acuity [VA] and contrast sensitivity were nearly identical we chose to include only visual acuity as that measure is more commonly available than measures of contrast sensitivity); inability to rise from a chair without using arms; gait time, hand grip strength, and peak expiratory flow rate (PEFR) were categorized in sex-specific quartiles. The poorest category for each function was considered to indicate the presence of frailty for that function. The total frailties were summed to give an index of biological aging (frailty) for each individual by adding 1 for any of the following: best corrected VA 20/40 or worse in the better eye; inability to rise from a chair without using arms; highest quartile for gait time (≥ 3.37 seconds for women, ≥ 3.19 seconds for men); lowest quartile for hand grip strength (≤ 18.5 kg for women, ≤ 34.5 kg for men); lowest quartile for PEFR (≤ 290 L/minute for women, ≤ 440 L/minute for men). Therefore, the minimum frailty score was 0 and the maximum score was 5. Persons with an index score of 0 or 1 and who were missing data on three or more of the tests were excluded from this analysis (N=237). The frailty index outcome was modeled with proportional odds models.

Biomarkers of frailty for age were evaluated using parental age group as the risk factor. In addition, all models controlled parental survival status and were stratified by gender. To determine if any significant relationships were independent from other comorbidities, we further adjusted for hypertension, diabetes, and history of cardiovascular disease. We also considered lifestyle factors (e.g., smoking status and education) as potential confounders.

3. RESULTS

The age of cohort members by the attained age of their parents indicates that greater attained age of parents is associated with older age of their children (Table 1). After controlling for age, older persons were more likely to have a parent with a higher attained age. Younger persons were more likely to have a living parent than older persons but the older the parent, irrespective of the age of the child, the more likely they were to be living (data not shown). In addition, persons with older parents' attained age were more likely to be free of cardiovascular disease.

In the following analyses, we controlled for age and parental survival status. Neither hand grip strength nor ability to rise from a chair without using hands was significantly associated with parents' attained age (Figures 1a and 1b). Gait time was faster and peak expiratory flow rate was greater for those with greater parents' attained age, but these trends were only significant in women (Figures 1c and 1d). Both best corrected visual acuity and contrast sensitivity were consistently and significantly better in those with greater parents' attained age (Figures 1e and 1f).

There were 2515 of the 2962 participants for whom we had data for best corrected visual acuity, gait time, peak expiratory flow rate, hand grip strength, and chair stand. Those without all measurements tended to be older, female, had poor peak flow, had poor grip, were less able to do the chair stand, had poor visual acuity, resided in a nursing home (Klein et al., 2005), and were more likely to have parents with lower attained age after controlling for age.

We computed the odds of having a poorer frailty score after adjusting for age and the survival status of the parent with the highest attained age (Table 2). For men, there was a trend across the categories of parents' attained age. The trend was no longer significant after additionally controlling for diabetes, hypertension, and history of cardiovascular disease. For women, the

trends were significant in both models. By combining both sexes and adding sex to both models, the trends were highly significant. Results were similar in models that additionally adjusted for history of cancer, smoking status, and education (data not shown).

4. DISCUSSION

Older attained parental age was associated with better values for biomarkers of aging in children. This is consistent with our finding of a beneficial effect of parents' attained age and survival in this cohort (Klein et al., 2007) and of our finding of increased morbidity and decreased survival in those who were frailer in the cohort (Klein et al., 2005). Terry et al. (Terry et al., 2007) has described a survival advantage specifically for cardiovascular disease of children with long-lived parents, but much of the effect was related to lifestyle risk factors for cardiovascular disease. When we adjust for cardiovascular disease (including hypertension and diabetes), we found a residual effect of parents' attained age on frailty, suggesting that the beneficial effects of longer-lived parents is not restricted to the cardiovascular system.

We found some differences between the apparent effects of parents' age on the biomarkers by the sex of the children with more significant associations in women. This may reflect better health care, nutrition, and lifestyles than men. However, this finding may also reflect more exposure to adverse environment for men than women thereby obscuring an inherent genetic or familial effect. Since we are ignorant of parents' medical and occupational history, we offer this discussion only as speculation. In addition, there are fewer men in each category of parental age rendering statistical significance less likely in men despite similar estimates of the odds ratio.

We included two measures of visual function in our 'battery' of biomarkers of aging. We have found that while age-related macular degeneration and the two most common forms of cataract that are often associated with decreased vision were not associated with parents' age (data not shown), visual functions were associated. We suspect that vision, as a measure of sensory neural function, adds important information to the concept of frailty that is not otherwise captured in the other measures.

Because we do not have the biomarkers of aging in the parents, we cannot address the question of whether the parents would have similar age-specific levels of the biomarkers that we found in their children. We might, however, infer that the older parents were probably less frail than their age peers and that frailty measures in them might have predicted their survival as it has in their children (Klein et al., 2007).

Limitations of our study include our not being able to address these relationships in the full cohort as defined at baseline because we did not have all the biomarkers measured at that visit. By the time of the second follow-up examination, some participants did not return. We cannot estimate the direction or magnitude of the effect this might have had on our findings. Also, at the baseline examination, more than a thousand persons in the cohort had at least one living parent. The attained age of those parents underestimates their actual lifespan and so potentially underestimates the effect of parents' length of life on their children.

5. CONCLUSION

In summary, parents' attained age is a significant correlate of frailty in their children. The effect is independent of specific diseases including cardiovascular disease and cancer. This is consistent with the hypothesis of specific genetic determinants of robustness and likely of longevity.

Acknowledgments

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Figure 1a.
Adjusted* mean hand grip strength (kg) by maximum parental age and gender.

* Adjusted for age and parental survival status

Figure 1b.
Adjusted* percent unable to rise from chair without using arms in 1 attempt by maximum parental age and gender.

Figure 1c.
Adjusted* mean gait time (seconds) by maximum parental age and gender.

Figure 1d.
Adjusted* mean peak expiratory flow rate (liters/min) by maximum parental age and gender.

Figure 1e. Adjusted* mean visual acuity (number of letters in better seeing eye) by maximum parental age and gender.

Figure 1f.
Adjusted* mean contrast sensitivity (log triplet score in better seeing eye) by maximum parental age and gender.

Table 1Population Characteristics^a at the 2nd Follow-up Examination by Maximum Parental Age

Characteristic	Maximum Parental Age			<i>p-value</i> ^c
	< 75 years (N=694) ^b	75-89 years (N=1637) ^b	90+ years (N=318) ^b	
Age, mean (SD) years	64.7 (9.9)	68.6 (8.9)	75.4 (7.8)	<.001
Male, %	40.9	43.2	35.3	.91
Max parent alive, %	27.3	41.1	51.9	<.001
Diabetes, %	12.2	11.6	9.8	.34
Cardiovascular disease history, %	20.3	16.8	15.7	.05
Hypertension, %	60.9	59.3	53.5	.16
Cancer, %	17.6	21.3	26.0	.06
Less than high school education, %	24.0	19.1	16.8	.03
Ever a smoker, %	55.1	51.5	48.5	.05

Note: SD=standard deviation

^aRates adjusted for age in 4 groups^bMaximum parental age groups: < 75 years, 75-89 years, and 90+ years: For men: 294, 715, 118, respectively and for women: 400, 922, 200, respectively^cF-test for age and age-adjusted Cochran-Mantel-Haenszel test for all other variables

Table 2
Adjusted Proportional Odds Models for Poorer Frailty Score and Maximum Parental Age

Gender	Parents Maximum Attained Age	Multivariate Model 1 ^a			Multivariate Model 2 ^b		
		OR	(95% CI)	p-value	OR	(95% CI)	p-value
Men	< 75 years	referent			referent		
	75-89 years	0.75	(0.56, 1.01)	0.06	0.75	(0.56, 1.00)	0.054
	90+ years	0.71	(0.45, 1.10)	0.12	0.75	(0.48, 1.17)	0.20
	Trend	0.82	(0.66, 1.01)	0.07	0.84	(0.67, 1.04)	0.11
Women	< 75 years	referent			referent		
	75-89 years	0.83	(0.64, 1.07)	0.16	0.85	(0.65, 1.10)	0.22
	90+ years	0.58	(0.40, 0.83)	0.003	0.59	(0.41, 0.86)	0.006
	Trend	0.77	(0.64, 0.92)	0.004	0.78	(0.65, 0.94)	0.007
Both	< 75 years	referent			referent		
	75-89 years	0.80	(0.66, 0.97)	0.02	0.80	(0.66, 0.98)	0.03
	90+ years	0.62	(0.47, 0.82)	<0.001	0.64	(0.48, 0.85)	0.002
	Trend	0.79	(0.69, 0.91)	<0.001	0.80	(0.70, 0.92)	0.002

^a adjusted for age, gender (where appropriate), and parent's survival status

^b adjusted for all variables in Model 1 and additionally for diabetes, hypertension and history of cardiovascular disease