Association of Cataract Surgery With Mortality in Older Women
Findings From the Women’s Health Initiative

Victoria L. Tseng, MD, PhD; Rowan T. Chlebowski, MD, PhD; Fei Yu, PhD; Jane A. Cauley, DrPH; Wenjun Li, PhD; Fridtjof Thomas, PhD; Beth A. Virnig, PhD; Anne L. Coleman, MD, PhD

IMPORTANCE Previous studies have suggested an association between cataract surgery and decreased risk for all-cause mortality potentially through a mechanism of improved health status and functional independence, but the association between cataract surgery and cause-specific mortality has not been previously studied and is not well understood.

OBJECTIVE To examine the association between cataract surgery and total and cause-specific mortality in older women with cataract.

DESIGN, SETTING, AND PARTICIPANTS This prospective cohort study included nationwide data collected from the Women’s Health Initiative (WHI) clinical trial and observational study linked with the Medicare claims database. Participants in the present study were 65 years or older with a diagnosis of cataract in the linked Medicare claims database. The WHI data were collected from January 1, 1993, through December 31, 2015. Data were analyzed for the present study from July 1, 2014, through September 1, 2017.

EXPOSURES Cataract surgery as determined by Medicare claims codes.

MAIN OUTCOMES AND MEASURES The outcomes of interest included all-cause mortality and mortality attributed to vascular, cancer, accidental, neurologic, pulmonary, and infectious causes. Mortality rates were compared by cataract surgery status using the log-rank test and Cox proportional hazards regression models adjusting for demographics, systemic and ocular comorbidities, smoking, alcohol use, body mass index, and physical activity.

RESULTS A total of 74,044 women with cataract in the WHI included 41,735 who underwent cataract surgery. Mean (SD) age was 70.5 (4.6) years; the most common ethnicity was white (64,430 [87.0%]), followed by black (5293 [7.1%]) and Hispanic (1723 [2.3%]). The mortality rate was 2.56 per 100 person-years in both groups. In covariate-adjusted Cox models, cataract surgery was associated with lower all-cause mortality (adjusted hazards ratio [AHR], 0.40; 95% CI, 0.39-0.42) as well as lower mortality specific to vascular (AHR, 0.42; 95% CI, 0.39-0.46), cancer (AHR, 0.31; 95% CI, 0.29-0.34), accidental (AHR, 0.44; 95% CI, 0.33-0.58), neurologic (AHR, 0.43; 95% CI, 0.36-0.53), pulmonary (AHR, 0.63; 95% CI, 0.52-0.78), and infectious (AHR, 0.44; 95% CI, 0.36-0.54) diseases.

CONCLUSIONS AND RELEVANCE In older women with cataract in the WHI, cataract surgery is associated with lower risk for total and cause-specific mortality, although whether this association is explained by the intervention of cataract surgery is unclear. Further study of the interplay of cataract surgery, systemic disease, and disease-related mortality would be informative for improved patient care.
Cataract surgery is the mainstay of treatment for visually significant cataract, and its primary purpose is to reverse the associated visual impairment. Previous studies from administrative databases have demonstrated that in addition to visual improvement, cataract surgery was also associated with a lower mortality risk. Although these studies hypothesized that the observed associations are mediated by improvements in health status and functional independence after cataract surgery, they have not examined whether the association between cataract surgery and lower mortality risk applies to women with different medical conditions that affect overall functioning to varying degrees, such as cancer, cardiovascular disease, and dementia.

The Women's Health Initiative (WHI) database contains detailed and extensively validated information on demographic, comorbidity, and lifestyle factors in a large cohort of US women with more than 20 years of follow-up. Furthermore, the WHI database contains information on total and cause-specific mortality, which is not available in other large databases of patients with cataract surgery in the United States. These factors make the WHI an ideal cohort in which to examine the interplay between eye disease and a wide variety of systemic and lifestyle factors in US women. Given these strengths of the WHI database and the need for further understanding of the association between cataract surgery and improved survival, the purpose of the present study is to examine the association between cataract surgery and total and cause-specific mortality in the WHI cohort, with the hypothesis that cataract surgery improves survival among women with cataract in the WHI.

Methods

Overview of the Women's Health Initiative
The WHI is a study of US postmenopausal women aged 50 to 79 years. The WHI included 4 overlapping, randomized clinical trials evaluating hormone therapy, diet modification, and calcium and vitamin D supplementation that enrolled 68 132 women and an observational study cohort that enrolled 93 676 women. Details of the study design have been previously published. The protocols were approved by the institutional review boards at all clinical sites, and all women provided written informed consent. The present study was additionally approved by the institutional review board at UCLA.

Data collection for the main WHI study started in January 1, 1993, and ended December 31, 2005, at 40 clinical centers, and additional observational data were collected in 2 WHI extension studies from January 1, 2005, through December 31, 2010, and from January 1, 2010, through December 31, 2015. For WHI participants who are also enrolled in Medicare, WHI data are linked on an individual level to all International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnostic codes and Current Procedural Terminology (CPT) codes in the administrative Medicare database.

Study Population
The study population consisted of all WHI participants who had an ICD-9-CM diagnosis code for cataract in the linked Medicare database at 65 years or older (eTable 1 in the Supplement). Participants younger than 65 years at the time of cataract diagnosis in Medicare were excluded owing to selective indications for Medicare enrollment before 65 years of age. Participants who were younger than 65 years at the time of WHI enrollment were not included in the study population until the age of cataract diagnosis in the Medicare database, which defined their age at study baseline.

Cataract Surgery Status
The exposure of interest was cataract surgery. The cataract surgery group consisted of all participants with an ICD-9-CM diagnosis code for cataract and a CPT code for cataract surgery (eTable 1 in the Supplement). The cataract diagnosis group consisted of all participants with an ICD-9-CM diagnosis code for cataract without a CPT code for cataract surgery. Patients in both groups were followed up starting from the date of earliest diagnostic code for cataract.

Outcome
The primary outcome of interest was all-cause mortality before December 31, 2015. Death and underlying cause of death were determined at the clinical coordinating center by review of medical records or death certificates and, in some cases, by reports from participants’ relatives or by the National Death Index. Of 31 311 total discovered deaths in the WHI cohort as of December 31, 2015, cause of death was ascertained from medical record review for 21 887 participants (69.9%), from the initial cause of death form for 2466 (7.9%), and from the ICD-9-CM code for 6958 (22.2%). In this study, causes of death were grouped into vascular, cancer-related, accident-related, neurologic, pulmonary, and infectious conditions (eTable 2 in the Supplement).

For both groups, time to death was calculated as the number of days from cataract diagnosis to death. Participants who did not have a recorded death in the study were censored on the last known date of WHI follow-up or on December 31, 2015, if they were still enrolled.

Covariates
Demographics that were collected included age at the time of cataract diagnosis in Medicare, race, US region of residence, educational level, annual income, health insurance status at the time of WHI enrollment, use of preventive health services (mammography and Papanicolaou smear), and WHI study
Arm. Systemic comorbidities in the Charlson Comorbidity Index (CCI) were assessed at the time of surgery and the time of diagnosis for the cataract surgery group and at the time of diagnosis for the cataract diagnosis group (eTable 3 in the Supplement). The CCI is a weighted index of systemic disease burden (range, 0-33), and a higher CCI score indicates a higher burden of systemic disease. Ocular comorbidities collected included age-related macular degeneration and glaucoma. A participant was counted as having a systemic or ocular comorbidity if she had the disease based on the WHI indicator variable for the disease, an ICD-9-CM code for the disease in Medicare, or both (eTable 4 in the Supplement). The WHI verified the following outcomes by central medical record review: all cancers, myocardial infarction, congestive heart failure, stroke, other cardiovascular events, pulmonary emboli, hip fracture, and dementia (only in the WHI Memory Study subcohort).

Because objective visual acuity data were not available, the presence of severe cataract was examined as a proxy for poor vision. Patients with ICD-9-CM codes for subcapsular cataracts, total or mature cataract, hypermature cataract, and combined cataracts were considered to have severe subtypes of cataract (eTable 1 in the Supplement).

Additional covariates collected included smoking status, alcohol intake, body mass index (BMI; calculated as weight in kilograms divided by height in meters squared), and physical activity. Smoking status and alcohol intake were self-reported at study baseline. We determined BMI based on height and weight measurements from study baseline. Physical activity was based on metabolic equivalent tasks per week, which were calculated from self-reported physical activity habits at baseline and at years 3 and 6.

### Statistical Analyses

Data were analyzed for this study from July 1, 2014, through September 1, 2017. Patient characteristics and mortality rates were compared by cataract surgery status descriptively. To compare the source of diagnosis for systemic comorbidities that were ascertained from the WHI and Medicare databases, we performed χ² tests for the diagnosis source for selected cardiovascular and cancer-related comorbidities. Log-rank tests were used to compare crude mortality rates by surgical status. Cox proportional hazards regression models were used to obtain covariate-adjusted associations from cataract surgery and time to death due to any cause and from cataract surgery and time to death attributed to vascular, cancer, accidental, neurologic, pulmonary, and infectious conditions. An additional analysis was performed for all-cause mortality treating cataract surgery status as a time-varying exposure variable. All demographic, CCI score, ocular comorbidities, cataract severity, smoking status, alcohol intake, physical activity, and BMI data were included as covariates in the model. To account for potential confounding by indication, propensity scores were created by reordering all covariates on cataract surgery status to determine the probability of cataract surgery. Participants were then grouped by propensity score strata, and time to all-cause mortality was compared between participants in the cataract surgery and cataract diagnosis groups within propensity score deciles with Cox models. P < .05 indicated significance.

### Results

#### Baseline Characteristics

Baseline characteristics are summarized in Table 1 and eTable 5 in the Supplement. The study cohort included 74,044 women (mean [SD] age, 70.5 [4.6] years), of whom 41,735 were in the cataract surgery group and 32,309 were in the cataract diagnosis group. The largest proportion of patients in the cataract surgery and cataract diagnosis groups were aged 65 to 69 years at the time of cataract diagnosis (45.6% and 55.6%, respectively). The remainder of demographic factors were similar in both groups. The most common systemic comorbidity in both groups was solid malignant neoplasm (29.9% in the cataract surgery and 23.6% in the cataract diagnosis groups), and the most common ocular comorbidity was glaucoma (31.6% in the cataract surgery and 17.5% in the cataract diagnosis groups). Higher proportions of most comorbidities were found in the surgery group at the time of surgery. When diagnosis sources for selected systemic comorbidities were compared, 6.2% to 40.8% of comorbidities were diagnosed in the WHI and Medicare databases, whereas the remainder were diagnosed in 1 database only (eTable 6 in the Supplement). In both groups, most participants were never smokers (51.5% in the cataract surgery and 51.8% in the cataract diagnosis groups, of those with available data), had 1 to less than 7 alcoholic beverages per week (25.8% in the cataract surgery and 27.1% in the cataract diagnosis groups, of those with available data), had a BMI of less than 25 (36.2% in the cataract surgery and 36.7% in the cataract diagnosis groups), and had activity levels of 5 to 12 MET/wk (64.8% in the cataract surgery and 64.5% in the cataract diagnosis groups, of those with available data).

#### Mortality Incidence

Data on mortality incidence are summarized in Table 2. The crude incidence of all-cause mortality was 1.52 deaths per 100 person-years in the cataract surgery group and 2.56 deaths per 100 person-years in the cataract diagnosis group (P < .001 for log-rank test comparing crude mortality incidence in both groups).

#### Multivariable Associations Between Cataract Surgery and Mortality

Multivariable associations between cataract surgery and each type of mortality are summarized in Table 3. Cataract surgery was associated with a lower risk for all-cause mortality in the unadjusted model (hazards ratio [HR], 0.51; 95% CI, 0.49-0.53) and adjusted model (adjusted HR [AHR], 0.40; 95% CI, 0.39-0.42). Cataract surgery was also associated with lower hazards for all-cause mortality and cause-specific death for every type of death in the unadjusted and adjusted models. The magnitudes of association were similar for all types of cause-specific mortality except for pulmonary causes of death, which had a weaker unadjusted (HR, 0.83; 95% CI, 0.71-0.98) and adjusted (AHR, 0.63; 95% CI, 0.52-0.78) association. When the analysis of all-cause mortality was repeated with cataract surgery status as a time-varying exposure variable, the HRs and CIs in the unadjusted and adjusted models were completely unchanged.
identical to the HRs and CIs in the models where cataract surgery status was not treated as a time-varying covariate (unadjusted HR, 0.51 [95% CI, 0.49-0.53]; AHR, 0.40 [95% CI, 0.39-
0.42]). In addition, we found associations of similar magnitude for all outcomes when adjusting for CCI score at the time of cataract diagnosis rather than at the time of cataract surgery.
Table 2. Mortality Rates in Older Women With Cataract by Surgical Care Status in the Women’s Health Initiative From 1993-2013a

<table>
<thead>
<tr>
<th>Cause of Mortality</th>
<th>Mortality Rate, No. of Deaths/Total Person-years (Incidence per 100 Person-years)</th>
<th>P Valueb</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cataract Surgery Group (n = 41 735)</td>
<td>Nonsurgery Group (n = 32 309)</td>
</tr>
<tr>
<td>All-cause</td>
<td>6878/552 798 (1.22)</td>
<td>6123/239 448 (2.56)</td>
</tr>
<tr>
<td>Vascular</td>
<td>2390/112 157 (0.58)</td>
<td>1982/213 659 (0.93)</td>
</tr>
<tr>
<td>Cancer</td>
<td>1650/403 957 (0.41)</td>
<td>1933/211 013 (0.92)</td>
</tr>
<tr>
<td>Accident</td>
<td>185/331 971 (0.05)</td>
<td>150/202 019 (0.07)</td>
</tr>
<tr>
<td>Neurologic</td>
<td>380/384 145 (0.10)</td>
<td>340/203 909 (0.17)</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>439/394 338 (0.13)</td>
<td>227/202 626 (0.13)</td>
</tr>
<tr>
<td>Infectious</td>
<td>411/394 196 (0.10)</td>
<td>283/203 116 (0.14)</td>
</tr>
</tbody>
</table>

aIncludes 74 044 participants. Person-years for cause-specific mortality exclude patients who died from other causes.
bCalculated using the log-rank test (excluding/including time from diagnosis to surgery).

Table 3. Hazards of Total and Cause-Specific Mortality in Patients With Cataract by Surgery Status in the WHI From 1993-2013a

<table>
<thead>
<tr>
<th>Cause (No. of Participants)</th>
<th>Unadjusted HR (95% CI)</th>
<th>AHR (95% CI)bc</th>
<th>AHR (95% CI)d,e</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause (62 544)</td>
<td>0.51 (0.49-0.53)a</td>
<td>0.40 (0.39-0.42)b</td>
<td>0.38 (0.36-0.39)</td>
</tr>
<tr>
<td>Vascular (55 408)</td>
<td>0.54 (0.50-0.57)</td>
<td>0.42 (0.39-0.46)</td>
<td>0.34 (0.31-0.37)</td>
</tr>
<tr>
<td>Cancer (54 875)</td>
<td>0.42 (0.39-0.45)</td>
<td>0.31 (0.29-0.34)</td>
<td>0.36 (0.33-0.39)</td>
</tr>
<tr>
<td>Accident (52 152)</td>
<td>0.55 (0.45-0.69)</td>
<td>0.44 (0.33-0.58)</td>
<td>0.32 (0.24-0.43)</td>
</tr>
<tr>
<td>Neurologic (52 454)</td>
<td>0.45 (0.39-0.52)</td>
<td>0.43 (0.36-0.53)</td>
<td>0.27 (0.22-0.33)</td>
</tr>
<tr>
<td>Pulmonary (52 438)</td>
<td>0.83 (0.71-0.98)</td>
<td>0.63 (0.52-0.78)</td>
<td>0.71 (0.57-0.88)</td>
</tr>
<tr>
<td>Infectious (52 437)</td>
<td>0.62 (0.53-0.72)</td>
<td>0.44 (0.36-0.54)</td>
<td>0.38 (0.30-0.46)</td>
</tr>
</tbody>
</table>

Abbreviations: AHR, adjusted hazard ratio (HR); WHI, Women’s Health Initiative.

aIncludes 74 044 participants.
bAdjusted for age, race, region of residence, use of preventive health services, health insurance at WHI baseline, Charlson Comorbidity Index score, smoking status, alcohol intake, metabolic equivalent tasks per week, cataract surgery severity.
cIndicates with systemic disease burden at the time of cataract surgery.
dIndicates with systemic disease burden at the time of cataract diagnosis.
eIdentical values were obtained when cataract surgery status was treated as a time-varying covariate.

for the cataract surgery group (AHR for all-cause mortality, 0.38; 95% CI, 0.36-0.39). Additional results are given in Table 3.

Propensity Score Analysis

Results from propensity score analyses are outlined in Table 4 and Table 5. A higher likelihood of receiving cataract surgery was associated with being in the clinical trial arm of the WHI, living outside of the Northeast, having insurance, undergoing routine mammography, having a CCI score higher than 0, having any ocular comorbidities, and having a high level of physical activity. Participants in the cataract surgery group had decreased hazards of all-cause mortality compared with participants in the cataract diagnosis group in all propensity score strata (Table 5). In addition, the association became progressively stronger in higher propensity deciles (HR for decile 1, 0.63 [95% CI, 0.53-0.75]; HR for decile 10, 0.21 [95% CI, 0.17-0.28]).

Discussion

In participants with cataract in the WHI, cataract surgery was associated with a lower risk for total and cause-specific mortality after adjusting for demographics, systemic and ocular comorbidities, and selected lifestyle factors. Specifically, WHI participants with cataract surgery had lower risks for dying due to any cause and due to vascular, cancer, accidental, neurologic, pulmonary, and infectious conditions compared with participants with a cataract who did not receive surgery. These results were further supported by findings from propensity score analyses, which demonstrated consistently lower hazards for mortality in participants with cataract surgery vs a cataract diagnosis when using propensity scores to account for potential confounding.

The findings on all-cause mortality in the present study parallel that of a previous study of cataract surgery and mortality in the US Medicare population. The study in Medicare reported that cataract surgery was associated with a lower hazard for all-cause mortality in patients with cataract after adjusting for demographics and systemic and ocular comorbidities, which was also seen in a subgroup analysis of women within the Medicare population. In the present study, we were able to adjust additionally for smoking, alcohol use, BMI, and physical activity, and the association between cataract surgery and lower mortality risk that was observed in the Medicare database persisted after adding these important covariates. In addition, the magnitude of the association was similar in both studies, suggesting that in US patients with cataract, a strong association exists between cataract surgery and a lower risk for mortality due to any cause. Furthermore, both studies found that patients in the highest propensity score decile experienced the highest reduction...
in mortality risk after cataract surgery, suggesting that cataract surgery may be especially beneficial for patients who are most likely to receive surgery.
systemic health care in addition to cataract surgery. This possibility is suggested by the higher odds of cataract surgery in WHI participants who underwent routine mammography and in those with health insurance. However, study findings did not change after attempting to equalize baseline characteristics between study groups with propensity score analyses.

An additional potential explanation is the possibility of healthier lifestyle in participants who underwent cataract surgery. Although this study examined BMI and physical activity scores and found similar distributions of these variables between the surgery and diagnosis groups, we did not explore additional important lifestyle factors such as healthy diets. The incorporation of additional lifestyle factors with variables such as the WHI healthy diet score would be of importance and interest for future studies. Further studies are needed to better understand mechanisms of association between cataract surgery and disease-related mortality and could specifically examine the effect of cataract surgery on factors such as quality of life, activities of daily living, access to medical care, and mental health.

Limitations
This study is mainly limited by its observational nature. Participation in the WHI is voluntary, and generalizability of findings from this cohort may be limited by differential participant dropout. In addition, because the WHI cohort is all female, findings from this study may not be generalizable to male patients, and additional studies of cataract surgery and mortality in a male population would be beneficial. Furthermore, WHI participants are long-term study participants, and their demographic and systemic disease profiles may differ from those of the general population of women in the United States. Another finding of interest in this study that may limit its generalizability is the unusually high proportion of patients with systemic comorbidities compared with previous studies, especially in the cataract surgery group. We hypothesize that the explanation for these differences is multifactorial and mainly related to the ability to combine the WHI and Medicare databases, which may lead to increased detection of comorbidities compared with a single data collection modality that was supported by the significant proportion of cardiovascular and cancer-related comorbidities that were only diagnosed in 1 of the 2 databases between WHI and Medicare. In addition, follow-up with primary care physicians may have been better among WHI participants who have proven reliable follow-up with regular study visits, which would lead to increased detection of systemic disease. The observational data in this study are also subject to misclassification bias, including the accuracy of cause-of-death data. Previous studies have demonstrated that cardiovascular disease is overrepresented as a cause of death, in addition to suggesting high rates of misclassification of causes of death from other sources of illness.

In the present study, higher rates of metastatic cancer but lower rates of cancer-related deaths in the cataract surgery vs cataract diagnosis group were found, suggesting that our findings should be interpreted in light of the inherent limitations of cause-of-death data. In addition, unmeasured confounding is a possibility, although the consistency of results in this study with previous studies of cataract surgery and mortality and the findings from propensity score analyses suggest that any potential confounding is minimal. Finally, although lower mortality rates were observed in the cataract surgery group, they do not prove a causal association between cataract surgery and decreased mortality, and additional study of the mechanisms and interplay between these associations is warranted.

Conclusions
This study found associations between cataract surgery and lower risks for total and cause-specific mortality in participants of the WHI. Further studies of the associations cataract surgery, systemic disease, and disease-specific mortality would be informative for improving patient selection and use of cataract surgery and for improved understanding of the benefits of cataract surgery beyond vision improvement.