Cataract-Related Visual Impairment Corrected by Cataract Surgery and 10-Year Mortality: The Liwan Eye Study

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Submitted: July 11, 2015
Accepted: March 2, 2016

Citation: Zhu Z, Wang L, Young CA, Huang S, Chang BHW, He M. Cataract-related visual impairment corrected by cataract surgery and 10-year mortality: The Liwan Eye Study. *Invest Ophthalmol Vis Sci*. 2016;57:2290–2295. DOI:10.1167/iovs.15-17673

Purpose. To assess 10-year mortality in people who had undergone cataract surgery with no residual visual impairment (VI) and those who had persistent VI due to cataract using a population-based cohort.

Methods. The Liwan Eye Study is a 10-year longitudinal study commenced in 2003. According to the World Health Organization, presenting VI was defined as visual acuity less than 20/63 in the better-seeing eye. History of cataract surgery was defined as cataract surgery performed on either eye. Information on the date of surgery was recorded. Dates of death occurring between baseline and April 30, 2014 were obtained from the National Death Index data. Information on socioeconomic factors was obtained from questionnaire interviews. Cox proportional hazards regression models were used to assess the hazard ratios (HRs) and 95% confidence intervals (CIs).

Results. Fifty-nine participants had undergone cataract surgery without residual VI and 67 participants had persistent cataract-related VI. The 10-year mortality rate for participants who had undergone cataract surgery without residual VI was statistically significant lower than that in participants who had VI due to cataract based on log-rank test (32.2% vs. 64.2%; $P = 0.002$). This finding remained significant in the unadjusted Cox proportional hazards model (HR, 0.43; 95% CI, 0.25–0.74; $P = 0.002$). After adjusting for age, sex, history of diabetes, and hypertension, body mass index (BMI), education level, and personal income, participants with cataract surgery and no residual VI did not have a higher chance of survival than participants with persistent VI due to cataract (HR, 0.56; 95% CI, 0.26–1.20; $P = 0.136$).

Conclusions. Cataract-related VI corrected by cataract surgery was not associated with better survival after adjusting for a number of possible confounders. Given our sample size is relatively small and limited power, further studies with larger sample are needed.

Keywords: cataract surgery, mortality, visual impairment

Visual impairment (VI) and blindness represent a major global health issue. According to the World Health Organization (WHO) estimation,[1] there are 161 million visually impaired persons and 37 million blind people around the world, with a large proportion residing in developing countries. Cataract remains the leading cause of visual impairment, accounting for almost one-half of all cases.[2] There is consistent evidence showing that persons with cataract have a higher risk of mortality compared with persons without cataract.[3–10] Cataract surgery is the only effective treatment for people with cataract, and is the most commonly performed clinical procedure in the medical field.[11] In addition to improving visual function, some evidences suggest that cataract surgery is associated with better chances of survival, although this has yet to be conclusive.[3–8,12–15] The Beaver Dam Eye Study (BDES)[5] found no association between cataract surgery and mortality in participants who did and did not undergo surgery, while in the Bristol Eye Hospital Study,[15] people who had undergone cataract surgery had a significantly lower mortality than the national and regional standardized mortality ratios (SMR = 0.88 vs. 0.87). Although many studies assessed the association of cataract surgery with mortality, they compared operated people with unoperated people with or without cataract, or people in the general population, which complicated the interpretation of the role cataract surgery played in its association with mortality. However, in the Blue Mountains Eye Study (BMES),[7] which addressed a slightly different study question, surgical correction of VI attributable to cataract was associated with better survival than survival among individuals who had cataract-related VI. Currently, little information is available regarding the survival between people with VI corrected by cataract surgery and those with persistent VI due to cataract in China, which accounts for one-fifth of the world's population. Our study, one that is population-based with long-term follow-up, provides an opportunity to explore the mortality risk amongst those who have undergone successful cataract surgery and those who had persistent VI due to cataract.

Therefore, we attempted to explore the 10-year mortality in people with cataract surgery-corrected VI and those with persistent VI due to cataract using a population-based cohort study in urban China.

Methods

Study Population

The methodology used in the Liwan Eye Study has been described in detail elsewhere.[16] Briefly, the study was conducted in the Liwan District of Guangzhou, chosen for its relatively stable population, representative of demographic and socioeconomic characteristics. Participants, aged 50 years and older that had resided in the Liwan District for over 6 months, were recruited via cluster sampling method. Of the 1864 eligible subjects, 1405 (75.4%) participated in the baseline survey. Comprehensive eye examinations and anthropometric measurements, such as weight and height, were obtained in the research clinic set up near the communities. All baseline participants were asked to fill out questionnaires to provide detailed information on their history of systemic diseases (hypertension and diabetes) and their level of education and income. All surviving participants were invited for reexaminations after 5 and 10 years using the same standardized protocol. To address our study question, participants who underwent cataract surgery before baseline or during the follow-up period and had no residual VI (59 participants) and those who had VI due to cataract (67 participants) were included.

The study was approved by the Ethics Committee of the Zhongshan Ophthalmic Center, the Guangzhou Liwan District Government, and the Research Governance Committee of Moorfields Eye Hospital (London, UK). The research was conducted adhering to the tenets of the World Medical Association's Declaration of Helsinki. Written informed consent was obtained from all participants.

Measurements

Confirmation and dates of death occurring between baseline and April 30, 2014 were obtained from the National Death Index of the Center for Disease Control (CDC) of the Liwan District. We provided the CDC with a list of personal information, including names, dates of birth, and home addresses for all the participants who did not show up at the 10-year follow-up examination. According to the list, the staff from the CDC provided a corresponding list of deaths after matching the names, sex, age, and home addresses with the National Death Index database. Participants who did not attend the 10-year follow-up examination and were not registered as having died in the National Death Index database were regarded as survivors. Most participants (94.4%) could be contacted by phone or home visits, which implied their survival. The date of death was not obtainable for 15 (24.2%) of the deceased.

Presenting VA was measured using an Early Treatment Diabetic Retinopathy Study logMAR E chart (Precision Vision, Villa Park, IL, USA) with a standard illumination box and the participant's habitual distance correction. Presenting VI was defined as visual acuity less than 20/63 in the better-seeing eye with habitual correction if worn based on the current World Health Organization (WHO) definition. According to the study protocol, the principal cause of VI was assigned by an experienced specialist (MH) using a 15-item diagnostic checklist. Visual impairment attributable to cataract was assumed for those with significant lens opacity that obscured observation of the fundus. History of cataract surgery was defined as participants who had received cataract surgery before the baseline examination or during the follow-up period, as confirmed by the same experienced ophthalmologist (MH). Information on the date of cataract surgery was recorded. The eye examination was performed with a slit lamp (SL-8Z; Topcon, Tokyo, Japan, with D1x digital image system; Nikon, Tokyo, Japan).

Hypertension was defined as high blood pressure diagnosed by a physician and for patients currently taking antihypertensive medications. Diabetes was defined as hyperglycemia diagnosed by a physician and for patients currently taking antidiabetic drugs. Body mass index (BMI) was calculated as weight (in kilograms) divided by the height squared (in meters). Body mass index was categorized as underweight (BMI < 18.5 kg/m^2), overweight or obese (BMI ≥ 25 kg/m^2), and normal ($18.5 \leq$ BMI < 25.0 kg/m^2, reference group). The level of education was defined as the highest level of education the participant attained according to their questionnaire answer. The education level was divided into two groups: lower than high school and high school or higher, with the former group regarded as the reference. The status of personal income was divided into two categories: less than 1000 renminbi (RMB) and more than 1000 RMB per month.

Statistical Analysis

All statistical analysis was performed using Stata (ver. 12.0; StataCorp., College Station, TX, USA). Student's *t*-test was used to compare continuous variables, while Pearson χ^2 or Fisher's exact test were used for the comparison of categorical data where appropriate. We used median survival time to impute the missing information of date of death for deceased participants. Plots of survival curves of people with cataract surgery-corrected VI and those with persistent VI due to cataract were generated using Kaplan-Meier estimates, and the log-rank test was used for comparing the survival distributions between the groups. Univariate and multivariate Cox proportional hazards regression models were used to assess the hazard ratios (HRs) and 95% confidence intervals (CIs) of all-cause mortality. Age, sex, BMI, history of hypertension and diabetes, level of education, and personal income were adjusted in the multivariate models. Proportional-hazards assumption test was based on Schoenfeld residuals with a *P* value less than 0.05 regarded as violate the assumption. All variables we included in the Cox regression models were found to be valid. Collinearity was examined using variance inflation factors (VIF) procedure and found VIF for all covariables less than 2 (mean: 1.47). Statistical significance was defined as a P value less than 0.05.

Results

At baseline, visual acuity measurements were available for 1399 of the 1405 participants. Among them, 1250 participants had no VI and 149 had VI. Of the 1250 participants without VI, 48 had undergone cataract surgery before the baseline examination. In the 149 visually impaired participants, 75 participants had not undergone cataract surgery and had VI due to cataract, three participants underwent cataract surgery and still had VI due to cataract or posterior capsular opacity. Among the 78 (75 + 3) participants with VI due to cataract at baseline, 11 had cataract surgery during the follow-up period and no residual VI, yielding 59 (48 + 11) participants (mean age: 72.4 ± 7.42 years) who had undergone cataract surgery with no residual VI and 67 (mean age: 78.4 ± 7.42 years) who had persistent VI due to cataract. In participants who had undergone cataract surgery and no residual VI, 29 (49.2%) participants returned for 10-year follow-up examination and 19 (32.2%) had died. The figures for the 67 participants with persistent VI due to cataract were 11 (16.4%) and 43 (64.2%), respectively (Fig. 1).

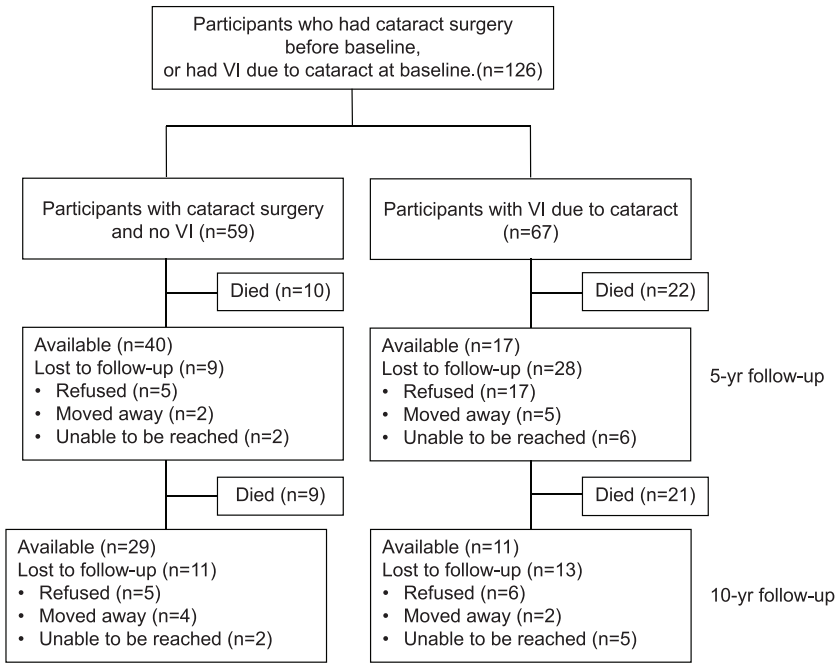

Figure 1. Schematic showing participants in the Liwan Eye Study at baseline, the time of 5- and 10-year follow-ups for the current study. A total 126 participants were included; 62 died during the 10-year follow-up.

Table 1 shows the baseline characteristics of participants included in our data analysis. Participants who had cataract surgery with no residual VI tended to be younger, more educated, and have higher income than persistent visually impaired participants due to cataract. In other aspects of demographic or medical history, there were no significant differences between these two groups at baseline.

By April 30, 2014, 62 (49.2%) of the 126 included participants were reported to have died of any cause. Table 2 gives the baseline characteristics of participants who died and survived. Participants who died were older and more likely to be male and underweight.

Participants with cataract surgery and no residual VI had a significantly reduced 10-year mortality compared with participants with VI due to cataract based on log-rank test (32.2% vs. 64.2%; $P = 0.002$). This finding remained significant in the unadjusted Cox proportional hazards model (HR, 0.43; 95% CI, 0.25–0.74; $P = 0.002$). However, after adjusting for age and sex in the Cox proportional hazards model, no significant association was found between VI corrected by cataract surgery and long-term mortality (HR, 0.57; 95% CI, 0.32–1.03; $P = 0.062$). After further adjustment for history of diabetes and hypertension, BMI, education level, and personal income level, participants who had undergone cataract surgery without residual VI had neither an increased nor decreased risk of mortality compared with participants who had cataract-related VI (HR, 0.56; 95% CI, 0.26–1.20; $P = 0.136$; Table 3); however, a post hoc power analysis indicated that we had only a 63% power to detect a statistically significant difference between the 2 groups due to the small sample size. The multivariate-adjusted survival curves based on Kaplan-Meier estimates are shown in Figure 2. Participants with cataract

Table 1. Baseline Demographic, Medical History and Socioeconomic Status of Participants Who Had Cataract Surgery with No Residual VI and Those Who Had Cataract-Related VI

Characteristics	*N**	Subsamples: Cataract Surgery and No VI, *n* = 59	Subsamples: Cataract-Related VI, *n* = 67	Unadjusted *P* Values
Age, mean ± SD, y	126	72.4 ± 7.4	78.3 ± 7.5	<0.001
Female	126	35 (59.3)	46 (68.7)	0.275
Hypertension	109	19 (35.8)	28 (50.0)	0.136
Diabetes mellitus	110	11 (20.8)	7 (12.3)	0.230
BMI				
Reference (18.5–25.0 kg/m^2)	36	18	18	-
Underweight (<18.5 kg/m^2)	11	8 (30.7)	3 (14.3)	0.185
Overweight/Obesity (>25.0 kg/m^2)	26	13 (41.9)	13 (41.9)	1.000
Higher education†	84	11 (26.8)	2 (4.65)	0.005
Higher income level‡	84	12 (29.3)	3 (6.98)	0.008

* Excludes missing data.
† Higher education was defined as an education level of at least high school.
‡ Higher income level was defined as personal income of more than 1000 RMB per month.

Table 2. Baseline Characteristics of Those Who Had Died and Survived Among the Participants

Characteristics	Participants, *N* (%)*		Unadjusted *P* Values	Adjusted Cox Regression Model *P* Value†
	Died, $n = 62$	Survived, $n = 64$		
Age, mean ± SD, y	78.5 ± 6.6	72.7 ± 8.2	<0.001	0.007
Female	35/62 (56.5)	46/64 (71.9)	0.071	0.026
Hypertension	25/52 (48.1)	22/57 (38.6)	0.318	0.556
Diabetes mellitus	7/53 (13.2)	11/57 (19.3)	0.388	0.935
BMI				
Reference (18.5–25.0 kg/m^2)	14	22	-	-
Underweight (<18.5 kg/m^2)	8/37 (21.6)	3/36 (8.33)	0.049	0.016
Overweight/Obesity (>25.0 kg/m^2)	15/37 (40.5)	11/36 (30.6)	0.143	0.253
Higher education‡	6/44 (13.6)	9/40 (22.5)	0.289	0.925
Higher income level§	6/44 (13.6)	7/40 (17.5)	0.625	0.875

* Excludes missing data.
† Adjustment for exposure (VI corrected by cataract surgery and persistent cataract-related VI).
‡ Higher education was defined as an education level of high school or higher.
§ Higher income level was defined as personal income of more than 1000 RMB per month.

surgery and no residual VI revealed higher long-term survival compared with participants with cataract-related VI, but did not reach statistical significance ($P = 0.136$).

Discussion

To the best of our knowledge, this is the first population-based study to document the long-term survival between people with VI corrected by cataract surgery and those who had persistent VI due to cataract in a Chinese population. We found that participants who had undergone cataract surgery and had no residual VI had the same mortality rate as those with VI due to cataract after adjusting for age, sex, history of diabetes and hypertension, BMI, education level, and personal income. The advantage of our analysis is that all the included cases are from a population-based study and therefore are likely representative in terms of severity of systemic and eye diseases, with a limited amount of selection bias.

Confirmation of death was obtained from National Death Index data, which is regarded as the most authoritative and comprehensive database for death information in China. The information on date of death was available for 75.8% (47/62) of the deceased people in our study. The reason for this is that the dates of death were not included in the death record and we could not trace the family to obtain this information for one-quarter of the participants. Data on the causes of death were not obtainable for almost one-half of the participants. Thus, the associations between cataract surgery and cause-specific death could not be assessed.

In our study, participants who had undergone cataract surgery without residual VI did not have a statistically significant difference in mortality compared with participants who had persistent VI due to cataract after adjusting for potential confounding factors. Our results differed from that of the Blue Mountains Eye Study (BMES),[7] which reported that cataract surgery reduced the long-term mortality risk by 40% compared with persons who had VI due to cataract in elderly population after adjusting for known mortality risk factors. The demographic discrepancies, as well as differences in ethnicity, study design, study sample size and age, methodology for controlling confounding factors, statistical methods of analysis, quality of medical service, age when cataract surgery was received, as well as the severity of lens opacity may explain some of the inconsistency between study results.

There is consistent evidence showing that persons with age-related cataract have a higher risk of mortality compared with those without.[3–10] It has been speculated that oxidation with aging and oxidative stresses on the lens[17] could explain some of the complex etiology of cataract. In addition, cataract is regarded as the translational "window to the rest of the body," suggesting cataract perhaps is a biomarker for aging at the molecular, epigenetic, cellular, and clinical levels.[18] The implications of these findings suggests that age-related cataract is a biomarker of aging and frailty.

Another possible hypothetical explanation for cataract and poor survival is in the consequences of VI. Persons with VI were more likely to have functional disability[19,20] and were more likely to have depression,[21,22] falls,[23] bone fractures[24] and accidents,[25] which may be associated with poor survival. Cataract surgery, an intervention that improves visual function, may therefore result in better survival rates. However, our study does not support this speculation.

There are other socioeconomics factors associated with those that do or do not receive surgery. Our study found that participants with cataract surgery and no residual VI tended to be younger, more educated and had a higher income. This is to be expected, as people with better knowledge of health and better access to health care services may be more likely to seek medical treatment. We did observe that participants that had

Table 3. Hazard Ratios of Participants Who Had Cataract Surgery With No Residual VI and Those Who Had Cataract-Related VI

	Participants, *n*	Died, *n*	Mortality Rate, %	HR (95% CI)	
				Age and Sex-Adjusted	Multivariate-Adjusted*
Cataract surgery and no VI	59	19	32.2	0.57 (0.32–1.03)	0.56 (0.26–1.20)
Cataract-related VI	67	43	64.2		

VI, Visual Impairment; HR, hazard ratio; CI, confidence interval.
* Adjustments for age, sex, history of diabetes and hypertension, BMI, education level, and personal income.

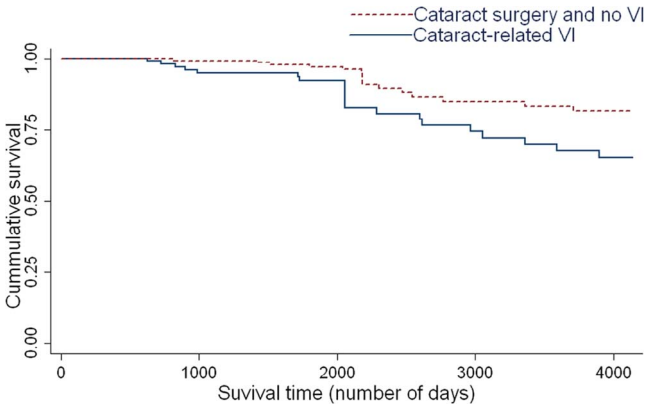

Figure 2. Survival curves of participants with cataract surgery and no VI (*short, dash line*) and those with cataract-related VI (*long, dash line*), after adjustments for age, sex, history of diabetes and hypertension, BMI, education level, and personal income. Participants with cataract surgery and no VI revealed higher long-term survival compared with those with cataract-related VI, but did not reach statistical significance ($P = 0.136$).

undergone cataract surgery with no residual VI had better chances of survival after cataract surgery because they were more health well-being and well-off. However, we did not find such an association between participants who had undergone cataract surgery with no residual VI and those whose who had persistent VI due to cataract in this population after adjusting for potential confounding factors. There is no clear explanation for this, but we might speculate that because cataract surgery alters vision but not the intrinsic causes of cataract, such as accelerated aging or the natural history of diseases, such as cardiovascular disease and cancer that are closely associated with mortality.[4,26] Though the information on systemic diseases was not studied comprehensively, we did find that older age and being underweight were important predictors of death in this study, similar to the findings in Swiss.[27]

There were a number of strengths of our study. Firstly, all the included cases were from a population-based study and therefore were likely representative in terms of severity of systemic and eye diseases, with a limited amount of selection bias. Secondly, we used the Cox proportional hazards regression model as a statistical method given that the data met the proportional-hazards assumption on the basis of Schoenfeld residuals. This model has an advantage over traditional logistic regression model on survival analysis for considering censored time. Thirdly, we had long-term follow-up data on survival time.

The study does have some limitations. Firstly, a relatively small number of included participants in our study may have less power. Post hoc power analysis was conducted and our study provided a power of 63% to detect the possible difference of mortality between participants who had undergone cataract surgery with no residual VI and those who had persistent VI due to cataract. With this moderate power, we cannot exclude the possibility of reporting false negative results in our study. Further studies are needed to investigate the effect of VI corrected by cataract surgery on survival. Secondly, it is possible that some important confounding factors, such as cardiovascular disease, the number of medical comorbidities, indicators of physical health, depression, and smoking and drinking status, may not have been controlled for and therefore we cannot completely exclude the uncontrolled confounders. Thirdly, date of death information was missing for 15/62 (24.2%) baseline participants. Although we used median survival time to impute the missing information of date of death for deceased participants, we still need to take into consideration the additional variance due to imputation, which may have potentially biased our findings. As a consequence of having no reliable information about the causes of death, the association between VI corrected by cataract surgery and specific-causes of death remains unknown in our study. Finally, with no data on the cause of cataract, we were not able to differentiate traumatic or congenital cataract from age-related cataract. However, it should be noted that age is the most common cause in older persons.

In summary, our study showed no significant difference in mortality between people who had undergone cataract surgery with no residual VI and people with cataract-related visual impairment after adjusting for age, sex, hypertension, diabetes, and lifestyle factors. This finding appears to indicate that the benefit of cataract surgery creating better visual function does not override the effects of lethal systemic diseases in this population. Further studies and clinical trials that investigate the effect of VI corrected by cataract surgery on survival may be useful to confirm these findings and elucidate the possible mechanisms.

Acknowledgments

Supported by grants from the National Natural Science Foundation of China (81125007; Beijing, China) and Fundamental Research Funds of the State Key Laboratory (Guangzhou, China).

Disclosure: **Z. Zhu**, None; **L. Wang**, None; **C.A. Young**, None; **S. Huang**, None; **B.H.W. Chang**, None; **M. He**, None

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