The Association of Cataract and Cataract Surgery With the Long-term Incidence of Age-Related Maculopathy

The Beaver Dam Eye Study

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Objective: To examine the association between cataract and cataract surgery and the 10-year incidence of age-related maculopathy (ARM).

Methods: A population-based cohort study of persons aged 43 to 86 years at baseline, living in Beaver Dam, Wis, of whom 3684 participated in a 5-year and 2764 in a 10-year follow-up. We used standardized protocols for physical examination, blood collection, health history, slitlamp and retroillumination photography of the lenses to determine the presence of cataract, and stereoscopic color fundus photography to determine the presence of ARM. We used the Kaplan-Meier (product-limit) survival approach and discrete linear logistic regression in analyses.

Main Outcome Measures: The risk ratios (RRs) of persons with cataract or cataract surgery at baseline.

Results: While controlling for age, sex, systolic blood pressure, history of heavy drinking and smoking, and vitamin use, cataract at baseline was associated with incidence of early ARM (RR, 1.30; 95% confidence interval [CI], 1.04-1.63), soft indistinct drusen (RR, 1.38; 95% CI, 1.08-1.75), increased retinal pigment (RR, 1.38; 95% CI, 1.07-1.79), and progression of ARM (RR, 1.37; 95% CI, 1.06-1.77). We found no association with the incidence of late ARM. In contrast, cataract surgery before baseline was associated with incidence of late ARM (RR, 3.81; 95% CI, 1.89-7.69), increased retinal pigment (RR, 1.89; 95% CI, 1.18-3.03), retinal pigment epithelial depigmentation (RR, 1.95; 95% CI, 1.17-3.25), pure geographic atrophy (RR, 3.18; 95% CI, 1.33-7.60), exudative macular degeneration (RR, 4.31; 95% CI, 1.71-10.9), and progression of ARM (RR, 1.97; 95% CI, 1.29-3.02), but not with the incidence of early ARM.

Conclusions: These findings indicate an association of cataract with subsequent risk for early ARM. Cataract surgery increased the risk for late ARM.

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AGE-RELATED maculopathy (ARM) is an important cause of loss of vision in older Americans.[1-6] Its pathogenesis is poorly understood.[6,7] Cataract and cataract surgery have been reported to be related to the development of ARM.[8-14] However, data from epidemiological studies regarding these associations have been inconsistent. In the Beaver Dam Eye Study, a positive cross-sectional association was found between nuclear sclerosis or cataract surgery and early ARM. The association with nuclear sclerosis was consistent with findings in the Chesapeake Bay Watermen Study,[13] but not with findings in the Framingham Eye Study[8,9] or the Blue Mountains Eye Study.[14] Certain types of cataract and ARM might occur together more frequently because of commonly shared genetic and environmental causes.

The association between cataract surgery and ARM is less clear. One hypothesis is that cataract surgery may simply be a surrogate for the severity of cataract. However, cataract removal also may result in increased risk because a barrier (cataract) to some exposure (eg, UV radiation) has been removed or because of the trauma to the eye incurred by surgery.

At the time of the 5-year follow-up in the Beaver Dam Eye Study, our group reported that, after controlling for age, eyes that had undergone cataract surgery before baseline were more likely to have progression of ARM and that signs of late ARM were more likely to develop than in eyes that were phakic at baseline.[15] No association was found between nuclear, cortical, or posterior subcapsular cataract (PSC) and the 5-year incidence or progression of ARM. The purpose of this report was to examine the associations of

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cataract and cataract surgery with the 10-year incidence of ARM in the population-based Beaver Dam Eye Study.

METHODS

POPULATION

Methods used to identify and describe the population have appeared in previous reports.[16-24] In brief, a private census of the population of Beaver Dam, Wis, was performed from September 15, 1987, through May 4, 1988, to identify all residents in the city or township of Beaver Dam who were aged 43 to 86 years. Of the 5924 eligible individuals, 4926 participated in the baseline examination between March 1, 1988, and September 14, 1990.[17] More than 99% of the population was white. Of these, 3684 persons (81.1% of survivors) participated in the 5-year follow-up examination between March 1, 1993, and June 30, 1995, and 2764 persons (82.9%) participated in the 10-year follow-up examination between March 1, 1998, and June 30, 2000. Comparisons between participants and nonparticipants at the time of the baseline and 5- and 10-year follow-up examinations have appeared elsewhere.[20-21]

In general, persons who were alive but did not participate at the 10-year examination were older at baseline than those who participated, and after adjusting for age, were more likely to have fewer years of education, lower income, poorer visual acuity, a poorer cardiovascular risk profile, a history of never drinking alcohol, and have more pack-years smoked than persons who participated. After adjusting for age and sex, participants with ARM at baseline were as likely to participate as those in whom ARM was absent (data not shown). After controlling for age, we found no differences in participation rates at follow-up examinations for men and women with a history of cataract and early ARM compared with those with a history of cataract without early ARM (data not shown).

PROCEDURES

Similar procedures have been used at the baseline and follow-up examinations and are described in detail elsewhere.[18,19] Informed consent was obtained from each participant. The examinations at baseline and follow-up included measurement of blood pressure (using a random-zero sphygmomanometer and following the Hypertension Detection and Follow-up Program protocol).[22] A standardized questionnaire was administered that included questions on vitamin use.

Slitlamp and retroillumination photographs of the lenses were graded using standardized systems reported previously.[23-25] For this report, nuclear cataract was defined as present if the photograph of the lens was graded as more severe than standard photograph 3. For grading the severity of cortical and posterior subcapsular opacities, a grid dividing the lens into 8 sectors and a central circle was used. Cortical opacity was considered present if, on grading the retroillumination photograph, 5% or more of the lens surface area was affected. Posterior subcapsular opacity was considered present if 5% or more of any of the 8 sectors or of the central circle of the surface area of the lens was involved. Any cataract was defined as the presence of nuclear or cortical cataract or PSC.

Stereoscopic 30° color fundus photographs centered on the disc (Diabetic Retinopathy Study standard field 1) and the macula (Diabetic Retinopathy Study standard field 2), and a nonstereoscopic color fundus photograph temporal to but including the fovea of each eye were obtained. For purposes of this report, the 2663 people (3570 at the first 2 examinations) with at least 1 eye free of confounding lesions (eg, retinal detachment or non–age-related chorioretinal scarring) at all 3 examinations are included in the analyses.

The Wisconsin Age-Related Maculopathy Grading System was used to assess the presence and severity of lesions associated with ARM.[26] Grading procedures, lesion descriptions, detailed definitions of the presence and severity of specific lesions, and 10-year incidence of specific lesions have appeared elsewhere.[26-30] Incidence implies the appearance of a lesion at follow-up when it was absent in all of the subfields that could be graded at baseline and follow-up examinations. Progression implies the presence of a lesion at baseline with a worsening at follow-up.[29]

Incidence was determined for the maximum size and type of each specific drusen class, increased drusen area, increased retinal pigment, retinal pigment epithelial (RPE) depigmentation, pigmentary abnormalities (defined as RPE depigmentation or increased retinal pigment), signs of exudative macular degeneration, and pure geographic atrophy. For example, if none of the subfields had soft indistinct drusen at baseline, and if soft indistinct drusen were present in one or more subfields at the 5- or 10-year follow-up, the eye would be considered to have incident soft indistinct drusen.

Early ARM was defined by the presence of soft indistinct drusen or the presence of any type of drusen associated with RPE depigmentation or increased retinal pigment. Late ARM was defined by the appearance of exudative macular degeneration or pure geographic atrophy.

For each eye, a 6-level severity scale for ARM was defined. Level 10 indicates no drusen of any type, or hard or small ($<$125 μm in diameter) soft drusen only, regardless of the area of involvement, and no pigmentary abnormality (increased retinal pigment or RPE depigmentation) present. Level 20 indicates hard drusen or small ($<$125 μm in diameter) soft drusen, regardless of the area of involvement, with increased retinal pigment but no RPE depigmentation present, or soft drusen ($\geq$125 μm in diameter) with a drusen area of less than 196 350 μm^2 (equivalent to a circle with a diameter of 500 μm) and no pigmentary abnormalities present. Level 30 indicates soft drusen ($\geq$125 μm in diameter) with a drusen area of less than 196 350 μm^2 and RPE depigmentation present or soft drusen ($\geq$125 μm in diameter) with a drusen area of at least 196 350 μm^2 with or without increased retinal pigment but no RPE depigmentation present. Level 40 indicates soft drusen ($\geq$125 μm in diameter) with a drusen area of at least 196 350 μm^2 and RPE depigmentation present with or without increased retinal pigment. Level 50 indicates pure geographic atrophy in the absence of exudative macular degeneration. Level 60 indicates exudative macular degeneration with or without geographic atrophy present.

Progression for a participant was defined as an increase in the maculopathy severity from baseline to the 5- or 10-year follow-up examination in either eye by 2 steps or more from levels 10 through 30 and 1 step or more from level 40 or 50.

Age was defined as the age at the time of the baseline examination. The mean systolic blood pressure was the average of the 2 systolic blood pressure determinations. Cigarette smoking status at the time of the baseline examination was determined. Subjects were classified as nonsmokers if they had smoked fewer than 100 cigarettes in their lifetime; as exsmokers if they had smoked more than this number of cigarettes in their lifetime but had stopped before the baseline examination; and as current smokers if they had not stopped smoking. Persons consuming 4 or more servings of alcoholic beverages daily were defined as current heavy drinkers; 4 or more servings daily in the past but not in the previous year, as former heavy drinkers; and never consuming 4 or more servings daily on a regular basis, as nonheavy drinkers. Persons who took at least 1 vitamin per week within the month before the baseline examination were classified as current vitamin users; at least once a week in the past but not within the last month, as past

Table 1. Prevalence of Cataract and Cataract Surgery by Eye and Age Group at Baseline in the Beaver Dam Eye Study*

Baseline Characteristic, Eye	Age Group, y							
	43-54		55-64		65-74		≥75	
	No. at Risk	Prevalence, No. (%)	No. at Risk	Prevalence, No. (%)	No. at Risk	Prevalence, No. (%)	No. at Risk	Prevalence, No. (%)
Cataract type								
Nuclear								
Right	1251	4 (0.3)	1017	40 (3.9)	884	171 (19.3)	316	140 (44.3)
Left	1248	3 (0.2)	1022	41 (4.0)	890	171 (19.2)	315	141 (44.8)
Cortical								
Right	1252	9 (0.7)	1023	62 (6.1)	882	157 (17.8)	317	100 (31.5)
Left	1252	11 (0.9)	1027	67 (6.5)	890	153 (17.2)	320	121 (37.8)
Posterior subcapsular								
Right	1256	13 (1.0)	1025	24 (2.3)	893	41 (4.6)	321	21 (6.5)
Left	1256	14 (1.1)	1032	22 (2.1)	901	31 (3.4)	321	21 (6.5)
Any cataract								
Right	1248	22 (1.8)	1012	111 (11.0)	878	313 (35.6)	318	202 (63.5)
Left	1244	27 (2.2)	1018	118 (11.6)	885	309 (34.9)	321	217 (67.6)
Prior cataract surgery								
Right	1272	8 (0.6)	1064	22 (2.1)	951	38 (4.0)	390	54 (13.8)
Left	1275	9 (0.7)	1062	19 (1.8)	953	32 (3.4)	390	51 (13.1)
Aphakia								
Right	1272	3 (0.2)	1064	5 (0.5)	951	11 (1.2)	390	12 (3.1)
Left	1275	3 (0.2)	1062	4 (0.4)	953	7 (0.7)	390	13 (3.3)
Intraocular lens								
Right	1272	5 (0.4)	1064	17 (1.6)	951	27 (2.8)	390	42 (10.8)
Left	1275	6 (0.5)	1062	15 (1.4)	953	25 (2.6)	390	38 (9.7)

*For all comparisons, $P<.001$, test for trend of increasing age.

vitamin users; and less than regular use at least once a week, as nonusers.

STATISTICAL METHODS

For these analyses, we examined the relationships between cataract and cataract surgery at baseline and the incidence or progression of each of the specific maculopathy lesions; the incidence of 2 end points of disease severity, early and late ARM; and the progression of ARM. For those with cataract surgery before baseline, we excluded nuclear and cortical cataract and PSC at baseline as risk factors. For those with cataract surgery between baseline and the first follow-up, nuclear and cortical cataract and PSC were included in the analyses as risk factors. We used SAS software to analyze the data.[31] The analytical approaches used allowed those persons who were right censored (not seen after the 5-year examination because of death or nonparticipation) to contribute information to the estimates. Cumulative events were estimated using the Kaplan-Meier (product-limit) survival approach.[32] Multivariate risk ratios (RRs) and 95% confidence intervals (CIs) were calculated from the discrete linear logistic model.[33] Age- and sex-adjusted models were constructed by outcome for each of the potential risk factors. Final models were then built by outcome for each risk factor by further adjusting the models for vitamin use, history of smoking and heavy drinking, and systolic blood pressure. In these models, smoking status, heavy drinking status, and vitamin use were each considered using the 2 indicator variables. We performed tests of trend that treated categorical risk factors as continuous variables in the discrete linear logistic model and computed the χ^2 statistic for the variable estimate. A generalized estimating equations model was used to assess multivariate relationships with data from both eyes.[34] This method adjusts for the correlation between both eyes.

RESULTS

The prevalences of nuclear and cortical cataract, PSC, aphakia, and pseudophakia increased with age at baseline (**Table 1**). After controlling for age, women had higher prevalences of nuclear cataract (right eye, 12.5% vs 8.5% [$P<.001$]; left eye, 13.1% vs 7.6% [$P<.001$]) and cortical cataract (right eye, 11.2% vs 8.0% [$P=.002$]; left eye, 12.0% vs 8.5% [$P=.001$]) compared with men. After controlling for age, women had a similar prevalence of cataract surgery (right eye, 3.7% vs 2.9% [$P=.14$]; left eye, 3.1% vs 2.9% [$P=.73$]) and PSC (right eye, 3.1% vs 2.5% [$P=.38$]; left eye, 2.6% vs 2.6% [$P=.81$]) as men.

The 10-year incidence and progression rates of ARM increased with age (**Table 2**). Late ARM developed in 41 right and 48 left eyes during the 10 years of the study. Geographic atrophy developed in 17 right and 23 left eyes. Exudative ARM developed in 24 right and 27 left eyes. Two left eyes that developed geographic atrophy at 5 years advanced to exudative ARM at 10 years, and 3 left eyes with geographic atrophy at baseline developed exudative ARM at 5 years.

Table 3 shows the incidence of signs of early and late ARM by the presence of cataract and cataract surgery, based on data on the right eye (results of the left eye are similar; not shown).

In multivariate analyses controlling for age, sex, systolic blood pressure, smoking and heavy drinking status, and vitamin use at baseline, the presence of cataract at baseline was associated with the incidence of early ARM,

Table 2. Ten-Year Cumulative Incidence and Progression of ARM by Eye and Age Group in the Beaver Dam Eye Study*

Incidence and Progression, Eye	Age Group, y: 43-54 No. at Risk	43-54 No. (%)†	55-64 No. at Risk	55-64 No. (%)†	65-74 No. at Risk	65-74 No. (%)†	≥75 No. at Risk	≥75 No. (%)†
Incidence								
Early ARM								
Right	1165	30 (2.7)	897	54 (6.7)	695	111 (18.9)	189	44 (28.9)
Left	1168	37 (3.4)	898	81 (10.1)	692	97 (16.7)	193	48 (32.2)
Drusen size ≥125 µm								
Right	1219	11 (1.0)	991	24 (2.7)	826	52 (7.7)	262	28 (16.2)
Left	1237	8 (0.7)	996	39 (4.6)	387	64 (9.8)	287	34 (15.9)
Soft indistinct drusen								
Right	1199	25 (2.2)	942	53 (6.2)	745	109 (17.3)	216	38 (22.2)
Left	1207	34 (3.0)	955	63 (7.4)	739	101 (16.5)	226	41 (23.2)
Increased pigmentation								
Right	1188	13 (1.2)	954	38 (4.6)	790	76 (11.4)	240	42 (23.2)
Left	1195	18 (1.6)	944	60 (7.3)	790	72 (11.0)	250	50 (25.8)
RPE depigmentation								
Right	1207	9 (0.8)	980	35 (4.1)	824	50 (7.5)	259	35 (19.5)
Left	1221	11 (1.0)	990	37 (4.4)	837	52 (7.9)	268	34 (18.0)
Pigmentary abnormalities								
Right	1187	15 (1.3)	949	38 (4.6)	788	75 (11.3)	242	42 (23.1)
Left	1195	18 (1.6)	943	59 (7.1)	790	74 (11.4)	247	47 (23.8)
Geographic atrophy								
Right	1234	0	1013	3 (0.3)	876	7 (1.1)	299	7 (3.1)
Left	1244	0	1017	1 (0.1)	891	12 (1.9)	307	10 (4.0)
Exudative ARM								
Right	1215	0	996	4 (0.5)	852	13 (2.0)	283	7 (3.8)
Left	1235	1 (0.1)	1002	5 (0.6)	859	11 (1.7)	277	13 (6.6)
Late ARM								
Right	1225	0	999	7 (0.8)	852	20 (3.2)	281	14 (6.6)
Left	1239	1 (0.1)	1006	5 (0.6)	870	22 (3.4)	291	20 (9.7)
Progression of ARM								
Right	1224	15 (1.4)	1002	45 (5.3)	858	91 (14.0)	287	53 (25.9)
Left	1237	20 (1.8)	1007	48 (5.5)	867	94 (13.9)	299	50 (24.3)

*ARM indicates age-related maculopathy; RPE, retinal pigment epithelium. For all comparisons, test for trend for increasing age, $P<.001$.
†Percentages for cumulative incidence and progression derived from Kaplan-Meier product-limit method (see "Statistical Methods" subsection of the "Methods" section).

drusen size of greater than or equal to 125 µm in diameter, soft indistinct drusen, increased retinal pigment, and progression of ARM, but not with incidence of late ARM (**Table 4**). When specific cataract types were analyzed, eyes with nuclear cataract present at baseline had a higher 10-year incidence of early ARM, soft indistinct drusen, increased retinal pigment, and increased RPE depigmentation. We found no association of nuclear cataract at baseline with the incidence of late ARM or the progression of ARM. Cortical cataract at baseline was associated with the incidence of soft indistinct drusen and progression of ARM. We found no significant associations of PSC at baseline with the incidence or the progression of ARM.

In contrast, cataract surgery before baseline was associated with a higher 10-year incidence of increased retinal pigment, RPE depigmentation, late ARM, pure geographic atrophy, exudative ARM, and progression of ARM (Table 4). These associations did not change when analyses were restricted to fundus photographs of fair to good quality (data not shown). Except for incident exudative ARM, the risk ratios for development of ARM lesions were higher in eyes that were aphakic at baseline compared with eyes that had intraocular lenses at baseline (Table 4). We found no association of time between cataract surgery before baseline and the incidence of ARM (data not shown).

After controlling for age and sex, we found no associations between eyes in which cataract developed between baseline and the 5-year follow-up examination and the incidence of early or late ARM compared with eyes without cataract (data not shown). When we controlled for age and sex, large drusen were more likely to develop at the 10-year follow-up in eyes that underwent cataract surgery between the baseline and 5-year follow-up examinations (RR, 2.93; 95% CI, 1.65-5.23 [$P<.01$]) compared with eyes that did not undergo cataract surgery. We found no statistically significant difference in the incidence of signs of late ARM (RR, 1.62; 95% CI, 0.60-4.40 [$P=.34$]) in eyes that underwent cataract surgery between the baseline and 5-year follow-up examinations compared with eyes that did not undergo cataract surgery.

One possible reason for the association between cataract surgery and the incidence of late ARM is that persons who have cataract and early ARM at baseline are more likely to have subsequent cataract surgery than persons

Table 3. Ten-Year Incidence of ARM by Cataract Type and Cataract Surgery at Baseline, Right Eye*

	No. at Risk (Incidence, %)									
	Early ARM	Size ≥125 µm	Soft Indistinct Drusen	Increased Pigmentation	RPE Depigmentation	Pigmentary Abnormalities	Late ARM	Pure Geographic Atrophy	Exudative ARM	Progression of ARM
Nuclear cataract										
Yes	204 (24.9)	256 (8.7)	223 (22.2)	255 (17.6)	263 (14.4)	257 (17.9)	271 (3.9)	295 (0.9)	276 (2.6)	277 (18.9)
No	2653 (7.6)	2923 (3.4)	2776 (6.8)	2803 (4.8)	2886 (3.5)	2795 (4.7)	2962 (1.1)	2998 (0.5)	2945 (0.6)	2965 (6.0)
Cortical cataract										
Yes	206 (19.2)	253 (8.5)	220 (16.3)	253 (13.4)	259 (10.5)	252 (13.0)	264 (2.8)	288 (2.0)	264 (1.3)	271 (15.5)
No	2651 (7.9)	2929 (3.4)	2781 (7.1)	2807 (4.9)	2892 (3.6)	2802 (5.0)	2973 (1.2)	3007 (0.4)	2957 (0.7)	2974 (6.1)
PSC										
Yes	60 (14.4)	71 (5.1)	65 (14.9)	73 (11.4)	75 (5.3)	72 (10.2)	78 (4.7)	83 (0.0)	76 (4.7)	78 (12.9)
No	2806 (8.5)	3122 (3.8)	2945 (7.5)	2997 (5.5)	3087 (4.2)	2992 (5.6)	3169 (1.2)	3223 (0.5)	3158 (0.7)	3178 (6.7)
Any cataract										
Yes	406 (19.7)	495 (8.5)	438 (17.8)	489 (14.2)	505 (11.1)	488 (13.8)	522 (3.7)	562 (1.5)	527 (2.4)	530 (15.8)
No	2438 (6.9)	2671 (3.1)	2548 (6.1)	2556 (4.1)	2631 (3.1)	2551 (4.2)	2698 (0.9)	2718 (0.4)	2681 (0.5)	2699 (5.4)
Cataract surgery										
Yes	64 (21.1)	88 (11.9)	76 (19.8)	82 (19.7)	89 (17.1)	82 (20.8)	91 (6.4)	94 (3.0)	96 (3.1)	96 (19.9)
No	2882 (8.7)	3210 (3.8)	3026 (7.7)	3090 (5.7)	3181 (4.2)	3084 (5.7)	3266 (1.3)	3328 (0.5)	3250 (0.8)	3275 (6.8)
Aphakic										
Yes	13 (15.4)	17 (20.6)	17 (17.6)	21 (33.3)	21 (33.3)	21 (37.0)	18 (9.1)	21 (7.7)	20 (0.0)	22 (13.6)
No	2895 (8.9)	3281 (3.9)	3085 (7.9)	3151 (5.8)	3249 (4.4)	3145 (5.8)	3339 (1.4)	3401 (0.5)	3326 (0.8)	3349 (7.1)
Intraocular lens										
Yes	51 (22.4)	71 (9.6)	59 (20.7)	61 (15.5)	68 (12.5)	61 (15.5)	73 (5.5)	73 (1.4)	76 (3.9)	74 (21.7)
No	2895 (8.7)	3227 (3.9)	3043 (7.8)	3111 (5.8)	3202 (4.4)	3105 (5.8)	3284 (1.3)	3349 (0.6)	3270 (0.8)	3297 (6.9)

*ARM indicates age-related maculopathy; PSC, posterior subcapsular cataract.

who have cataracts without early ARM. However, when we controlled for age and sex, we found that persons with cataract at baseline in whom early ARM developed at the 5-year follow-up had a similar incidence of cataract surgery by the 10-year follow-up as persons with cataract in whom incident ARM did not develop at the 5-year follow-up (data not shown).

COMMENT

Data from this population-based study show an association of baseline cataract and cataract surgery before baseline with the 10-year incidence of signs of ARM. In addition, we found differences in the pattern of association for cataract compared with cataract surgery. Cataract at baseline, in particular nuclear cataract, was associated with an increased but modest risk for early ARM. In contrast, cataract surgery before baseline was mainly associated with increased risk for signs of late ARM.

In fact, signs of geographic atrophy were approximately 4 times as likely to develop in eyes that had undergone cataract surgery before the baseline examination, and signs of exudative macular degeneration were 3 times as likely to develop by the time of the 10-year examination. At the 5-year follow-up in Beaver Dam, we reported that eyes that had undergone cataract surgery before baseline were more likely to have progression of ARM and development of signs of late ARM than phakic eyes.[15] The 10-year incidence data from Beaver Dam provide a longer-term follow-up with more incident cases of late ARM.

The association between cataract surgery and progression of ARM and the risk for late ARM has broad clinical implications. Most reports regarding this association have come from clinical case series, case-control studies, and cross-sectional studies, and the results have been inconsistent.[8-11-14,35-41] In the National Health and Nutrition Examination Survey, a significant association was found between aphakia and age-related macular degeneration (odds ratio, 2.00; 95% CI, 1.44-2.78).[10] In a clinic-based study, Pollack et al[36,38] reported a higher risk for progression of eyes with moderate ARM after cataract surgery. In that study, exudative macular degeneration developed during the first postoperative year in 19% of the eyes that underwent surgery compared with 4% of the fellow eyes in patients older than 65 years. These findings are also consistent with a higher frequency of exudative macular degeneration found by results of histopathologic study of eyes that underwent implantation of an intraocular lens compared with phakic eyes.[12] However, no association was found between cataract surgery and ARM prevalence in the Rotterdam Study.[37]

Eyes that had undergone cataract surgery before baseline in Beaver Dam might have been ones in which early ARM was progressing and causing additional visual symptoms to warrant cataract surgery. However, we did not find that cataract, in the presence of signs of early ARM, was more likely to lead to subsequent cataract surgery

Table 4. Relationship of Cataract and Cataract Surgery to the 10-Year Incidence and Progression of ARM by Means of Generalized Estimating Equation Models in the Beaver Dam Eye Study*

	Nuclear Cataract	Cortical Cataract	Posterior Subcapsular Cataract	Any Cataract	Cataract Surgery	Aphakic Cataract Surgery	Intraocular Lens Cataract Surgery
Early ARM	1.46 (1.11-1.92) $P = .01$	1.24 (0.93-1.64) $P = .14$	1.03 (0.61-1.76) $P = .90$	1.30 (1.04-1.63) $P = .02$	1.36 (0.82-2.23) $P = .23$	1.85 (0.56-6.08) $P = .31$	1.24 (0.73-2.11) $P = .43$
Drusen size ≥125 µm	1.40 (0.98-2.00) $P = .06$	1.22 (0.83-1.80) $P = .31$	1.38 (0.72-2.65) $P = .34$	1.33 (0.97-1.83) $P = .07$	1.24 (0.70-2.21) $P = .47$	3.08 (1.22-7.76) $P = .02$	0.86 (0.43-1.75) $P = .68$
Soft indistinct drusen	1.37 (1.03-1.82) $P = .03$	1.39 (1.04-1.86) $P = .03$	1.24 (0.72-2.11) $P = .44$	1.38 (1.08-1.75) $P = .01$	1.31 (0.81-2.12) $P = .27$	2.34 (0.82-6.64) $P = .11$	1.07 (0.64-1.77) $P = .81$
Increased retinal pigment	1.54 (1.13-2.10) $P = .01$	1.13 (0.82-1.55) $P = .46$	0.87 (0.44-1.74) $P = .69$	1.38 (1.07-1.79) $P = .01$	1.89 (1.18-3.03) $P = .01$	3.39 (1.68-6.81) $P < .01$	1.36 (0.74-2.49) $P = .32$
RPE depigmentation	1.62 (1.12-2.34) $P = .01$	1.17 (0.80-1.71) $P = .42$	0.60 (0.25-1.44) $P = .25$	1.31 (0.96-1.81) $P = .09$	1.95 (1.17-3.25) $P = .01$	3.61 (1.70-7.68) $P < .01$	1.37 (0.71-2.67) $P = .35$
Pigmentary abnormalities	1.58 (1.16-2.15) $P < .01$	1.06 (0.77-1.47) $P = .71$	0.79 (0.38-1.64) $P = .53$	1.30 (1.00-1.69) $P = .05$	1.96 (1.23-3.13) $P < .01$	3.75 (1.86-7.55) $P < .01$	1.37 (0.75-2.51) $P = .30$
Late ARM	1.30 (0.69-2.44) $P = .42$	1.30 (0.72-2.35) $P = .39$	1.86 (0.73-4.71) $P = .19$	1.42 (0.83-2.43) $P = .21$	3.81 (1.89-7.69) $P < .01$	3.99 (1.53-10.4) $P < .01$	3.25 (1.38-7.69) $P = .01$
Pure geographic atrophy†	0.84 (0.31-2.23) $P = .72$	1.73 (0.76-3.92) $P = .19$	0.84 (0.13-5.40) $P = .85$	1.27 (0.59-2.76) $P = .54$	3.18 (1.33-7.60) $P = .01$	7.31 (2.24-23.9) $P < .01$	1.60 (0.48-5.38) $P = .45$
Exudative ARM	1.66 (0.72-3.83) $P = .24$	1.36 (0.62-3.00) $P = .44$	2.58 (0.86-7.68) $P = .09$	1.74 (0.86-3.51) $P = .12$	4.31 (1.71-10.9) $P < .01$	2.35 (0.57-9.69) $P = .24$	4.47 (1.62-12.4) $P < .01$
Progression of ARM	1.18 (0.87-1.60) $P = .28$	1.54 (1.14-2.08) $P < .01$	1.49 (0.88-2.53) $P = .14$	1.37 (1.06-1.77) $P = .02$	1.97 (1.29-3.02) $P < .01$	2.78 (1.23-6.31) $P = .01$	1.69 (1.05-2.74) $P = .03$

*Data are given as risk ratio (95% confidence interval). Controlled for age, sex, smoking and heavy drinking status, vitamin use, and systolic blood pressure. ARM indicates age-related maculopathy; RPE, retinal pigment epithelium.

†In people 55 years and older who did not smoke at baseline.

than in the absence of early ARM. In addition, we have not found that eyes with cataract at baseline with incident early ARM at the 5-year follow-up were more likely to have poorer visual acuity at baseline than eyes with cataract without incident ARM (R.K., unpublished data, June 2001). The association we report may be a result of easier visualization and detection of ARM lesions after cataract surgery. However, when analyses were restricted to eyes with fair or good quality fundus photographs, these associations did not change, suggesting that better visualization did not explain this association. Some of the signs of ARM in eyes that underwent cataract surgery before the baseline examination may be related to photic retinal injuries (increased retinal pigmentation and RPE depigmentation) due to the operating microscope.[42-44] Inflammatory changes, with or without the development of transient cystoid macular edema, that may occur in eyes after cataract surgery have been hypothesized to be related to the development of late ARM.[12] In our study, the relationship between cataract surgery and the progression of ARM and incidence of late ARM remained significant after controlling for systolic blood pressure, cigarette smoking, history of heavy drinking, and vitamin consumption at baseline. Other common environmental exposures, not measured in the study, may explain the association.

Eyes that were aphakic at baseline had higher relative risks for the incidence and progression of most of the ARM end points compared with eyes that had intraocular lenses at baseline. This relationship was independent of time after cataract surgery. It is likely that surgical aphakia was a result of intracapsular cataract extraction, and those subjects who were aphakic would, on average, have undergone their cataract surgery at an earlier date and a greater age than those who had intraocular lens insertions and who were more likely to have undergone an extracapsular cataract extraction. Extracapsular cataract surgery has been thought to be somewhat more protective of the retina than intracapsular cataract surgery because of the decrease in endophthalmodonesis, presumably because of the stabilizing effects of the posterior lens capsule and possibly also because of an intact anterior hyaloid.[45] Although data show that extracapsular cataract surgery with (or without) posterior chamber lens implantation protects the retina somewhat from cystoid macular edema,[46,47] no evidence suggests a protective effect for ARM.

Results from previous cross-sectional population-based studies have been inconsistent regarding the relationship of nuclear cataract and ARM.[8,10,11] In Beaver Dam, we found an association between the presence of nuclear cataract at baseline and the 10-year incidence of early ARM (soft indistinct drusen and pigmentary abnormalities). This has been postulated to be due to environmental factors such as diet[48,49] or light exposure[13,50,51] or genetic factors[52,53] that may be related to both conditions.

The association of increased risk for progression to late ARM in eyes after cataract surgery is important because of the high frequency of cataract and early ARM in the population. In Beaver Dam, 27% of those aged at least 75 years had at least 1 eye with both conditions present at baseline (R.K. and B.E.K.K., unpublished data, June 2001). Armbrecht et al,[41] in a prospective study with 3 to 5 months of follow-up of patients with and without ARM who were undergoing cataract surgery, found significant improvement in terms of quality of life and visual function measures after cataract surgery, irrespective of the severity of ARM. Greater improvement in

function was reported in eyes that had more severe cataract before extraction. For these reasons, they concluded that cataract surgery was justified in eyes with ARM. Similarly, Shuttleworth et al,[39] in a retrospective study of people older than 50 years, also reported that the benefits of cataract surgery in eyes with ARM outweighed the risks. Although data from these and other studies cannot be used to provide guidelines for cataract surgery in eyes with moderate ARM, they suggest that cataract extraction is best considered in eyes in which the cataract has caused a decrease in function and that close follow-up of such eyes is indicated. Too few subjects in Beaver Dam had cataract surgery in eyes with late ARM to evaluate the effect on visual function. Data from a small study of 12 patients with a diagnosis of bilateral late ARM showed that within an average of 4 weeks of follow-up, no further deterioration of ARM or vision in the operated-on eye occurred, and self-reported visual function improved, suggesting a possible benefit of cataract surgery in some individuals with late ARM.[54]

Many statistical tests were performed in evaluating the potential risk factors and end points. Although we cannot exclude the possibility of chance associations, our findings exhibit biological rationale and consistency. In addition, the concomitant low frequency of some conditions (eg, PSC) and of the incidence of some lesions (eg, exudative macular degeneration) limits our ability to detect (or reject) meaningful relations. For example, in Beaver Dam, with 3234 participants, 76 of whom had a PSC in the right eye at baseline and 21 of whom had development of exudative macular degeneration by the 10-year examination, we would be able to detect an odds ratio of about 5.0 with a power of 0.80 with an $\alpha = .05$ for this association.

CONCLUSIONS

The 10-year incidence data from our study show an increased risk for early ARM in eyes with cataract at baseline, particularly nuclear cataract, and for progression of ARM and incidence of late ARM in eyes that underwent cataract surgery. These findings need further confirmation in other studies, but may have important clinical implications.

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