THE ROLE OF PATIENT AGE AND INTRAOCULAR GASES IN CATARACT PROGRESSION FOLLOWING VITRECTOMY FOR MACULAR HOLES AND EPIRETINAL MEMBRANES

BY *John T. Thompson MD*

ABSTRACT

Purpose: To evaluate the rate of increase in nuclear sclerosis and posterior subcapsular cataracts in eyes as a function of patient age and use of intravitreal gas at the time of vitrectomy.

Methods: Nuclear sclerotic cataracts and posterior subcapsular cataracts were graded on a scale of 0 to 4.0 in 301 consecutive eyes prior and subsequent to vitrectomy for macular holes, epiretinal membranes, or vitreomacular traction syndrome. Linear regression analysis was performed to compare the rate of change in cataract score.

Results: Nuclear sclerotic cataracts showed minimal increase in patients younger than 50 years of age following vitrectomy (.13 grades per year). Nuclear sclerotic cataracts increased at a rate of .7 to .9 grades per year (mean, .812) in patients from age 50 to 60, 60 to 70, 70 to 80, and 80+ years, even though the baseline nuclear sclerosis scores were progressively greater for each decade. The increase in nuclear sclerotic cataracts in patients younger than 50 years was significantly less ($P<.001$) than in patients 50 years or older. The fellow nonsurgical eyes of patients 50 years or older also showed smaller increases in nuclear sclerotic cataracts over time (.091 to .342 grades per year; mean, .139). Eyes with intraocular gas use had a higher rate of nuclear sclerosis progression (.8 grades per year) compared to eyes without intraocular gas bubbles (.5 grades per year) ($P<.001$). Posterior subcapsular cataract scores showed minimal or no increases in all groups.

Conclusions: Patients older than 50 years have a similar rate of increase in nuclear sclerotic cataracts independent of age. The rate is sixfold greater than in patients younger than 50 years and also sixfold greater than the progression of nuclear sclerosis in the fellow nonsurgical eyes. Intravitreal gas bubbles cause nuclear sclerosis to increase by 60%, compared to eyes without use of a gas bubble.

Trans Am Ophthalmol Soc 2003;101:479-492

INTRODUCTION

Accelerated progression of nuclear sclerotic cataracts is an important complication of vitrectomy, particularly in an era where severe complications such as retinal detachment and infectious endophthalmitis are infrequent.[1-3] Vitrectomy is currently being performed in eyes with relatively good visual acuity, because the threshold for surgery for macular holes and epiretinal membranes has decreased due to improvements in surgical techniques. In such cases, nuclear sclerotic cataract formation frequently causes decreased visual acuity, compared to the preoperative visual acuity, within 1 to 2 years of vitreous surgery. Progression of nuclear sclerotic cataracts following vitrectomy has been recognized for many years. Prior reports have evaluated the development of nuclear sclerosis in clear lenses, the percentage of eyes that progress at least 1 grade, or the percentage of eyes undergoing cataract surgery since vitrectomy.[4-7] The limitation of these methods is that the percentage of eyes with cataract progression or cataract surgery is strongly influenced by the duration of postoperative follow-up. The percentage of eyes with nuclear sclerosis progression is much higher in eyes followed for a mean of 2 years than in eyes followed for a mean of 1 year. Although more accurate quantitative methods have been developed to measure lens opacities, the rate of change in cataract score per unit of time using quantitative scoring has not been studied in any large series of eyes following vitrectomy.[8-11]

The purpose of this study was to test two primary hypotheses: (1) Is the rate of increase in nuclear sclerosis or posterior subcapsular cataracts greater in patients as they age? For example, does a 55-year-old with no preexisting cataract at the time of vitrectomy have the same or a different rate of cataract progression compared to a 75-year-old patient with a 1+ nuclear sclerotic cataract prior to vitrectomy? (2) Does the use of intravitreal air or perfluoropropane gas alter the progression of nuclear sclerotic or posterior subcapsular cataracts compared to

From the Greater Baltimore Medical Center, the Wilmer Institute of the Johns Hopkins University, and the University of Maryland.

eyes in which no intraocular gas bubbles are used? A related question is, Do eyes with macular holes, which are typically treated with long-acting intraocular gas bubbles, have a different rate of cataract progression compared to eyes with epiretinal membranes/vitreomacular traction syndrome, which usually do not require any gas bubbles or use only a short-acting gas bubble?

HISTORICAL REVIEW

Nuclear sclerotic cataract progression was not immediately recognized during the early years of vitrectomy development for several possible reasons.[12] First, lensectomy combined with vitrectomy was more common during the evolution of vitrectomy techniques for diabetic retinopathy. Younger patients undergoing vitrectomy for complications of diabetic retinopathy also were less likely to develop nuclear sclerotic cataracts. One study in the early 1980s reported visually significant posterior subcapsular cataracts in 17% of eyes following vitrectomy for diabetic retinopathy compared to only 7% of eyes developing nuclear sclerosis.[13] The development of cataracts following vitrectomy was noted with the increasing use of vitrectomy for the treatment of epiretinal membranes in the late 1970s.[14-16] Posterior subcapsular cataract progression was also noted to be relatively infrequent in eyes with vitrectomy for epiretinal membranes.[4,5] The recognition of nuclear sclerotic cataract progression following vitrectomy required that surgeons measure cataract severity before and after surgery. Early qualitative methods for grading lens opacities used terms such as clear, mild, moderate, or severe for nuclear sclerosis. This grading scheme was used in a report showing that operated eyes with idiopathic epiretinal membranes had substantially greater progression of nuclear sclerosis than fellow phakic eyes.[4] Progression of nuclear sclerosis was defined as the development of nuclear sclerosis in a clear lens or progression of nuclear sclerosis from one level to the next level, such as mild to moderate nuclear sclerosis. The incidence of nuclear sclerosis progression in this study was 31% in surgical eyes at 12 months compared to 0% in fellow eyes, and 72% in surgical eyes by 24 months compared to 15% in fellow eyes.[4] These investigators did not find any relationship between greater nuclear sclerosis progression in older patients, but most patients in this study were older than 50 years.

Increased nuclear sclerosis was first reported with vitrectomy for epiretinal membrane but will develop following vitrectomy for a variety of other indications.[11] Nuclear sclerosis progression has been reported following macular hole surgery.[7,17-21] Increased nuclear sclerosis has also been noted after vitrectomy for vitreomacular traction syndrome with or without epiretinal membrane removal,[22-26] as well as when vitrectomy is used for repair of rhegmatogenous retinal detachment.[27]

ETIOLOGY OF NUCLEAR SCLEROSIS FOLLOWING VITRECTOMY

The etiology of accelerated nuclear sclerosis is uncertain, but a number of potential causes have been postulated over the past 25 years. Causative factors that have been suggested include (1) physiologic differences between the ionic composition of vitrectomy infusion solution and native vitreous during vitrectomy, (2) differences in temperature between room temperature infusion solution and the body temperature of the normal vitreous/lens, (3) light toxicity to the crystalline lens from the operating microscope during surgery, and (4) increased oxidation of the crystalline lens proteins, possibly due to changes in posterior lens capsule permeability.

Infusion Solution Composition and Temperature

The vitrectomy irrigating solution has been implicated as a possible source of the increased nuclear sclerosis. Vitrectomy infusion solutions have been formulated to try to simulate aqueous, but none of the infusion solutions precisely match the chemical composition of aqueous. BSS Plus, which was used in all eyes in the current study, has been found to cause less damage to the corneal endothelium than lactated Ringer's solution[28] but appeared to have similar effects on nuclear sclerosis progression.[5] It was also thought that the practice of using high glucose concentrations in the infusate, which had been developed for diabetic patients, might be causing the nuclear sclerosis in nondiabetic patients. Prior studies had demonstrated increased cataract due to glycosylation of lens proteins in patients with elevated glucose levels from diabetes.[29] Hyperglycemic vitrectomy infusion solution, though, gave similar nuclear sclerosis progression compared to normoglycemic infusion solution in a study that evaluated eyes treated with epiretinal membranes with and without glucose supplementation.[5]

Temperature differences between the room-temperature infusion solution and body-temperature crystalline lens could also lead to biochemical changes in the lens, leading to increased nuclear sclerosis. The effect on nuclear sclerosis of warming the infusion solution to body temperature has not been investigated in any publication to the author's knowledge, but increased duration of exposure of the lens to room-temperature infusion solution does not appear to increase cataract formation.[30]

Light Toxicity

Light toxicity has been evaluated as a possible mechanism for cataract progression. The operating microscope produces ultraviolet light, so it was believed that crystalline lens exposure to ultraviolet light from the microscope during vitrectomy might produce nuclear sclerotic cataracts. This hypothesis was supported by the observation that exposure to high levels of ultraviolet light causes cataracts in mice.[31] These ultraviolet-induced cataracts are primarily manifest as a diffuse lens opacity rather than the typical clinical characteristics of nuclear sclerosis seen following vitrectomy. Ultraviolet radiation at the levels found in human eyes exposed to high cumulative sun exposure which exceeds that of the operating microscope did not cause increased nuclear sclerosis in a study of Chesapeake Bay watermen.[32] Cortical cataracts were increased in persons exposed to high levels of ambient ultraviolet light,[32] but cortical cataracts do not appear to increase following vitrectomy.[4] The absence of nuclear sclerosis progression in eyes with vitreous surgery where the vitreous is not removed during surgery also suggests that ultraviolet light from the operating microscope is not the cause of increased nuclear sclerosis following vitrectomy.[10]

Oxidation of the Crystalline Lens

Increased oxidation of the lens following vitrectomy is another possible mechanism for nuclear sclerosis acceleration. It is postulated that removal of the vitreous gel changes the microenvironment surrounding the lens, which leads to increased oxidation of lens proteins. The increased oxidation of lens proteins may be due to several mechanisms, including increased permeability of the posterior lens capsule and increased oxidation from changes in the ionic composition of the vitreous fluid following vitrectomy. Several different experimental studies support this hypothesis.[33-35] Clinical observations also support the hypothesis of increased oxidation of lens proteins as the cause of increased nuclear sclerosis following vitrectomy. Some recent publications have described modified techniques for epiretinal membrane removal to try to minimize the development of nuclear sclerotic cataracts.[10,36] The surgical technique avoids any vitrectomy or intravitreal saline infusion. The surgeon uses a vitreoretinal pick to peel the epiretinal membrane, which is then either left in the vitreous cavity or removed by forceps through the sclerotomy. A study of 21 eyes using "nonvitrectomizing" vitreous surgery for epiretinal membranes in patients older than 50 years showed no increased nuclear sclerosis in surgical eyes compared to fellow eyes during a mean follow-up of 9.7 months.[36] A second study was reported by the same authors using these techniques in 41 eyes of patients older than 50 years.[10] This study included longer follow-up of the 21 eyes in their prior study[36] and again reported no significant difference in nuclear sclerosis or myopic shift between the surgical and fellow eyes after a mean follow-up of 22 months. The two studies suggest that it is removal of the vitreous gel itself that directly or indirectly produces nuclear sclerosis after vitrectomy in elderly patients.

INTRAVITREAL GAS AND CATARACT FORMATION

It was recognized during the early years of vitrectomy surgery that intraocular gas contact with the posterior lens capsule will cause posterior subcapsular lens feathering. This will evolve into a posterior subcapsular cataract in many eyes if the patient does not improve compliance with prone positioning. Suboptimal compliance with prone positioning explains why some children develop posterior subcapsular cataract after use of an intravitreal gas bubble even though they do not develop any nuclear sclerosis. The literature has made conflicting claims about whether intraocular gas bubbles increase nuclear sclerosis. Two studies[4,11] found no definite increase in nuclear sclerosis with use of air or sulfur hexafluoride compared to eyes without intravitreal gas bubbles. Another report[37] did find evidence of increased nuclear sclerosis in eyes treated with gas tamponade.

MEASUREMENT OF CATARACTS FOLLOWING VITRECTOMY

Several lens opacity grading systems have been developed and refined for the purpose of grading cataracts in multicenter studies. The Lens Opacity Classification System II (LOCS II) uses color lens photograph standards, which are compared to the patient. The patient's lens is graded on a scale of 0 to 4 by comparison to these standards.[8] This lens classification system was confirmed in an independent study to be highly reproducible.[9] The current report uses the same lens grading scheme as the LOCS II clinical grading system, except that grading was performed by the author based on recall of the standard photographs rather than comparing the patient lens to the lens photographs during the patient examination. A more quantitative version of the LOCS II method was created and named the LOCS III scale, which uses slit-lamp photographs of the lens for each patient in the study with grading of nuclear color and opalescence on a scale of .1 (clear) to 6.9 (very opaque) by masked graders rather than the physician examiner.[38] The LOCS III system was used in a study of 56 eyes which reported that eyes of patients younger than 50 years had less nuclear sclerosis progression following vitrectomy than eyes of patients 50 years or older.[39]

A similar lens grading protocol to the LOCS III is the Wisconsin system for grading cataracts, which was modified for use in the Age-Related Eye Disease Study (AREDS).[40,41] The AREDS classification system grades nuclear sclerosis, posterior subcapsular cataracts, and cortical changes using two methods. In the first method, patient lens photographs were sent to a reading center and graded on a scale of .9 to 6.1 using optical density measured with a digital image processor.[40] A second set of clinical photographic standards was prepared by the AREDS group for use by clinicians when patients were examined and was based on a scale of 0 to 4. Fractional scores such as 1.5 can be used to describe a nuclear sclerotic cataract between standard photographs 1 and 2.

Another quantitative method to measure nuclear sclerosis changes uses lens photographs taken by a Scheimpflug camera. The density of the lens photograph is measured to derive a quantitative measure of nuclear sclerosis. Scheimpflug photographs were used in two studies of nuclear sclerosis lens changes in eyes with epiretinal membrane removal but without vitrectomy.[10,36] All of the nuclear sclerosis grading systems described above use color photographs of eyes with nuclear sclerosis. A different approach is to measure lens autofluorescence by fluorophotometry. In one study of nuclear sclerosis following vitrectomy, 13 surgical eyes were compared to fellow nonsurgical eyes using lens autofluorescence. A significant increase in lens autofluorescence was demonstrated following vitrectomy.[11] Lens autofluorescence does not measure nuclear sclerosis in the same way as the AREDS, LOCS II, and LOCS III methods. Hence, the results of lens autofluorescence would not necessarily parallel those the LOCS and AREDS systems.

METHODS

The study consisted of a retrospective analysis of 301 consecutive phakic eyes treated by one surgeon using vitrectomy for eyes with macular holes, epiretinal membranes, or vitreomacular traction syndrome from 1992 through 2001. Patients were excluded if any of the following factors were present: prior cataract surgery, vitrectomy, retinal detachment, diabetes, uveitis, known ocular trauma, prolonged use of topical or systemic steroids, prior glaucoma filtering surgery, use of silicone oil intravitreal tamponade at the time of vitrectomy, simultaneous cataract surgery, or any other known condition that may have altered the rate of cataract progression following the vitrectomy. Patients with less than 6 months of follow-up after vitrectomy were also excluded. Lenses were graded by the surgeon at all time points using the Chylack LOCS II lens grading scale of nuclear sclerosis and posterior subcapsular cataracts.[8,42] Nuclear sclerosis and posterior subcapsular cataracts were graded on a scale of 0 to 4.0. Fractional numbers were allowed, such as .5 for trace nuclear sclerosis judged between 0 and 1+ standard photographs or 1.5 for moderate nuclear sclerosis between 1+ to 2+ standard photographs. Cortical spoking was not routinely recorded, so this cataract variable was not analyzed, but prior reports have shown minimal effects of vitrectomy on cortical cataract.[4]

Cataracts were evaluated at the time of the preoperative visit closest to the date of surgery and on all subsequent postoperative visits. Cataract scoring for the first 6 weeks following vitrectomy was not recorded in the database, so that the first postoperative visit at which the lens was graded was usually between 6 and 12 weeks following vitrectomy. Cataract severity was graded on all subsequent postoperative visits until cataract surgery was performed or until the patient was discharged from care or was lost to follow-up. Patient characteristics and examination scores at baseline (preoperative) and final examination were explored using summary statistics and tables. Paired t tests and independent sample t tests were used to compare numeric variables at baseline and final examination.

Cataract progression was measured with the date of surgery becoming the baseline time for the cataract score (time = 0), since cataract progression was typically minimal between the preoperative examination and the date of surgery. Most preoperative visits were typically within several weeks of the surgery date. General linear models were used to estimate the average change in cataract score per year follow-up for each individual patient. This measure is commonly referred to as a slope or a rate of change in regression analysis (Figure 1). This model allowed for patients to have their cataracts measured at different time points following surgery for different follow-up durations. Nonlinear regression models were also evaluated but did not appear to fit the data any better than linear regression analysis. Standard analysis of variance (ANOVA) procedures were used to compare the average slopes within subgroups of patients of different age ranges or other categories, such as use of intraocular gases. When multiple comparisons between subgroups were made, such as in multiple age ranges, the Bonferroni correction was applied to all P values to correct for the possibility of chance associations due to the multiple comparisons.[43]

RESULTS

The baseline demographic variables for the 301 eyes in the study are summarized in Table I and Figure 2. The mean preoperative logMAR visual acuity was .731, which corresponds to a Snellen equivalent of 20/100 –2. The mean nuclear sclerosis score was .70 in study eyes at baseline and .75 in the fellow eyes that were phakic (n = 288). Few eyes in the study had posterior subcapsular cataracts, and this is reflected in the posterior subcapsular score of .01 at baseline. Cataract surgery had been performed in 156 of 301 phakic surgical eyes (51.8%) by the time of the final examination at a mean of 2.1 years following surgery. Cataract surgery had been performed in 39 of 288 phakic fellow (nonsurgical) eyes (13.5%) by the final examination.

COMPARISON OF BASELINE AND FINAL PHAKIC CATARACT SEVERITY

Table II compares the baseline to final cataract and visual acuity scores in pairs of eyes that remained phakic

TABLE I: DEMOGRAPHICS AT BASELINE AND FINAL EXAMINATION

FACTOR	MEAN (±SEM)
Age at surgery date (yr)	67.36 ± .621
Duration of follow-up	2.10 ± .102
Nuclear sclerosis score (0 to 4.0 scale)	
At baseline (n=301)	.70 ± .024
Fellow eye at baseline (n=288)	.75 ± .030
Final examination* (n=145)	1.94 ±.069
Fellow eye final examination* (n=249)	.90 ± .045
Posterior subcapsular cataract score (0 to 4.0 scale)	
At baseline (n=301)	.01 ± .004
Fellow eye at baseline (n=288)	.01 ± .008
Final examination* (n=145)	.07 ± .021
Fellow eye final examination* (n=249)	.01 ± .005
LogMAR visual acuity	
Preoperative	.731 ± .018 (20/100 –2)
Final examination (all eyes)	.529 ± .021 (20/63 –1)
Change between preoperative and final examination	+.202 ± .024 (+2 lines)

*Score in eyes that were still phakic at final examination.

TABLE II: COMPARISON OF PREOPERATIVE AND FINAL EXAMINATION IN PAIRED EYES THAT REMAINED PHAKIC AT FINAL EXAMINATION

	PREOPERATIVE	FINAL EXAMINATION IN PHAKIC EYES (MEAN ± SEM)*	*P* VALUE (PAIRED *t* TEST)
Nuclear sclerosis score (n=145)	.68 ± .035	1.94 ±.069	<.001
Posterior subcapsular cataract score (n=145)	.01 ± .006	.07 ± .021	.005
Fellow eye nuclear sclerosis score (n=249)	.69 ± .029	.90 ± .045	<.001
Fellow eye posterior subcapsular cataract score (n=249)	.01 ± .004	.01 ± .005	.276
logMAR visual acuity (n=145)	.758 ± .025 (20/125 +2)	.662 ± .031 (20/100 +2)	.009

*Final examination mean ± standard error of the mean in eyes that remained phakic at a mean of 1.22 years.

throughout the study. The mean nuclear sclerosis score in eyes that were still phakic at the final examination following vitrectomy had increased to 1.94, and the posterior subcapsular cataract score had increased to .07. The increases in cataract scores for nuclear sclerosis and posterior subcapsular cataracts were both statistically significant. The mean nuclear sclerosis score increased from .69 to .90 in fellow eyes that were still phakic (n = 249) at the final examination, and this was also statistically significant. Posterior subscapsular cataract scores did not increase significantly in fellow eyes during the study. Visual acuity did improve significantly, from 20/125 +2 to 20/100 +2, in paired eyes that remained phakic at the final examination, but this included many eyes with visually significant cataracts on the final examination. Figure 3 shows the mean cataract score in all eyes at baseline, 6 to 12 weeks, and at the final phakic examination. The mean nuclear sclerosis score increased from .70 at baseline, to 1.046 at 6 to 12 weeks postoperatively, to 1.967 at a mean of 1 year postoperatively. Posterior subcapsular cataract showed a minimal change during the same interval. Table III makes a similar comparison, but this was performed using the means for all eyes (n = 301) at baseline and for the final phakic examination (n = 301), including eyes with subsequent cataract surgery. Often the eyes with subsequent cataract surgery had substantial cataracts on the final phakic examination. The increase in nuclear sclerosis and posterior subcapsular cataract was statistically significant for surgical eyes. Nonsurgical fellow eyes also showed statistically significant, although small, increases in nuclear sclerosis. However, posterior subcapsular cataracts did not increase significantly in these eyes. The final phakic visual acuity did not improve, since many eyes had visually significant cataracts on the final examination.

CATARACT PROGRESSION BY AGE IN SURGICAL EYES

The effect of age on progression of cataracts was evaluated by dividing the eyes into five age ranges: 10 to 49.99 years, 50 to 59.99 years, 60 to 69.99 years, 70 to 79.99 years, and 80+ years. The progression of nuclear sclerotic and posterior subcapsular cataracts was evaluated using linear regression analysis of eyes in each age range. The

TABLE III: COMPARISON OF PREOPERATIVE AND FINAL PHAKIC EXAMINATION

	PREOPERATIVE	FINAL EXAMINATION IN PHAKIC EYES (MEAN ± SEM)*	*P* VALUE (INDEPENDENT SAMPLE *t* TEST)
Nuclear sclerosis score (n=301)	.702 ± .024	1.967 ± .004	<.0001
Posterior subcapsular cataract score (n=301)	.011 ± .004	.094 ± .019	<.0001
Fellow eye nuclear sclerosis score (n=288)	.750 ± .030	.944 ± .043	.0002
Fellow eye posterior subcapsular cataract score (n=288)	.013 ± .008	.014 ± .006	.9590
logMAR visual acuity (n=301)	.731 ± .018 (20/100 –2)	.707 ± .020 (20/100)	.3788

*Final examination in eyes that remained phakic at a mean of 1.03 years ± standard error of the mean.

baseline nuclear sclerosis scores were higher for each successive age range, as expected (Table IV). The average slopes, which represent the average change in nuclear sclerosis cataract scores per year, were compared to one another using ANOVA. The Bonferonni correction for multiple comparisons was applied. Eyes of patients younger than 50 years had small increases in nuclear sclerosis (.128 grades per year), while patients 50 years and older had substantial progression of nuclear sclerosis (.707 to .897 grades per year; mean, .812). The higher rate of increased nuclear sclerosis in surgical eyes in all groups of older patients was statistically significant when compared to patients younger than 50 years (Table IV). The coefficient of correlation squared was between .328 and .748, indicating a reasonably good correlation between the x variable (time since surgery) and the y variable (cataract score). The coefficient of correlation squared also denotes the percentage of variability in nuclear sclerosis explained by the regression equation for the variables studied. Between 32.8% and 74.8% of variability in nuclear sclerosis score was predicted by the independent variable of time since vitrectomy. Figure 4 plots the regression data showing the similarity in the slope of increased nuclear sclerosis in patients older than 50 years compared to small increases in patients younger than 50 years. Regression analysis was performed for eyes with posterior subcapsular cataracts but there was minimal increase in posterior subcapsular cataract scores, so the slopes were close to 0 for all age ranges (Table V). There was no difference in rates of change in posterior subcapsular cataracts between different age ranges. The coefficient of correlation squared for posterior subcapsular cataract was .004 to .486, indicating a poorer correlation between elapsed time since surgery and posterior subcapsular cataract scores.

CATARACT PROGRESSION BY AGE IN NONSURGICAL EYES

Nuclear sclerosis also increased in fellow nonsurgical eyes, but the rate of increase was less than in surgical eyes (Table VI). The baseline nuclear sclerosis scores were higher for older patients, as expected. The rate of increase in nuclear sclerosis was negligible in fellow eyes of patients younger than 50 years and varied between .091 to .342 in fellow eyes (mean = .139 grades per year) of patients older than 50 years. Patients younger than 50 years had lower rates of increased nuclear sclerosis (mean = .039 grades per year) compared to other age ranges, and this difference was statistically significant when comparing patients younger than 50 years to patients 50 to 60 years and 70 to 80 years. The higher rate of increased nuclear sclerosis in patients 50 to 60 years compared to all other age ranges was also significant. Figure 5 plots the regression data showing the lower rate of increase in nuclear sclerosis in patients older than 50 years compared to the surgical eyes in Figure 4. Again, patients younger than 50 years had a small increase in nuclear sclerosis during the study interval. Posterior subcapsular cataract progression was minimal in phakic fellow eyes. The baseline posterior subcapsular cataract scores were essentially 0, and the rate of increase was also about 0 for nonsurgical fellow eyes (Table VII). The differences in posterior subcapsular cataract progression between different age ranges were not statistically significant.

CATARACT PROGRESSION BY INTRAOCULAR GAS USE

Cataract progression was also compared in surgical eyes according to whether intraocular gases were used at the time of surgery (Table VIII). The baseline nuclear sclerosis scores were similar between the two groups (.697 versus .704). The rate of increase in nuclear sclerosis was less in eyes without use of any intraocular gas bubble (.519) than it was in eyes treated with air or C_3F_8 (.807), and this difference was statistically significant (P<.001). The mean patient age at the time of surgery was 69.3 years for eyes without intravitreal gas versus 66.7 years for eyes with use of gas. This difference in age was not statistically significant (P = .08), and the older mean ages of eyes without gas, if anything, would have caused more nuclear sclerosis progression rather than less. Baseline posterior subcapsular cataract scores were similar between the two groups, and the increased rate of posterior subcapsular

TABLE IV: COMPARISON OF NUCLEAR SCLEROSIS PROGRESSION BY AGE IN SURGICAL EYE

AGE	n	BASELINE NUCLEAR SCLEROSIS SCORE*	NUCLEAR SCLEROSIS SCORE INCREASE/YR (MEAN ± SEM)†	ADJUSTED R^2‡
<50 yr	13	.039	.128 ± .046	.328
50-60 yr	27	.324	.786 ± .111	.434
60-70 yr	133	.641	.897 ± .042	.592
70-80 yr	108	.903	.707 ± .034	.644
>80 yr	20	.963	.853 ± .070	.748

Comparison of rate of nuclear sclerosis progression by age range using analysis of variance with Bonferroni correction for multiple comparisons:
<50 yr versus all other age ranges: $P<.001$
50-60 yr versus all older age ranges: $P>.05$
60-70 yr versus 70-80 yr: $P<.01$
60-70 yr versus 80+ yr: $P>.05$
70-80 yr versus 80+ yr: $P>.05$
*Average nuclear sclerosis score at baseline.
†Mean slope and standard error of the mean for average nuclear sclerosis score increase per year.
‡Coefficient of correlation squared.

TABLE V: COMPARISON OF POSTERIOR SUBCAPSULAR CATARACT PROGRESSION BY AGE IN SURGICAL EYE

AGE	n	BASELINE POSTERIOR SUBCAPSULAR CATARACT SCORE*	POSTERIOR SUBCAPSULAR CATARACT SCORE INCREASE/YR (MEAN ± SEM)†	ADJUSTED R^2‡
<50 yr	13	.077	.052 ± .048	.192
50-60 yr	27	.000	.012 ± .016	.004
60-70 yr	133	.004	.037 ± .013	.486
70-80 yr	108	.016	.012 ± .013	.372
>80 yr	20	.000	.027 ± .038	.382

None of the comparisons of posterior subcapsular cataract progression between different age ranges were statistically significant ($P>.05$) using Bonferroni correction for multiple comparisons.
*Average nuclear sclerosis score at baseline.
†Mean slope and standard error of the mean for average nuclear sclerosis score increase per year.
‡Coefficient of correlation squared.

cataract in eyes with use of intraocular gas, although small (–.003 versus .040 grades per year), was statistically significant ($P = .022$) (Table IX).

CATARACT PROGRESSION BY SURGICAL INDICATION

Cataract progression was also evaluated on the basis of surgical indication. This analysis was very similar to the analysis of cataract progression by use of intraocular gases, since most eyes with macular holes were treated with long-acting gas bubbles. An intraocular gas bubble was required in 24 (24.2%) of 99 eyes with epiretinal membranes or vitreomacular traction syndrome, and this was usually a short-acting air bubble. The baseline scores for nuclear sclerosis were very similar (.722 for macular hole eyes versus .662 for epiretinal membrane/vitreomacular traction syndrome eyes). The rate of increase in nuclear sclerosis was .795 grades per year in eyes with macular holes compared to .561 grades per year in eyes with epiretinal membranes or vitreomacular traction syndrome (Table X). The higher rate of nuclear sclerosis progression in eyes with macular holes was significantly greater than in eyes with epiretinal membrane/vitreomacular traction syndrome ($P<.0001$). The baseline posterior subcapsular cataract scores were similar, and the rate of increase in posterior subcapsular cataract score was small but was significantly higher in eyes with macular holes compared to eyes with epiretinal membrane/vitreomacular traction syndrome (–.003 versus .041, $P = .0125$, Table XI).

DISCUSSION

The goal of the current study was to answer two primary questions about nuclear sclerosis following vitrectomy for

TABLE VI: COMPARISON OF NUCLEAR SCLEROSIS PROGRESSION BY AGE IN FELLOW (NONSURGICAL) EYE

	n	BASELINE NUCLEAR SCLEROSIS SCORE*	NUCLEAR SCLEROSIS SCORE INCREASE/YR (MEAN ± SEM) †	ADJUSTED R^2‡
<50 yr	13	.039	.017 ± .015	.109
50-60 yr	26	.346	.342 ± .022	.688
60-70 yr	128	.717	.091 ± .012	.717
70-80 yr	102	.936	.147 ± .017	.669
>80 yr	19	.987	.146 ± .038	.501

Comparison of rate of fellow eye nuclear sclerosis progression by age range using analysis of variance with Bonferroni correction for multiple comparisons
<50 yr versus 50-60 yr: P<.001
<50 yr versus 60-70 yr: P>.05
<50 yr versus 70-80 yr: P<.05
<50 yr versus 80+ yr: P>.05
50-60 yr versus 60-70 yr: P<.001
50-60 yr versus 70-80 yr: P<.001
50-60 yr versus 80+ yr: P<.001
60-70 yr versus 70-80 yr: P<.05
60-70 yr versus 80+ yr: P>.05
70-80 yr versus 80+ yr: P>.05
*Average nuclear sclerosis score at baseline.
†Mean slope and standard error of the mean for average nuclear sclerosis score increase per year.
‡Coefficient of correlation squared.

TABLE VII: COMPARISON OF POSTERIOR SUBCAPSULAR CATARACT PROGRESSION BY AGE IN FELLOW (NONSURGICAL) EYE

	n	BASELINE POSTERIOR SUBCAPSULAR CATARACT SCORE*	POSTERIOR SUBCAPSULAR CATARACT INCREASE/YR (MEAN ± SEM)†	ADJUSTED R^2‡
<50 yr	13	.000	.000 ± .000	
50-60 yr	26	.000	.000 ± .000	
60-70 yr	128	.006	.006 ± .003	.446
70-80 yr	102	.029	.006 ± .003	.698
>80 yr	19	.000	–.008 ± .009	.425

None of the comparisons of fellow eye posterior subcapsular cataract progression between different age ranges were statistically significant (P>.05) using Bonferroni correction for multiple comparisons.
*Average nuclear sclerosis score at baseline.
†Mean slope and standard error of the average nuclear sclerosis score increase per year.
‡Coefficient of correlation squared..

epiretinal membranes or macular holes. The first question concerned the relationship between patient age and progression of nuclear sclerosis. The study demonstrated that the absolute increase in nuclear sclerosis was small in patients younger than 50 years (.13 grades increase per year) but was significantly greater and relatively constant in patients older than 50 years (.7 to .9 grades increase per year), for a sixfold greater increase in older patients compared to those younger than 50 years. Patients who are in their 80s have greater nuclear sclerosis at baseline (mean nuclear sclerosis score = .96) compared to patients in their 50s (mean nuclear sclerosis score = .32), but the rate of increase in nuclear sclerosis from their preoperative baseline was relatively constant. The mean increase in nuclear sclerotic cataracts in surgical eyes of patients older than 50 years was .812 grades per year compared to .139 grades per year for fellow eyes of patients older than age 50, and this also represents a sixfold greater rate of nuclear sclerosis following vitrectomy. Patients younger than 50 years had a mean rate of increase in nuclear sclerosis of .128 grades per year in surgical eyes compared to .017 grades per year in nonsurgical eyes, and this is a sevenfold increase in nuclear sclerosis following vitrectomy. Thus, the increase in nuclear sclerosis in the surgical eyes compared to the fellow eyes was about sixfold to sevenfold in all patient age ranges following vitrectomy, even though the absolute rate of increase in nuclear sclerosis was much less in patients under age 50 years.

The second question to be answered concerned the effects of intraocular gas on progression of nuclear sclero-

TABLE VIII: COMPARISON OF NUCLEAR SCLEROSIS PROGRESSION BY USE OF INTRAOCULAR GAS IN SURGICAL EYES

	n	Baseline nuclear sclerosis score*	Nuclear sclerosis score increase/yr (mean ± SEM)†	Adjusted R^2‡
No gas	75	.697	.519 ± .044	.552
Gas (air or C3F8)	226	.704	.807 ± .030	.625

Comparison of rate of nuclear sclerosis progression by use of intraocular gas using independent sample *t* test:
No gas versus use of intraocular gas: $P<.001$.
*Average nuclear sclerosis score at baseline.
†Mean slope and standard error of the mean for average nuclear sclerosis score increase per year.
‡Coefficient of correlation squared.

TABLE IX: COMPARISON OF POSTERIOR SUBCAPSULAR CATARACT PROGRESSION BY USE OF INTRAOCULAR GAS IN SURGICAL EYES

	n	Baseline posterior subcapsular cataract score*	Posterior subcapsular cataract score increase/yr (mean ± SEM)†	Adjusted R^2‡
No gas	75	.023	–.003 ± .044	.435
Gas (air or C3F8)	226	.007	.040 ± .030	.400

Comparison of rate of posterior subcapsular cataract progression by use of intraocular gas using independent sample t test:
No gas versus use of intraocular gas: $P = .022$.
*Average nuclear sclerosis score at baseline.
†Mean slope and standard error of the mean for average nuclear sclerosis score increase per year.
‡Coefficient of correlation squared.

TABLE X: COMPARISON OF NUCLEAR SCLEROSIS PROGRESSION BY SURGICAL INDICATION

	n	Baseline nuclear sclerosis score*	Nuclear sclerosis score increase/yr (mean ± SEM)†	Adjusted R^2‡
Macular hole	202	.722	.795 ± .031	.611
Epiretinal membrane/ vitreomacular traction syndrome	99	.662	.561 ± .042	.550

Comparison of rate of nuclear sclerosis progression by surgical indication (macular hole versus epiretinal membrane/vitreomacular traction syndrome) using independent sample *t* test:
Macular hole versus epiretinal membrane/vitreomacular traction syndrome: $P<.0001$.
*Average nuclear sclerosis score at baseline.
†Mean slope and standard error of the mean for average nuclear sclerosis score increase per year.
‡Coefficient of correlation squared.

sis. The current report determined that eyes with intraocular gas bubbles had a different rate of increase in nuclear sclerosis compared to eyes without use of intraocular gas bubbles. Eyes with intraocular gas bubbles had a higher rate of increase in nuclear sclerosis (.81 grades increase per year) compared to eyes without use of intraocular gas bubbles (.52 grades increase per year), and this difference was statistically significant. A corollary of the effect of gas tamponade on nuclear sclerosis is that eyes with macular hole surgery using long-acting intraocular gas bubbles developed nuclear sclerotic cataracts more rapidly than eyes with epiretinal membranes in which intraocular gas bubbles were less frequently used. Posterior subcapsular cataracts showed small increases in the study when evaluated by patient age, by use of intraocular gas bubbles, or by surgical indication (macular hole versus epiretinal membrane/vitreomacular traction syndrome). The increases in posterior subcapsular cataracts, although statistically significant between the initial and final examination in surgical eyes, were not visually significant compared to the effects of nuclear sclerosis on visual acuity.

TABLE XI: COMPARISON OF POSTERIOR SUBCAPSULAR CATARACT PROGRESSION BY SURGICAL INDICATION

	n	BASELINE POSTERIOR SUBCAPSULAR CATARACT SCORE*	POSTERIOR SUBCAPSULAR CATARACT SCORE INCREASE/YR (MEAN ± SEM)†	ADJUSTED R^2‡
Macular hole	202	.007	.041 ± .011	.402
Epiretinal membrane/ vitreomacular traction syndrome	99	.018	−.003 ± .011	.435

Comparison of rate of posterior subcapsular cataract progression by surgical indication (macular hole versus epiretinal membrane/vitreomacular traction syndrome) using independent sample *t* test:
Macular hole versus epiretinal membrane/vitreomacular traction syndrome: $P = .0125$.
*Average nuclear sclerosis score at baseline.
†Mean slope and standard error of the mean for average nuclear sclerosis score increase per year.
‡Coefficient of correlation squared.

A limitation of the current study was that it was retrospective with variable length of follow-up. A few patients were followed for only 6 months, whereas most were followed for 1 or more years. A second limitation was that cataracts were graded subjectively by the surgeon rather than by a masked examiner evaluating standard lens photographs. The fact that all lenses were evaluated by the author would tend to decrease variability in lens grading inherent in multicenter studies where the lenses are graded by many surgeons. Neither of these limitations was likely to have substantially altered the two primary conclusions of the study.

The author has not been able to identify any reports in the literature that have used linear regression analysis to calculate the rate of progression of cataract following vitrectomy. Earlier reports of nuclear sclerosis following vitrectomy used measurement of the percentage of eyes that either developed cataracts in clear lenses or had one grade progression (from mild to moderate or moderate to severe) during the study interval.[4,5] Comparisons were made using Kaplan-Meier life table analysis. The first report found a cumulative incidence of progression of nuclear sclerosis of 31% in vitrectomy eyes at 1 year and 0% of control eyes.[4] The incidence of nuclear sclerosis progression increased to 72% in surgical eyes by 24 months compared to 15% in fellow eyes.[4] The incidence of nuclear sclerosis progression was 68.4% in operated eyes compared to 12.8% in nonsurgical fellow eyes by 24 months in a second larger study using the same techniques.[5] These techniques were sufficiently sensitive to identify the large difference in nuclear sclerosis progression between surgical and fellow eyes, but these studies do not take into account the baseline cataract score for any eyes. An eye that has a clear lens at baseline and progresses to a mild nuclear sclerotic cataract at 12 months has progressed one grade and is counted as identical to an eye that starts with a moderate nuclear sclerotic cataract and progresses to a severe nuclear sclerotic cataract at 12 months. Linear regression analysis allows both the baseline nuclear sclerosis score and the rate of increase in nuclear sclerosis score to be measured and analyzed in groups of eyes of multiple patient age ranges as was performed in the current study. It would have been difficult to detect small differences in nuclear sclerosis changes by decade with the previous methods of assessing nuclear sclerosis progression using life table analysis. Linear regression also predicts the time it takes to progress by a certain number of grades. For example, the mean time for progression of nuclear sclerosis by one grade was 1.23 years for surgical eyes compared to 7.19 years in fellow eyes without vitrectomy in patients older than 50 years in the current study. The mean time to progress one grade was 7.7 years in patients younger than 50 years, which agrees with clinical observations that patients younger than 50 years still develop premature nuclear sclerotic cataract that may require removal 5 or more years following vitrectomy.

Patient age is an important factor in determining the rate of increase in nuclear sclerosis, and multiple studies have found that younger patients have less cataract progression. The first study reported that nuclear sclerosis increased in a lower percentage of eyes in a subgroup of 11 patients aged 50 years or younger at the time of vitrectomy for idiopathic epiretinal membranes.[5] This finding was confirmed in a second study, which found that patients younger than 50 years developed visually significant nuclear sclerotic cataracts in only 7% of eyes using densitometry measurements of lens photographs with the LOCS III scale compared to 79% of eyes in patients older than 50 years after a mean follow-up of about 2 years.[39] A significant increase in cataract was defined in this study as either an increase in .9 units on the LOCS III scale or cataract surgery in the study eye. The minimal nuclear sclerosis increase in patients younger than 50 years of age

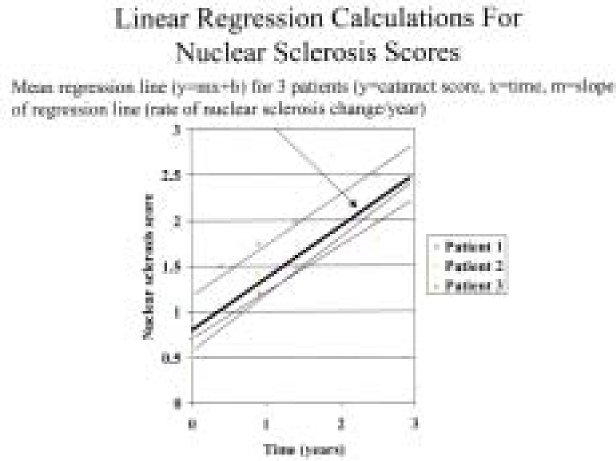

FIGURE 1
Nuclear sclerosis score (y-axis) is plotted over time (x-axis) in three patients. The statistical software's general linear model calculated a regression line for each patient individually and computed a composite regression line for all patients (darker line), which represents the mean change in cataract score over time.

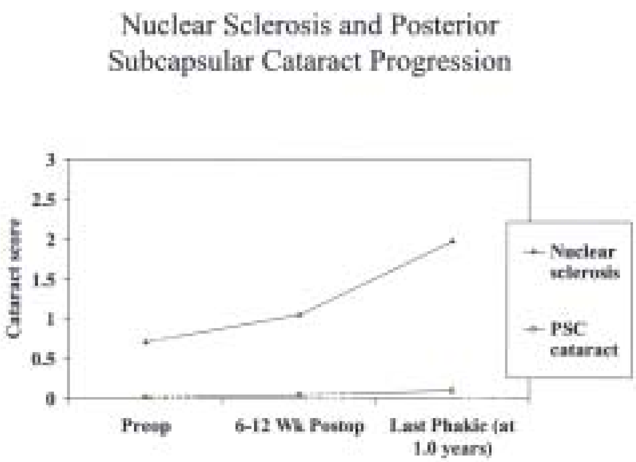

FIGURE 3
Mean nuclear sclerosis score increased between preoperative and final phakic examination at a mean of 1 year following vitrectomy. Posterior subcapsular scores increased minimally during the same interval.

following vitrectomy was confirmed in two additional studies.[44,45]

Another measure of nuclear sclerosis is the use of lens autofluorescence. Lens autofluorescence was found to develop or increase in older patients following vitrectomy, but the authors found no correlation with longer length of postoperative follow-up and/or with use of intraocular gas.[11] The increase in lens autofluorescence plotted against age suggested an exponential increase in autofluorescence in older patients, although the number of eyes was too small to distinguish whether the increase was linear, as found in the current study. The current study was able to evaluate the change in nuclear sclerosis by decade and confirmed that there is a relatively abrupt transition at around the age of 50 years, with slow

FIGURE 2
Demographics for 301 phakic eyes. About two thirds of patients were female and macular hole accounted for about two thirds of surgical indications. One quarter of eyes had no intraocular gas bubble, while two thirds had use of perfluoropropane.

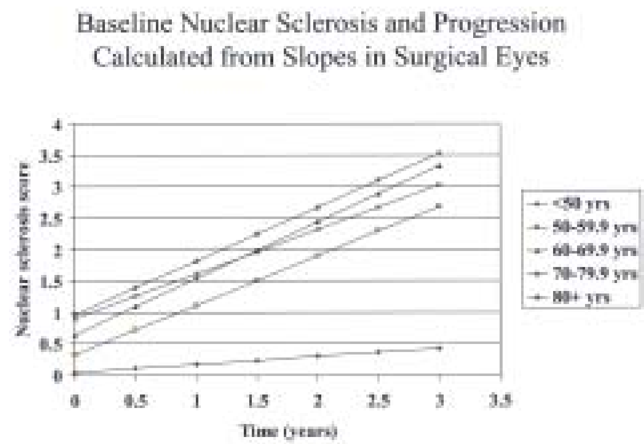

FIGURE 4
Nuclear sclerosis scores in surgical eyes of patients younger than 50 years showed minimal increase, while eyes of patients older than 50 years showed similar increases in nuclear sclerosis.

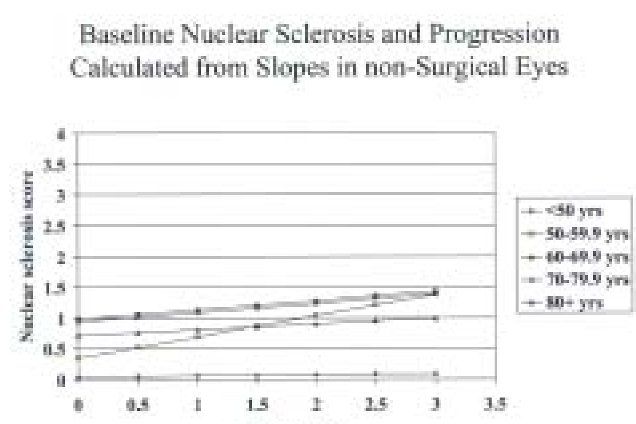

FIGURE 5
Nuclear sclerosis scores in nonsurgical eyes of patients younger than 50 years showed minimal change. Eyes of patients older than 50 years showed a slow increase in nuclear sclerosis, as expected, with eyes 50 to 60 years showing a slightly higher rate of increase but still substantially less than surgical eyes in Figure 4.

progression of nuclear sclerosis in patients younger than age 50 and a higher rate of nuclear sclerosis progression in patients older than age 50.

A recent study looked at the duration of vitrectomy surgery and severity of nuclear sclerosis following macular hole surgery to determine if the duration of surgery influenced nuclear sclerosis progression. The investigators found that eyes with longer-duration surgeries had no increased rate of nuclear sclerosis progression compared to eyes with shorter-duration surgeries.[30] This study suggests that neither light toxicity from the operating microscope nor temperature of the infusion solution plays a significant role in nuclear sclerosis progression following vitrectomy.

The effect of intraocular gas bubbles on cataract has not been evaluated systemically in many studies. Two studies have found no effect of intraocular gas bubbles on cataract progression,[4,11] while a third found increased nuclear sclerosis progression in eyes with intraocular gas bubbles.[37] The effect of intraocular gas bubbles on cataract formation has not been evaluated in any large series of eyes prior to the current study. The relatively small increase in nuclear sclerosis progression (1.6-fold) with use of intraocular gas bubbles found in the current study would have been much more difficult to detect in smaller series using life table analysis for detecting cataract progression.

Posterior subcapsular cataracts also increase following vitrectomy, but the increase is relatively small and is not visually significant in most eyes. The baseline posterior subcapsular cataract score of .01 increased to .07 to .09 by the final examination, but the rate of increase did not appear to be related to patient age by regression analysis. It is of interest that eyes with intraocular gas bubbles did have a small but significant increase in posterior subcapsular cataract formation, as did eyes with vitrectomy for macular holes.

The relatively rapid development of nuclear sclerotic cataracts following vitrectomy has led some surgeons to advocate simultaneous cataract surgery whenever vitrectomy is performed in elderly patients. The overall results for combined vitrectomy and cataract surgery are good in a number of reports for a variety of vitrectomy indications.[46-50] Combined vitrectomy and cataract surgery has some advantages in efficiency and decreased cost, but pupillary capture and posterior synechiae also appear more frequent when simultaneous surgery is performed.[51,52] Pupillary capture and posterior synechiae appear to be more common following vitrectomy with use of an intraocular gas bubble and in eyes with proliferative diabetic retinopathy.

Cataract formation following vitrectomy does reduce the visual acuity benefits of vitrectomy for macular holes and epiretinal membranes reported at 1 year or more following surgery. Progression of nuclear sclerotic cataracts leads to substantial visual loss by 1 to 2 years following vitrectomy in most patients older than 50 years. This factor has caused most previous reports of vitrectomy for epiretinal membranes and macular hole surgery to potentially underestimate the benefits of vitreous surgery, since a majority of series included eyes with visually significant cataracts at the date of their final examination. Long-term studies of the visual results of vitrectomy in eyes following cataract surgery or studies of vitrectomy in the subset of pseudophakic eyes will provide a more accurate assessment of the visual benefits of vitrectomy for a variety of indications in patients older than 50 years.

ACKNOWLEDGMENT

The author wishes to thank Elizabeth Johnson, MS, of the Johns Hopkins Biostatistics Center for statistical assistance with this study.

REFERENCES

1. Tabandeh H, Chaudhry NA, Smiddy WE. Retinal detachment associated with macular hole surgery: characteristics, mechanism and outcomes. *Retina* 1999;19:281-286.
2. Cohen SM, Flynn HW Jr, Murray TG, et al. Endophthalmitis after pars plana vitrectomy. The Postvitrectomy Endophthalmitis Study Group. *Ophthalmology* 1995;102:705-712.
3. Eifrig CW, Flynn HW Jr, Scott IU, et al. Acute-onset postoperative endophthalmitis: review of incidence and visual outcomes (1995-2001). *Ophthalmic Surg Lasers* 2002;33:373-378.
4. de Bustros S, Thompson JT, Michels RG, et al. Nuclear sclerosis after vitrectomy for idiopathic epiretinal membranes. *Am J Ophthalmol* 1988;105:160-164.
5. Cherfan GM, Michels RG, de Bustros S, et al. Nuclear sclerotic cataract after vitrectomy for idiopathic epiretinal membranes causing macular pucker. *Am J Ophthalmol* 1991;111:434-438.
6. Michels RG. Vitrectomy for macular pucker. *Ophthalmology* 1984;91:1384-1388.
7. Freeman WR, Azen SP, Kim JW, et al. Vitrectomy for the treatment of full-thickness stage 3 or 4 macular holes: results of a multicentered randomized clinical trial. *Arch Ophthalmol* 1997;115:11-21.
8. Chylack LT Jr, Leske C, McCarthy D, et al. Lens opacity classification system II (LOCS II). *Arch Ophthalmol* 1989;107:991-997.
9. Maraini G, Pasquini P, Tomba M, et al. An independent evaluation of the lens opacities classification system II (LOCS II). *Ophthalmology* 1989;96:611-615.
10. Sawa M, Saito Y, Hayashi A, et al. Assessment of nuclear sclerosis after nonvitrectomizing vitreous surgery. *Am J Ophthalmol* 2001;132:356-362.

11. Ogura Y, Takanashi T, Ishigooka H, et al. Quantitative analysis of lens changes after vitrectomy by fluorophotometry. *Am J Ophthalmol* 1991;111:179-183.
12. Blankenship G, Cortez R, Machemer R. The lens and pars plana vitrectomy for diabetic retinopathy. *Arch Ophthalmol* 1979;97:1263-1267.
13. Novak MA, Rice TA, Michels RG, et al. The crystalline lens after vitrectomy for diabetic retinopathy. *Ophthalmology* 1984;91:1480-1484.
14. Michels RG. Surgical management of epiretinal membranes. *Trans Ophthalmol Soc U K* 1979;99:54-62.
15. Margherio RR, Cox MS Jr, Trese MT, et al. Removal of epimacular membranes. *Ophthalmology* 1985;92:1075-1083.
16. Machemer R. The surgical removal of epiretinal macular membranes (macular puckers). *Klin Monatsbl Augenheilkd* 1978;173:36-42.
17. Wendel RT, Patel AC, Kelly NE, et al. Vitreous surgery for macular holes. *Ophthalmology* 1993;100:1671-1676.
18. Korobelnik JF, Hannouche D, Balayachi N, et al. Autologous platelet concentrate as an adjuct in macular hole healing: a pilot study. *Ophthalmology* 1996;103:590-594.
19. Smiddy WE, Sjaarda RN, Glaser BM, et al. Reoperation after failed macular hole surgery. *Retina* 1996;16:13-18.
20. Ie D, Glaser BM, Thompson JT, et al. Retreatment of full-thickness macular holes persisting after prior vitrectomy. *Ophthalmology* 1993;100:1787-1793.
21. Thompson JT, Smiddy WE, Williams GA, et al. Comparison of recombinant transforming growth factor-beta-2 and placebo as an adjunctive agent for macular hole surgery. *Ophthalmology* 1998;105:700-706.
22. Smiddy WE, Michels RG, Glaser BM, et al. Vitrectomy for macular traction caused by incomplete vitreous separation. *Arch Opththalmol* 1988;106:624-628.
23. Margherio RR, Trese MT, Margherio AR, et al. Surgical management of vitreomacular traction syndrome. *Ophthalmology* 1989;96:1437-1445.
24. Pournaras CJ, Kapetanios AD, Donati G. Vitrectomy for traction macular edema. *Doc Ophthalmol* 1999;97:439-447.
25. Massin P, Erginay A, Haouchine B, et al. Results of surgery of vitreomacular traction syndromes. *J Fr Ophthalmol* 1997;20:539-547.
26. McDonald HR, Johnson RN, Schatz H. Surgical results in the vitreomacular traction syndrome. *Ophthalmology* 1994;101:1397-1402.
27. Van Effenterre G, Ameline B, Campinchi F, et al. Is vitrectomy cataractogenic? Study of changes of the crystalline lens after surgery of retinal detachment. *J Fr Ophthalmol* 1992;15:449-454.
28. Edelhauser HF, Gonnering R, Van Horn DL. Intraocular irrigating solutions. A comparative study of BSS Plus and lactated Ringer's solution. *Arch Ophthalmol* 1978;96:516-520.
29. Stevens VJ, Rouzer CA, Monnier VM, et al. Diabetic cataract formation: potential role of glycosylation of lens crystallins. *Proc Natl Acad Sci U S A* 1978;75:2918-2922.
30. Cheng L, Azen SP, El-Bradey MH, et al. Duration of vitrectomy and postoperative cataract in the vitrectomy for macular hole study. *Am J Ophthalmol* 2001:132:881-887.
31. Michael R. Development and repair of cataract induced by ultraviolet radiation. *Ophthalmic Res* 2000;32(Suppl 1):1-44.
32. Taylor HR, West SK, Rosenthan FS, et al. Effect of ultraviolet radiation on cataract formation. *N Engl J Med* 1989;319(22):1429-1433.
33. Lou MF, Dickerson JE Jr, Tung WH, et al. Correlation of nuclear color and opalescence with protein S-thiolation in human lenses. *Exp Eye Res* 1999;68:547-552.
34. Boscia F, Grattagliano I, Vendemiale G, et al. Protein oxidation and lens opacity in humans. *Invest Ophthalmol Vis Sci* 2000;41:2461-2465.
35. Bron AJ, Vrensen GF, Koretz J, et al. The ageing lens. *Ophthalmologica* 2000;214:86-104.
36. Saito Y, Lewis JM, Park I, et al. Nonvitrectomy vitreous surgery: a strategy to prevent postoperative nuclear sclerosis. *Ophthalmology* 1999:106:1541-1545.
37. Hsuan JD, Brown NA, Bron AJ, et al. Posterior subcapsular and nuclear cataract after vitrectomy. *J Cataract Refract Surg* 2001;27:437-444.
38. Chylack LT Jr, Wolfe JK, Singer DM, et al. The Lens Opacities Classification System III. The Longitudinal Study of Cataract Study Group. *Arch Ophthalmol* 1993:111:831-836.
39. Melberg NS, Thomas MA. Nuclear sclerotic cataract after vitrectomy in patient younger than 50 years of age. *Ophthalmology* 1995;102:1466-1471.
40. Age-Related Eye Disease Study Research Group. The Age-Related Eye Disease Study (AREDS) system for classifying cataract from photographs: AREDS report No. 4. *Am J Ophthalmol* 2001;131:167-175.
41. Braccio L, Camparini M, Baratta GP, et al. An independent evaluation of the Age-Related Eye Disease Study (AREDS) cataract grading system. *Curr Eye Res* 1998;17:53-59.
42. Thompson JT, Glaser BM, Sjaarda RN, et al. Progression of nuclear sclerosis and long-term visual results of vitrectomy with transforming growth factor beta-2 for macular holes. *Am J Ophthalmol* 1995;119:48-54.
43. Motulsky H. *Intuitive Biostatistics*. New York: Oxford University Press, 1995:259.
44. Banach MJ, Hassan TS, Cox MS, et al. Clinical course and surgical treatment of macular epiretinal membranes in young subjects. *Ophthalmology* 2001;108:23-26.
45. Blodi BA, Paluska SA. Cataract after vitrectomy in young patients. *Ophthalmology* 1997;104:1092-1095.
46. Benson WE, Brown GC, Tasman W, et al. Extracapsular cataract extraction, posterior chamber lens insertion and pars plana vitrectomy in one operation. *Ophthalmology* 1990:97:918-921.
47. Koenig SB, Han DP, Mieler WF, et al. Combined phacoemulsification and pars plana vitrectomy. *Arch Ophthalmol* 1990;108:362-364.
48. Jun Z, Pavlovic S, Jacob KW. Results of combined vitreoretinal surgery and phacoemulsification with intraocular lens implantation. *Clin Exp Ophthalmol* 2001;29:307-311.
49. Lahey JM, Francis RR, Fong DS, et al. Combining phacoemulsification with vitrectomy for treatment of macular holes. *Br J Ophthalmol* 2002;86:876-878.
50. Rahman R, Rosen PH. Pupillary capture after combined management of cataract and vitreoretinal pathology. *J Cataract Refract Surg* 2002;28:1607-1612.

51. Shinoda K, O'hira A, Ishida S, et al. Posterior synechia of the iris after combined pars plana vitrectomy, phacoemulsification and intraocular lens implantation. *Jpn J Ophthalmol* 2001;45:276-280.
52. Suzuki Y, Sakuraba T, Mizutani H, et al. Postoperative complications after simultaneous vitrectomy and cataract surgery. *Ophthalmic Surg Lasers* 2001;32:391-396.