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# Change in refraction after lens-sparing vitrectomy for rhegmatogenous retinal detachment and epiretinal membrane

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**Abstract**

The aim of this study was to compare changes in refraction following lens-sparing vitrectomy between patients with rhegmatogenous retinal detachment (RRD) and epiretinal membrane (ERM) and to investigate factors associated with the change in refraction.

We reviewed medical records of 49 eyes of 49 patients with RRD (53.6 ± 7.8 years, mean ± standard deviation) and 24 eyes of 24 patients with ERM (50.9 ± 15.7 years) who underwent lens-sparing vitrectomy. Spherical equivalent refractive power was evaluated before and up to 18 months after surgery. The relationship between the change in refraction and several parameters was evaluated.

A significant progressive myopic shift in refractive power was observed after vitrectomy in operated RRD and ERM eyes ($P < 0.001$, $P = 0.016$, respectively), with no significant difference in fellow eyes. The refraction values observed at ≥3 and ≥12 months following vitrectomy were significantly different as compared with those observed at baseline in the RRD group ($P < 0.001$) and the ERM group ($P < 0.05$), respectively. The change in refraction between the RRD and ERM groups was significant ($P = 0.030$). The multiple linear regression analysis showed that only age was significantly correlated with the change in refraction in RRD ($P = 0.018$) and ERM ($P < 0.001$) groups. The change in refraction was significantly and positively correlated with age in RRD ($r = -0.461$, $P = 0.001$) and ERM ($r = -0.687$, $P < 0.001$) groups. Following lens-sparing vitrectomy, cataract surgery was performed on 30 eyes after 0.89 ± 0.26 years in the RRD group and on 10 eyes after 1.11 ± 0.14 years in the ERM group; there was a significant difference in time to cataract surgery between the groups ($P = 0.007$). Kaplan–Meier survival analysis demonstrated that there was a significant difference in the rate of cataract surgeries between the RRD and ERM groups ($P = 0.022$).

Following lens-sparing vitrectomy for RRD and ERM, a progressive myopic shift in refraction owing to nuclear sclerosis was observed. Core vitrectomy itself would cause a myopic shift of refraction. The only risk factor associated with cataract progression following lens-sparing vitrectomy is age for both types of patients.

**Abbreviations:** C3F8 = octafluoropropane, ERM = epi-retinal membrane, ILM = internal limiting membrane, IOP = intraocular pressure, RRD = rhegmatogenous retinal detachment, SER = spherical equivalent refraction, SF6 = sulfur hexafluoride.

**Keywords:** cataract, epiretinal membrane, lens-sparing vitrectomy, nuclear sclerosis, refraction, rhegmatogenous retinal detachment, vitreous

*Editor: Alparslan Sahin.*

*Contributions of authors: TI contributed in design and conduct of the study; TI, KY, and MK contributed in the collection of data; TI, KY, ER, and HT contributed in management, analysis, and interpretation of data; TI, KY, MK, ER, and HT contributed in preparation, review, and approval of the manuscript.*

*This work was supported by a Grant-in-Aid for Scientific Research (C) (TI) and a Grant-in-Aid for Scientific Research (B) (HT).*

*This manuscript is an original submission and has not been considered elsewhere.*

*The authors report no conflicts of interest.*

*Supplemental Digital Content is available for this article.*

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*Medicine (2016) 95:32(e4317)*

*Received: 30 December 2015 / Received in final form: 7 May 2016 / Accepted: 14 June 2016*

*http://dx.doi.org/10.1097/MD.0000000000004317*

## 1. Introduction

Vitrectomy was first developed by Machemer et al in 1971.[1] Vitrectomy has revolutionized the treatment of posterior segment disorders and improved visual outcomes in patients with retinal diseases requiring surgical intervention. During vitrectomy surgery, 3 small incisions are made in the eye to enable the placement of instruments: a vitreous cutter, a fiberoptic light source to illuminate the inside of the eye, and an infusion cannula to maintain proper intraocular pressure (IOP) during the surgery. Lens-sparing vitrectomy is a procedure in which only vitrectomy is performed for the phakic eye with the lens being retained. These procedures could compromise visual acuity by inducing cataract development or progression in the phakic eyes.

The occurrence of progressive nuclear cataract after lens-sparing vitrectomy was first described in patients undergoing vitrectomy for proliferative diabetic retinopathy.[2] Since then, many reports have described the development of nuclear cataract following lens-sparing vitrectomy.[3–6] In a series of 75 patients, the cumulative incidence of progressive nuclear sclerosis was 72% in the operated eye and 15% in the fellow eye after 24 months.[7,8]

Following lens-sparing vitrectomy, the lens develops a fast and persistent clouding of the nucleus in almost all eyes, resulting in a myopic shift in the refractive state of the eye.[9] However, there are few reports describing a myopic shift following surgery.

Tseng et al[10] were the first to report on a myopic shift after lens-sparing vitrectomy; however, the study did not involve longitudinal evaluation. Okamoto et al[11] evaluated refractive changes following lens-sparing vitrectomy for rhegmatogenous retinal detachment (RRD) and found that a significant myopic progression occurred from the early postoperative period. However, patients who underwent cataract surgery because of a myopic shift and anisometropia by the progression of nuclear sclerotic cataracts dropped out from the study, which resulted in the number of the remaining eyes becoming smaller; therefore, the mean refraction value over time did not reflect the actual situation. Therefore, it is difficult to evaluate the relationship between the actual change in refraction and other factors in such situations.

It has been reported that nuclear cataract develops more rapidly following lens-sparing vitrectomy plus gas tamponade.[12] Various procedures are required for the treatment of RRD by vitrectomy, such as sufficient vitrectomy to the periphery, fluid-gas exchange, and endo-photocoagulation. However, the vitrectomy procedure for the epiretinal membrane (ERM) is simpler, typically only involving core vitrectomy and ERM peeling. In core vitrectomy, vitreous near the lens is undisturbed and this type of vitrectomy incurs fewer complications than general vitrectomy because of the selective removal of the vitreous material. Therefore, a comparison of the change in refraction between RRD and ERM following lens-sparing vitrectomy may reveal which vitrectomy procedure causes a faster progression of cataract and severe myopic shift.

Thus, the purpose of this study was to evaluate the changes in refraction over time following lens-sparing vitrectomy for RRD and ERM and to investigate the factors associated with these changes.

## 2. Methods

### 2.1. Ethics statement

This study was conducted in adherence with the tenets of the Declaration of Helsinki. This was a retrospective, observational comparative, single-center study, and the procedures were approved by the Institutional Review Board and the Ethics Committee of the Nagoya University Graduate School of Medicine (Nagoya, Japan).

### 2.2. Subjects

We reviewed the medical records of all patients who underwent lens-sparing vitrectomy for RRD or ERM at the Nagoya University Hospital from January 2008 to January 2014. Identical measurements were performed in fellow eyes as controls. To be included in the study, patients had to have primary RRD or idiopathic ERM and be phakic. The visual acuity was 20/20 or more than 20/20 in the fellow eye, and the lens did not have obvious opacification in both the operated and fellow eyes. Accordingly, none of the eyes were judged as having a significant visual disturbance because of cataract at the time of surgery. All patients signed an informed consent form before surgery.

All patients underwent a comprehensive ophthalmic examination including measurement of IOP, slit-lamp examination, fundus examination, and optical coherence tomography preoperatively as well as refraction analysis at 1, 3, 6, 12, and 18 months following lens-sparing vitrectomy. Refraction was measured with a refractometer (RK-2; Canon Inc, Tokyo, Japan), and the spherical equivalent refraction (SER) was calculated using the formula SER = sphere + 0.5 cylinder.

We evaluated the change in refraction using a mixed linear model to incorporate appropriate covariates between repeated measured values over time, and the selected order of polynomials was used to evaluate the correlation between the change in refraction and independent variables.

When the refractive power could not be measured before lens-sparing vitrectomy because of macular detachment or vitreous hemorrhage, the refraction obtained at the first post-vitrectomy visit (postoperative 1–2 weeks) was defined as the baseline refraction.

Patients with proliferative vitreo-retinopathy grade C or greater[13] in the RRD group; those with a history of ocular surgery, diabetes, or ocular disease that could affect refraction, and/or those with visual function were excluded from this study. In addition, eyes subject to endophotocoagulation were excluded in the ERM group.

### 2.3. Surgical technique

Standard 3-port PPV was performed with either 20-, 23-, or 25-gauge instruments after retrobulbar anesthesia with 2.5 mL of 2% lidocaine and 2.5 mL of 0.5% bupivacaine. None of the patients had concurrent scleral buckling surgery.

A trocar was inserted at an angle of approximately 30 degree parallel to the limbus. Once the trocar was past the trocar sleeve, the angle was changed to be perpendicular to the surface. After developing the 3 ports, vitrectomy was performed using the Constellation system (Alcon Laboratories, Inc, Fort Worth, TX).

In eyes with RRD, after complete removal of the vitreous to the periphery, fluid-air exchange and subretinal fluid drainage from the causative retinal tear(s) or iatrogenic hole were performed, and endophotocoagulation was applied to the causative retinal tear(s) or iatrogenic hole (if present). Gas consisting of 20% sulfur hexafluoride ($SF_6$) or 12% octafluoropropane ($C_3F_8$) was injected into the vitreous upon completion of the vitrectomy.

In eyes with ERM, after core vitrectomy, the ERM and internal limiting membrane (ILM) were peeled from the retina using ILM-peeling forceps (25 + Grieshaber revolution DSP ILM forceps, Alcon Laboratories). Next, air was administered into the vitreous cavity to close the scleral port, if needed.

After the IOP was adjusted to normal tension, the cannulas were withdrawn. The sclera was pressed and massaged with an indenter or sutured with 8–0 vicryl to close the wound.

### 2.4. Statistical analysis

We evaluated the changes in refraction using a mixed model to incorporate appropriate covariates between repeated measured values over time.

Specifically, we assumed the following model:

$$y_{ij} = a_i + f(t_j, G_i : b) + \varepsilon_{ij}$$

i(subject) = 1, . . . ,73, j(time) = 0, 1, 3, 6, 12, 18, 24 where $y_{ij}$ is the refraction value at time j on subject i. $a_i$ is a subject-specific random effect, $G_i = 1$ indicates ERM and 0 indicates RRD. The function $f(t_j{:}b)$, which represents a fixed effect of time on the refraction, was specified as a polynomial function:

$$\begin{aligned} f(t_j, G_i : b) &= b_0 + b_1 G_i + b_{11} t_j + b_{12} t_j G_i + b_{21} t_j^2 + b_{22} t_j^2 G_i + \cdots \\ &\quad + b_{k1} t_j^k + b_{k2} t_j^k G_i. \end{aligned}$$

**Table 1**

**Patients' demographics and surgical characteristics in patients undergoing lens-sparing vitrectomy.**

| Characteristic | RRD (n=49) | ERM (n=24) | P |
|---|---|---|---|
| Age, y | 53.6±7.8 | 50.9±15.7 | 0.291 |
| Sex (male/female) | 36/13 | 13/11 | 0.108 |
| Axial length, mm | 26.9±1.8 | 24.9±1.6 | <0.001 |
| Base line refraction (diopter) | -5.8±3.7 | −3.1±3.8 | 0.005 |
| 20/23/25 gauge vitrectomy | 19/11/19 | 7/6/11 | 0.723 |
| Use of triamcinolone acetonide (yes/no) | 38/11 | 17/7 | 0.542 |
| Photocoagulation burns | 1183±940 | 0 | <0.001 |
| Operation time, min | 103.5±31.3 | 50.7±15.7 | <0.001 |
| None/air /$SF_6$ | 0/0/49 | 12/12/0 | <0.001 |

ERM=epi-retinal membrane, RRD=rhegmatogenous retinal detachment, SF6=sulfur hexafluoride.

The parameters *b's* represent fixed time effects and interaction between time and group effects, respectively. The order of polynomials in f($t_j$,$G_i$:b) was selected on the basis of the Akaike information criteria (AIC). For the residual term εij of the refraction value, we assumed a heterogeneous compound symmetry structure within patients.

$\chi^2$ tests were used to compare categorical data, and independent *t* tests were used to compare normally distributed data. Repeated 1-way analysis of variance with post hoc Bonferroni corrections was used to evaluate changes in refraction. Pearson correlation coefficient test was used to determine the correlation between age and the slope of the refraction change. Multiple linear regression analysis was used to evaluate the correlation between the change in refraction and independent variables such as age, axial length, sex, operation time, and use of tamponade. All statistical analyses were performed with SAS9.4 (SAS Inc, Cary, NC). A *P* value <0.05 was considered statistically significant.

## 3. Results

### 3.1. Patient demographics and surgical characteristics

The demographics and surgical characteristics of all patients are shown in Table 1, demonstrating the mean±standard deviation of the continuous variables. Forty-nine eyes of 49 patients with RRD (mean age, 53.6±7.8 years) and 24 eyes of 24 patients with ERM (mean age, 50.9±15.7 years) were studied. There were significant differences in the axial length ($P<0.001$), base line refraction ($P=0.005$), operation time ($P<0.001$), and use of tamponade ($P<0.001$) between the 2 groups.

### 3.2. Refractive changes in eyes with RRD and ERM

Table 2 demonstrates the time course of the mean refraction value following lens-sparing vitrectomy for RRD and ERM. The operated eyes demonstrated a significant progressive myopic shift in both RRD ($P<0.001$) and ERM ($P=0.016$) groups. The mean refraction values observed at ≥3 and ≥12 months following vitrectomy were significantly different compared with those observed at baseline in the RRD group ($P<0.001$) (Fig. 1) and the ERM group ($P<0.05$), respectively. Meanwhile, the mean refraction values in the contralateral eyes were stable throughout the study period (Fig. 1, Table 2).

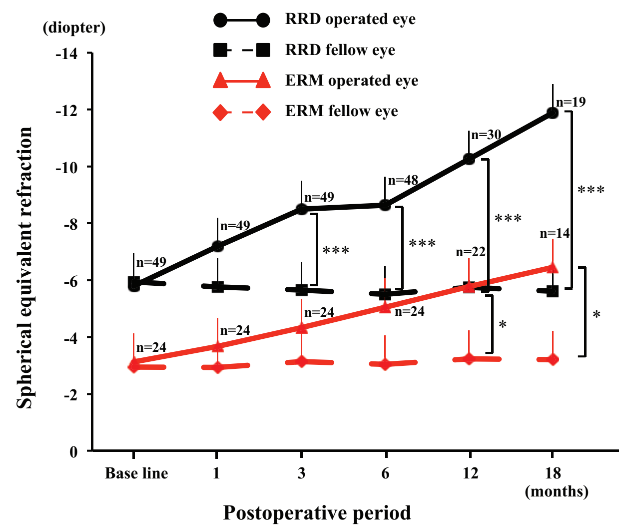


Figure 1. Changes in the spherical equivalent refraction over time in eyes following lens-sparing vitrectomy for rhegmatogenous retinal detachment (RRD) and epi-retinal membrane (ERM). The refraction of operated eyes progressively significantly moved towards a myopic shift in both RRD and ERM patients. n indicates the number of eyes measuring the refraction value at each time point. Values are presented as means±standard error (SE). ***$P<0.001$, *$P<0.05$.

The change in this refraction value over time can be best described by a linear regression equation based on AIC using a linear mixed model (Table 3). Therefore, the progression rate of the refractive value in each case was calculated as the slope of refractive changes over time using a linear regression equation (see supplement figure S1, http://links.lww.com/MD/B178). The mean progression rate of the refractive value was −0.40 (diopter/month) in the RRD group and −0.28 (diopter/month) in the ERM group (Table 4). Moreover, there was a significant progression rate of refraction between patients in the RRD and the ERM groups ($P=0.030$) (Fig. 2), whereas no significant progression rate of refraction was observed between ERM air tamponade (+) and ERM air tamponade (−) patients.

The results of the multiple linear regression analysis of the progression rate of refraction in the RRD group and the ERM group are shown in Tables 5 and 6, respectively. Only age significantly correlated with the progression rate of refraction in

**Table 2**

**Change of refraction after lens-sparing vitrectomy.**

| | | Base line | Month 1 | Month 3 | Month 6 | Month 12 | Month 18 | *P*-value |
|---|---|---|---|---|---|---|---|---|
| RRD | Operated eye | −5.8±3.6 | −7.2±3.9 | −8.4±3.7 | −8.5±3.8 | −10.25±5.4 | −11.9±7.3 | <0.001 |
| | Fellow eye | −5.6±3.2 | −5.8±3.3 | −5.6±2.8 | −5.5±2.9 | −5.7±4.0 | −5.6±3.1 | 0.994 |
| ERM | Operated eye | −3.1±3.9 | −3.7±3.8 | −4.3±3.8 | −5.0±4.2 | −5.8±4.3 | −6.5±6.1 | 0.016 |
| | Fellow eye | −2.9±3.5 | −2.9±3.4 | −3.1±3.6 | −3.0±4.0 | −3.2±3.7 | −3.2±3.8 | 0.910 |

One-way analysis of variance was used to evaluate the change of each parameter with time. ERM=epi-retinal membrane, RRD=rhegmatogenous retinal detachment.

**Table 3**

**Comparing polynomial equation and the Akaike information criteria.**

| Polynomial equation | Akaike information criteria |
|---|---|
| linear regression equation (k=1) | 1508.1 |
| quadratic polynomial equation (k=2) | 1508.2 |
| cubic polynomial equation (k=3) | 1525.6 |

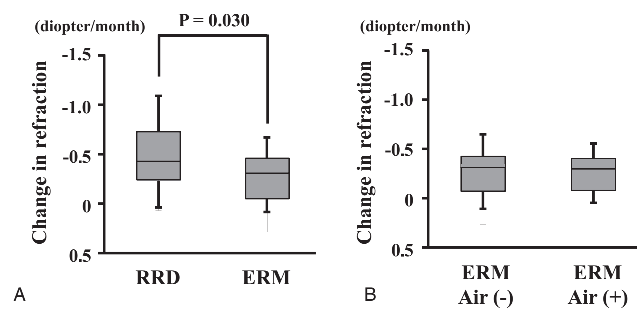


Figure 2. Box-and-whisker plot of differences in refraction changes following lens-sparing vitrectomy. The bottom and top of the box are the first and third quartiles, and the band inside the box is the median. The ends of the whiskers represent the minimum and maximum of all the data. The change in refraction was significantly higher in the rhegmatogenous retinal detachment (RRD) group than in the epiretinal membrane (ERM) group ($P=0.030$) (A). There was no significant difference in the change in refraction between ERM air tamponade (+) and ERM air tamponade (–) patients (B).

the RRD group ($P=0.018$) and the ERM group ($P<0.001$). The progression rate of refraction significantly and positively correlated with age both in the RRD ($r=-0.461$, $P=0.001$; Fig. 3A) and ERM groups ($r=-0.687$, $P<0.001$; Fig. 3B).

### *3.3. Frequency of cataract surgery in eyes with RRD and ERM*

The type of cataract was nuclear sclerosis in all of the eyes, and none of the eyes had cortical and posterior subcapsular cataract. Following lens-sparing vitrectomy, cataract surgery was performed on 30 eyes 0.89±0.26 years after in the RRD group and in 10 eyes 1.11±0.14 years after in the ERM group, and there was a significant difference in time to cataract surgery between the groups ($P=0.007$, Table 7).

In the RRD group, patients who underwent cataract surgery were 55.3±6.1 years' old and those who did not undergo surgery were 49.2±10.3 years' old ($P=0.016$) (Fig. 4). In the ERM group, patients who underwent cataract surgery were 58.4±6.7 years' old, whereas those who did not undergo surgery were 38.4±18.5 years' old ($P<0.001$).

Kaplan–Meier survival analysis demonstrated that there was a significant difference in the rate of cataract surgery between the RRD and ERM groups ($P=0.022$, Fig. 5).

**Table 5**

**Results of multiple regression analysis of factors independently contributing to the progression rate of refraction in RRD group.**

| Variable | | | |
|---|---|---|---|
| Dependent | Independent | β | *P* |
| Refraction change | Age | −0.425 | 0.018 |
| | Axial length | −0.351 | 0.053 |
| | Sex | −0.221 | 0.181 |
| | Operation time | −0.100 | 0.533 |
| | Tamponade | 0.012 | 0.940 |

RRD=rhegmatogenous retinal detachment.

**Table 6**

**Results of multiple regression analysis of factors independently contributing to the progression rate of refraction in ERM group.**

| Variable | | | |
|---|---|---|---|
| Dependent | Independent | β | *P* |
| Refraction change | Age | −0.736 | <0.001 |
| | Sex | −0.344 | 0.067 |
| | Operation time | −0.304 | 0.088 |
| | Axial length | −0.075 | 0.668 |
| | Tamponade | −0.031 | 0.853 |

ERM=epiretinal membrane.

## 4. Discussion

Our results showed a significant and progressive myopic shift in eyes with RRD and ERM compared with fellow eyes over the 18 months following lens-sparing vitrectomy. Linear single regression analysis showed that the progression rate of refraction, that is, the change in refraction, correlated with age in both groups. The multiple stepwise regression analysis revealed that age was an independent factor, indicating a change in refraction in both groups. In addition, patients undergoing cataract surgery were significantly older than those who did not undergo cataract surgery in both the RRD and ERM groups; moreover, Kaplan–Meier survival analysis demonstrated that eyes in the RRD groups underwent cataract surgery earlier and at a higher rate than those in the ERM groups.

Nuclear sclerotic cataract following lens-sparing vitrectomy morphologically and histologically resembles age-related cata-

**Table 4**

**Linear regression analysis of the relation between changes of refraction and time.**

| Variable | Category | Coefficient | 95% CI | | *P* |
|---|---|---|---|---|---|
| Intercept ($b_0$) | | −7.1471 | −8.1110 | −6.1833 | <0.0001 |
| Time ($b_1$) | | −0.4034 | −0.4628 | −0.3439 | <0.0001 |
| Group ($b_2$) | ERM | 3.4330 | 1.7650 | 5.1009 | 0.0001 |
| | RRD | 0 | – | – | |
| Time × group ($b_3$) | ERM | 0.1187 | 0.0189 | 0.2185 | 0.0202 |
| | RRD | 0 | – | – | |

Prediction formula: refraction $= b_0 + b_1$ (time) $+ b_2$(group) $+ b_3$ (time) × (group). ERM refraction = −7.1471 −0.4034 (time) + 3.4330 + 0.1187 (time) = −3.7141 −0.2847 (time). RRD refraction = −7.1471 − 0.4034 (time). ERM=epiretinal membrane, RRD=rhegmatogenous retinal detachment.

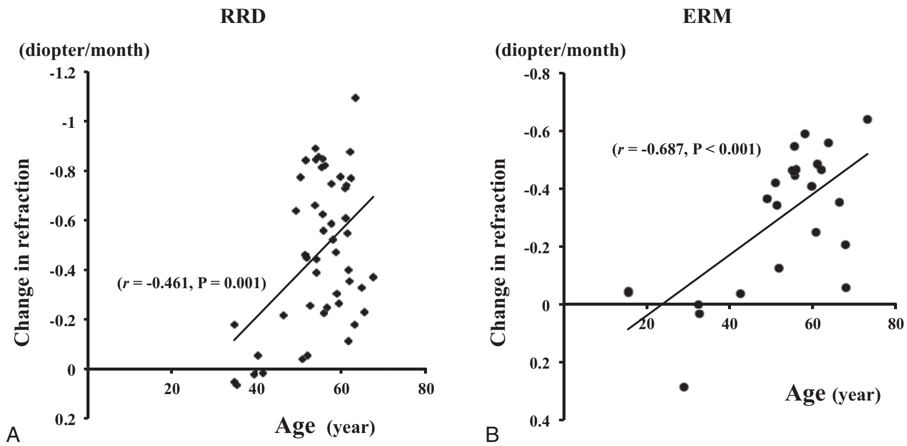


**Figure 3.** Relationship between age and change in refraction following lens-sparing vitrectomy for rhegmatogenous retinal detachment (RRD) and epiretinal membrane (ERM). The change in refraction was significantly and negatively correlated with age in both RRD ($r=-0.461$, $P=0.001$) and ERM ($r=-0.687$, $P<0.001$) patients.

**Table 7**

**Patients undergoing cataract surgery after lens-sparing vitrectomy.**

| Parameters | RRD | ERM | P |
|---|---|---|---|
| Cataract surgery (+/−) | 30/19 | 10/14 | 0.119 |
| Time to cataract surgery, y | 0.89 ± 0.26 | 1.11 ± 0.14 | 0.007 |

ERM = epiretinal membrane, RRD = rhegmatogenous retinal detachment.

ract, but exhibits a much faster progression. Cataract can be classified into 3 types according to the location of the opacity: cortical, nuclear sclerotic, and posterior subcapsular.[14] Vitrectomy causes the progression of nuclear sclerotic cataract, leading to increased lens opacity and myopic shift.[15,16] Wong et al[12] quantified nuclear sclerosis progression using Scheimpflug image analysis in patients undergoing surgery for idiopathic full-thickness macular hole and found that the increase in nuclear density from baseline was 24 times greater in the surgical group than in the observation group at 6 months. Okamoto et al observed a significant and continuous myopic shift because of nuclear sclerosis developing after vitrectomy for the treatment of RRD throughout the study period.[11] In the present study, the cataract type was nuclear sclerosis in all of the eyes, and the mean refraction significantly and progressively moved toward a myopic shift over time in the ERM group as well as in the RRD group following lens-sparing vitrectomy. Our results are in concordance with previous reports.

Patients having a stronger visual disturbance from myopic shift and anisometropia by the progression of nuclear sclerotic cataracts following lens-sparing vitrectomy tend to undergo earlier cataract surgeries. In such situations, patients with higher myopic-shifted eyes typically drop out from studies, which results in the fact that the mean change in refraction in the remaining eyes does not reflect the overall change. Therefore, we assessed what polynomial function was the best fitting for the change in

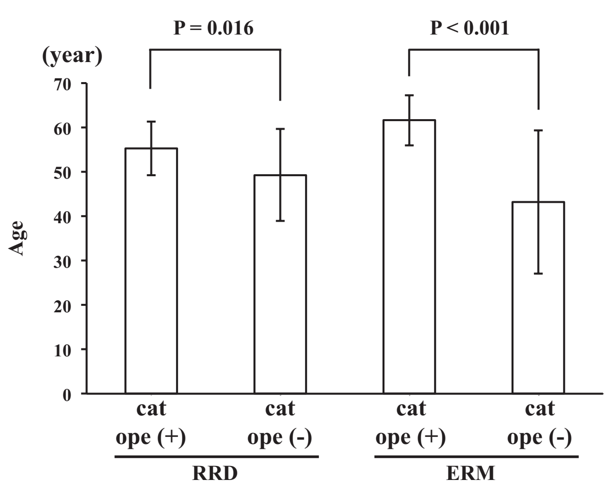


**Figure 4.** Comparison of the age of patients undergoing and not undergoing cataract surgery. There was a significant difference in the age between patients who underwent cataract surgery and those who did not undergo cataract surgery in the RRD group ($P=0.016$) and in the ERM group ($P<0.001$). Values are presented as means ± standard deviation (SD).

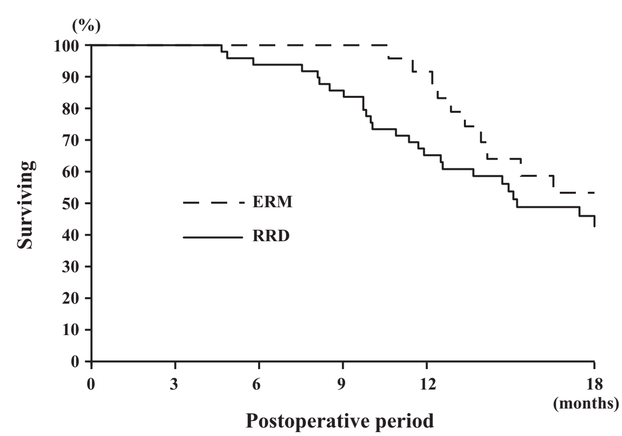


**Figure 5.** Kaplan–Meier survival curves showing the cumulative proportion of patients undergoing cataract surgery with respect to rhegmatogenous retinal detachment (RRD) and epiretinal membrane (ERM) following lens-sparing vitrectomy. There was a statistically significant difference between the RRD and the ERM group ($P=0.022$).

the refraction value over time using a mixed linear model, which can incorporate appropriate covariates between repeated measured values over time and can use all the observed data even under the condition of missing at random. Moreover, a linear regression equation was used for selection of the best fitting for the change in refraction over time in both the RRD and ERM groups. Therefore, we used the progression rate in refraction as a measure for the change in refraction to resolve the inherent problem in such studies. We found that the change in refraction correlated only with age by single and multiple regression analyses in both groups.

It has been reported that several factors are associated with cataract progression after lens-sparing vitrectomy, including the gauge of the vitrectomy system, operation time, and the use of gas tamponade.[5,17,18] However, Okamoto et al[11] reported that a change in refraction correlated only with age. Our results show that none of the intraoperative factors mentioned above were significantly associated with cataract progression, thereby corroborating Okamoto results. Patients below the age of 50 years are relatively protected from developing postsurgical accelerated nuclear sclerosis.[5,7] With the progression of nuclear sclerosis of the lens associated with aging, refractive values tend toward myopia in age-related cataract progression.[16,19] Okamoto et al[11] reported that myopia following lens-sparing vitrectomy significantly progressed with age. Our results corroborate the finding that patient age is a significant risk factor for cataract progression. Phacovitrectomy would be an option to resolve this problem when performing vitrectomy in older patients.

Considering the pathogenic mechanism of cataract progression following lens-sparing vitrectomy, several studies have recently suggested that vitrectomy surgery increases oxygen tension within the eye; the partial oxygen pressure is highly elevated in the vitreous cavity following vitrectomy and posterior to the lens because the vitreous is lacking as a diffusion barrier for the oxygen.[20–22] This elevated partial oxygen pressure may lead to increased oxygen stress to the lens and thus to lens opacification by the oxidation of structural proteins. It has been reported that nonvitrectomizing vitrectomy surgery does not cause accelerated postsurgical nuclear sclerotic cataract.[23,24] In the present study, the refraction in the ERM group was subject to a myopic shift, although we merely performed core vitrectomy and ERM and ILM peeling. Our result indicates that core vitrectomy itself can cause oxidative stress and the progression of nuclear sclerosis, corroborating previous results.

There was a significant difference in the change in refraction, time to undergo cataract surgery, and survival rate to undergo cataract surgery between the RRD and ERM groups in the present study. Although age was only correlated with the refraction change within each group, the possibility cannot be denied that the difference in procedures between the groups could cause the progression of nuclear sclerosis. The RRD group should have surgically induced alteration of the lens's biochemical microenvironment. One possibility is that core vitrectomy for ERM results in an amount of vitreous remaining in the ERM group, which would lead to higher intraocular oxygen gradients, lower oxygen delivery to the lens, and slower progress of nuclear sclerosis than the RRD group.

Interestingly, the refraction change in the ERM group was more significantly related to age than in the RRD group, as revealed by single and multiple regression analyses. The correlation coefficient in the RRD group was $r=-0.46$, which is not very high. Moreover, it would be statistically significant only because a large number of patients were included in the analysis. Eyes undergoing intraoperative laser photocoagulation were excluded from the ERM group, which indicates that the vitrectomy procedure for ERM was simple and uniform. However, the procedure used in the RRD group varied widely because the extent of RD and the number of laser photocoagulation burns and tears vary among the cases. These differences may, at least in part, explain the stronger relationship between myopic shift and age in the ERM group.

Taken together, the use of multiple procedures could lead to the progression of nuclear sclerosis, but the resistance to oxidative stress in the lens reduces with aging, which means that older patients may easily be affected by oxidative stress and tend to a faster progression of nuclear sclerosis.

Our study has some limitations such as it being retrospective with a relatively small sample size. Triamcinolone was used for assisting membrane removal, and cataract may develop as a complication. Another limitation was that the clinical criteria for performing cataract surgery were not predefined, which indicates that bias because of subjective decisions made by the patients cannot be rejected. Therefore, some patients with a severe visual disturbance resulting from progressed cataract did not undergo the procedure. A prospective study using a large sample size, objective assessments of crystalline lenses, and objective criteria for cataract surgery are warranted in future studies.

In conclusion, refraction following lens-sparing vitrectomy for RRD and ERM is subject to a progressive myopic shift owing to nuclear sclerosis. The results suggest that core vitrectomy itself could cause a myopic shift in refraction. The only risk factor associated with cataract progression following lens-sparing vitrectomy was age in both RRD and ERM patients.

## References

[1] Machemer R, Buettner H, Norton EW, et al. Vitrectomy: a pars plana approach. Trans Am Acad Ophthalmol Otolaryngol 1971;75:813–20.
[2] Michels RG, Ryan SJJr. Results and complications of 100 consecutive cases of pars plana vitrectomy. Am J Ophthalmol 1975;80:24–9.
[3] 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;111:434–8.
[4] Hsuan JD, Brown NA, Bron AJ, et al. Posterior subcapsular and nuclear cataract after vitrectomy. J Cataract Refract Surg 2001;27:437–44.
[5] Thompson JT. The role of patient age and intraocular gas use in cataract progression after vitrectomy for macular holes and epiretinal membranes. Am J Ophthalmol 2004;137:250–7.
[6] van Effenterre G, Haut J, Larricart P, et al. Gas tamponade as a single technique in the treatment of retinal detachment: is vitrectomy needed? A comparative study of 120 cases. Graefes Arch Clin Exp Ophthalmol 1987;225:254–8.
[7] Melberg NS, Thomas MA. Nuclear sclerotic cataract after vitrectomy in patients younger than 50 years of age. Ophthalmology 1995;102: 1466–71.
[8] de Bustros S, Thompson JT, Michels RG, et al. Nuclear sclerosis after vitrectomy for idiopathic epiretinal membranes. Am J Ophthalmol 1988;105:160–4.
[9] Chang S. LXII Edward Jackson lecture: open angle glaucoma after vitrectomy. Am J Ophthalmol 2006;141:1033–43.
[10] Tseng PCW, Tseng GL, Tsai GL, et al. Refractive change after pars plana vitrectomy. Taiwan J Ophthalmol 2012;2:18–21.
[11] Okamoto Y, Okamoto F, Hiraoka T, et al. Refractive changes after lens-sparing vitrectomy for rhegmatogenous retinal detachment. Am J Ophthalmol 2014;158:544–9. e541.
[12] Wong SC, Clare G, Bunce C, et al. Cataract progression in macular hole cases: results with vitrectomy or with observation. J Cataract Refract Surg 2012;38:1176–80.
[13] Machemer R, Aaberg TM, Freeman HM, et al. An updated classification of retinal detachment with proliferative vitreoretinopathy. Am J Ophthalmol 1991;112:159–65.
[14] Chylack LTJr, Wolfe JK, Singer DM, et al. The Lens Opacities Classification System III. The Longitudinal Study of Cataract Study Group. Arch Ophthalmol 1993;111:831–6.

[15] Wong TY, Foster PJ, Johnson GJ, et al. Refractive errors, axial ocular dimensions, and age-related cataracts: the Tanjong Pagar survey. Invest Ophthalmol Vis Sci 2003;44:1479–85.
[16] Samarawickrama C, Wang JJ, Burlutsky G, et al. Nuclear cataract and myopic shift in refraction. Am J Ophthalmol 2007;144:457–9.
[17] 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;132:881–7.
[18] Almony A, Holekamp NM, Bai F, et al. Small-gauge vitrectomy does not protect against nuclear sclerotic cataract. Retina 2012;32:499–505.
[19] Richter GM, Choudhury F, Torres M, et al. Risk factors for incident cortical, nuclear, posterior subcapsular, and mixed lens opacities: the Los Angeles Latino eye study. Ophthalmology 2012;119:2040–7.
[20] Holekamp NM, Shui YB, Beebe DC. Vitrectomy surgery increases oxygen exposure to the lens: a possible mechanism for nuclear cataract formation. Am J Ophthalmol 2005;139:302–10.
[21] Palmquist BM, Philipson B, Fagerholm P. Nuclear cataract–a microradiographic study. Acta Ophthalmol (Copenh) 1988;66:671–7.
[22] Barbazetto IA, Liang J, Chang S, et al. Oxygen tension in the rabbit lens and vitreous before and after vitrectomy. Exp Eye Res 2004;78:917–24.
[23] Sawa M, Saito Y, Hayashi A, et al. Assessment of nuclear sclerosis after nonvitrectomizing vitreous surgery. Am J Ophthalmol 2001;132:356–62.
[24] Saito Y, Lewis JM, Park I, et al. Nonvitrectomizing vitreous surgery: a strategy to prevent postoperative nuclear sclerosis. Ophthalmology 1999;106:1541–5.