

Cataract, AMD are Associated With Increased Mortality

Further studies are needed to clarify whether visual impairment in older people accelerates aging and frailty.

BY CONNI BERGMANN KOURY, EDITOR-IN-CHIEF

In an Australian population-based cohort, age-related macular degeneration (AMD) independently predicted all-cause and vascular mortality in people ages 49 to 75 years, and cataract predicted mortality in people aged ≥ 49 years. The investigators reported in *Archives of Ophthalmology*¹ that the visual impairment, AMD, cataract, and mortality associations all seemed to be independent of each other.

“Several studies have consistently shown an association between visual impairment and increased mortality in older persons,” wrote Sudha Cugati, MS, and colleagues from the Department of Ophthalmology at the University of Sydney. “The mechanisms for higher mortality associated with visual impairment remain unclear.”

The mortality increase may be linked to age-related ocular conditions or cataract, which can be markers for biological aging, or it could be that visual impairment and its related factors share a similar pathogenesis with other conditions linked with increased mortality. To date, studies have been inconsistent, the investigators said.

BLUE MOUNTAINS EYE STUDY

In the current investigation, the authors sought to assess the longer-term mortality risk associated with visual impairment and its two principal causes, AMD and cataract, in an older Australian cohort in the Blue Mountains Eye Study. The Blue Mountains Eye Study is a population-based cohort investigation of vision and common eye disorders among a suburban Australian population, aged ≥ 49 years at baseline. The Blue Mountains Eye Study research team examined 3,654 people from 1992 to 1994.

Initial visual acuity was assessed using a logarithm of the minimum angle of resolution chart. Dr. Cugati wrote that if the initial visual acuity was < 54 letters read correctly (20/20 Snellen equivalent), refraction was performed. Retinal photographs were also taken at baseline (FF3; Zeiss, Oberkochen, Germany) and graded for AMD lesions. Baseline cataract was documented from slit lamp (Topcon Medical, Tokyo) and retroillumination (Neitz Instruments, Tokyo) lens photos.

Other baseline tests included blood pressure and body mass index. Patients were classified as current or nonsmokers, and diabetes was defined as a history of physician-diagnosed diabetes and the use of diabetic medications of diet control or fasting blood glucose ≥ 126 mg/dL at the time of examinations. The investigators also noted history of angina, myocardial infarction (MI), and stroke at baseline.

CAUSES OF DEATH OBTAINED

According to the report, mortality and causes of death occurring between baseline and Dec. 31, 2003 were obtained using data linkages with the Australian National Death Index. Age-standardized mortality rates were then calculated, and hazard ratios (HR) and 95% confidence intervals (CI) were assessed using Cox models.

During an average period of 11 years, 1,051 participants (28.9%) died of any cause (28.9%) and 483 (13.3%) died of vascular causes. “Participants who died were more likely to be male, current smokers, overweight, have diabetes, hypertension, and a history of angina, acute MI, and stroke,” Dr. Cugati wrote.

Visual impairment was identified in 132 participants

TABLE 1. BASELINE CHARACTERISTICS ASSOCIATED WITH MORTALITY IN THE MULTIVARIATE-ADJUSTED COX REGRESSION MODEL*

Status at Baseline	Participants	
	Died n=1051	Survived n=2582
Age, mean \pm SD, years	73.7 \pm 9.36	63.1 \pm 8.11
Sex		
Female	516 (49.1%)	1,546 (59.9%)
Male	535 (50.9%)	1,036 (40.1%)
Body mass index [†]		
<20 (underweight)	90 (9.2%)	108 (4.3%)
20-25	397 (40.6%)	957 (37.6%)
25-30 (overweight)	341 (40.6%)	1,021 (40.2%)
>30 (obese)	150 (15.3%)	457 (18.0%)
Diabetes	113/1,051 (10.8%)	169/2,582 (6.6%)
Hypertension	563/1,034 (54.4%)	1,073/2,572 (41.7%)
Current smoker	165/982 (16.8%)	330/2,507 (13.2%)
History of angina	204/1,039 (19.6%)	245/2,574 (9.5%)
History of acute MI	154/1,039 (14.8%)	179/2,574 (7.0%)
History of stroke	114/1,042 (10.9%)	77/2,571 (3.0%)

* $P < .001$ for all characteristics
[†] BMI is expressed as weight in kilograms divided by height in meters squared

(3.6%) (24 aged <75 years and 108 aged \geq 75 years). The cumulative 11-year mortality was higher in participants with versus without visual impairment (75.0% vs 26.9%), with age-standardized mortality of 54.0% and 34.0% in participants with and without visual impairment, respectively, according to the report.

VISUAL IMPAIRMENT AND REDUCED SURVIVAL

“An association between visual impairment and reduced survival (around 40%) was observed in the age- and gender-adjusted model (HR, 1.4; 95% CI, 1.1-1.7), but this association became weaker after adjusting for other known factors significantly associated with poor survival (HR, 1.3; 95% CI, 0.98-1.7),” the researchers said. “Among persons aged <75 years, however, visual impairment predicted an almost three-fold higher all-cause mortality (HR, 2.9; 95% CI, 1.6-5.5). They added that the association remained in people aged <75 years, but became attenuated after further adjustment for triglyceride level, fibrinogen level, education, and walking disability.

A similar association was found between visual impairment and vascular mortality in participants aged <75 years, after gender and age adjustment, but after adjustment for other factors became nonsignificant.

Among the 3,553 patients with retinal photograph data available, 6.9% had AMD at baseline. Seventy-two patients had late AMD, of those, 12 were aged <75 years at baseline.

Cumulative 11-year mortality was higher among participants with AMD versus those without AMD (55.8% vs 25.9%), with age-standardized mortality of 45.8% and 33.7% in people with and without AMD, respectively. No significant difference was seen in all-cause mortality risk between those with and those without AMD. In participants aged <75 years, however, AMD predicted 70% higher all-cause mortality (HR, 1.7; 95% CI, 1.2-2.4). This association in participants aged <75 years remained similar after adjustment for the previously mentioned confounders. The researchers said in those participants aged <75 years, early AMD (HR, 1.5; 95% CI, 1.0-2.2) and late AMD (HR, 2.5; 95% CI, 1.2-5.0) significantly predicted higher all-cause mortality.

AMD PREDICTIVE OLDER PEOPLE

“Cumulative 11-year vascular mortality was higher in participants with versus without any AMD (26.5% vs 11.9%), although AMD was not associated with higher adjusted vascular mortality risk for all ages,” Dr. Cugati and colleagues wrote. “In participants younger than 75 years, any AMD predicted increased vascular mortality risk (HR, 2.1; 95% CI, 1.2-3.8).” This association remained after further adjustment for visual impairment and cataract, however, the association became attenuated in participants aged <75 years after adjusting for the confounders.

They further found that, in analyses using three categories of AMD (early, late, none), in patients aged <75 years at the baseline exams, late AMD predicted higher vascular mortality and early AMD did not.

Any cataract (HR, 1.3; 95% CI, 1.0-1.5), cortical (HR, 1.2; 95% CI, 0.97-1.4), nuclear (HR, 1.2; 95% CI, 0.98-1.5), and posterior subcapsular cataract (HR, 1.3; 95% CI, 1.0-1.7) were also associated with modest, independent increases in all-cause mortality, Dr. Cugati and colleagues found.

The investigators compared the primary cause of death between participants with and without AMD and cataract. Vascular deaths were more frequent among participants with visual impairment of cataract compared with those without visual impairment or cataract ($P = .004$ and $P < .001$, respectively)

In summary, among Australians in this study, AMD in those aged <75 years significantly predicted higher all-cause and vascular mortality. “The association of visual impairment and all-cause mortality among persons older than 75 years became nonsignificant after adjusting for other potential economic and biological confounders, although reduced power could have contributed here,” Dr. Cugati wrote. This age-stratified difference is not uncommon in such studies, because effects of age alone tend to dominate influences on mortality in very old people. They also found that any type of cataract were significant predictors of all cause mortality in the overall population.

“The implications of these findings also remain uncertain: whether such an association indicates that visual impairment, age-related eye disease, or both are markers of aging and frailty or whether these ocular conditions accelerate aging, thus leading to relatively earlier death in older persons,” they wrote. “The present findings suggest that the association between visual impairment and all-cause mortality is mainly observed in persons younger than 75 years at baseline.”

The investigators went on to say that this is important given that a major proportion of visual impairment is due to treatable causes.

HYPOTHETICAL EXPLANATIONS

Several hypothetical explanations may explain the relationship between visual impairment and earlier mortality, such as reduced functional ability, loss of independence, need for community support, reduced social interaction, and depression, the authors said. Additionally, the findings with regard to AMD may confirm previous work that has shown AMD to be a predictor of vascular mortality. This finding appears to support the hypothesis that AMD may share common antecedents as cardiovascular disease, including chronic inflammation.

“Further studies are needed to confirm these findings ... If a direct or indirect causal effect from visual impairment on earlier death is confirmed, regular assessment of vision in older persons may lead to early detection, facilitating treatments that could reduce the impact of visual impairment,” the investigators wrote. ■

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1. Cugati S, Cumming RG, Smith W, et al. Visual impairment, age-related macular degeneration, cataract, and long-term mortality. *Arch Ophthalmol*. 2007;125:917-924.

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