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Original Article – Clinical Science

Effect of phacoemulsification cataract surgery on intraocular pressure in early glaucoma: A prospective multi-site study

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ABSTRACT

Importance: Cataract and primary open angle glaucoma (POAG) commonly coexist, and cataract surgery is thought to reduce intraocular pressure (IOP), the major modifiable risk factor of POAG.

Background: Previous studies exploring the effect of cataract surgery on IOP are limited by retrospective design, lack of a control group, medication use and washout, and loss to follow-up.

Design: Prospective, multicentre, matched case-control Australian study.

Participants: 171 eyes of 108 POAG patients who underwent cataract surgery, matched to 171 control eyes.

Methods: Serial longitudinal IOP measurements was compared before and after cataract surgery, and relative to the controls. A mixed-effect model was used for the longitudinal data.

Main Outcome Measures: Change in IOP.

Results: The mean follow-up time was 4.8 (1.4) years. Cataract surgery reduced mean IOP by 2.22 mmHg (95% confidence interval [CI]: 1.93-2.52 mmHg, $P<0.001$) with 59 eyes (34%) achieving at least 3 mmHg reduction. Compared to matched controls, the mean reduction in IOP was 1.75 mmHg (95% CI 1.15 - 2.33 mmHg;; $P<0.001$). Higher preoperative IOP and being on fewer topical glaucoma medications preoperatively were strongly predictive of a larger IOP reduction in a multivariable model. Anterior chamber depth was not associated with IOP reduction. Eyes with preoperative IOP $\geq$ 24 mmHg had a mean IOP reduction of 4.03 mmHg with 81% experiencing at least 3 mmHg reduction. Sub-analysis of medication naïve and pseudoexfoliation patients showed similar results.

Conclusions and Relevance: Cataract surgery has a confirmed effect in reducing IOP in a "real world" setting of early glaucoma patients.

Keywords: Open angle glaucoma, Cataract surgery, Phacoemulsification, Cataract, Biometry

1. INTRODUCTION

Glaucoma is a progressive optic neuropathy characterised by accelerated loss of retinal ganglion cells, leading to visual field loss.[1] The most common subtype of glaucoma is primary open angle glaucoma (POAG) in which the iridocorneal angle is unobstructed by the iris and there is no secondary cause of intraocular pressure (IOP) elevation. The prevalence of POAG and cataract are strongly associated with older age, and thus both conditions commonly coexist.[2,3] Glaucoma and cataract represent the second and third most common causes of blindness in Australia, respectively.[4] Cataract is the commonest cause of non-refractive error-related low-vision in Australia and worldwide.[4]

Currently, lowering IOP is the only demonstrably therapeutic treatment for POAG. Both topical medical therapy and selective laser trabeculoplasty (SLT) are effective and commonly used to treat POAG.[5,6] Filtration surgery is a more widely effective means of lowering IOP but carries higher morbidity compared to medical or laser therapy and thus is commonly reserved for more recalcitrant disease not responding to other therapies.[7,8]

While cataract surgery is not a procedure for IOP lowering in open angle glaucoma, several studies have reported a reduction of IOP following cataract surgery in patients with open angles.[9,10] A recent meta-analysis of the studies on the effects of phacoemulsification on IOP has identified the lack of a control group, medication use and washout, and the loss to follow-up as sources of bias which potentially undermine certain conclusions in the reported literature.[11] In this study, we aim to address these issues and characterise the effects of cataract surgery on IOP in a large prospectively monitored early glaucoma cohort with pragmatic study design

across multiple clinics in Australia. In the following text, cataract surgery refers to phacoemulsification with posterior chamber intraocular lens insertion.

2. METHODS

2.1 Study participants

This study cohort formed a sub-population of PROGRESSA study (Progression Risk Of Glaucoma; RElevant SNPs with Significant Association), an Australia-wide multicentre prospective cohort study of progression risk in glaucoma.

Participants were enrolled if they had optic nerve head appearance suspicious or probable for early stage glaucoma based on the disk damage likelihood scale (DDLS)[12] with Humphrey visual field mean deviation better than -6 db (Humphrey Field Analyzer; Carl Zeiss Meditec; Dublin, CA). Patients with angle closure on gonioscopy, secondary causes of elevated IOP or other ophthalmic conditions causing reduced visual acuity were excluded. Patients were reviewed 6-monthly with complete ophthalmic examination including visual acuity and IOP measurements using Goldmann Applanation Tonometry (GAT). Dilated fundoscopy and central corneal thickness (CCT) measurement by pachymetry (Pachmate DGH55; DGH Technology Inc, Exton, PA) were performed annually. If a participant had glaucoma filtration surgery, then only those visits prior to this operation were included in the analysis.

Eligible participants were those who had undergone cataract surgery via phacoemulsification with intraocular lens implant in either eye during their period of longitudinal monitoring, and had at least one visit 6-months post procedure. The indication for surgery was visually significant cataract interfering with vision. Surgical technique and IOP management was at the discretion of the treating glaucoma specialist. Case notes were then reviewed to record the pre-treatment maximum

IOP, and the preoperative ocular biometry: anterior chamber depth and axial length (IOL Master, Carl Zeiss, Germany).

A matched sample of the PROGRESSA cohort who had not undergone any ocular surgery during their follow-up were selected as controls. These were enrolled and followed up under the same protocol as outlined above. To account for confounding factors that could affect IOP measurements over time, the control group were matched to the cases (who underwent cataract surgery) by age, gender, duration of study follow-up, baseline IOP at enrolment, and treatment intensity during follow-up.

Formal participant information was provided and informed consent was obtained from all study participants. The study was approved by the The Southern Adelaide Clinical Human Research Ethics Committee (SACHREC) and adheres to the tenets of the Declaration of Helsinki.

2.2 Statistical analysis

All statistical analyses were performed using R (version 3.5.1, RCore Team, Austria).[13] Both eyes, if applicable, were included in the study. Controls were matched by dissimilarity matrix calculation using *cluster* (version 2.0.7.1) and *e1071* (version 1.7.0.1) packages in R.[14,15] Analysis of variance between the cases and controls was done using Kruskal–Wallis test for continuous variables and Chi-squared test for categorical variables. To account for the correlated nature of these measurements, we used a mixed-effects linear model with random intercepts per patient.[16] Longitudinal IOP measurements from each visit was used in the primary analysis; within-eye correlation was adjusted for using two-level random intercepts per patient then per eye.[16] In the case-control analysis, we calculated the mean difference between all the IOP measurements before and after cataract surgery for

the cases. For the controls, the median visit per patient was used as the point in time to calculate the "change in IOP". To account for the random effects of the clinic sites, we included the recruitment and follow-up location as another random intercept in the model. Models were fitted using *lme4* package (version 1.1.20),[17] and hypothesis testing of the model was done using Satterthwaite's degrees of freedom method. The pseudo-R^2 of the mixed-effects model was calculated based on the fixed-effects only as described by Nakagawa *et al.*[18] The cut-off of statistical significance (alpha level) was set at P = 0.05.

3. RESULTS

In total, 171 eyes of 108 patients from 8 clinics across Australia met the case eligibility criteria for this study. All cases were enrolled in PROGRESSA and underwent cataract surgery electively during routine follow-up. The mean (SD) age of the patients at the time of cataract extraction was 72.8 (6.8) years. Cases had clinical data recorded for 3.9 (3.4) years before the operation with a mean follow-up time of 2.7 (1.7) years post procedure. The majority of our patients had at least one year of follow-up (n = 145, 85%). Follow-up rates at 18 and 24 months post procedure were 73% (n = 125) and 59% (n = 100) respectively. Five eyes (2.9%) underwent trabeculectomy surgery at a later date due to progressive glaucoma not responding to medical treatment. IOP measurements following the trabeculectomy were not included in the analysis.

For our control group, we matched 171 eyes of 144 patients enrolled in PROGRESSA and follow-up by the same protocol as the cases, who have not undergone cataract surgery. As cataract surgery was indicated for visually significant cataracts, there was a significant difference in the best corrected visual acuity (BCVA) between the cases (prior to cataract surgery) and the controls (median [IQR] BCVA 6/9.5 [4.5] vs

6/7.6 [3.5] respectively; P = $3.3x10^{-8}$). The distribution of the cataract density of the cases and the controls using The Lens Opacities Classification System III is presented in Supplementary Figure 1. Detailed clinical and demographic characteristics of the study cohort is summarised in Table 1.

Table 1: Clinical and demographic characteristics of study participants

Characteristics	**Cases**	**Controls**	**P**
Number: eyes / patients	171 / 108	171 / 144	-
Gender, male (%)	56 (51.9)	69 (47.9)	0.62
Age at recruitment, years	69.2 (6.8)	69.0 (6.5)	0.93
Study follow-up duration, years	4.8 (1.4)	4.43 (1.5)	0.05
Number with 5 year follow-up, patients (%)	55 (50.9)	58 (40.3)	0.12
Pseudoexfoliation syndrome, patients (%)	5 (4.6)	4 (2.8)	0.66
Central corneal thickness, µm	546 (35)	538 (31)	0.05
IOP at recruitment, mmHg	16.7 (4.2)	16.5 (3.6)	0.90
Maximum recorded IOP, mmHg	20.6 (5.8)	20.4 (5.2)	0.88
Vertical cup-to-disc ratio	0.71 (0.12)	0.67 (0.13)	0.01
Visual field mean deviation, dB	-2.72 (3.95)	-2.38 (3.14)	0.65
Number of glaucoma medications	1.0 (1.0)	0.9 (0.9)	0.52
Selective laser trabeculoplasty, eyes (%)	57 (34.1)	43 (25.1)	0.09
Number of treatment naive patients (%)	27 (25.0)	43 (29.9)	0.47

Values displayed are mean (standard deviation) for continuous variables and N (%) for categorical variables. P values represent the statistical significance of the analysis

of variance for continuous variables (Kruskal–Wallis test) or Chi-squared test for categorical variables.

IOP: intraocular pressure.

Using the longitudinal data of all IOP measurements, cataract surgery reduced the mean IOP by 2.22 mmHg (95% confidence interval [CI]: 1.93 - 2.52 mmHg; $P < 2x10^{-16}$). The effect was most pronounced in the first 18 months after cataract surgery then diminished to some extent although remaining below pre-operative mean measurements (Figure 1A). The magnitude of reduction differed between eyes, with 59 eyes (34%) achieving at least 3 mmHg reduction within two years of cataract surgery, and 34 eyes (20%) having no, or a positive, change in IOP. A breakdown of the change in IOP per eye within two years of the cataract surgery is summarised in Table 2 and Figure 2. Ongoing glaucoma management was at the discretion of the treating clinicians and was individualised to each patient. Thus, only 5 eyes (3%) stopped at least one glaucoma medication post cataract surgery. Escalation in medical treatment was similar between the cases (29 eyes) and controls (27 eyes; $P = 0.9$).

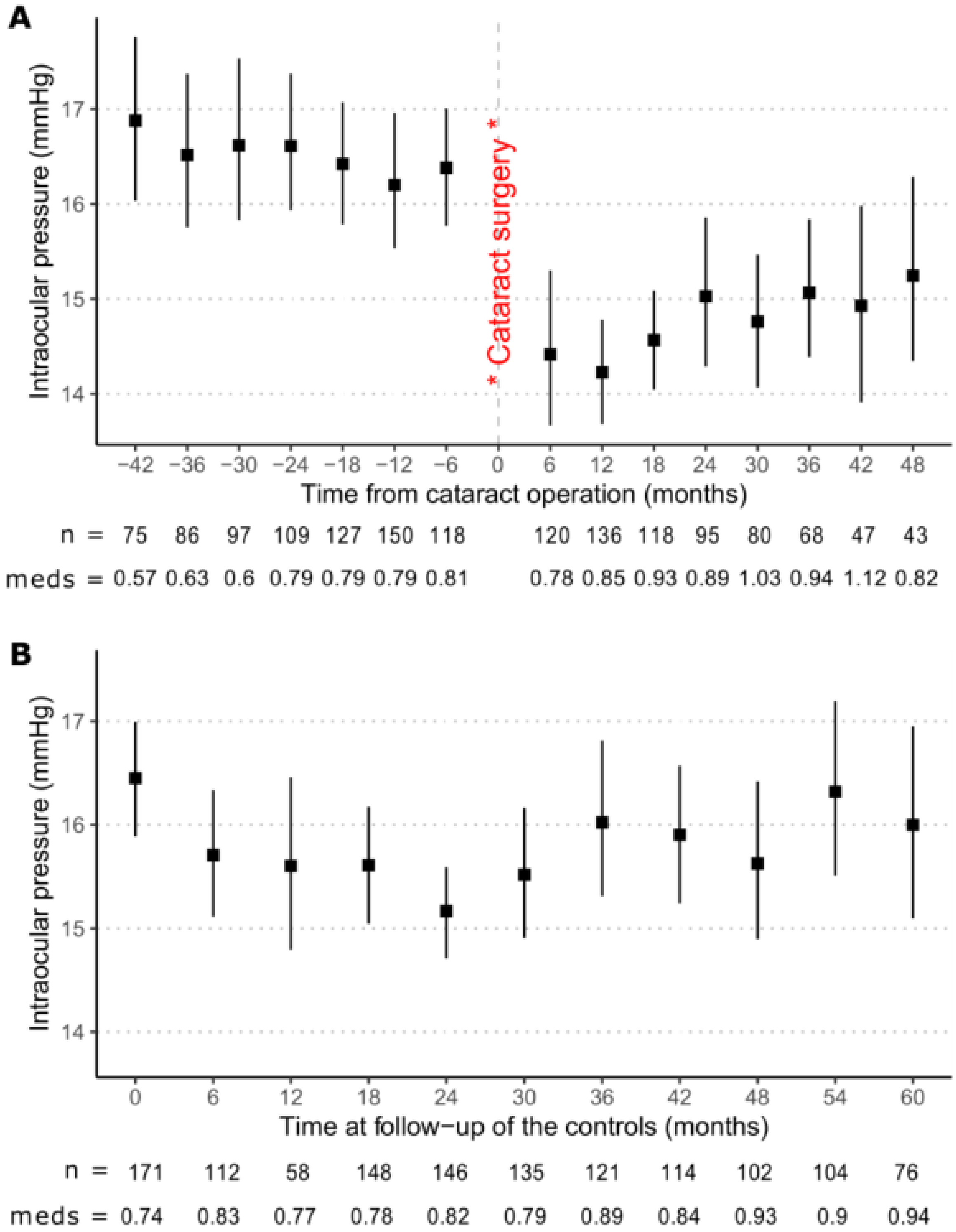
A
Intraocular pressure (mmHg)
17
16
15
14
* Cataract surgery *
−42 −36 −30 −24 −18 −12 −6 0 6 12 18 24 30 36 42 48
Time from cataract operation (months)
n = 75 86 97 109 127 150 118 120 136 118 95 80 68 47 43
meds = 0.57 0.63 0.6 0.79 0.79 0.79 0.81 0.78 0.85 0.93 0.89 1.03 0.94 1.12 0.82
B
Intraocular pressure (mmHg)
17
16
15
14
0 6 12 18 24 30 36 42 48 54 60
Time at follow−up of the controls (months)
n = 171 112 58 148 146 135 121 114 102 104 76
meds = 0.74 0.83 0.77 0.78 0.82 0.79 0.89 0.84 0.93 0.9 0.94

Figure 1: Longitudinal change in intraocular pressure (IOP) after cataract surgery (A) in the cases n = 171, and (B) in the control group n = 171 eyes. The square dot represents the mean IOP at each time point, and the error bars represent the 95% confidence interval of the mean. The number of eyes with IOP data recorded and the mean number of topical glaucoma medications at each time point is reported below each figure.

Table 2: Number and percent of eyes with the corresponding two-year mean change in intraocular pressure following cataract surgery

Two-year absolute change in IOP after cataract surgery	Number of eyes	Percent of eyes
At least -6 mmHg	7	4.1%
-6 up to -5 mmHg	11	6.4%
-5 up to -4 mmHg	15	8.8%
-4 up to -3 mmHg	19	11%
-3 up to -2 mmHg	33	19.3%
-2 up to -1 mmHg	23	13.5%
-1 up to 0 mmHg	29	17%
No or positive change	34	19.9%

IOP: intraocular pressure.

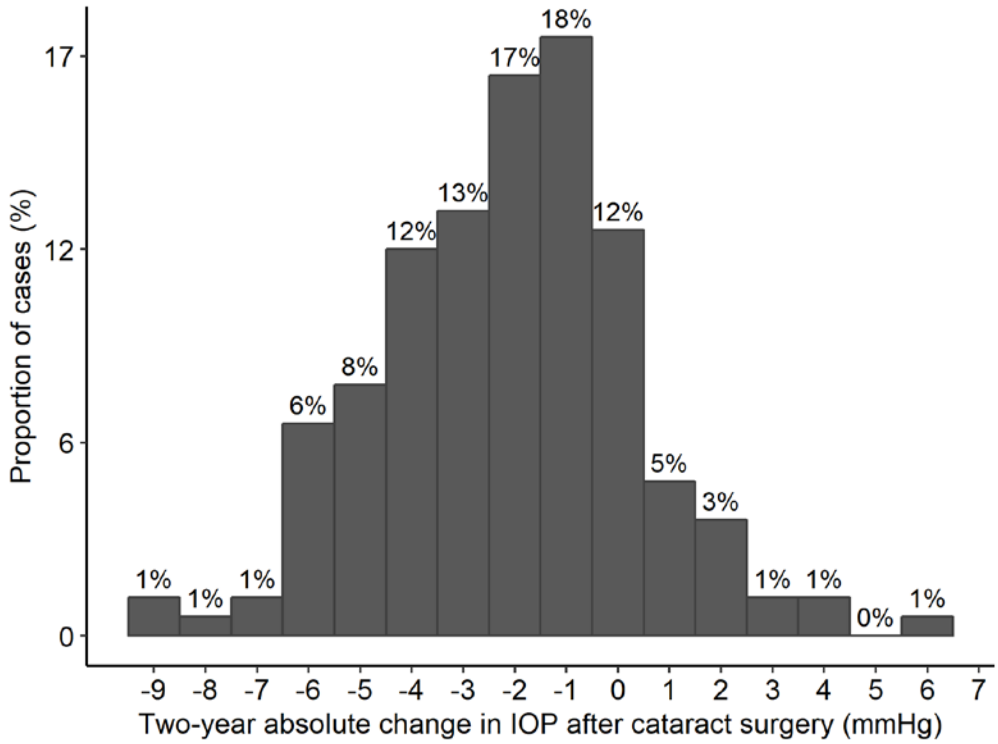

Figure 2: Histogram of the absolute change in intraocular pressure (IOP) within 2 years after cataract surgery in the PROGRESSA cohort (N = 171 eyes).
IOP: intraocular pressure.

To further isolate the effect of cataract surgery from the change of IOP over time, we conducted a case-control analysis, comparing the change in IOP in those who underwent cataract surgery (*i.e.* the group reported above) to matched controls (no cataract surgery; N = 171 eyes). The controls had similar age, gender, IOP at enrolment, duration of follow-up, and medical treatment compared to the cases (Table 1). Compared to the controls, and accounting for the intereye correlation of IOP and the clinic site as a random effect, cataract surgery reduced IOP by 1.75 mmHg (95% CI 1.15 - 2.33 mmHg; $P = 1.6\text{x}10^{-8}$).

To identify predictors of the change in IOP for inclusion in a multiple variable model, we conducted univariate linear regressions with the following variables: gender, age

at operation, maximum recorded IOP prior to the operation, baseline IOP at study enrollment, central corneal thickness, axial length, anterior chamber depth, history of pseudoexfoliation syndrome, and the number of topical glaucoma medications prior to the operation (Supplementary Table 1). Variables with P-values < 0.2 were then used in a multiple variable model. When the maximum recorded IOP was limited to two years prior to cataract surgery, the strength of the association and the goodness-of-fit of the change in IOP improved significantly with 23% of the variance in the postoperative IOP change explained compared to 7% when the all-time maximum IOP was used. We have thus included the two-year maximum in the multiple variable model. Interestingly, preoperative anterior chamber depth and axial length were not associated with the change in IOP postoperatively (Supplementary Figure 2).

In the multiple variable model, elevated preoperative IOP was strongly predictive of a larger reduction in IOP post cataract surgery (Table 3). For each 1 mmHg higher maximum preoperative IOP (in the preceding 2 years), there was an estimated reduction of 0.33 mmHg (95% CI: 0.23-0.42 mmHg) of IOP post cataract surgery ($P = 1.4x10^{-10}$). The number of glaucoma medications preoperatively was inversely associated with the change in IOP. That is, patients who were on more intensive glaucoma medical therapy experienced a lower reduction in IOP than those with fewer topical glaucoma drops (Supplementary Figure 3). This may suggest that cataract surgery is subject to the so-called 'law of diminishing returns', in producing a lesser yield of IOP-lowering benefit in those already on treatment.[19] Finally, male participants experienced an estimated 1 mmHg (95% CI: 0.30-1.7 mmHg) greater reduction in IOP than females ($P = 7.5x10^{-3}$)

Table 3: Multiple variable model of clinical predictors of IOP reduction following cataract surgery.

Variable	Estimate	Standard error	P-value
Number of glaucoma medications preoperatively	0.77	0.21	3.0×10^{-4}
Maximum IOP in the last 2 years prior to cataract operation	-0.33	0.048	1.4×10^{-10}
Baseline study IOP	0.073	0.037	0.05
Gender (male)	-1.01	0.37	7.5×10^{-3}

Results are the coefficients of a linear mixed-effects model with the post cataract change in IOP as the response and the variables as fixed predictors. The model random effects were the patients (to account for the intereye correlation) and clinic site. Pseudo-R-squared (fixed effects only) = 35%.

IOP: intraocular pressure.

We further examined the impact of high preoperative IOP on the expected postoperative reduction in pressure (Figure 3). Eyes with 2-year preoperative maximum IOP of at least 24 mmHg (N = 16) had a mean IOP reduction of 4.03 (3.27) mmHg in the first 2 years, with 13 of the eyes (81%) experiencing at least 3 mmHg reduction. The outlier in the top right of Figure 3 was a patient with POAG and a persistently high IOP despite maximal medical therapy (4 medications). The cataract operation was done in anticipation of a trabeculectomy which was done 6 months later (no post-trabeculectomy IOP data was included in the analysis).

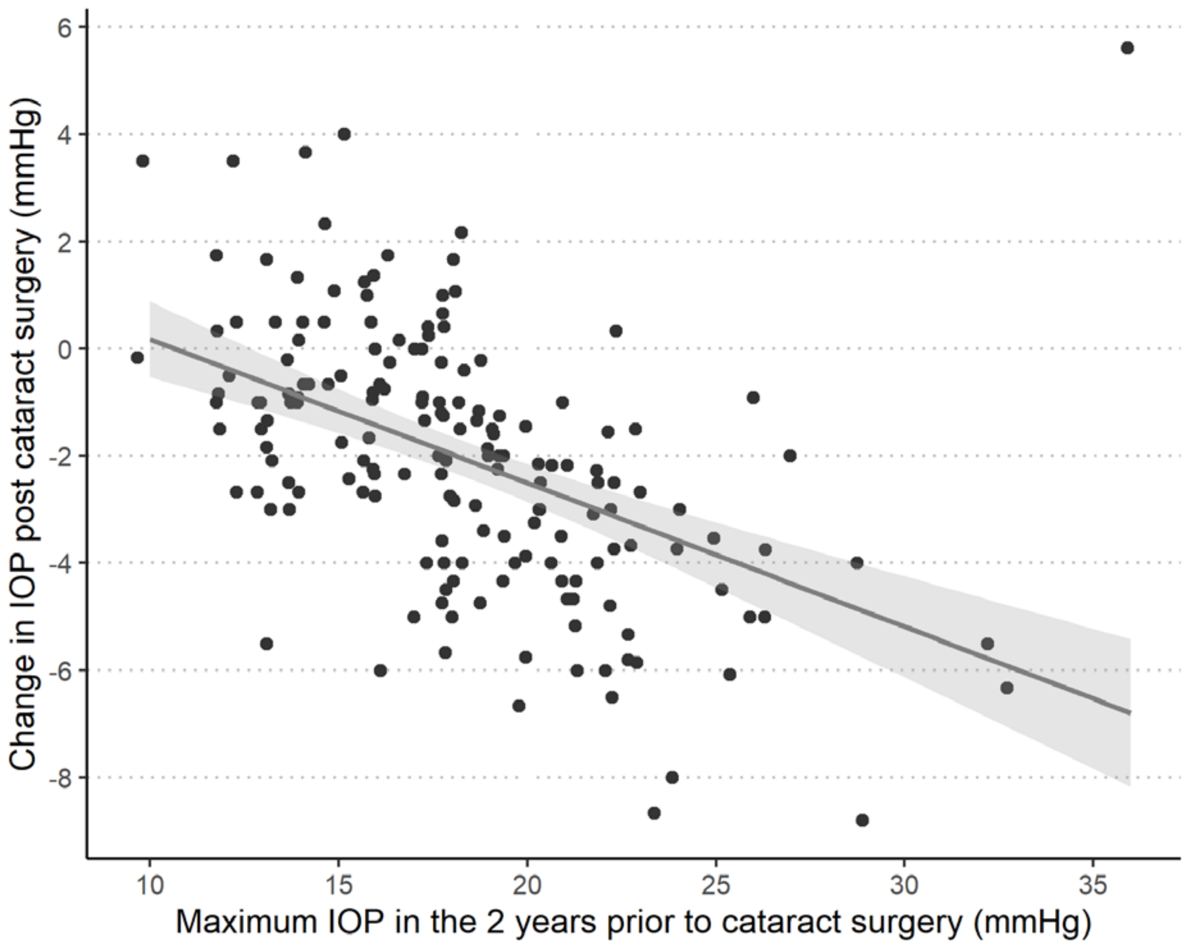

Figure 3: Observed difference in the mean intraocular pressure (IOP) within two years post cataract surgery. Each point represents a study eye. The grey line is the line of best fit with the 95% confidence interval shaded in light grey (P-value for trend = 3.3×10^{-10}).

IOP: intraocular pressure.

To improve the generalisability of our results we performed various sensitivity analyses. Topical medications used to treat glaucoma will invariably affect the IOP changes measured during follow-up. To account for this important covariate, we performed a subgroup analysis on medication naive participants - *i.e.* those who have not been on any topical ocular hypotensive drops during the study period (N =

43 eyes). In this subgroup, cataract surgery was associated with a mean reduction of IOP of 2.4mmHg (95% CI 1.9 - 2.9 mmHg; $P < 2x10^{-16}$). Only one eye had prior peripheral iridotomy and had a mean reduction of 3.8 mmHg. Exclusion of this case did not change the results. Eyes with pseudoexfoliation syndrome may experience IOP reduction via a different mechanism than POAG eyes. 7 eyes had pseudoexfoliation syndrome and in this subgroup with a mean IOP reduction of 2.7 mmHg (95% CI 1.2 - 4.1 mmHg; $P = 4.7x10^{-4}$). This change in IOP was no statistically significantly different than the rest of the study cohort ($P = 0.6$).

4. DISCUSSION

This study demonstrated the effects of cataract surgery on intraocular pressure (IOP) in early open angle glaucoma patients in a “real world” setting from 8 clinics in Australia. Patients were enrolled in the study for glaucoma monitoring, and the treatment of cataract was based on symptoms and clinical assessment. We demonstrated a reduction in IOP after cataract surgery that was statistically significant, which persisted for the duration of follow-up, although was most pronounced in the first 18 months. A third of the cases had at least 3 mmHg of mean IOP reduction in 2 years. Patients with higher IOP before the operation, and those on fewer glaucoma medications had a larger reduction in IOP. The cataract surgery in this cohort was not aimed to modify the glaucoma medical therapy, and we did not observe a significant number of patients who had their glaucoma medications reduced.

Our findings are consistent with previously published studies on the effect of cataract surgery on IOP in glaucoma.[9–11,20] In a study of 55 eyes with POAG, Shingleton *et al.* reported a mean reduction of 1.4 ± 3.3 mmHg at the three-year follow-up post cataract surgery, which has persisted at their last follow-up

appointment (mean of 5 years).[16] Hayashi *et al.* observed a mean reduction of 4.3 ± 4.2 mmHg in 68 eyes with POAG at 1 year post cataract surgery, which has persisted for patients followed up to 2 years.[9] This larger effect size may be attributable to the relatively higher preoperative IOP in this study (mean of 20.7mmHg). Other studies have demonstrated a comparable reduction in ocular hypertensives and normal eyes without glaucoma.[10,21,22] Cataract surgery may therefore be a useful treatment option in the management in early high tension glaucoma patients with comorbid cataracts.

Microinvasive glaucoma surgery (MIGS) has recently been introduced as a treatment option for early glaucoma.[23] The currently available devices are usually inserted during cataract surgery. The effect of combined MIGS and cataract surgery relative to cataract surgery alone has been reported in several studies.[24–28] Of note, these comparative studies only recruited eyes with high tension glaucoma, where our study and others show that cataract removal is most likely to be efficacious, and the results are often reported after medication washout, which whilst valid as a trial tool, is less relevant in a clinical scenario where IOP reduction from the *treated* IOP is the therapeutic aim.[11,20]

For instance, Craven *et. al.* reported that cataract surgery alone reduced IOP by 7.5 mmHg at 24 months post procedure.[25] In this high tension POAG cohort, the mean pre-procedure IOP was 25.2 mmHg after medication washout period, thus regression to the mean is expected. Similarly, Pfeiffer *et. al.* reported 9.2 mmHg IOP reduction at 12 months post cataract surgery in their high tension POAG cohort (mean baseline IOP of 26.6 mmHg).[27] The effect size has diminished at 24 months to a net IOP reduction of 7.4 mmHg, consistent with our results and others that the effect of cataract surgery on IOP may reduce in some patients over time.[22,27]

The mechanism of the IOP reduction seen after cataract surgery may partly be related to the anatomical changes due to the crystalline lens removal. Issa *et al.* have developed an index for predicting the reduction in IOP post cataract surgery in non-glaucomatous eyes.[29] Elevated preoperative IOP and shallower anterior chamber depth (ACD) were both predictive of greater IOP reduction post-operatively, consistent with the experience in angle closure eyes.[29] The ratio of preoperative IOP to preoperative ACD was positively correlated to the magnitude of IOP reduction and there was at least 4 mmHg IOP reduction in those with a ratio higher than 7.0.[29] The authors believe that any role of ACD is likely related to the effect of lens thickness on this parameter. It should be noted that gonioscopy was not performed on the participants of this study. In our study, all participants had open angles by gonioscopy and we found no correlation between the ACD or axial length and the change in IOP. This suggests that ACD is not a crucial predictor of IOP reduction post cataract surgery in those with open angles by clinical examination.

Using anterior segment optical coherence tomography in open angle glaucoma patients undergoing cataract operation, Lin *et al.* reported the angle-opening distance, iris thickness, iris area and the lens vault (the area between the anterior pole of the phakic lens and the line between the two scleral spurs) were associated with greater IOP reduction post surgery,[30] although other studies have struggled to use such parameters to predict IOP lowering after cataract surgery.[31] Lensectomy is also speculated to possibly improve aqueous drainage by providing posterior traction on the ciliary body and scleral spur resulting in widening of the trabecular meshwork and Schlemm's canal.[32]

In PXF, reversal of anterior chamber shallowing due to zonular laxity as well as anterior chamber lavage of PXF material have been postulated as reasons for greater

IOP lowering in PXF cataract patients, and one cannot exclude the possibility that such lavage and simple trabecular meshwork stretching may contribute to the transitory nature of the IOP lowering after routine cataract surgery.[33] Finally, the phacoemulsification ultrasound may improve trabecular meshwork aqueous drainage. DeVience *et al.* reported that intraoperative phacoemulsification time was associated with greater IOP reduction in normal eyes.[34] This is supported by an in-vitro study of phacoemulsification ultrasound on trabecular meshwork cells activating cellular pathways leading to improved aqueous outflow and lower IOP.[35] This stress-mediated pathway may be similar to the effects of laser trabeculoplasty on the trabecular meshwork.[35,36]

The strengths of this study are the prospective follow-up of a large sample size from multiple clinics and specialists. The pragmatic design reflects the current clinical practice in the management of early glaucoma patients with cataracts. We have also used improved statistical modelling that utilises this longitudinal data and adjustments for several covariates including the clinic site.[16] This study has some limitations. Our cohort represents early open angle glaucoma cases, and thus our results are not directly applicable to normal eyes or those with other forms or degrees of glaucoma. The cataract density and type may be a factor that contributes to the differences observed between the cases and controls. Other treatments were not standardised by protocol, and thus patients were medically treated per their glaucoma specialists. We have performed sub-analysis to address this, with similar findings to our primary analysis.

In this prospectively monitored early open angle glaucoma cohort, cataract surgery has a confirmed effect in reducing intraocular pressure. The magnitude of effect is largest among those with higher pressures and fewer glaucoma medications. The magnitude of the IOP reduction is generally small. It will remain a point of debate as

to whether this magnitude of reduction is clinically useful in glaucoma care, particularly if as a deliberate surgical intervention for progressive glaucoma.

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SUPPLEMENTARY MATERIALS

Supplementary Table 1: Univariate linear mixed-effects models of the clinical predictors of the intraocular pressure reduction following cataract surgery in PROGRESSA (N = 172 eyes).

Variable used in the univariate model	Estimate	Standard error	P-value	Pseudo-R^2
Gender (male)	-0.83	0.44	**0.06**	**2.7%**
Age at operation	0.02	0.03	0.55	0.3%
Maximum recorded IOP prior to operation	-0.13	0.04	**$1.1x10^{-03}$**	**7.3%**
Maximum IOP in the last 2 years prior to cataract operation	-0.28	0.04	**$3.3x10^{-10}$**	**22.5%**
Baseline study IOP	-0.05	0.04	**0.18**	**1.3%**
Central corneal thickness	0.00	0.01	0.69	0.1%
Preoperative axial length†	-0.09	0.22	0.68	0.1%
Preoperative anterior chamber depth‡	-0.24	0.65	0.71	0.1%
Pseudoexfoliation syndrome (yes)	-0.42	1.09	0.70	0.1%
Number of glaucoma medications preoperatively	0.84	0.23	**$4.4x10^{-04}$**	**8.4%**

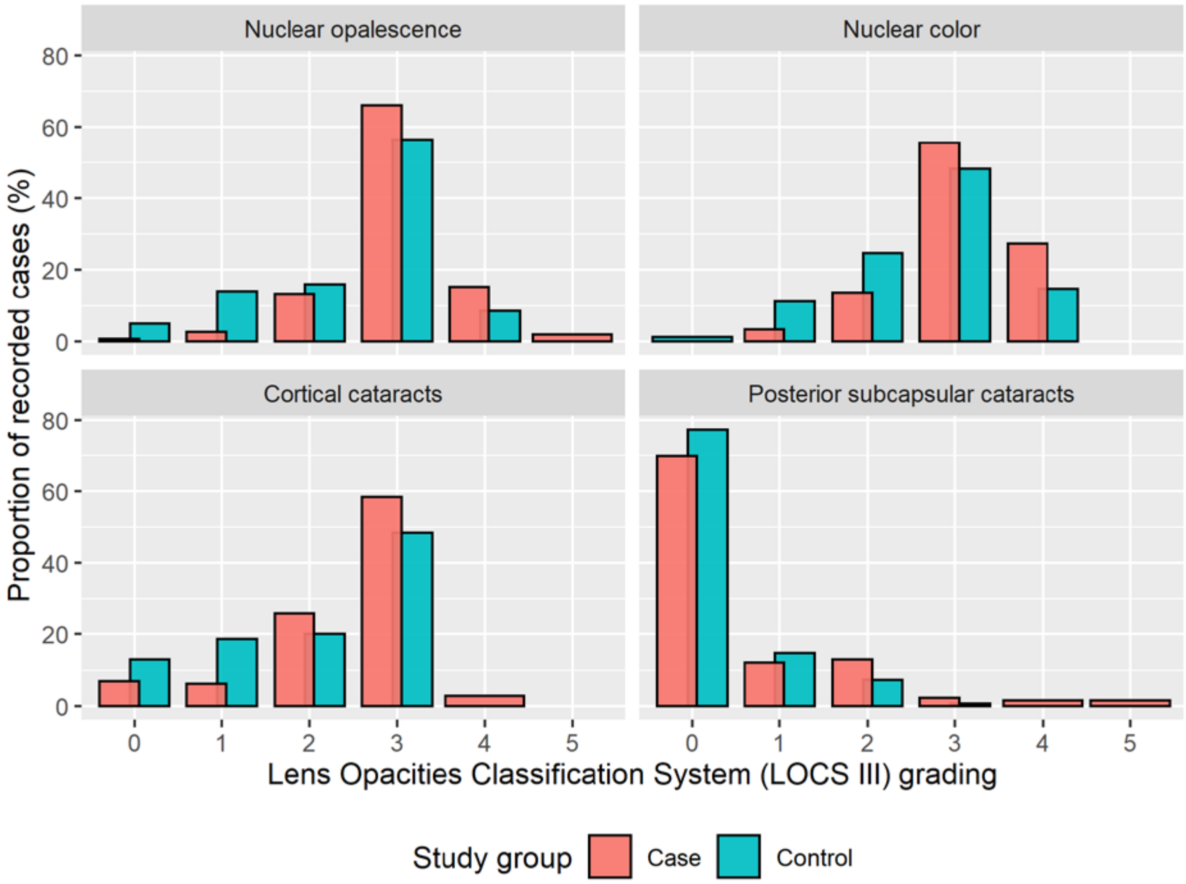
Psuedo-R^2 is the variance explained by the fixed effects only of the generalized linear mixed-effects model.[18]

† Axial length was missing for 5 cases

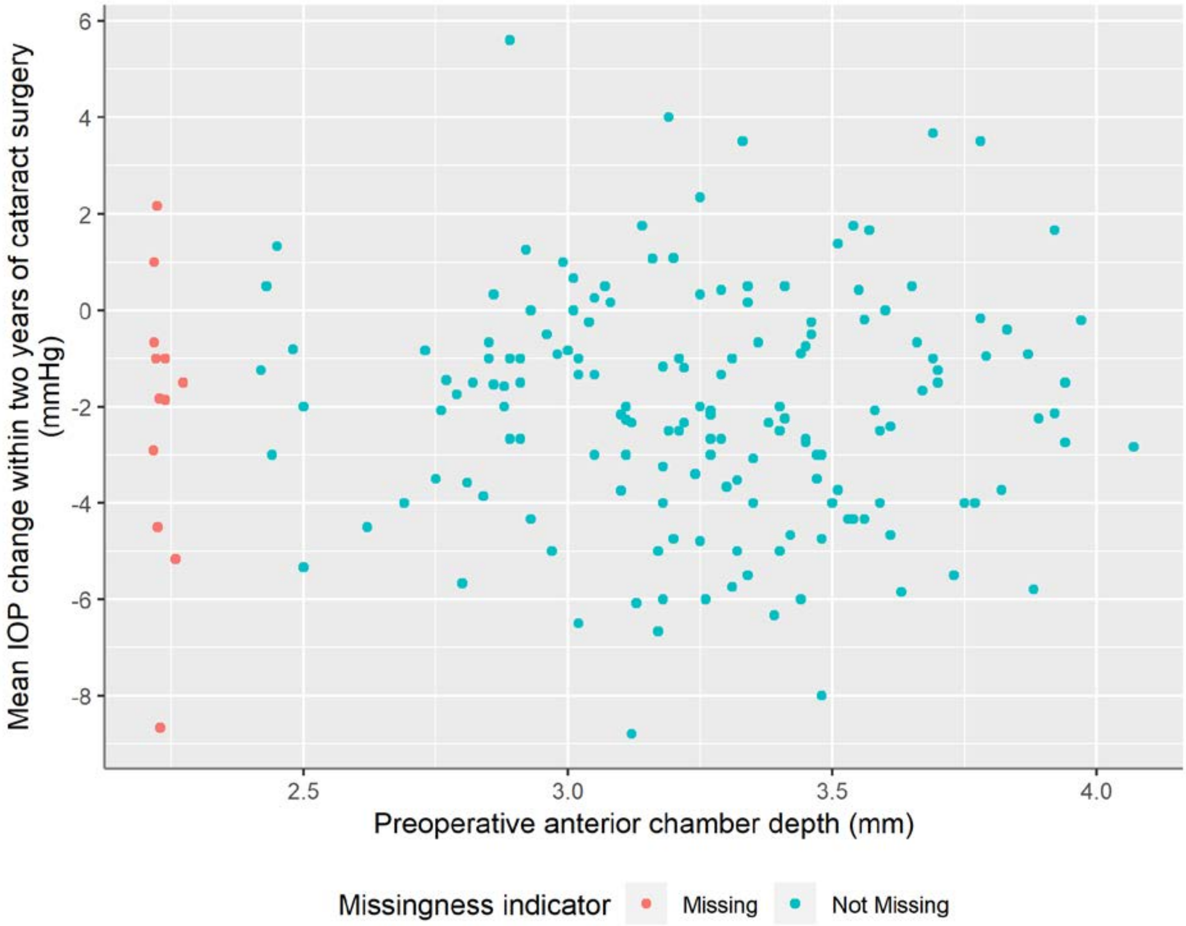
‡ Anterior chamber depth was missing for 12 cases

IOP: intraocular pressure.

Supplementary Figure 1: Cataract grading using the The Lens Opacities Classification System III of the cases and controls. This data was available for 153 cases and 164 controls.

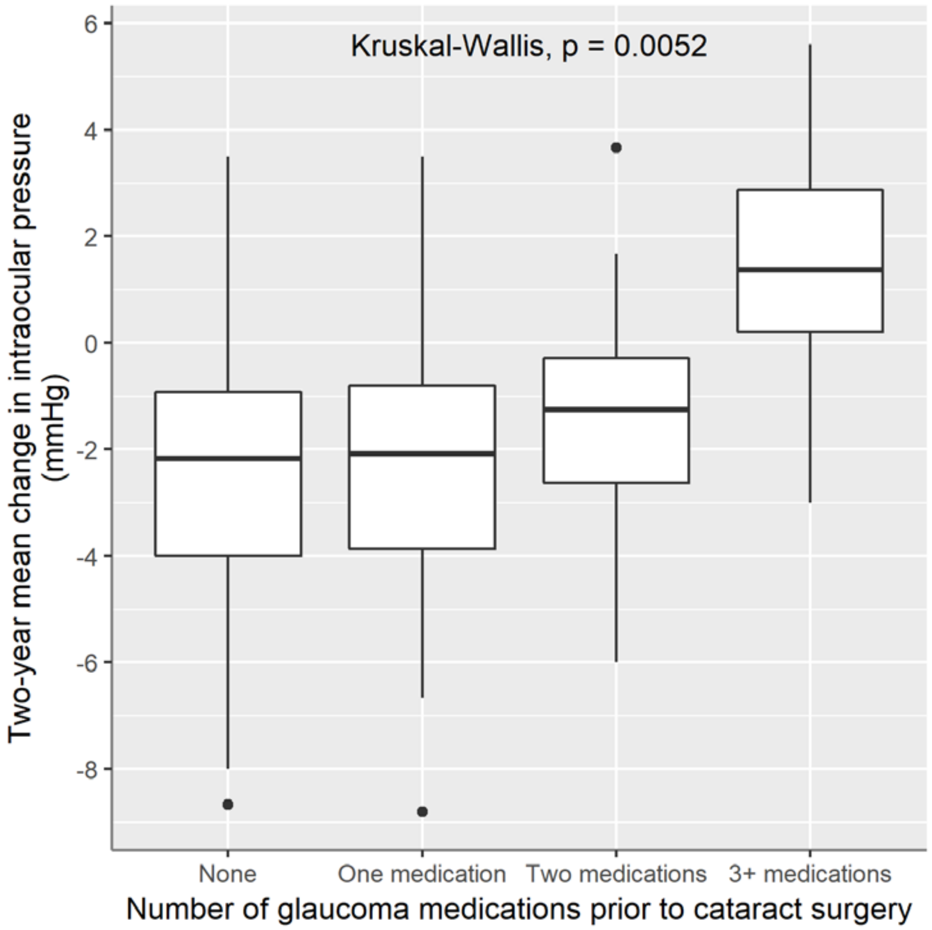


Supplementary Figure 2: Scatter plot of the preoperative anterior chamber depth and observed two-year mean change in intraocular pressure following cataract surgery.



Each blue point represents an eye (N = 159). Red points (N = 12) are cases with missing preoperative anterior chamber depth. These are plotted on the left margin of the plot to assess for missingness bias. The missing cases appear to be missing-at-random.

Supplementary Figure 3: Boxplot of the observed two-year mean change in intraocular pressure following cataract surgery based on the number of preoperative glaucoma medications.



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