ORIGINAL ARTICLE

Mortality following cataract surgery in patients taking warfarin

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Abstract

Aims: To study the long-term survival of warfarin users after cataract surgery.

Methods: This retrospective study involved 200 consecutive patients taking warfarin and 129 patients who had phacoemulsification at the same surgical sessions between January 2001 and December 2006. Their clinical characteristics and survival were retrieved from the hospital medical records and the electronic Patient Record of the Hospital Authority, Hong Kong. Standardized mortality ratios were computed and survival after cataract surgery was compared using the log rank test.

Results: Patients taking warfarin had shorter survival after cataract surgery (log rank test, $p < 0.001$); their standardized mortality ratios being 1.95 (95% confidence interval, 1.56 - 2.44). Survival in both groups appeared similar in the initial 2 years postoperatively, but a difference emerged thereafter. No difference in the causes of death was detected in the two groups ($p = 0.33$).

Conclusions: Patients taking warfarin had shorter survival after cataract surgery. This was likely an effect due to selection of healthier patients for surgery.

Key words: Cataract extraction; Models, statistical; Risk assessment; Survival rate; Warfarin

Introduction

Cataract surgery is regarded as a safe operation. In the immediate postoperative period, there were few systemic adverse events,[1,2] and survival appeared not to be affected.[3,4] Among the cataract patient population, those taking warfarin constitute a subgroup with cardiovascular or cerebrovascular comorbidities, such as atrial fibrillation, valvular heart diseases and venous thromboembolism.[5] Anticoagulation is indicated for thromboprophylaxis, but may confer a higher risk of intraoperative and postoperative hemorrhage. In the literature, most studies reporting complications surrounding cataract surgery in warfarin users highlighted the low rates of ocular bleeding complications. The majority of incidents were minor and not vision-threatening,[6-15] and systemic adverse events were very few.[13,16-18] However, the postoperative follow-up periods covered by these reports were short, spanning 3 months or less post-surgery. There is no long-term information on the mortality rate of warfarin users who had cataract surgery.

Methods

We conducted a retrospective study on the mortality of patients taking warfarin who had undergone cataract surgery during a 6-year period, between January 2001 and December 2006 in Hong Kong Eye Hospital, which is a public hospital providing secondary and tertiary ophthalmic care. The study was approved by the hospital clinical research ethics committee. Consecutive patients taking warfarin who underwent cataract surgery with phacoemulsification were identified via the hospital theatre registry. A comparison

group was drawn from consecutive patients who had phacoemulsification in the same operating sessions. If a patient had a second cataract surgery within this period, only the first surgery was included in the analysis. The hospital preoperative and operation records were reviewed to retrieve clinical characteristics. Information on medical comorbidities and survival status was obtained from the electronic Patient Record (e-PR), which is a central database of medical records for all public hospitals in Hong Kong. Data retrieved from the e-PR included systemic comorbidities, warfarin dosage and international normalized ratio (INR), other medications and medical events, and in particular any warfarin overdose resulting in admission to a general hospital for treatment. If the e-PR showed a date of death, the principal medical diagnosis of the last hospital admission was taken as the cause of death. The study was closed on March 31, 2010, with the potential follow-up period of 9 years.

Comparisons between the groups were conducted with a statistical package (SAS 9.1.3; SAS Inc. Cary NC, USA), using the Mann-Whitney *U* tests for demographic and clinical characteristics, and the log rank tests for survival. The log rank test was repeated after adjustment for gender and diabetic status. The expected number of deaths for each 5-year age band in a calendar year was calculated using the age-specific mortality rates in the local population for each age band and year.[19] At the time when data analysis was conducted, the age-specific mortality rates for the calendar year 2010 were not available. The rates for 2009 were adopted for the calculation of expected mortality for the period from January 1 to March 31, 2010. The expected number of deaths for each group was obtained from the sum of all combinations of age bands and calendar years. Finally, a standardized mortality ratio (SMR) was obtained by dividing the observed and expected numbers in each group.[20] A 95% confidence interval (CI) was calculated according to the method provided by Clayton and Hills.[21] For those who had died, the principal diagnoses at their last hospital admissions were compared using Fisher's exact test.

Results

Two hundred consecutive warfarin users who had cataract surgery during the 6-year period were recruited. Among this group, 38 patients also had cataract surgery on the other eye during this period, for whom only the first operation was included for analysis. The comparison group comprised 129 patients who had cataract surgery in the same operation sessions as the warfarin group. All the patients were Chinese. There were more females in both groups, in whom the gender ratios were comparable (p = 0.85) [**Table 1**]. Patients taking warfarin were older (median age, 75; range, 47 to 90 years) than controls (median age, 74; range 41 to 96 years) but the difference was not statistically significant (Mann-Whitney *U* test, p = 0.09). Cardiac arrhythmias were the most frequent (71%) indication for anticoagulation (**Table 2**). Chronic rheumatic heart disease with valvular incompetence or a prosthetic heart valve was also a common indication (29%). Deep vein thrombosis and pulmonary embolism were not common reasons (9%). The mean daily dose of warfarin was 2.4 (standard deviation [SD], 0.9) mg, and the mean INR was 2.1 (SD, 0.6). In all, 26 (13%) of the patients in the warfarin group were also taking an antiplatelet agent, whilst 44 (22%) of them had experienced warfarin overdosing in the past.

The preoperative regimen was identical for both groups, and consisted of topical mydriatics and an antibiotic (tropicamide 1.0%, phenylephrine 2.5%, and tobramycin). No systemic sedative was administered. In the majority of patients (91%), warfarin was continued during the perioperative period. Cataract surgery was conducted under topical anesthesia in 192 (96%) eyes. Warfarin users had poorer visual acuities before surgery (p = 0.03) [**Table 3**]. There were substantial visual improvements, such that the final visual acuities were similar in both groups (p = 0.31). In both groups, blood pressure, pulse rates and oxygen saturation were stable in the entire perioperative period. One warfarin user suffered from suprachoroidal hemorrhage during surgery and subsequently

Table 1. Demographic and clinical characteristics (n = 329).

Characteristic	No. of patients / Mean ± standard deviation		p Value
	Warfarin group (n = 200)	Comparison group (n = 129)	
Age at operation (years)	74 ± 7	72 ± 11	0.09*
Gender (M:F)	88:112	56:73	0.85†
Daily warfarin dose (mg)	2.4 ± 0.9	-	-
International normalized ratio	2.1 ± 0.6	-	-
Antiplatelet agent use	26 (13%)	25 (19%)	0.11†
Blood pressure (mm Hg)			
Systolic	147 ± 21	150 ± 21	0.33‡
Diastolic	74 ± 12	77 ± 12	0.03‡
Pulse (beats/min)	78 ± 16	79 ± 15	0.65‡
Visual acuity (logMAR)	1.5 ± 0.7	1.3 ± 0.6	0.03*

* Mann-Whitney *U* test.
† Chi-square test.
‡ Analysis of variance.

Table 2. Systemic morbidities as shown in the electronic Patient Record (n = 328).

Systemic morbidities	No. (%) of patients*		p Value
	Warfarin group (n = 200)	Comparison group (n = 128)	
Cardiac arrhythmias	141 (71)	1 (1)	< 0.0001†
Valvular heart diseases, including cardiac valve replacement	57 (29)	0	< 0.0001†
Cerebrovascular accidents	39 (20)	12 (9)	0.013‡
Ischemic heart diseases, including myocardial infarction	35 (18)	15 (12)	0.19‡
Deep vein thrombosis or pulmonary embolism	17 (9)	1 (1)	0.002†
Primary hypertension	33 (17)	66 (52)	< 0.0001‡
Diabetes mellitus	43 (22)	38 (30)	0.17‡

* The percentages do not total 100% because a patient could have multiple diagnoses.
† Fisher exact test.
‡ Chi-square test.

Table 3. Visual improvement after surgery (n = 315).

Visual acuity	Mean ± standard deviation		p Value*
	Warfarin group (n = 198)	Comparison group (n = 117)	
Visual acuity (logMAR)			
Preoperative	1.48 ± 0.65	1.31 ± 0.63	0.03
Postoperative	0.32 ± 0.24	0.36 ± 0.30	0.31
Visual acuity improvement, lines	11.5 ± 7.0	8.9 ± 6.0	0.003

* Mann-Whitney *U* test.

Table 4. Principal diagnoses for the last hospital admissions (n = 105). Diseases of the circulatory system include principal diagnoses coded under I00 to I99 of the International Classification of Diseases and Related Health Problems, 10th Revision. The proportions of deaths from diseases of the circulatory system and other causes in the local population for the calendar year 2010 are provided for comparison.*

Leading causes of death	No. (%) of patients	
	Warfarin group (n = 77)	Comparison group (n = 28)
Diseases of the circulatory system	24 (31)	7 (25)
Others	37 (48)	18 (64)
Unknown	16 (21)	3 (11)

* Chi-square test, p = 0.33.

lost vision in that eye. The indication for anticoagulation was paroxysmal atrial fibrillation. Her daily warfarin dosage and preoperative INR were 1.5 mg and 1.5, respectively.

Within the first month after surgery, one patient in the control group died of metastatic carcinoma of the liver, and another was hospitalized for hypoglycemia. One patient in the warfarin group was hospitalized for an exacerbation of congestive heart failure. By the end of the study, 77 (39%) of patients in the warfarin group had succumbed; in 24 (31%) of them cardiovascular or cerebrovascular diseases were the principal diagnoses during their last hospital admissions (**Table 4**). In all, 16 patients were not admitted to a public hospital at the time of death and no principal diagnosis was recorded in the e-PR. There was no statistical difference between the groups with respect to the principal diagnoses at their last hospital admissions (Chi-square test, p = 0.33).

Warfarin users had a higher SMR (2.0; 95% CI, 1.6 to 2.4) than the controls (SMR = 1.1; 95% CI, 0.8 to 1.6). The warfarin group had decreased survival than in the comparison group following cataract surgery (log rank test, p = 0.001). This difference persisted after adjustment for gender or diabetic status. From the Kaplan-Meier survival plot, survival after surgery appeared similar in both groups in the first 2 years, but was worse in the warfarin group thereafter. *Post hoc* analysis of survival data indicated that a statistical difference between the groups could be detected if survival longer than 3 years was set as censored. The median survival after cataract surgery for warfarin users was 8 years. Survival for those who had a history of warfarin overdose did not differ from those who had not experienced such episodes (log rank test, p = 0.49).

Discussion

Recent reports on the systemic complications and mortality surrounding modern cataract surgery concluded that it was associated with low mortality. Greenberg et al[4] studied the mortality of 45,082 cataract patients in the Veterans Health Administration, and found that the 90-day postoperative mortality was 0.3%. Blundell et al[3] studied the survival in a

cohort of 933 patients who had cataract surgery in 2000-01 with a follow-up period of 6 years. They reported increased survival after cataract surgery compared to reference regional and national populations. Their findings contrasted with early reports that cataract surgery was associated with increased mortality.[22,23]

Adverse events surrounding cataract surgery remains a concern because the majority of patients are elderly, some of whom have multiple comorbidities. Cardiovascular diseases were more prevalent in patients with cataract.[24] A Cochrane review on medical adverse events associated with cataract surgery showed that most adverse events were cardiovascular and happened during the intraoperative period.[25] Patients taking warfarin constituted a particular subgroup with more severe cardiovascular or cerebrovascular comorbidities.[26] A higher incidence of adverse events in this group in the perioperative period therefore appeared likely. Previous studies reported cataract surgery in warfarin users was safe. In the majority of studies, however, the number of warfarin users was small, or the reports covered events that occurred within 3 months or less postoperatively.[6-14] Katz et al[17] studied perioperative adverse events of anticoagulant users that ensued within 7 days of cataract surgery. Among 734 warfarin users, there were 9 adverse events — 5 myocardial infarctions or episodes of ischemia, 3 cerebrovascular accidents and 1 deep vein thrombosis. In our study, there was only one adverse systemic event in the warfarin group in the first postoperative month. This finding appeared to agree with other studies that adverse events in the early postoperative period were uncommon.

To study the survival after cataract surgery, the SMR for warfarin users who had phacoemulsification was constructed. This allowed comparison of observed mortality against a reference population, while controlling for the differences in age distribution between the cohort of interest and the reference population.[20] Our results suggested that warfarin users had shortened survival after cataract surgery in comparison to the local population. To elucidate whether cataract surgery in local hospital settings was associated with an increased mortality, a comparison group was drawn from consecutive cataract patients who had surgery in the same operative sessions as the warfarin users. Both groups thus received identical perioperative care, though the comparison group (controls) was not an exact age-match for the warfarin group. The SMR for the latter group showed that cataract surgery in the hospital setting was not associated with an increased mortality. This was consistent with Blundell et al's finding.[3]

With long follow-up, we were able to detect a difference in survival that emerged only after a long postoperative period had lapsed. The Kaplan-Meier plot showed survival in both groups was very similar in the first 24 months after surgery (**Figure**). After this initial period, the curves diverged; the warfarin group showed decreased survival. We postulate this phenomenon could be the result of a selection bias. Healthier warfarin patients had cataract surgery, whereas those in poor

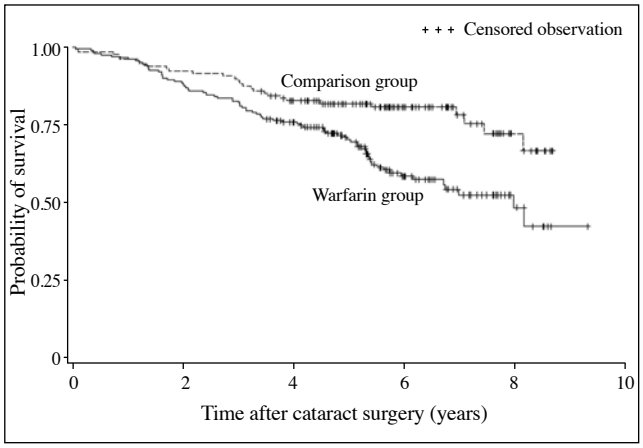

Figure. Kaplan-Meier plot of survival after cataract surgery. The median survival in the warfarin group was 8.0 years.

health did not. Diseases of circulatory system were more prevalent in patients taking warfarin. Hypertension and cardiac conditions were frequent reasons for cancellation of cataract surgery.[25] If those who were in a worse physical state proceeded to surgery, the mortality figures would have been higher in the early postoperative period. In the two studies conducted by Greenberg et al[4] and Blundell et al,[3] the mortality rates for patients aged 80 years and older were lower than those in reference populations. They postulated healthier patients were selected for surgery that could bias towards lower mortality in this age-group. In a cohort study, McGwin et al[27] reported that patients with cataract who did not elect to have cataract surgery had a borderline higher mortality than those who had such surgery. At the time of the study, patients had to wait up to 37 months for elective cataract surgery.[28] The long waiting time could have selected out those who were in poor health. A prospective cohort study recruiting warfarin users declining cataract surgery for health or other reasons may provide more information on the survival of warfarin users with or without cataract surgery.

Shortcomings of this study included the small number of warfarin users among cataract patients and the low mortality rate in the early postoperative period. A longer study period was necessary to recruit patients and for following patients to obtain adequate statistical power. By including all consecutive warfarin users who had cataract surgery within the 6-year period, the potential bias of missed patients in a retrospective study was avoided. Our patients' ages ranged from 47 to 90 years. Since survival was expected to decrease with advancing age, analysis of survival for each age-band could be informative. However, there were only a few deaths in each age-band during each calendar year; construction of SMR rates for individual age-bands lacked precision and was therefore omitted. We also expected a higher proportion of warfarin users to be diagnosed with circulatory system diseases at their last admissions, because warfarin was indicated for the control of such comorbidities, but could not detect a statistically significant difference

between the groups. The number of deaths was small and a significant portion of warfarin users were not admitted to a public hospital at the time of death. Causes of their deaths were therefore not recorded in the e-PR. Diseases of the circulatory system are the major cause of death in elderly cataract patients,[19,23] whereas patients in the control group were likely to succumb to diseases of the circulatory system. This could have conferred an insignificant result in the comparison of the causes of death.

Conclusion

This study showed that after cataract surgery, survival in warfarin users was shorter than in other patients. Survival was similar between the groups in the initial 24 postoperative months; a difference emerged thereafter. The mortality rate in the immediate postoperative period was low. Cataract surgery was unlikely to have contributed to shortened survival. Among patients taking warfarin, relatively healthier patients may have been selected to undergo cataract surgery, but their comorbidities could have conferred overall shortened survival. Patients taking warfarin may be reassured of the visual benefits of cataract surgery. They should not defer surgery unless their systemic status precludes such therapy.

Declaration

No author has a financial or proprietary interest in any material or methods mentioned.

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