Visual Acuity Change and Mortality in Older Adults

Ellen E. Freeman,1 Brian L. Egleston,2 Sheila K. West,1 Karen Bandeen-Roche,2 and Gary Rubin5

PURPOSE. Several studies indicate an increased mortality rate in older adults who have visual impairment, but few have attempted to address a potential causal mechanism. The goals of this study are to determine whether visual acuity loss increases the risk of dying and to examine whether depressive symptoms act as a mediator in this relationship.

METHODS. Data were derived from the 2520 older adults who participated in the Salisbury Eye Evaluation project, a population-based prospective 8-year cohort study. Presenting binocular visual acuity was measured with the Early Treatment Diabetic Retinopathy Study [ETDRS] eye chart and depressive symptoms with the General Health Questionnaire Part D subscale. Mortality data were collected by staff follow-up. Analyses were performed with the Cox proportional hazards regression.

RESULTS. Worse baseline acuity was associated with a higher mortality rate (hazard ratio [HR] = 1.05; 95% confidence interval [CI], 1.01–1.09). Also, those who gained two or more lines of visual acuity over 2 years had a lower adjusted risk of dying (HR = 0.47; 95% CI, 0.23–0.95). An interaction was detected, in that women who lost ≥3 lines of visual acuity over a 2-year period had a higher adjusted risk of dying (HR = 3.97; 95% CI, 2.21–7.15), whereas men did not (HR = 1.32; 95% CI, 0.66–2.63). Depressive symptoms did not mediate these relationships.

CONCLUSIONS. If the relationship between visual acuity and mortality is indeed causal, it most likely acts via numerous pathways through a variety of intervening variables. The identification of these intervening variables could give additional targets for intervention if acuity cannot be restored. (Invest Ophthalmol Vis Sci. 2005;46:4040–4045) DOI:10.1167/iovs.05-0687

Older adults frequently lose visual acuity as they age because of conditions such as age-related macular degeneration, cataract, diabetes, and glaucoma.1,2 Prior population-based studies have found that visual impairment is associated with increased risk of subsequent death.3–7 For example, the Blue Mountains Eye Study found that visual impairment is independently associated with an increased 5-year mortality rate, even after adjustment for demographic factors and a variety of health conditions, including cataract (relative risk [RR] = 1.7; 95% confidence interval [CI], 1.2–2.3).7

There are a variety of mechanisms by which visual impairment could be associated with dying. One mechanism is that a condition such as diabetes may directly cause visual impairment and increase one’s risk of dying. Second, other age-related conditions (heart disease, for example) may simply coexist with, but not cause, visual impairment, and these conditions may increase the risk of dying. Third, visual impairment itself may increase the risk of death by increasing the likelihood of an accident. Finally, visual impairment may cause psychological changes that over time increase the risk of death.

If the visual impairment–mortality relationship is indeed causal, an important goal is to identify any mediators or intervening variables, in the causal pathway, which are amenable to intervention, particularly since acuity cannot always be restored. It is possible that depression is one such mediator. Depression may result from vision loss due to feelings of increased dependence, less social interaction, and increasing disability. In the literature, depression has been associated with both visual impairment8–11 and death12–17 and thus is a possible mediator in this causal pathway.

The goals of this analysis were to examine whether visual acuity loss increases the 8-year risk of subsequent mortality in a cohort of older adults and then to test our hypothesis that incident depressive symptoms may explain part of this relationship. Loss of acuity over a 2-year period was examined while adjusting for baseline acuity, because it was expected that recent changes in vision would be most likely to affect psychological health.

METHODS

Study Population

In this analysis, we used data from the Salisbury Eye Evaluation, a population-based cohort study of 2520 older adults between the ages of 65 and 84 years who were residents of Salisbury, Maryland.18 The study was consistent with the Declaration of Helsinki and was approved by the Joint Committee on Clinical Investigation at Johns Hopkins University. Informed consent was obtained from all participants. Eligibility criteria included age between 65 and 84 years, residence near Salisbury and not in a nursing home, ability to communicate, and a score greater than 17 on the Mini Mental State examination. Of those approached, 65% completed both the home questionnaire and the medical examination at baseline.

Participants returned for round 2 approximately 2 years later, when the same questionnaires and clinical procedures were performed. Of 2520 individuals, 2240 (89%) returned for round two. Of the 280 who did not return, 147 died and 133 withdrew or moved away.

Of the 2240 who returned for round 2, the analysis required that we exclude those with depressive symptoms at baseline, as defined later in the article, (n = 204) or those without information on depression at baseline (n = 21). Finally, of these 2015 people, there were 17 who did not have depression information at round 2, and an additional 7 who did not have their visual acuity measured at round 2. This gave a final sample size of 1991.

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Questionnaire and Clinical Examination

Participants were given an interviewer-administered questionnaire at home. Demographic, medical history, and behavioral information were collected. The presence of depressive symptoms was assessed with Part D of the General Health Questionnaire. Questions were asked about a physician diagnosis of 15 medical conditions.

At the clinical examination, trained observers measured height and weight using methods described by Caulfield et al. Body mass index was calculated as weight (in kilograms) divided by height (square meters). Visual function was evaluated during an eye examination described by West et al. Presenting visual acuity was measured binocularly with the Early Treatment Diabetic Retinopathy Study (ETDRS) eye chart under normal illumination. Acuity was then converted to log_{10} minimum angle of resolution (logMAR).

Vision and Depression Variables

Presenting visual acuity was used instead of best corrected acuity, because it is the vision that individuals are able to use in the real world. It is this type of vision, as opposed to the best theoretical vision one could have, that was hypothesized to affect eventual mortality through its action on depressive symptoms.

A change in visual acuity was defined as the difference between the two presenting visual acuity logMAR scores in the second and first rounds. For ease of interpretation, it was decided a priori that a four-category variable would be created. Those who lost between 2 and 3 lines of visual acuity had “mild loss,” those who lost ≥3 lines of visual acuity had “moderate loss,” and those who gained ≥2 lines of visual acuity had “vision gain.” The reference group included those who had not gained or lost ≥2 lines of acuity.

Baseline visual acuity was examined categorically as well, but was then used as a continuous variable, since it appeared to have a linear relationship with mortality. The β coefficient for baseline visual acuity was multiplied by 0.1 to give more meaningful units. Therefore, the β coefficient for baseline acuity equaled the log odds ratio for a 1-line increase (worsening) in acuity score rather than a 1-letter increase.

Incident depressive symptoms were defined if a person answered affirmatively to one or more of the seven questions of the General Health Questionnaire (GHQ-28) Part D at round 2 but not at round 1. These questions ask about feelings of worthlessness, hopelessness, and suicidal thoughts.

Mortality Follow-up

All participants enrolled at baseline were called yearly by telephone for follow-up. Information on mortality was obtained by report from family members, by the local newspapers, and by staff follow-up. All deaths reported by July 2003 were used in the current analysis. If the year of death was known, but the day and/or month were missing, then the midpoint of the time between their last round attended and the end of the study.

The proportionality assumption was checked by examining scaled Schoenfeld residual plots versus time for each variable, to determine whether the slope deviated systematically from zero, and also by examining log-log survival curves versus log(time) and adjusting for the mean values of the other variables to see whether the curves were roughly parallel. The correlation of the covariates was checked to assess colinearity. Ties in hazard times were handled by the Breslow method. Effect modifiers including visual impairment (worse than 20/40) at baseline, diabetes, and gender were evaluated by stratification and by including interaction terms with visual acuity change into the regression model.

To determine whether incident depressive symptoms were a mediator in the relationship between visual acuity loss and time to death, the methods of Baron and Kenney were used. Briefly, the relationship between visual acuity loss and mortality should be reduced once depressive symptoms are in the model, if depressive symptoms act as a mediator.

RESULTS

The baseline characteristics of individuals by change in visual acuity category are compared in Table 1. The groups were similar except that those who gained visual acuity were more likely to be women and African-American and to have had worse baseline visual acuity than the other groups. Those who had moderate visual acuity loss were much more likely to have reported diabetes than were the other groups.

In the 1991 participants used in the analysis, there were 481 (24%) deaths as of July 2003. Those who died were more likely to be older men, African-American, and less educated and to have had worse baseline visual acuity, to have had conditions such as diabetes, stroke, hypertension, and to be current smokers (P < 0.05 from t-test or Pearson χ² test; data not shown).

Compared to the 24% of those who died in the group who did not change acuity, a greater percentage of those with moderate visual acuity loss died (47.1%), whereas a smaller percentage of those who gained acuity died (14.5%; Pearson χ² test, P < 0.00; Table 2).

After adjusting for age, sex, race, diabetes history, body mass index, comorbidity number, and smoking history, we found that moderate 2-year acuity loss, gain in acuity, and baseline visual acuity were associated with death (Table 3). Those who had a moderate 2-year loss in acuity had an increased hazard of dying (HR = 2.23; 95% CI, 1.43–3.46), whereas a gain in acuity was associated with a decreased hazard (HR = 0.47; 95% CI, 0.25–0.90; Table 3, model 1). Also, those who gained visual acuity had an increased risk of death, so that there was a 5% increased risk of death per 1-line loss of acuity (HR = 1.05; 95% CI 1.01–1.10; Table 3, model 1).

In model 2, incident depressive symptoms at round 2 were included in the model, to determine whether it would explain the relationship between acuity loss and subsequent death. The HRs for moderate acuity loss in models 1 and 2 are nearly identical, suggesting that depressive symptoms do not mediate this relationship. In fact, incident depressive symptoms, as measured by the General Health Questionnaire Part D, were not strongly associated with the hazard of death (HR = 1.23; 95% CI, 0.89–1.74). Education, history of hypertension, and history of stroke at baseline were not included in the final models due to both their lack of statistical significance and their lack of an effect on visual acuity change after their removal.

Those 56 individuals who had died but for whom the date of death was unknown were at first excluded from the analyses. Then, sensitivity analyses were performed including them and assuming their date of death to be the midpoint of the time between their last round attended and the end of the study.
The adjusted survival curves derived from the Cox regression model are shown in Figure 1. The figure shows that those who gained visual acuity had the longest time until death, whereas those who had a moderate visual acuity loss had the shortest time to death.

An interesting interaction was found between gender and moderate vision loss (Table 4). The men who had moderate vision loss did not have a significantly higher hazard of mortality (HR = 1.32; 95% CI, 0.66–2.63), whereas the women did (HR = 3.97; 95% CI, 2.21–7.15). The P-value from a model with an interaction term for moderate acuity loss and gender was statistically significant (P = 0.01). Other interactions with diabetes and baseline acuity were not found.

The characteristics of those who died before round 2 were compared with the characteristics of those who were still living (data not shown). As expected, those who died were older and more likely to be men than those who were still living. In addition, after age and sex adjustment, those who died were more likely to be nonwhite, to have a higher mean number of comorbidities, to have diabetes and a history of stroke, and to be current smokers (data not shown).

Analyses were rerun including the 56 individuals who had died but had no death date and using the midpoint of the follow-up time between their last round attended and the end of the study as their date of death. The inferences remained the same (data not shown). In addition, the mean visual acuity was no different between those with a known date of death and those with an unknown date of death (logMAR 0.04 vs. logMAR 0.07; ANOVA P = 0.29), and there were no meaningful differences in the percentages of those with 2-year visual acuity change between those with a known date of death and those with an unknown date of death (Pearson \( \chi^2 \) test, \( P = 0.71 \)).

The proportionality assumption was checked for all variables and was appropriate.

**DISCUSSION**

We have confirmed that worse baseline visual acuity is associated with the risk of mortality and have also found that the women who had a moderate loss of acuity over a 2-year period had a higher risk of mortality whereas the men with a moderate loss did not. In addition, we report that those who gained \( \geq 2 \) lines of visual acuity had a lower risk of dying than those whose acuity did not change. We did not find that incident depressive symptoms at round 2 explained any of the observed relationship between acuity loss and mortality.

The finding that a 2-year gain in visual acuity was associated with a decreased risk of death is novel, to our knowledge. Almost half (47%) of those who had a 2-year gain in visual acuity had cataract surgery during that time. The other 53%...
who gained visual acuity presumably had their refractive errors corrected in the interim period. Although we are limited by the small sample, it appears that the reduced risk of death was mostly in the group who had their refractive errors corrected (7% died vs. 24% in the reference group) as opposed to those who had cataract surgery (19% died). Nevertheless, if the association between a gain in acuity and a reduced risk of mortality is causal, one explanation may be that having taken action to reverse visual acuity loss resulted in increased feelings of self-efficacy\textsuperscript{23} that may have encouraged other actions to improve health. Unfortunately, we do not have the data to address this question, but perhaps future studies could resolve it. The association could also be due to residual confounding, in that it could be that persons who had a 2-year gain in acuity differ in other factors that explain the decreased risk of mortality. For example, it could be that those with a gain in acuity had a higher socioeconomic status (SES) than those who did not have a visual acuity change, and SES has been associated with mortality.\textsuperscript{24} Although we do not have data on SES, there are no differences in education, which is sometimes used as a surrogate for SES, between those who had a moderate acuity loss and those who had a 2-year gain in acuity. It could also be that those who gained in visual acuity were healthier than those who had no change, although there were no meaningful differences in the number of comorbidities between the groups with change in visual acuity, and those who gained acuity were more likely to be currently smoking, which is not consistent with their being healthier.

We chose to use presenting visual acuity because we hypothesized that a person’s actual acuity (as opposed to best possible acuity) would affect psychological health. However, our results were very similar when we used best corrected visual acuity, although gain in acuity was not statistically significantly related to mortality, because of the smaller number of people who had a gain in best corrected acuity ($n=36$).

The association between loss in visual acuity and an increased risk of death is consistent with other findings in studies that looked at visual impairment and death.\textsuperscript{3-7} To our knowledge, this is the first study in which recent visual acuity change was examined (as opposed to just visual impairment of unknown duration) and mortality. Our finding that a 2-year gain in acuity is associated with a decreased risk of death is not

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**Table 3. Results from Cox Proportional Hazards Regression Models**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model 1 ($n=1911$)</th>
<th></th>
<th>Model 2 ($n=1911$)</th>
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</thead>
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<tr>
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<td>Adjusted Hazard of Death*</td>
<td></td>
<td>Adjusted Hazard of Death*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HR</td>
<td>95% CI</td>
<td>HR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Visual Acuity Change</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>No Change</td>
<td>1.00</td>
<td>Reference</td>
<td>1.00</td>
<td>Reference</td>
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<tr>
<td>Mild Loss</td>
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<td>0.61–1.37</td>
<td>0.91</td>
<td>0.61–1.36</td>
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<td>Moderate Loss</td>
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<td>1.45–3.46</td>
<td>2.26</td>
<td>1.45–3.52</td>
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<td>Gain</td>
<td>0.47</td>
<td>0.23–0.96</td>
<td>0.47</td>
<td>0.23–0.95</td>
</tr>
<tr>
<td>Baseline visual acuity†</td>
<td>1.05</td>
<td>1.01–1.10</td>
<td>1.05</td>
<td>1.01–1.09</td>
</tr>
<tr>
<td>Incident depressive symptoms</td>
<td></td>
<td></td>
<td>1.00</td>
<td>Reference</td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
<td>1.23</td>
<td>0.89–1.74</td>
</tr>
<tr>
<td>Yes</td>
<td></td>
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</tr>
</tbody>
</table>

Models examined how visual acuity affects the hazards of death and whether incident depression acts as a mediator. Acuity loss is as described in Table 1.

* Adjusted for age, sex, race, diabetes history, body mass index, comorbidities, and smoking history.

† Per 0.1 logMAR (1 line) change in acuity.

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**Figure 1.** Cox proportional hazards regression adjusted survival curves by visual acuity change category. Those who had moderate acuity loss over 2 years had a worse adjusted survival than those who did not have a change in visual acuity, whereas those who gained acuity had a better adjusted survival. The curves were adjusted for age, sex, race, baseline visual acuity, diabetes history, body mass index, comorbidity number, and smoking history.
consistent with previous findings that those with cataract surgery (most of whom would presumably gain acuity) had an increased risk of death.\textsuperscript{25–27} It is difficult to compare these findings directly with the results of our analysis because our analysis examined gain in acuity, whereas the others examined cataract surgery without regard to change in acuity.

Our results also corroborate a previous study that found a relationship between visual impairment and mortality only in women.\textsuperscript{3} We did not find an interaction between baseline acuity and gender, but we did find an interaction between moderate acuity loss and gender. These findings suggest that women may be more vulnerable to a rapid loss of vision in older age than are men. The reasons for this are not known. There may be interactions between moderate acuity loss and gender for outcomes like falling, car accidents, medication errors, or decreased social support that then have an impact on mortality risk. Because studying interactions requires much larger sample sizes, a large, longitudinal study with detailed cause of death information would be needed to evaluate this more thoroughly.

To attempt to delineate a causal pathway, we explored whether depressive symptoms explain the relationship between visual acuity and mortality. We found no evidence of that they do. It is likely that we underestimated those with depressive symptoms, by using the GHQ-28. Reporting information on feelings of hopelessness and worthlessness is a sensitive topic, and some individuals may not have felt comfortable revealing that information in person, especially in this age group. This underestimation of depressive symptoms may have biased any association between depressive symptoms and mortality toward the null, because it is unlikely that the underreporting would have differed by subsequent mortality status. In addition, the correlation between a clinical diagnosis of depression and depressive symptoms on the GHQ-28 Part D subscale is 0.56,\textsuperscript{19} which could have further biased our results toward the null. Despite the imperfect nature of our depression variable, we still think it was important to examine whether it explained any of the observed relationship between visual acuity and mortality and to report that it did not.

Because 2-year visual acuity loss and incident depressive symptoms were both measured at round 2, reverse causality could be a concern. For example, depression may have caused individuals to lose vision because they did not receive care (untreated cataract, refractive error). However, depression at round 1 was not associated with incident visual impairment at round 2, suggesting that this is not a major concern.

Some individuals died before round 2, precluding us from measuring the change in their visual acuity. If these people were less likely to have had moderate acuity loss before they died, then our reported association between moderate acuity loss and mortality might be upwardly biased. However, because those who died before round 2 were older and had more diabetes and because these are risk factors for moderate visual acuity loss, they probably would have been more likely to have had moderate visual acuity loss, which would have strengthened our results. In addition, a sensitivity analysis assuming that all those who died before round 2 did not have moderate acuity loss supported our results (data not shown). Similarly, if those who died before round 2 were more likely to have had a gain in visual acuity before they died, then our reported association between gain in visual acuity and decreased mortality might be exaggerated. However, it is probably less likely that these individuals would have undergone cataract surgery or correction of refraction to achieve a gain in acuity if they were undergoing the health problems that often occur before death.

There are now several studies that indicate an increased risk of mortality in people with impaired visual acuity, two of which have found this to be true mainly in women. If the relationship between acuity and mortality is indeed causal, it most likely acts via numerous pathways through a variety of intervening variables. Future work using large datasets should investigate how vision loss is associated with different causes of death, should examine whether factors such as a clinical diagnosis of depression, falls, or other accidents act as intervening variables in this relationship, and should examine why this relationship may be limited to women. The identification of these factors could give additional targets for intervention if acuity cannot be restored.

\textbf{References}


\textbf{Table 4. Results from Cox Proportional Hazards Regression Model Examining Visual Acuity and Its Relation to the Hazard of Death Stratified by Gender}

<table>
<thead>
<tr>
<th>Strata (n)</th>
<th>Variables</th>
<th>HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women (n = 1114)</td>
<td>Baseline visual acuity†</td>
<td>1.06</td>
<td>1.00–1.13</td>
</tr>
<tr>
<td></td>
<td>Visual acuity change over 2 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No change</td>
<td>1.00</td>
<td>Reference</td>
</tr>
<tr>
<td></td>
<td>Mild loss</td>
<td>0.65</td>
<td>0.30–1.39</td>
</tr>
<tr>
<td></td>
<td>Moderate loss</td>
<td>3.97</td>
<td>2.21–7.15</td>
</tr>
<tr>
<td></td>
<td>Gain</td>
<td>0.37</td>
<td>0.14–1.03</td>
</tr>
<tr>
<td>Men (n = 797)</td>
<td>Baseline visual acuity†</td>
<td>1.04</td>
<td>0.98–1.10</td>
</tr>
<tr>
<td></td>
<td>Visual acuity change over 2 years†</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No change</td>
<td>1.00</td>
<td>Reference</td>
</tr>
<tr>
<td></td>
<td>Mild loss</td>
<td>1.12</td>
<td>0.70–1.81</td>
</tr>
<tr>
<td></td>
<td>Moderate loss</td>
<td>1.32</td>
<td>0.66–2.63</td>
</tr>
<tr>
<td></td>
<td>Gain</td>
<td>0.58</td>
<td>0.21–1.60</td>
</tr>
</tbody>
</table>

\textsuperscript{†} For a 0.1 logMAR (1 line) change in acuity.

\textsuperscript{*} Adjusted for age, race, diabetes history, body mass index, comorbidities, incident depression, smoking history.

\textsuperscript{‡} For a 0.1 logMAR (1 line) change in acuity.


