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Outcomes and predictive factors after cataract surgery in patients with neovascular age-related macular degeneration. The Fight Retinal Blindness! Project

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**Outcomes and predictive factors after cataract surgery in patients with neovascular age-related macular degeneration. The Fight Retinal Blindness! Project**

**Purpose:** To evaluate outcomes and predictive factors of visual acuity (VA) change after cataract surgery in patients being treated for neovascular age-related macular degeneration (nAMD).

**Design:** Retrospective, matched case-control study.

**Methods:** We studied eyes undergoing cataract surgery that had been tracked since they first started treatment for nAMD. These eyes were compared with a cohort of unoperated phakic eyes being treated for nAMD (three per case) matched for treatment duration before cataract surgery, baseline VA, age and length of follow-up.

**Results:** We included 124 patients that had cataract surgery and 372 matched controls. The mean (95% CI) VA gained was 10.6 letters (7.8, 13.2;  $P < 0.001$ ) 12 months following surgery; 26.0% had gained  $\geq 3$  lines and 1.6% had lost  $\geq 3$  lines of VA. Visual acuity (mean [SD]) 12 months after surgery was higher in eyes that had cataract extraction compared with controls (65.8 [17.1] vs. 61.3 [20.8] letters respectively,  $P = 0.018$ ). The proportion of visits where the choroidal neovascular (CNV) lesion was graded active and the mean number of injections were similar before and after surgery ( $P = 0.506$  and  $P = 0.316$ , respectively), while both decreased in the control group, suggesting that surgery modestly increased the level of activity of the CNV lesion. Mean [SD] VA prior to surgery was lower in eyes that gained  $\geq 15$  letters compared with eyes that gained 0-14 letters (40.2 [21.4] vs. 62.1 [15.1],  $P < 0.001$ ). Patients undergoing cataract surgery within the first 6 months of anti-VEGF therapy were more likely to lose rather than gain vision (20.8% lost vision vs. 12.8% and 4.4% gaining  $\geq 15$  or 0-14 letters respectively,  $P = 0.023$ ). Age, receiving an injection at least 2 weeks before surgery, and the CNV lesion type had no discernible association with VA outcomes.

**Conclusions:** We found evidence of a modest effect of cataract surgery on CNV lesion activity in eyes being treated for nAMD. Despite this, visual outcomes were reassuringly good. Cataract surgery within 6 months of starting treatment for nAMD should be avoided if possible.

1 **Outcomes and predictive factors after cataract surgery in patients with neovascular**  
2 **age-related macular degeneration. *The Fight Retinal Blindness! Project***

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22

## 1 Introduction

2 Cataract and age-related macular degeneration (AMD), common causes of reduced  
3 vision, often occur together in elderly people. The prevalence of late AMD, including  
4 neovascular AMD (nAMD) or geographic atrophy, and cataract in the same eye after  
5 80 years of age in the USA has been estimated at 12% and 68%, respectively.<sup>1,2</sup>

6 A recent Cochrane collaboration report could not draw reliable conclusions from the  
7 available data on whether cataract surgery was beneficial or harmful in people with  
8 dry AMD. Although cataract surgery has been reported to provide better visual  
9 outcomes in eyes with AMD 6 months after surgery compared with eyes that were  
10 observed, it is unclear whether the timing of surgery in relation to commencement of  
11 treatment for AMD influences long-term outcomes.<sup>3</sup>

12 Visual acuity (VA) improvement after cataract surgery was less in patients with  
13 nAMD than in patients without retinal disease in the Age-Related Eye Disease  
14 Study.<sup>4</sup> A history of intravitreal injections (IVT) may be a risk factor for complications  
15 of cataract surgery, including intra-operative posterior capsule rupture<sup>5</sup> and post-  
16 operative endophthalmitis.<sup>6</sup> Cataract surgery may increase the risk of progression to  
17 choroidal neovascularization (CNV) in eyes with intermediate AMD;<sup>7</sup> it may also  
18 activate existing CNV through inflammatory mediators released at the time of  
19 surgery.

20 Data on how cataract surgery influences the course of treatment of patients with  
21 nAMD receiving intravitreal vascular endothelial growth factor (VEGF) inhibitors are  
22 encouraging.<sup>8-14</sup> However, many of the reports on cataract surgery outcomes in eyes  
23 with nAMD lack a control group, making it difficult to estimate the effect of cataract  
24 surgery on injection frequency or lesion activity post cataract surgery.

25 The aim of this study was to evaluate the long-term change in VA after cataract  
26 surgery in nAMD and to compare outcomes with a control group matched for similar  
27 baseline characteristics. The secondary objective was to evaluate the CNV lesion  
28 activity and number of anti-VEGF injections before and after cataract surgery. We  
29 also assessed factors that predicted VA outcomes.

30

## 31 Methods

1 This study followed the STROBE checklist items for reporting observational data.<sup>15</sup>

## 2 ***Study Design***

3 Retrospective, matched case-control analysis performed of data from a prospectively  
4 designed observational database study.

## 5 ***Setting***

6 Data were obtained from the Fight Retinal Blindness! (FRB!) observational database  
7 which tracks outcomes of nAMD and is compliant with the International Consortium  
8 for Healthcare Outcome Measures (ICHOM) macular degeneration standard set.<sup>16</sup>  
9 Ethics approval was obtained from the Human Research Ethics Committees of the  
10 Royal Victorian Eye and Ear Hospital, the Royal Australian and New Zealand  
11 College of Ophthalmologists, the University of Sydney, and the Cantonal Ethics  
12 Committee Zurich, Switzerland. This study adhered to the tenets of the Declaration  
13 of Helsinki. This study included patients from Australia, New Zealand and  
14 Switzerland.

## 15 ***Data Sources/Measurements***

16 Details of the FRB! database have been published elsewhere.<sup>17</sup> Briefly, data were  
17 obtained from each clinical visit, including: the number of letters read on a logarithm  
18 of the minimum angle of resolution (LogMAR) VA Chart (best of uncorrected,  
19 corrected with the current spectacle or according to the refraction, or pinhole);  
20 treatment given, if any; lesion activity (lesions were graded at each visit as active “if  
21 there was intraretinal or subretinal fluid attributable to leak from choroidal  
22 neovascularisation lesion or fresh hemorrhage”); additional procedures including  
23 cataract surgery; ocular adverse events. Lesion size (greatest linear dimension),  
24 lesion type and prior treatment, if any, were recorded during the baseline visit (when  
25 intravitreal therapy for nAMD was started). Treatment decisions, including drug  
26 choice and treatment regimen, were at the discretion of the treatment physician,  
27 thereby reflecting routine clinical practice.

## 28 ***Participants***

29 Treatment-naïve phakic eyes with nAMD tracked by the FRB! registry commencing  
30 anti-VEGF therapy between Jan. 1, 2006 and May. 7, 2014 and undergoing cataract

1 surgery were considered for this analysis. Analysis of outcomes also required that  
2 eyes have at least 12 months of follow-up prior to and following cataract surgery.

3 A cohort of phakic eyes from the FRB! database that did not undergo cataract  
4 surgery was used to assess the effect of cataract surgery on the course of nAMD.  
5 This cohort consisted of three phakic controls per case matched on the following  
6 characteristics: treatment duration before cataract surgery, baseline VA and baseline  
7 age and length of follow-up. The controls had no history of cataract surgery and no  
8 surgery during the study period. Matched controls were only identified for cases that  
9 had at least 12 months of follow-up prior to and following cataract surgery to  
10 compare visual outcomes before and after surgery.

### 11 **Outcomes**

12 The primary outcome was the change in VA 12 months following cataract surgery.  
13 We also analyzed the proportion of eyes that gained  $\geq 15$  or lost  $\geq 15$  letters from pre-  
14 operative VA.

15 Secondary outcomes were the proportion of visits where the CNV lesion was graded  
16 active as well as the number of anti-VEGF injections.

17 Visual acuity and CNV lesion activity were assessed 12 months before vs. 12  
18 months after surgery. The pre-operative VA was defined as VA recorded at the visit  
19 immediately prior to cataract surgery.

20 Predictive factors were assessed by comparing baseline characteristics of patients  
21 (at presentation for nAMD) classified into 3 groups: those showing a decrease in VA;  
22 those displaying a change in LogMAR letter score between 0 to 15; and those who  
23 achieved an increase in VA  $\geq 15$  letters. Variables considered in the analyses of  
24 predictive factors included the baseline age, lesion type, the time to cataract surgery,  
25 whether an injection in the 2 weeks before the surgery, the interval between the last  
26 IVT and cataract surgery and lesion activity prior to cataract surgery.

### 27 **Statistical Analyses**

28 For bilateral patients, the first eye, or the worse eye when both eyes presented  
29 simultaneously, was used.

1 Descriptive data were summarized using the mean (standard deviation [SD]),  
2 median (quantiles [Q1, Q3]) and percentages where appropriate. Within-group  
3 change in VA after cataract surgery was analyzed using paired t-tests.

4 The proportion of visits where CNV was active before and after cataract surgery was  
5 compared using logistic regression for both within-group and between-group  
6 comparisons between cases and matched controls with eye included as a random  
7 effect for repeated visits. Between-group comparison of VA between cases and  
8 matched controls was performed using mixed-effects models. The number of  
9 injections before and after surgery was compared using Poisson regression for  
10 within-group and between-group analyses with an offset for log days' follow-up.  
11 Between-group logistic, mixed-effects and Poisson regression models also included  
12 an identifier variable to indicate matched patients as a nested random effect.

13 Comparisons of characteristics between eyes categorized by change from pre-  
14 operative VA (gain  $\geq 15$  letters, gain 0-14 letters, and loss  $\geq 1$  letter) was performed  
15 by several univariable models using ANOVA, Kruskal-Wallis or log-rank tests,  
16 followed by pairwise comparisons using Holm-Bonferroni adjustments where  
17 appropriate.

18 All analyses were conducted using R V.3.3.2 with the *lme4* package (V 1.1-12) for  
19 logistic, mixed-effects and Poisson regression<sup>18-20</sup> and the *MatchIt* package (V 3.0.1)  
20 to identify matched controls.<sup>21</sup>

## 21 Results

### 22 Study Population (Table 1)

23 We identified 302 eyes from 273 patients from the FRB! database that underwent  
24 cataract surgery in the registry; considering only the first (or worse) eye in bilateral  
25 patients, 162 eyes of 162 patients had at least 12 months of follow-up that was  
26 required for the predictive analysis with no limit to the time prior to surgery; Their  
27 median (IQR) time until cataract surgery was 28 (12-52) months. The median (Q1,  
28 Q3) interval between the last IVT and cataract surgery was 61 (36, 115) days. Of  
29 these eyes, 124 also had the 12 months of follow-up *prior to and following surgery*  
30 that was required to compare the frequency of injections and lesion activity before  
31 vs. after the cataract surgery. Therefore, the primary outcome analysis was

1 performed on 124 eyes of 124 patients (with 372 matched controls) and the  
2 predictive factor analysis on 162 eyes of 162 patients.

3 Demographic characteristics are summarized in Table 1. Mean (SD) VA at baseline  
4 (time of first injection for nAMD) was 60.4 (14.5) letters and VA prior to cataract  
5 surgery was 55.2 (20.1) letters.

### 6 ***Visual Acuity Outcomes after Cataract Surgery (Table 2, Figure 1)***

7 Eyes undergoing cataract surgery gained a mean of 10.6 letters (95%CI: 7.8, 13.2; P  
8 < 0.001) 12 months following the surgery compared with the last pre-operative visit;  
9 26.0% gained  $\geq 3$  lines and 1.6% lost  $\geq 3$  lines (Table 2 and Figure 1). Cataract  
10 surgery patients also had higher mean [SD] VA 12 months after surgery compared  
11 with their matched controls during the same time period (65.8 [17.1] vs. 61.3 [20.8]  
12 letters respectively, P = 0.018).

### 13 ***Effect of Cataract Surgery on Lesion Activity and Treatment Patterns (Table 3)***

14 The proportion of visits where the CNV lesion was graded as active remained  
15 constant before and after cataract surgery (51.7% vs. 52.2%, P = 0.506), and  
16 decreased in the control group during the same period after starting anti-VEGF  
17 therapy (47.9% vs. 43.0%, P < 0.001; Table 3). The median treatment interval [Q1,  
18 Q3] when the CNV lesion was graded as active was the same before and after the  
19 surgery (53 [42, 84] vs. 51 [41, 81] days, P = 0.665) whereas it increased for  
20 matched controls during the same period (56 [46, 77] vs. 60 [48, 88] days, P < 0.001;  
21 Table 3). The mean [SD] number of injections was similar in the 12 months before  
22 vs. after cataract surgery (5.4 [3.3] vs. 5.4 [3.3] injections P = 0.316) in the operated  
23 group and decreased in the control group during the same period after starting anti-  
24 VEGF therapy (5.4 [2.8] vs. 4.9 [2.9] injections P = 0.316; Table 3).

### 25 ***Analysis of predictive factors for VA change after cataract surgery (table 4)***

26 The mean (SD) VA prior to surgery was lower in eyes that gained  $\geq 15$  letters  
27 compared with eyes that gained 0-14 letters (40.2 [21.4] vs. 62.1 [14.9], P < 0.001).  
28 Cataract surgery in the 6 first months of anti-VEGF therapy was associated with a  
29 higher risk of vision loss (P = 0.023). Other factors including age (P = 0.154), lesion

1 activity prior the surgery ( $P = 0.858$ ), an injection at least 2 weeks prior to surgery ( $P$   
2  $= 0.862$ ), and the lesion type ( $P = 0.261$ ), had no discernible predictive effect.

### 3 **Discussion**

4 The prospective design of the FRB! registry allowed us to assess the effect of  
5 cataract surgery on long-term VA outcomes and on the course of nAMD, including  
6 CNV lesion activity and number of anti-VEGF injections before and after surgery.  
7 There was a mean gain in VA of around 10 letters (2 lines) and 26% of eyes had  
8 gained more than 3 lines of VA 12 months after surgery. Patients undergoing  
9 cataract surgery had better VA, were more likely to have active lesions and more  
10 anti-VEGF injections than their matched unoperated controls in the 12-months  
11 following surgery. We found that VA outcomes were associated with the level of  
12 vision immediately prior to surgery and that cataract surgery performed within 6  
13 months of starting anti-VEGF therapy was associated with an increased risk of vision  
14 loss.

15 Lee et al. suggested cataract surgery should not be performed in the first 12 months  
16 of anti-VEGF therapy.<sup>13</sup> The average time from the first injection to cataract surgery  
17 was 14 months in the post-hoc analysis of ANCHOR (Anti-VEGF Antibody for the  
18 Treatment of Predominantly Classic Choroidal Neovascularization in AMD) and  
19 MARINA (Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab in  
20 the Treatment of Neovascular AMD) trials.<sup>10</sup> We found patients that had cataract  
21 surgery within 6 months of initiating anti-VEGF therapy were more likely to lose  
22 vision. Since most eyes in the FRB! database were likely to be on treat-and-extend,<sup>22</sup>  
23 it is possible that only after the first 6 months after commencing anti-VEGF therapy  
24 were lesions sufficiently controlled to allow for an increase in VA and a reduced risk  
25 to lose vision.

26 Previous studies have generally reported improvements in mean VA in eyes  
27 receiving IVT for nAMD that had their cataract removed. The VA improvement was 2  
28 lines from the pre-operative VA 3 months after surgery in a retrospective analysis of  
29 the ANCHOR and MARINA trials.<sup>10</sup> A VA improvement of 7 letters at 6 months after  
30 cataract surgery was observed in another retrospective study of 89 eyes.<sup>14</sup> Lee et al.  
31 reported that 39% of 39 eyes gained more than 3 lines of VA, 54% remained stable,  
32 but 7% had lost more than three lines 6 months after the cataract surgery.<sup>13</sup> Eyes

1 with mild AMD undergoing cataract surgery gained a mean of 6 letters, eyes with  
2 moderate AMD gained 4 letters, and eyes with advanced AMD gained 2 letters in the  
3 Age-Related Eye Disease Study.<sup>4</sup> A mean improvement of 10 letters (2 lines) was  
4 observed in the present study 12 months after cataract surgery with 27.5% of eyes  
5 gaining more than 3 lines and 2.2% of eyes losing more than 3 lines. Unsurprisingly  
6 our analysis of predictive factors showed patients with worse vision had more  
7 improvement after cataract surgery. Several studies have reported similar trends  
8 whereby eyes with worse vision at presentation for nAMD tend to have greater  
9 improvement in VA as there is a limit to how much eyes with better vision can  
10 improve further. It has been speculated that intravitreal injections may work better in  
11 eyes with a posterior vitreous detachment,<sup>23</sup> which is often induced by cataract  
12 extraction.<sup>24</sup>

13 It has been proposed that the level of activity of the CNV in eyes on treatment for  
14 nAMD should be considered before performing cataract surgery.<sup>13</sup> This parameter  
15 was not available in the post-hoc analysis of MARINA and ANCHOR trials, but  
16 presence of ongoing exudation may explain why cataract surgery was not performed  
17 in any of the sham-treated patients in the MARINA trial.<sup>10</sup> In the present study, the  
18 proportion of visits where the CNV lesion was graded active was similar before and  
19 after the cataract operation while lesion activity decreased in the control group during  
20 the same period after starting anti-VEGF therapy. Although it did not increase, the  
21 relatively higher CNV activity state after cataract extraction compared with controls  
22 may be related to the release of inflammatory mediators associated with cataract  
23 surgery. Such mediators are the likely cause of post-surgical cystoid macular edema,  
24 the commonest macular complication of cataract surgery.<sup>25</sup>

25 The frequency of anti-VEGF injections did not change 6 months before vs. 6 months  
26 after cataract surgery in the studies conducted by Kessel et al.<sup>14</sup> and Grixti et al.<sup>12</sup>  
27 The authors of these two studies concluded cataract surgery did not influence the  
28 course of nAMD but neither study compared its outcomes with a control group of  
29 unoperated eyes. We also did not observe any difference in the number of anti-  
30 VEGF injections in the 12 months before vs. after the surgery. However, the number  
31 of injections decreased in the control group in the same period after starting anti-  
32 VEGF therapy, suggesting that the requirement for treatment was increased  
33 somewhat in the postoperative period. It is possible that anti-VEGF agents last

1 longer in phakic eyes, however, it has been reported that there was no difference in  
2 visual and anatomical outcomes between phakic and pseudophakic eyes being  
3 treated for nAMD.<sup>26–28</sup>

4 It has been proposed that IVT with a VEGF inhibitor should be considered during  
5 cataract surgery to reduce the risk of activating the CNV lesion.<sup>8,9</sup> We did not  
6 observe any relationship between a IVT performed in the 2 weeks before the  
7 cataract surgery and VA outcomes. A preoperative exudation-free period may be  
8 another important parameter when considering cataract surgery.<sup>13</sup>

9  
10 Several limitations to the present study should be noted. Details were not available  
11 on the rationale for surgery, timing of the surgery, the grade of cataract or the type,  
12 duration and complications of cataract surgery performed. It was therefore possible  
13 that there was selection bias in our study as the decision to operate was purely at  
14 the discretion of the treating physicians. Nor was information available on the type  
15 and duration of topical anti-inflammatory drops used after surgery, which may have  
16 influenced the degree of activity of the CNV lesion. Also, it may occasionally be  
17 challenging to differentiate pseudophakic cystoid macular edema from CNV  
18 recurrence in clinical practice. Our results are likely, however, to be applicable to a  
19 broader category of patients with nAMD than have been studied in randomized  
20 clinical trials.

21 The main strengths of the present study are the documentation of VA from when  
22 eyes first started treatment, inclusion of a matched control group and a detailed  
23 analysis of the period 12-months prior to cataract surgery and the 12-month  
24 outcomes after cataract surgery. Observational data may be the best way to study  
25 the safety and efficacy of cataract surgery in this context since there may be ethical  
26 issues with randomized clinical trials which would require randomization of a group  
27 with clinically significant cataract to observation only.

28 This study found evidence of a modest effect of cataract surgery on CNV lesion  
29 activity in eyes being treated for nAMD. Despite this, visual outcomes were  
30 reassuringly good. Cataract surgery within 6 months of starting treatment for nAMD  
31 should be avoided if possible.

32

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1 **Figure legends**

2 **Figure 1.** Locally weighted scatterplot smoothing (LOESS) regression curves of  
3 mean visual acuity 12 months before vs. 12 months after the cataract surgery for  
4 cases and matched controls.

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**Table 1. Demographic characteristics of patients with neovascular age-related macular degeneration undergoing cataract surgery and phakic controls.**

	<b>Cataract Surgery Patients N=124</b>	<b>Matched phakic Controls* N=372</b>
<b>Eyes</b>	124	372
<b>Females, %</b>	61.3%	65.6%
<b>Baseline Age, Mean Years (SD)</b>	77.8 (6.3)	77.9 (6.3)
<b>Baseline VA , Mean Letters (SD)</b>	60.4 (14.5)	60.8 (13.6)
<b>Baseline Lesion Size, Median <math>\mu\text{m}</math> (Q1, Q3)</b>	2525 (1688, 3214)	2375 (1216, 3463)
<b>Lesion Type, %</b>		
<i>Occult</i>	56.5%	51.3%
<i>Minimally Classic</i>	10.5%	14.8%
<i>Predominantly Classic</i>	20.2%	20.2%
<i>Other</i>	11.3%	4.0%
<i>Not Recorded</i>	1.6%	9.7%

**Abbreviations:** VA: Visual acuity in number of letters read on a logarithm of the minimum angle of resolution (LogMAR) VA Chart; SD: Standard Deviation; 95% CI: 95% Confidence Interval; Q1, Q3: 25th and 75th percentiles

\*Three controls per case were matched on the following characteristics: time duration before cataract surgery, baseline visual acuity, baseline age, and length of follow-up. The controls had no history of cataract surgery and no surgery during the study period.

**Table 2. Visual acuity outcomes 12 months after cataract surgery in patients with neovascular age-related macular degeneration**

	<b>Cataract Surgery Patients (N=124)</b>	<b>Matched phakic Controls (N=372)</b>
<b>VA at Baseline, Mean Letters (SD)</b>	60.4 (14.5)	60.8 (13.6)
<b>Time Until Surgery, Median Months (Q1, Q3)</b>	34 (22, 56)	-
<b>VA prior to Surgery, Mean Letters (SD)*</b>	55.2 (20.1)	63.1 (19.5)
<b>VA 12 months after cataract surgery, endpoint for VA evaluation, Mean Letters (SD)**</b>	65.8 (17.1)	61.3 (20.8)
<b>Proportion of eyes with <math>\Delta</math>VA 12 months from pre-op VA, %</b>		
<i>Loss <math>\geq</math>15 Letters</i>	1.6%	8.9%
<i>Loss 1-14 Letters</i>	11.4%	42.3%
<i>Gain 0-14 Letters</i>	61.0%	44.7%
<i>Gain <math>\geq</math>15 Letters</i>	26.0%	4.0%

**Abbreviations:** VA: Visual acuity in number of letters read on a logarithm of the minimum angle of resolution (LogMAR) VA Chart; SD: Standard Deviation; Q1, Q3: 25th and 75th percentiles

\*Phakic controls were matched on time duration before cataract surgery to assess the final endpoint (VA 12 months after cataract surgery) fairly between cases and controls. VA prior to surgery in the phakic neovascular age-related macular degeneration control group corresponded to the same time period as their matched cases i.e. a median time of 34 (22-56) months after commencement treatment for neovascular age-related macular degeneration.

\*\* The mean (SD) VA 12 months following the surgery was better in cases than in unoperated phakic controls ( $P = 0.018$ ).

**Table 3. Comparison of treatment and lesion activity patterns before and after surgery and between cases and matched phakic controls in patients with neovascular age-related macular degeneration**

	12 Months		P-value**
	Before Surgery	After Surgery	
<b>Injections, Mean (SD)</b>			
<i>Cases</i>	5.4 (3.3)	5.4 (3.3)	0.316
<i>Controls*</i>	5.4 (2.8)	4.9 (2.9)	<b>&lt;0.001</b>
<i>P-value**</i>	0.703	<b>0.014</b>	
<b>Proportion Visits CNV Lesion Active, %</b>			
<i>Cases</i>	51.7%	52.2%	0.506
<i>Controls*</i>	47.9%	43.0%	<b>&lt;0.001</b>
<i>P-value**</i>	0.674	0.079	
<b>Treatment Interval CNV lesion Active, Median Days (Q1, Q3)</b>			
<i>Cases</i>	53 (42, 84)	51 (41, 81)	0.665
<i>Controls*</i>	56 (46, 77)	60 (48, 88)	<b>&lt;0.001</b>
<i>P-value**</i>	0.242	<b>0.009</b>	

**Abbreviations:** CNV: Choroidal neovascular membrane; Q1, Q3: 25th and 75th percentiles

\*Three controls per case were matched on the following characteristics: time duration before cataract surgery, baseline visual acuity, baseline age and length of follow-up.

\*\* P-values in columns are comparing within-group changes before and after surgery and p-values in rows are comparing between cases and controls.

The proportion of visits where the CNV lesion was graded as active and mean injection frequency in the 12 months following the cataract surgery was higher in eyes undergoing cataract surgery than in matched controls.

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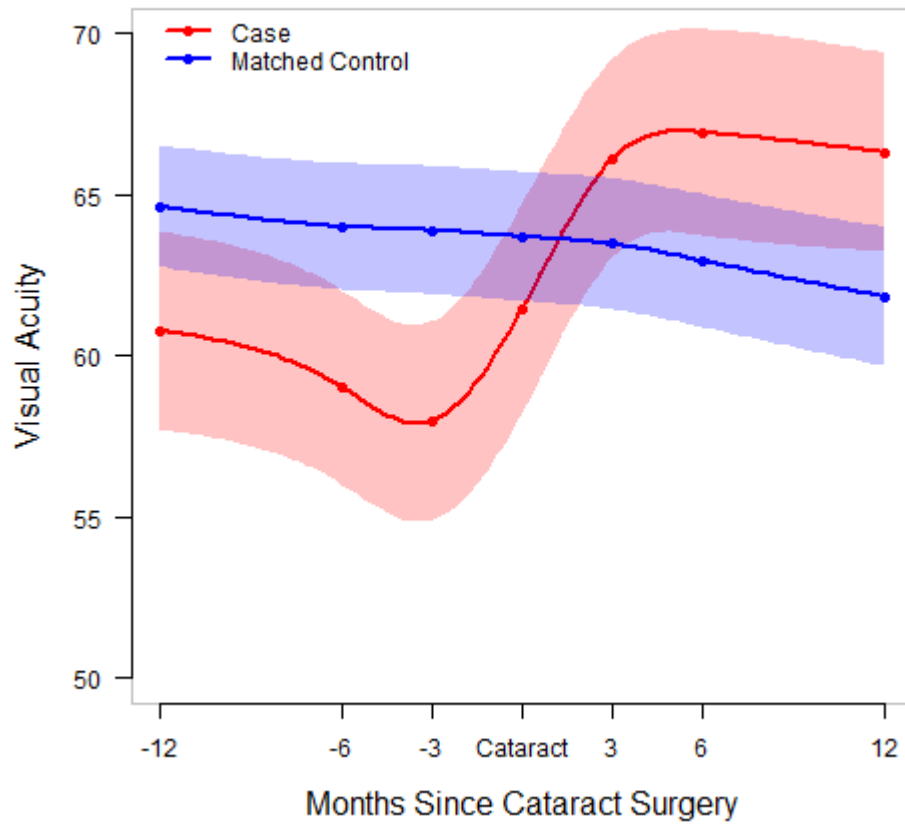
**Table 4: Predictive factor for 12 months visual acuity change after cataract surgery (from pre-operative) in patients with neovascular age-related macular degeneration**

12 months' visual acuity change	Gained $\geq 15$ Letters	Gain 0-14 Letters	Lost $\geq 1$ Letter	P-value**
<b>Eyes</b>	47	91	24	
<b>Baseline Age, Mean Years (SD)</b>	80.1 (6.4)	78.1 (6.8)	90.2 (6.1)	0.154
<b>VA Prior to Surgery, Mean Letters (SD)</b>	40.2 (21.4)	62.1 (14.9)	53.5 (20.2)	<b>&lt;0.001</b>
<b>Lesion Type, %</b>				
<i>Occult</i>	68.1%	56.0%	50.0%	0.261
<i>Minimally Classic</i>	10.6%	11.0%	12.5%	
<i>Predominantly Classic</i>	8.5%	22.0%	20.8%	
<i>Other</i>	6.4%	11.0%	16.7%	
<i>Not Recorded</i>	6.4%	0.0%	0.0%	
<b>Time Until Surgery, Median Months (Q1, Q3)*</b>	18.1 (10.3, 43.5)	29.2 (14.2, 47.2)	19.7 (10.3, 31.1)	0.332
<i>&lt;6 months between the beginning of anti-VEGF and cataract extraction, n (%)</i>	6 (12.8%)	4 (4.4%)	5 (20.8%)	<b>0.023</b>
<i>&gt;6 months between the beginning of anti-VEGF and cataract extraction, n (%)</i>	41 (87.2%)	87 (95.6%)	19 (79.2%)	
<b>Lesion Activity in the Visit Immediately Prior to the Surgery, n (%)</b>				
<i>Active</i>	21 (44.7%)	36 (39.6%)	10 (41.7%)	0.858
<i>Inactive</i>	26 (55.3%)	55 (60.4%)	14 (58.3%)	
<b>Prophylactic Injection in the 2 Weeks Before the Surgery, n (%)</b>				
<i>Yes</i>	1 (2.1%)	4 (4.4%)	1 (4.2%)	0.862
<i>No</i>	46 (97.9%)	87 (95.6%)	23 (95.8%)	
<b>Interval Between the Last Injection and Cataract Surgery, Median Days (Q1, Q3)</b>	56 (35, 137)	49 (35, 91)	53 (29, 96)	0.509

**Abbreviations:** VA: Visual acuity in number of letters read on a logarithm of the minimum angle of resolution (LogMAR) VA Chart; SD: Standard Deviation; Q1, Q3: 25th and 75th percentiles; ANOVA (analysis of variance)

\*No restriction of time to surgery but at least 12 months of follow-up post-surgery and only the first or worse eye in bilateral patients (n = 162 eyes).

\*\* P-values are global tests comparing characteristics between eyes that gained  $\geq 15$  letters, gained 0-14 letters, or lost  $\geq 1$  letter using ANOVA, Kruskal-Wallis or log-rank tests where appropriate.



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