RELATIONSHIP OF MEASURES OF FRAILTY TO VISUAL FUNCTION: THE BEAVER DAM EYE STUDY

BY *Barbara E. K. Klein MD*,* *Ronald Klein MD*, *Michael D. Knudtson MS*, AND *Kristine E. Lee MS*

ABSTRACT

Purpose: To investigate the association of standard measures of frailty to visual acuity and contrast sensitivity.

Methods: Time to walk a measured course, handgrip strength, peak expiratory flow rate, ability to stand from a sitting position without using arms, best-corrected visual acuity, and contrast sensitivity were assessed at the third examination (1998-2000) of the Beaver Dam Eye Study. The study is population-based with the initial census in 1988-1990.

Results: All measures of frailty and vision were significantly associated with age (poorer function at older ages). In general, women had poorer function than men in each age category. An "index of frailty" consisting of highest quartile (slowest) gait time, lowest quartile of peak expiratory flow rate, lowest quartile of handgrip strength, and inability to stand from sitting in one try (for those not in a wheelchair) was constructed for women and men. A score of 0 was the minimum amount of frailty, while a score of 4 indicated the maximum amount. Controlling for age, those with no evidence of frailty (score = 0) were likely to have the best visual acuity and best contrast sensitivity, while those with maximum evidence of frailty (score = 4) were likely to have poorest visual acuity and contrast sensitivity.

Conclusion: Greater frailty was associated with poorer visual functions. Including a measure of visual function when assessing frailty may improve upon the usefulness of an index of frailty in predicting incidence of chronic systemic diseases and survival.

Trans Am Ophthalmol Soc 2003;101:191-200

INTRODUCTION

Frailty is the vulnerability to adverse outcomes resulting from declines in multiple systems[1-4] as distinguished from disability.[5,6] Markers of frailty include age-related decreases in balance, muscle strength, mobility, gait time, "shrinking,"[5,6] and, in some investigations, poor lung function.[7] These clinical and measurable signs are likely accompanied by diminished physiologic reserve, which may result in a reduced ability to rebound from challenges, leading to increased morbidity and mortality.[5,7]

Visual function declines with age, and for various functions the decline is consistent and predictable.[8] This is true even after excluding from consideration persons with age-related eye diseases (eg, cataract, age-related macular degeneration). Visual impairment is also associated with subsequent mortality[9-11] and so may also be a useful measure of frailty. It is the purpose of this report

to describe the distributions of measures of frailty and their association with visual function in a large population-based study.

METHODS

A private census of the population of Beaver Dam, Wis, was performed from 1987 to 1988, to identify all persons 43 years and older.[12] Persons aged 43 to 86 years participated in the study evaluation that was performed during a 2.5-year period beginning March 1, 1988.[13] The examined group was 99% white. Tenets of the Declaration of Helsinki were followed, the institutional review board approval was granted, and informed consent was obtained from each subject. During the study visit, standard measurements were made, and a questionnaire was administered. All subjects who were identified at the initial census[13] were invited for a second examination 5 years later and for a third examination 10 years after the baseline examination. The differences between participants and nonparticipants at the baseline,[13] 5-year,[14] and 10-year follow-up[15] examinations have been previously published. Those who were alive but not participating at later visits were older and had poorer visual acuity. Those who had

died were older, were more likely to be men, had poorer visual acuity, and were more likely to have diabetes.[13-15]

For purposes of this inquiry, we use measurements at the 10-year examination of the cohort because some of the measurements were not taken at previous examinations. Only pertinent parts of the examination are described.

Distance visual acuity was measured according to a modification of the Early Treatment Diabetic Retinopathy Study (ETDRS) protocol[16] for each eye and was denoted as best-corrected visual acuity. Results were given as the number of letters read, as well as Snellen equivalents ranging from 20/10 to no light perception. We use the Snellen equivalents in tables. The Pelli-Robson letter charts were used to measure contrast sensitivity for each eye.[17] Log contrast sensitivity scores were calculated and ranged from 0 to 1.95 based on the triplet score.

Preliminary analyses were performed for each eye. There were no systematic differences between the eyes. We present data for responses in the better eye based on the assumption that performance in real life situations is a function of vision in the better eye. However, there were no systematic differences in the associations of visual function in either eye or the better eye with the measures of frailty.

Ambulatory subjects were instructed to walk a measured course of 10 feet at their usual pace. The time was recorded.[18] The participant was then seated in a standard chair (seat 19.5 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 their arms. If unable to rise without using arms, participants were instructed to stand up using their arms. The number of attempts to rise was recorded. The method (with or without arms) was recorded.

The peak expiratory flow rate was measured using the mini-Wright meter.[19] The participant stood and was instructed to take as deep a breath as possible and to blow as hard and fast as she or he could. This was repeated two more times. The best value (greatest flow rate) was used in the analysis.

Dynamometry was performed in each hand two times. The mean of two measures for the dominant hand was used in these analyses.[19]

A frailty index was devised according to the following scheme: highest quartile of gait time (≥3.37 seconds in women, ≥3.19 seconds in men); lowest quartile of peak expiratory flow rate (≤290 L/minute for women, ≤440 L/minute for men); lowest quartile for handgrip strength for the dominant hand (≤18.5 kg for women, ≤34.5 kg for men); and not being able to stand without using their arms from a sitting position in one try. Individuals who had none of these conditions were assigned a score of 0; those who had all of these conditions were assigned a score of 4.

Each component was given equal weight. Analytical techniques include computations of means, standard deviations, chi-square statistics, computation of Spearman and Pearson correlation coefficients, and linear regression.

RESULTS

Of the 2,962 participants seen at the third examination, 87% had data on gait time, 90% had data on handgrip strength, 90% had data on peak expiratory flow rate, and 91% had data on chair stand. Those without all measurements tended to be older and female, had poorer peak expiratory flow rate, had poorer handgrip strength, were less able to stand from sitting in a chair, and resided in a nursing home. Values for gait time, handgrip strength in the dominant hand, and peak expiratory flow rate differed by age and sex (Table I). For the chair stand, there was decreased ability to rise in one attempt with age, but differences between women and men were not significant ($P = .80$).

The four measures of frailty were significantly correlated with each other with absolute value of correlations ranging from 0.31 to 0.52 (Table II). The correlation coefficients were slightly stronger for women than for men. Best-corrected visual acuity in the better eye was better for men than for women and was decreased in both sexes in older age-groups (Table IIIA). Contrast sensitivity in the better eye was better for men than for women ($P < .001$) and diminished in both groups with increasing age ($P < .001$) (Table IIIB). The vision variables were significantly correlated with the measures of frailty (Table IV). The associations were similar in magnitude for best-corrected visual acuity and contrast sensitivity except that the chair stand had slightly higher correlations for visual acuity than for contrast sensitivity. The correlation coefficients were a bit stronger for women than men.

Table V gives the frailty scores for women and men by age. Persons without all four frailty measurements were excluded from this analysis (N = 446). The frailty score increased with age ($P < .001$). Best-corrected visual acuity (as described in the "Methods" section) (Table VIA) and contrast sensitivity (Table VIB) were strongly associated with the frailty score.

DISCUSSION

We had hypothesized that visual function might add to the ability of the index of frailty based on other functional measures to estimate the hazard of morbidities related to a variety of disease conditions and to survival. We used visual function rather than specific age-related eye diseases, because our concept of frailty, as in the Cardiovascular Health Study,[5] is that frailty differs from
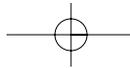
Relationship of Measures of Frailty To Visual Function: The Beaver Dam Eye Study

TABLE I: FRAILTY MEASURES BY AGE AND SEX

A. GAIT TIME (SECONDS)

		WOMEN				MEN		
AGE (YR)	N	MEAN	SD	*P**	N	MEAN	SD	*P**
53-64	592	2.64	0.649		496	2.62	0.559	
65-74	467	2.98	0.795		364	2.89	0.791	
75-84	338	3.58	1.149		228	3.26	0.899	
85+	71	4.61	1.916	<.001	26	3.95	1.069	<.001

Age-adjusted *P* value women versus men: <.001.
*Test of trend.

B. HANDGRIP, DOMINANT HAND (KG)

		WOMEN				MEN		
AGE (YR)	N	MEAN	SD	*P**	N	MEAN	SD	*P**
53-64	586	27.3	5.62		492	46.5	8.80	
65-74	468	23.3	5.81		371	40.1	9.30	
75-84	370	18.8	5.57		234	33.9	9.14	
85+	102	14.6	5.15	<.001	42	25.3	9.08	<.001

Age-adjusted *P* value women versus men: <.001.
*Test of trend.

C. MAXIMUM PEAK EXPIRATORY FLOW RATE (L/MIN)

		WOMEN				MEN		
AGE (YR)	N	MEAN	SD	*P**	N	MEAN	SD	*P**
53-64	585	408	74.8		493	550	91.2	
65-74	471	356	83.5		372	498	104.2	
75-84	369	302	93.4		233	434	109.1	
85+	99	237	94.4	<.001	39	350	122.6	<.001

Age-adjusted *P* value women versus men: <.001.
*Test of trend.

D. CHAIR STAND

		WOMEN (%)						MEN (%)					
AGE (YR)	N	RISES 1 TRY	RISES >1 TRY	RISES W/ARMS	WHEEL- CHAIR	NOT SAFE UNABLE	*P**	N	RISES 1 TRY	RISES >1 TRY	RISES W/ARMS	WHEEL- CHAIR	NOT SAFE UNABLE	*P**
53-64	592	98.5	0.2	0.7	0.3	0.3		499	96.8	0.6	0.6	0.4	1.6	
65-74	479	93.1	2.3	2.3	0.4	1.9		373	93.3	1.3	3.2	0.8	1.3	
75-84	371	75.7	8.1	5.9	3.2	7.0		241	80.5	4.6	4.2	2.1	8.7	
85+	115	41.7	7.8	6.1	17.4	27.0	<.001	39	43.6	12.8	2.6	15.4	25.6	<.001

Age-adjusted *P* value women versus men: 0.80.
* Mantel-Haenszel test for general association.

specific disabling conditions. We did not limit our analyses to only those without diagnosed eye diseases, because this would be akin to eliminating those with cardiovascular disease and other specific diseases from our evaluation of other measures of frailty. This is because we view frailty as general functional decline. Our data are compatible with the notion that visual function is another characteristic to be considered when evaluating frailty. It may be that with longer follow-up for incident morbidities and for survival, the visual function will improve the informativeness of an expanded index of frailty. The likelihood of this is supported by the finding that poor visual function has been shown to be associated with mortality.[21,22]

While frailty is used here to denote diminished func-

TABLE II: CORRELATION COEFFICIENTS BETWEEN FRAILTY MEASURES

	WOMEN				MEN			
FRAILTY MEASURE	GAIT TIME (SEC)	GRIP STRENGTH, DOMINANT HAND (kg)	PEAK EXPIRATORY FLOW RATE (L/MIN)	CHAIR STAND°	GAIT TIME (SEC)	GRIP STRENGTH, DOMINANT HAND (kg)	PEAK EXPIRATORY FLOW RATE (L/MIN)	CHAIR STAND°
Gait time (sec)	1.00	−0.42	−0.41	0.37	1.00	−0.39	−0.38	0.31
Grip strength, dominant hand (kg)	−0.42	1.00	0.52	−0.35	−0.39	1.00	0.52	−0.30
Peak expiratory flow rate (L/min)	−0.41	0.52	1.00	−0.31	−0.38	0.52	1.00	−0.27
Chair stand°	0.37	−0.35	−0.31	1.00	0.31	-0.30	−0.27	1.00

°Chair stand correlations are Spearman correlations (all others are Pearson correlations); all correlation coefficients are significant at $P <.001$.

TABLE III: BEST-CORRECTED VISUAL ACUITY AND CONTRAST SENSITIVITY BY AGE AND SEX

A. BEST-CORRECTED VISUAL ACUITY: BETTER EYE

		WOMEN (%)					MEN (%)			
AGE (YR)	N	20/20 AND BETTER	20/25 TO 20/32	20/40 AND WORSE	P°	N	20/20 AND BETTER	20/25 TO 20/32	20/40 AND WORSE	P°
53-64	595	85.9	13.3	0.8		503	93.2	5.2	1.6	
65-74	489	66.9	30.1	3.1		376	84.0	14.9	1.1	
75-84	397	42.1	48.4	9.6		250	52.8	37.6	9.6	
85+	142	11.3	50.7	38.0	<.001	48	22.9	47.9	29.2	<.001

Age-adjusted P value women versus men: <.001.
°Test of trend.

B. LOG CONTRAST SENSITIVITY (BASED ON LOG-TRIPLET SCORE): BETTER EYE

		WOMEN (%)					MEN (%)			
AGE (YR)	N	GOOD ≥1.80	FAIR 1.65-1.8	POOR <1.65	P°	N	GOOD ≥1.80	FAIR 1.65-1.8	POOR <1.65	P°
53-64	586	15.5	76.3	8.2		491	22.8	69.9	7.3	
65-74	467	6.2	66.4	27.4		370	9.7	66.5	23.8	
75-84	340	0.9	41.8	57.4		227	0.9	48.5	50.7	
85+	74	0.0	12.2	87.8	<.001	29	0.0	13.8	86.2	<.001

Age-adjusted P value women versus men: <.001.
°Test of trend.

TABLE IV: CORRELATION COEFFICIENTS OF VISUAL ACUITY (VA) AND CONTRAST SENSITIVITY (CS) IN THE BETTER EYE TO OTHER MEASURES OF FRAILTY

	WOMEN					MEN				
	N*	GAIT TIME	STRENGTH DOMINANT HAND	PEAK EXPIRATORY FLOW RATE	CHAIR STAND†	N*	GAIT TIME	STRENGTH DOMINANT HAND	PEAK EXPIRATORY FLOW RATE	CHAIR STAND†
Log CS	1,467	−0.33	0.37	0.38	−0.21	1,117	−0.29	0.35	0.29	−0.22
VA	1,623	0.29	−0.35	−0.36	0.31	1,177	0.21	-0.32	−0.26	0.33

*Number of people with the vision measure; correlations may have smaller N's due to missing information.
†Spearman correlation (all others are Pearson correlations); all correlation coefficients are significant at $P < .001$.

TABLE V: FRAILTY SCORE† BY AGE AND SEX

		WOMEN (%) SCORE							MEN (%) SCORE					
AGE (YR)	N	0	1	2	3	4	P*	N	0	1	2	3	4	P*
53-64	581	81.4	14.8	3.6	0.2	0.0		488	74.8	17.6	6.6	0.8	0.2	
65-74	456	54.4	29.4	11.6	3.3	1.3		361	50.1	30.5	14.4	3.9	1.1	
75-84	328	24.7	31.7	23.5	14.9	5.2		217	24.0	27.7	26.3	15.7	6.5	
85+	61	8.2	21.3	24.6	23.0	23.0	<.001	24	0.0	12.5	37.5	25.0	25.0	<.001

Age-adjusted *P* value women versus men: 0.004.
*Test of trend.
† Frailty score was increased by 1 if any of the following occurred:
  Highest quartile for gait time: (≥3.37 sec females, ≥3.19 sec males)
  Lowest quartile for peak flow: (≤290 L/min females, ≤440 L/min males)
  Lowest quartile for handgrip (dominant): (≤18.5 kg females, ≤34.5 kg males)
  Not able to do the chair stand in one try and not in a wheelchair

TABLE VI: RELATIONSHIP OF VISION VARIABLES TO FRAILTY SCORE

		WOMEN (%) SCORE							MEN (%) SCORE					

A. VISUAL ACUITY: BETTER EYE

VISUAL ACUITY	N	0	1	2	3	4	P*	N	0	1	2	3	4	P*
20/20 and better	983	65.9	22.5	8.1	3.0	0.5		899	59.3	24.0	11.8	3.9	1.0	
20/25 to 20/32	403	38.0	25.8	18.6	10.7	7.0		166	33.1	22.3	23.5	13.3	7.8	
20/40 and worse	39	12.8	30.8	28.2	18.0	10.3	<.001	25	40.0	24.0	20.0	4.0	12.0	0.07

*Age-adjusted test for trend.

B. LOG CONTRAST SENSITIVITY (BASED ON LOG-TRIPLET SCORE): BETTER EYE

CONTRAST SENSITIVITY LEVEL	N	0	1	2	3	4	P*	N	0	1	2	3	4	P*
Good (≥1.80)	121	79.3	16.5	2.5	1.7	0.0		148	73.7	19.6	5.4	1.4	0.0	
Fair (1.65-1.80)	895	65.1	23.1	8.0	3.0	0.7		693	59.6	23.8	12.7	3.2	0.7	
Poor (<1.65)	403	31.3	26.8	22.3	12.4	7.2	<.001	246	30.1	26.4	22.0	13.8	7.7	<.001

*Age-adjusted test for trend.

tional abilities, it can also be construed to mean diminished life span or early mortality.[22-24] It may be that using a frailty index as a quantitative phenotypic trait would enhance the investigations of genetic determinants of longevity.

REFERENCES

1. Campbell AJ, Buchner DM. Unstable disability and the fluctuations of frailty. *Age Ageing* 1997;26:315-318.
2. Bortz WM II . The physics of frailty. *J Am Geriatr Soc* 1993;41:1004-1008.
3. Lipsitz LA, Goldberger AL. Loss of 'complexity' and aging: potential applications of fractals and chaos theory to senescence. *JAMA* 1992;267:1806-1809.
4. Hammerman D. Toward an understanding on frailty. *Ann Intern Med* 1999;130:945-950.
5. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;56:M146-156.
6. Chin A Paw MJ, Dekker JM, Feskens EJ, et al. How to select a frail elderly population? A comparison of three working definitions. *J Clin Epidemiol* 1999;52:1015-1021.
7. Sharp DS, Burchfiel CM, Curb JD, et al. The synergy of low lung function and low body mass index predicting all-cause mortality among older Japanese-American men. *J Am Geriatr Soc* 1997;45:1464-1471.
8. Klein BEK, Klein R, Lee KE, et al. Associations of performance-based and self-reported measures of visual function. The Beaver Dam Eye Study. *Ophthalmic Epidemiol* 1999;6:49-60.
9. Klein R, Klein BEK, Moss SE. Age-related eye disease and survival. The Beaver Dam Eye Study. *Arch Ophthalmol* 1995;113:333-339.
10. Wang JJ, Mitchell P, Simpson JM, et al. Visual impairment, age-related cataract and mortality. *Arch Ophthalmol* 2001;119:1186-1190.
11. Klein R, Klein BEK, Moss SE, et al. Association of ocular disease and mortality in a diabetic population. *Arch Ophthalmol* 1999;117:1487-1495.
12. Campbell JA, Palet CD. Total digit dialing for a small area census by phone. *Proceedings of the Section on Survey Research Methods*. Alexandria, Va: American Statistical Association, 1988:549-551.
13. Klein R, Klein BEK, Linton KLP, et al. The Beaver Dam Eye Study: visual acuity. *Ophthalmology* 1991;98:1310-1315.
14. Klein R, Klein BEK, Lee KE. Changes in visual acuity in a population: the Beaver Dam Eye Study. *Ophthalmology* 1996;103:1169-1178.
15. Klein R, Klein BEK, Lee KE, et al. Changes in visual acuity in a population over a 10-year period: the Beaver Dam Eye Study. *Ophthalmology* 2001;108:1757-1766.
16. Klein R, Klein BEK, Lee KE. Changes in visual acuity in a population. The Beaver Dam Eye Study. *Ophthalmology* 1996;103:1169-1178.
17. Pelli DG, Robson JG, Wilkins AJ. The design of a new letter chart for measuring contrast sensitivity. *Clin Vis Sci* 1988;2:187-199.
18. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol* 1994;49:M85-94.
19. Klein R, Klein BEK. *Beaver Dam Eye Study III*. Manual of Operations. Springfield, Va: US Dept of Commerce; 1999. NTIS accession No. PB 99-137861.
20. Evans J. Exercise, nutrition and aging. *Clin Geriatr Med* 1995;11:725-734.
21. Wang JJ, Mitchell P, Simpson JM, et al. Visual impairment, age-related cataract, and mortality. *Arch Ophthalmol* 2001;119:1186-1190.
22. Begun A, Desjardins B, Iachine I, et al. Multivariate frailty model with a major gene: application to genealogical data. *Stud Health Technol Inform* 2000;77:412-416.
23. Kohler HP, Kohler I. Frailty modelling for adult and old age mortality: the application of a modified DeMoivre hazard function to sex differentials in mortality. *Demogr Res* 2000;3:[32] p.
24. Yashin AI, De Benedictis G, Vaupel JW, et al. Genes, demography, and life span: the contribution of demographic data in genetic studies on aging and longevity. *Am J Hum Genet* 1999;65:1178-1193.

DISCUSSION

DR ALFREDO A. SADUN. I am grateful to the program committee for granting me this opportunity to discuss Dr Klein's paper, and to Barbara for having sent it to me early. Dr Barbara Klein and colleagues have presented here further data and analysis from the Beaver Dam Eye Study. This is a private census population based cohort study, begun in 1988, of all persons over 43, which employed baseline questionnaires and examinations. Follow-up examinations occurred 5 and 10 years after, the results of which have been published elsewhere.

In the present study, nearly 3000 patients were considered. Measurements of visual acuity and contrast sensitivity taken at the 10-year mark were compared to measurements of frailty. Dr Klein has already carefully defined frailty as diminishments in multiple systems resulting in decreases in balance, muscle strength, and the resultant functions. A frailty index, based on measures of gait, grip strength, ability to standing and expiration flow rate, was calculated and compared to various visual functions.

All measures of frailty correlated well with each other. Visual functions declined with age, and correlated well with the measures of frailty. Men were more likely to be frail than women, not only in functions of strength, but in visual acuity as well. However, women were more likely to suffer losses of contrast sensitivity that may be a better and more global measure of visual function. Age-related impairments of vision did not yet predict morbidity.

However, this study suggests that these age-related visual deficits may complement and enhance present measures in the assessment of frailty in their predictive value for mortality and morbidity. Other studies, have shown that poor visual function, in disease, is associated with mortality.[1-3]

I have a few concerns and questions with this manuscript:

1. Persons without all four frailty measurements were excluded from analysis; did this create a selection bias by not considering the most frail?
2. How well does the population of Beaver Dam reflect the general U.S. population? For example, 99% were white.
3. How does the population of Beaver Dam compare in access to good health care? Might they have better control of diabetes or cardiovascular disease compared to the general population?
4. The study excluded patients with specific diseases and visual function deficits. If these impairments were related to aging, does this create a selection bias?
5. How can the many confounders be controlled for? For example, many diseases of aging may share common pathological mechanisms.

This work of the Kleins is the latest pearl in a long string of related investigations. The Beaver Dam investigators have designed and executed a prospective study of patients in a captured population and then persistently followed this large group for decades.

Such studies are important for several reasons:
1. They allow us to better understand the baseline of function against which to compare disease. It's easy but sloppy to overlook and hence fail to investigate subpar visual parameters and dismiss them as being due to aging.
2. These investigations also permit us to carefully consider which visual functions are most vulnerable to age and disease.
3. These studies provide us with a better understanding of the process of senescence by looking at the effects of age on the visual system.
4. They also allow us to take into account the reductions of vision in the elderly for purposes of social planning. For example, understanding the loss of contrast sensitivity with aging would lead to improved signage on the freeways as well as in hospital corridors. It would also be useful to measure these functions when making legal determinations such as disability or the eligibility to drive.

There are, of course, a number of age related diseases that have a major negative impact on various measures of visual function. Some, like glaucoma, have a predictable impact on visual fields. Others, like ARMD directly affect visual acuity. A third group, like the optic neuropathy of Alzheimer's disease, produce serious impairments of visual function best measured as loss of contrast sensitivity.[4,5] If we seek to capture such visual impairments with only a single index, it might be best to consider the integral of the contrast sensitivity/spatial frequency curve (since looking at the area beneath the entire curve takes into account all conditions of contrast and target size).

There is an interesting but not surprising parallel between the visual dysfunctions associated with Alzheimer's disease and senescence. Schefrin and colleagues showed that with aging comes severe losses of contrast sensitivity functions at all spatial frequencies.[6] These scotopic contrast sensitivity losses were deemed as primarily due to neural and not optical (e.g. lenticular) factors.[6] Specifically, the psychophysical characteristics of these impairments point to M-cell retinal ganglion cell impairments.

Selective loss of retinal M-cells has also been reported in Alzheimer's disease.[5] The retinal ganglion cells first affected in Alzheimer's are those with the largest dendritic fields and largest caliber axons that connect to layers 1 and 2 of the lateral geniculate nucleus (the M, or magnocellular layers). These cells are thought to mediate contrast sensitivity but not to be involved in high resolution or color vision.[7] Hence Alzheimer patients–and the elderly as a whole–probably do well enough with Snellen acuity when the letters are black on a bright white background as in the controlled circumstances of the examination room. However, in the real world of suboptimal contrast, they perform much worse.[4,5]

Histopathological and ultrastructural examination of optic nerves obtained at necropsy from Alzheimer's disease patients and from patients spanning a broad range of ages do, in fact, demonstrate a decline in the axonal population that correlates with age and disease.[4,5,8,9] Balazsi and colleagues calculated the loss to be about 5,600 axons/year.[9] However, this number represented a major interpolation to account for the middle years for which they did not have cases. In a study of 16 eyes from 13 patients, we found the axonal population to be about 1.2 million for each optic nerve in a young adult, a count that remains steady until about age 60, after which it plummets to about 900,000 by age 72.8. It fell to less than 750,000 in Alzheimer's disease.[4,5] It would be presumptuous to conclude that such losses do not reflect on function.

Dr Klein and her colleagues were wise to use contrast sensitivity to capture dysfunctions associated with the axonal structural losses. However, if instead of Pelli-Robson letter charts, measurements of contrast sensitivi-

ties were made at different spatial frequencies, it would then be possible to separate out the effects of the selective losses of retinal M-cells as shown by Schefrin and colleagues.

As the population continues to age, age-related diminishments visual function and their clinical impacts take on greater importance. This is true not only for the diagnosis, care, and treatment of older patients, but also for the making of important social decisions that will affect this increasingly large subpopulation that hopes for, and deserves, not only maximum independence, but also the opportunity to continue to make contributions. Dr Barbara Klein and her colleagues are to be commended for undertaking such an exhaustive and valuable enterprise.

REFERENCES

1. Klein R, Klein BEK, Moss SE. Age-related eye disease and survival. The Beaver Dam Eye Study. *Arch Ophthalmol* 1995;113:333-339.
2. Klein R, Klein BEK, Moss SE, et al. Association of ocular disease and mortality in a diabetic population. *Arch Ophthalmol* 1999;17:1487-1495.
3. Wang JJ, Mitchell P, Simpson JM, et al. Visual impairment, age-related cataract, and mortality. *Arch Ophthalmol* 2001;119:1186-1190.
4. Sadun AA, Borchert M, DeVita E, et al: Assessment of visual impairment in patients with Alzheimer's disease. *Am J Ophthalmol* 1987;104:113-120.
5. Sadun AA and Bassi C: Optic nerve damage in Alzheimer's disease. *Ophthalmology* 1990;97:9-17.
6. Schefrin BE, Tregear SJ, Harvey, Jr. LO, and Werner JS: Senescent changes in scotopic contrast sensitivity. *Vision Research* 1999;39:3728-3736.
7. Sadun AA: Dyslexia at the New York Times: (Mis) understanding of parallel visual processing. *Arch Ophthalmol* 1992;110:933-934.
8. Johnson BM, Miao M and Sadun AA: Age-related decline of human optic nerve axon populations. *Age* 1987;10:5-9.
9. Balazsi AG, Rootman J, Drance SM, Schulze M and Douglas GR: The effect of age on the nerve fiber population of the human optic nerve. *Am J Ophthalmol* 1984;97: 760-766.

DR GEORGE L. SPAETH. Congratulations on trying to move us away from visual acuity and things like that and into function, which is really what we should be interested in. There are some concerns about what you presented to us. The correlation between acuity or field or contrast sensitivity and function, taken by itself, is extremely poor. When you include only one eye that correlation plummets. Dr Richard Mills and some others as well as ourselves have shown that the correlation between measures of actual function, such as walking, working on a computer screen, and the Esterman method of assessing binocular visual field is better than with any of the other

visual functions that have been studied (such as visual acuity, monocular visual field etc). But even that correlation is still poor. Developing meaningful performance-based measures of function related to vision is an important matter to accomplish.

In your frailty index, you indicated that there was a statistical, and perhaps clinical, difference between men and women. But something did not fit. In your study the women were more frail that the men, yet, we all know that elderly women are more functional and live longer than men. How do you explain that discrepancy?

DR JAMES C. BOBROW. I was wondering whether or not the frailty index is reversible, and whether or not some of these measures of mobility such as gait might be ones that we could strengthen in patients and whether or not that ultimately that would alter the conclusions from the frailty index. I also wondered whether or not loss of visual function might then be subject to any kind of manipulation and what implications these alterations might have on the index as Dr Spaeth already indicated. You used here a fairly crude measurement: the percentage of patients with 20/20 acuity and also contrast sensitivity on the Pelli-Robinson Scale. I wonder whether looking at visual acuity levels rather than just presence or absence of 20/20 acuity might give you a scalable parameter.

DR ROBERT C. DREWS. Since you're using frailty to try to predict mortality and since there's a dramatic decline in visual acuity in 85 year olds and older, I have to wonder how much of that is macular degeneration. I'm reminded of a study that I did in my own office some years back in which we found, surprisingly, that patients with macular degeneration lived significantly longer.

DR BARBARA E.K. KLEIN. With regard to Dr Sadun's comments, I will look further into the literature as I was unaware of the association between change in contrast sensitivity and a potential correlate in Alzheimer's disease.

For an individual's data to contribute to the analyses he or she had to have a value for each frailty marker. We did not exclude participants with specific disease and visual deficits. It appears that those who did not complete the battery of tests were likely to be older and sicker than those who did perform all the tests. This has also been found in the Cardiovascular Health Study. People who were in a nursing home could perform very few of these functions on average and their mortality rate was much greater.

Dr Spaeth commented about using values from both eyes. For the two-vision test considered here, we had data for each eye individually. We have a measure of binocular acuity with individual's current correction before the

study refraction. We can certainly look at the question as to whether binocular acuity is more informative or helps more in trying to assess of frailty.

Dr Bobrow raises the interesting question about reversibility of frailty. Of course we take this as a point estimate since it is the only measure we have. There are papers in the aging literature that suggest that with increased muscle tone and exercise capacity their frailty will diminish and this will increase their ability to be independent. I cannot draw inferences from our data, but I think this is an important concept; namely that we should not give up on people because there are interventions that do work.

Dr Bobrow also questions our use of defined cut points for our vision markers of frailty. We did do some analyses using the measures as quantitative continuous markers and those analyses were compatible with the notion of a continuous spectrum of frailty related to vision. However, in constructing an index that might have clinical utility we dichotomized each marker so that a zero or 1 would be the value for each.

Dr Drew raises the interesting point about decreased visual acuity resulting from macular degeneration. Macular degeneration is not, at least in our data, associated with subsequent mortality, whereas visual acuity is. Better methods to help people cope with low vision associated with macular degeneration, until we can prevent it, are what is called for here.