Title

Predictors of long-term intraocular pressure control after lens extraction in primary angle closure glaucoma: results from the EAGLE trial

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Lens extraction was >10-times likelier than LPI to control IOP without drops in PAC/PACG. Chinese ethnicity, baseline IOP, and drop-use at baseline were the strongest predictors for success.

Abstract

Background/Aims:

To assess baseline ocular parameters in the prediction of long-term intraocular pressure (IOP) control after clear lens extraction (CLE) or laser peripheral iridotomy (LPI) in patients with primary angle closure disease using EAGLE trial data.

Methods:

This study is a secondary analysis of EAGLE data where we define primary outcome as 'good responders' as those with IOP <21mmHg without requiring additional surgery and 'optimal responders' as those who in addition were medication-free, at 36-months follow up. Primary analysis was conducted using a multi-variate logistic regression model to assess how randomized interventions and ocular parameters predict treatment response.

Results:

A total of 369 patients (182 in CLE arm and 187 in LPI arm) completed the 36-month follow up exam. After CLE, 90% met our pre-defined 'good response' criterion compared to 67% in the LPI arm, and 66% met 'optimal response' criterion compared to 18% in the LPI arm, with significantly longer drops/surgery-free survival time ($p < 0.05$ for all). Patients randomized to CLE [OR=10.1 (6.1-16.8)], Chinese [OR=2.3 (1.3-3.9)], those who had not previously used glaucoma drops [OR=2.8 (1.6-4.8)] were more likely to maintain long-term optimal IOP response over 36 months.

Conclusion:

Patients with PACG/PAC are ten times more likely to maintain drop-free good IOP control with initial CLE surgery than LPI. Non-Chinese ethnicity, higher baseline IOP and using glaucoma drops prior to randomization are predictors of worse long-term IOP response.

Key messages

What is already known on this topic: clear lens extraction (CLE) has greater efficacy and is more cost-effective than laser peripheral iridotomy (LPI) in patients with primary angle closure (PAC) disease.

What this study adds: Among patients with PAC disease, we found that those with initial CLE were 10x more likely to maintain good drop-free IOP control over 3 years vs LPI. We also identified Chinese ethnicity, lower preoperative intraocular pressure (IOP), not using glaucoma drops, and no glaucomatous changes to be baseline factors associated with drop-free post-operative IOP control.

How this study might affect research, practice or policy: in the context of shifting global management standards for angle closure disease, this study is important in guiding management decisions and further research.

Introduction

In 2016 we published the results of a randomized clinical trial comparing initial clear lens extraction (CLE) to laser peripheral iridotomy (LPI) for primary angle closure (PAC) and primary angle closure glaucoma (PACG) and reported better outcomes with CLE. Those undergoing CLE reported higher mean quality of life scores and had lower mean intraocular pressure (IOP -1.18 mmHg (95% CI -1.99 to -0.38, p=0.004)) after intervention, with fewer medications and glaucoma surgery, with an incremental cost effectiveness ratio of £14,284.[1]

Higher baseline IOP has been shown to predict higher post-surgery IOP for both non-glaucomatous[2-7] and open angle glaucoma eyes with cataract.[2,3,8-12] However, understanding which populations with PAC or PACG stand most to benefit from CLE remains to be determined. A recent paper found that higher baseline IOP was a predictor of higher IOP up to 48 months postoperatively for those with PACG and cataract undergoing phacoemulsification surgery.[13] Assessing *proportionate* change in IOP, others have reported that higher baseline IOP was associated with greater IOP reduction after phacoemulsification surgery, for both non-glaucomatous and glaucomatous eyes with cataract.[5] Only one paper has reported on anatomic predictors of IOP lowering, reporting that circumferential iridotrabecular contact was the best baseline parameter for prediction of postoperative IOP reduction for patients with PAC and IOP >30mmHg and cataract undergoing surgery.[14]

To date, there has been no analysis of predictors of IOP reduction after CLE in patients with non-cataractous lenses in either PAC or PACG. We aimed to identify baseline parameters associated with postoperative IOP reduction for those with PAC (with IOP > 30 mmHg) or PACG undergoing CLE vs LPI, using data from the EAGLE trial up to 36 months postoperatively.

Methods

Analysis cohort

Details of the EAGLE trial design and baseline characteristics are described elsewhere.[1,15] In brief; the EAGLE trial was a multicentre, international, randomized controlled trial comparing CLE with LPI. A total of 419 newly diagnosed PAC with IOP ≥30 mmHg or PACG patients were recruited from 30 hospitals across the UK, mainland China, Singapore, Malaysia, Hong Kong and Australia. PAC was defined as iridotrabecular contact of at least 180 degrees on gonioscopy, and PACG as reproducible glaucomatous visual field defects, glaucomatous optic neuropathy or both, and IOP ≥21 mmHg on at least one occasion. Individuals with symptomatic or clinically significant cataract, advanced glaucoma, or previous acute closed-angle glaucoma attacks were excluded.

The trial was prospectively registered with the ISRCTN registry, number ISRCTN44464607. The original EAGLE study adhered to the tenets of the Declaration of Helsinki and was approved by local institutional review boards. Study participants provided written informed consent. An independent data monitoring committee and an independent trial steering committee provided oversight.

EAGLE Procedures

Topical medications started at the time of diagnosis were continued and the allocated interventions were performed within 60 days of randomization. Participants randomized to CLE underwent phacoemulsification with a monofocal intraocular lens implant. Synechiolysis during lens extraction was allowed according to local practice. Patients randomized to standard of care underwent LPI. Laser iridoplasty was allowed if angle closure persisted after LPI, although this was rare.[1]

A target IOP of 15-20 mmHg was set at baseline dependent on the level of nerve damage.[15] Topical therapy could be escalated after intervention as needed to achieve this target. In the instance that maximal medical therapy did not control the IOP, the ophthalmologist could offer glaucoma surgery (including lens extraction in the LPI group). Patients assigned to LPI could undergo lens extraction for reduced vision (i.e. cataract surgery) as well.

EAGLE Assessments

Assessments were done at baseline and 6, 12, 24 and 36 months after randomization. IOP was the average of two readings by Goldmann tonometry. Two observers at each site, following a masking protocol, were

involved in the IOP measurements. Best-corrected visual acuity was tested using the Early Treatment Diabetic Retinopathy Study (ETDRS) vision charts. The extent of peripheral anterior synechiae (PAS) and iridotrabecular contact were determined by gonioscopy. Anterior chamber measurements (axial length (AL) and anterior chamber depth (ACD)) were performed using an IOLMaster. Participants underwent two visual field tests at baseline, and one at 6, 12, 24 and 36 months using a standard automated perimetry test (Humphrey SITA 24-2 test). Further detail of the original EAGLE procedures and assessments can be found in the original trial.[1]

Definition of success

For the present study, we defined "good responders" as those with an IOP <21 mmHg and without additional glaucoma surgery or lens extraction (vs all others, termed "poor responders"). We further defined "optimal responders" as those with an IOP <21 mmHg and without glaucoma surgery or lens extraction, who were additionally using no topical glaucoma medications at 36 months postoperatively (vs all others, termed "suboptimal responders"). In sensitivity analyses, patients in the LPI arm who underwent subsequent LE for low vision (i.e. cataract) rather than glaucoma management (with an IOP<21mH) will not be considered treatment failure. We also performed survival analysis assessing time to treatment failure, which was defined as either IOP ≥21 mmHg, needing additional topical medications after intervention, or requiring an additional glaucoma surgery or lens extraction in the originally treated eye.

Statistical analyses

All analyses were based on complete case analysis principles and no imputation was performed for missing data. Only the study eye of each patient was included in the analyses. The following baseline parameters were assessed: race, age, gender, diagnosis (PAC vs PACG), visual field loss (MD index), visual acuity, baseline IOP, anterior chamber depth, peripheral anterior synechiae, glaucoma medications.

Outcome measurements were compared by t-tests for continuous outcome variables, and chi-squared tests for dichotomous outcome variables. Univariate and multivariate logistic regression models were used to assess the association between baseline characteristics and the response to interventions. Hazard ratios (HRs) with 95% confidence intervals (CIs) were estimated using a Cox proportional hazards model between eyes randomized to CLE versus LPI. We used Kaplan Meier survival curves to display failure rates, where failure was defined as either (i) IOP >21mmHg, (ii) reoperation, or (iii) the need for medications to control IOP, and log-rank tests to test for equality of survival curves. All statistical analyses were performed using Stata version 14.2. The significance level was set at 5% in all analyses.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, interpretation, or writing of the report.

Results

Among 419 randomized participants, a total of 369 (182 in CLE arm and 187 in LPI arm) completed the 36-month follow up or were censored owing to having undergone additional surgeries. Only one study eye randomized to CLE underwent trabeculectomy to control IOP (0.5%) while six had trabeculectomy (2.8%) and 29 underwent lens extraction (13.7%) in the LPI arm.

CLE resulted in greater long-term IOP reduction than LPI. 89.6% of eyes had good pressure control after CLE with concurrent topical IOP-lowering medication, and 65.9% of them did not require topical glaucoma drops at 36 months. Among the LPI arm, 66.8% had good IOP control at 36 months with concurrent glaucoma drops, and only 17.7% of them remained off IOP lowering drops at 36 months (Table 1). Interval IOP between CLE versus LPI are shown in Figure 1. Despite similar IOP between CLE vs LPI at each interval, there was a substantially lower need for drops to control IOP for the CLE arm at 36 months.

After initial CLE, good responders were more likely to be of Chinese ethnicity (30.7% for good responder vs 0% for poor responder, p=0.005) and have shallower ACD (2.53mm versus 2.71mm, p=0.03) than poor responders (Table 2.1); and optimal responders more likely to have shallower ACD (2.51mm versus 2.61mm, p=0.048) and be drop-free at baseline (p=0.04) than suboptimal responders (Table 2.2). Patients who were not prescribed any glaucoma drops at baseline were more likely to be drops free after both CLE (p=0.04) and LPI (p=0.01, Table 2.2). After LPI, good responders were more likely to have lower IOP at baseline (29.6mmHg for good responders versus 32.3mmHg for poor responders, p=0.02) compared to poor responders; and optimal responders were more likely to be of Chinese ethnicity (p=0.01), more likely to have had PAC and less likely PACG (p<0.001), and lower refractive error (spherical equivalence +0.40D versus +1.48D, p=0.02) compared to suboptimal responders (Table 2.2). Sensitivity analyses demonstrated similar associations between Chinese ethnicity and PAC (rather than PACG) and optimal response after LPI (Table S1). In contrast to the CLE cohort, baseline ACD was not associated with optimal response after LPI. There was otherwise no statistically significant difference in age, gender, gonioscopic findings, axial length, visual field (VF), visual acuity, or central corneal thickness measurement at baseline between good versus poor responders or optimal vs suboptimal responders for either group.

The 3-year failure rate was 38% after initial CLE and 72% after initial LPI (p<0.001, Figure 2). The LPI-treated eyes had a >2.5 times higher risk of failure compared to those treated initially with CLE over 36 months (p<0.001) (Table 3). Non-Chinese [HR=1.52 (1.14-2.05)], those who had used glaucoma drops before randomization [HR=1.48 (1.12-1.95)] and those who had higher baseline IOP [HR=1.08 (1.01-1.16) per 5mmHg] were at higher risk of failure (Table 3). In multivariate logistic regression, patients of Chinese origin [OR=2.26, 95% CI: (1.31-3.89)], with PAC [OR=2.10, 95% CI: (1.26-3.49)], on no glaucoma drops

[OR=2.77 (1.61-4.78)] and with better visual field measurements at baseline [OR=1.06, 95% CI: (1.01-1.12) per 1dB better] were more likely to be optimal responders at 36 months (Table 4). Other baseline characteristics such as age, gender, presence of peripheral anterior synechiae, ACD, and visual acuity were not associated with long-term IOP control.

Among patients who randomized to initial CLE, shallower ACD [OR=1.18, 95% CI: (1.02-1.36) per 0.1mm shorter], not on glaucoma medications at baseline [OR=2.25, 95% CI: (1.12-4.54)] and worse visual acuity [OR=0.88, 95% CI: (0.77-1.00) per 1 line worsen] were predictors for either good or optimal response after surgery (Table 5). Among patients who were randomized to initial LPI, Chinese-origin [OR=2.76, 95% CI: (1.26-6.05)], PAC [OR=3.80, 95% CI: (1.67-8.63)], no glaucoma medications at baseline [OR=4.62 (1.86-11.48)], better baseline visual field [OR=1.12, 95% CI: (1.00-1.25) per 1dB better] and lower baseline IOP [OR=1.30, 95% CI: (1.05-1.60) per 1mmHg lower] were factors associated with either good or optimal long-term IOP control (Table 5).

Discussion

In the EAGLE trial patients undergoing initial CLE were almost 5 times more likely to have better long-term IOP control and 10 times more likely to be free of drops or surgery as compared to those undergoing LPI as initial management of PAC with high IOP or PACG with IOP 21 mmHg or greater (Table 4). Chinese ethnicity, no glaucomatous damage, lower pre-operative IOP and no glaucoma medications at baseline were associated with a higher probability of achieving adequate IOP control without the need for daily medications regardless of initial treatment (Table 4).

Despite the real difference in IOP reduction between CLE vs LPI being small at 36 months (1mmHg), there was a substantially lower need for drops to control IOP for the CLE arm. While no other trials describe the effect of CLE on long-term IOP outcomes in PAC or PACG to our knowledge, others also describe significant IOP reduction following standalone cataract extraction for PAC or PACG at 6 to 24 months postoperatively, between -1.8 and -8.3mmHg.[16-19]

A shallower anterior chamber has been associated with greater IOP reduction after surgery for patients with PACG and cataract,[13] in agreement with findings here for those randomized to CLE. A recent study of 18 PAC patients in a tertiary centre in India undergoing cataract surgery with baseline IOP >30 mmHg found that greater preoperative iridotrabecular contact was associated with a greater proportionate drop in IOP.[14] We did not find this to be the case in the current study, possibly due to our larger, more diverse patient population that included PAC and PACG patients and different ethnicities. The authors did not report on concurrent medical therapy requirements for IOP control postoperatively, and only reported one-month postoperative data.

Similar to previous studies, we found that higher baseline IOP was associated with poorer IOP outcomes for those undergoing either CLE or LPI. Given our IOP success threshold of <21 mmHg, it is not surprising that those with higher baseline IOP were *less* likely than those with lower baseline IOP to fall below this benchmark at 36 months postoperatively. This finding has also been reported by others. A recent paper on long-term IOP outcomes for those undergoing cataract surgery for PACG found that higher baseline IOP was associated with higher IOP postoperatively.[13] Others have also described the association between baseline IOP and postoperative IOP control after cataract surgery, although not for those undergoing clear lens extraction or in the setting of glaucoma management exclusively. In these studies, higher baseline IOP was reported to be associated with higher postoperative IOP after cataract surgery,[20] and associated with greater proportionate IOP reduction after cataract surgery.[9] An important limitation for direct comparisons between these studies and our own is that none of the above-mentioned studies explicitly report whether good postoperative IOP control was contingent on concurrent topical medication use.

Chinese ethnicity was identified as a predictor for better overall IOP response in this study. All Chinese patients were able to maintain IOP<21mmHg for 3 years after CLE (Table 2) and Chinese patients were 2 times more likely to be drops free after either CLE or LPI as compared to non-Chinese patients (Table 4). While few have examined the effect of ethnicity on IOP reduction after lens extraction, those that have similarly describe Asian ethnicity to be associated with postoperative IOP reduction vs non-Asian ethnicity (albeit for cataractous lenses).[20] Our findings are particularly important given the preponderance of PACG over POAG in East Asian populations, who account for around half of all glaucoma sufferers worldwide.[21] The prevalence of PACG in East Asia has been attributed toward a number of biometric factors including shallow ACD, lens thickness, and shorter AL.[21] These factors may in part explain why both CLE and LPI were of particular benefit for patients of Chinese ethnicity here, decreasing lens thickness and deepening ACD.

Lastly, better baseline VF was predictive of optimal IOP control for those undergoing LPI (albeit not reaching significance in sensitivity analyses). While better preoperative VF may be reflective of less severe disease and preserved integrity of angle structures at baseline – with subsequently greater likelihood of response – this has not been well-described elsewhere.[22] Poor baseline VA was associated with lower likelihood of optimal response for those undergoing CLE, also possibly reflective of those with more advanced disease at baseline (and progressive structural angle damage) being less likely to benefit from CLE.

The EAGLE trial is a prospective randomized multicentre trial that employed masking of the IOP outcome measure, collected data in a standard fashion (albeit missing baseline gonioscopic data for 247 patients), and included patients operated on by many surgeons across the globe. [23] We also had good follow up over 36 months with 88% completed 36-month visit or censored due to additional surgery. That said, the findings only apply to individuals meeting the enrolment criteria for the current study and the results may not be applicable to primary angle closure suspects with IOP below 30 mmHg or those with PACG and IOP < 21 mmHg. Further, those with symptomatic cataract were ineligible for this trial, and therefore it is not certain that the current findings translate to those with cataractous lens changes. Notably, of the 29 in the LPI arm who underwent subsequent lens extraction, 12 (6%) underwent surgery for clinically significant cataract rather than IOP control.[1] While not controlled for, given the demonstrated effect of lens extraction on IOP and the lower need for drops, this would have reduced our ability to detect a difference between the two arms. Sensitivity analyses also show similar associations between LPI and optimal response. Variable postoperative IOP goals dictating drops or reoperation may have made those with higher acceptable IOP (closer to 20 than 15 mmHg) more likely to be both good and optimal responders.[15] However, details of IOP

goals was not available as a covariable for the current study and should affect both LPI and CLE arms equally.

We have previously reported that in this multicentre randomized controlled trial, CLE had greater efficacy and was more cost-effective than laser peripheral iridotomy in patients with primary angle closure disease. Here we demonstrate that those undergoing CLE were 10 times more likely to achieve IOP control postoperatively without the need for topical therapy or surgery up to 3 years. For those undergoing any intervention, we identified Chinese ethnicity, lower preoperative IOP, not using glaucoma drops at randomization, and no glaucomatous changes (PAC) are baseline factors associated with optimal post-operative response. This study is of particular importance in the context of shifting global management standards for angle closure disease – and useful in guiding management decisions and further research.

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Author Contributions

WGM, DSF and DSC were responsible for conceptualization and methodology. AAB, PJF, JMB, CR, DC, CC and JN were responsible for the original investigation and data curation. DSC was responsible for data analyses and validation. WGM, DSF and DSC were responsible for initial manuscript composition. WGM, AAB, PJF, OH, JMB, CR, DC, CC, JN, DSF and DSC were responsible for final manuscript reviews and edits.

Competing Interests

None declared.

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Table 1: Treatment response by visits.

	CLE	LPI
Good response		
6-month visit [n (%)]	179 (91.8)	129 (63.9)
12-month visit [n (%)]	178 (92.7)	121 (62.1)
24-month visit [n (%)]	161 (86.6)	108 (58.1)
36-month visit [n (%)]	163 (89.6)	125 (66.8)
Optimal response		
6-month visit [n (%)]	130 (66.7)	43 (21.3)
12-month visit [n (%)]	136 (70.8)	42 (21.4)
24-month visit [n (%)]	121 (65.1)	35 (18.8)
36-month visit [n (%)]	120 (63.9)	33 (17.7)

Good response defined by IOP<21mmHg and not had additional lens extraction or glaucoma surgery at each visit.
Optimal response defined by IOP<21mmHg without any medication and has not had additional lens extraction or glaucoma surgery at each visit.
CLE, clear lens extraction; LPI, laser peripheral iridotomy

Table 2.1: Baseline demographics by responding to CLE versus LPI. Good responder defined by IOP<21mmHg at 36 months and not had additional lens extraction or glaucoma surgery

	CLE (n=182)		LPI (n=187)	
	Good responder	**Poor responder**	**Good responder**	**Poor responder**
Number (%)	163 (89.6%)	19 (10.4%)	125 (66.8%)	62 (33.2%)
Age (mean±SD)	68.1±8.1	66.5±6.8	66.7±8.5	68.5±8.2
Female [n (%)]	93 (57.1%)	14 (73.7%)	68 (54.4%)	38 (61.3%)
Chinese origin [n (%)]	50 (30.7%)*	0 (0%)*	38 (30.4%)	18 (29.0%)
Diagnosis (n (%))				
PAC	64 (39.3%)	9 (47.4%)	50 (40.0%)	23 (37.1%)
PACG	99 (60.7%)	10 (52.6%)	75 (60.0%)	39 (62.9%)
Spherical equivalence, Diopter (mean±SD)	+1.66±2.44	+1.64±1.29	+1.27±2.34	+1.34±2.26
Glaucoma medication used at baseline [n (%)]	95 (61.3%)	12 (63.2%)	76 (63.3%)	42 (68.9%)
Gonioscopy measurements				
Peripheral anterior synechiae, degree (mean±SD)	42.4±78.7	14.2±43.2	46.0±80.9	38.6±72.3
Irido-trabecular contact, degree (mean±SD)	292.5±79.1	264.7±74.4	303.7±72.1	306.1±72.6
IOLMaster (mean±SD)				
Axial length, mm	22.53±0.93	22.69±0.56	22.59±0.98	22.71±1.05
Anterior chamber depth, mm	2.53±0.32*	2.71±0.31*	2.54±0.34	2.55±0.42
Visual fields MD, dB (mean±SD)	-4.89±5.30	-2.44±5.07	-4.14±4.47	-5.57±6.22
Visual acuity, ETDRS letter	76.8±11.8	77.4±20.5	76.0±14.2	74.5±14.1
Intraocular pressure, mmHg (mean±SD)	29.64±8.13	29.47±7.19	29.59±6.87*	32.31±9.18*
Central corneal thickness, μm (mean±SD)	550.1±38.0	557.6±40.9	554.9±41.5	545.6±36.6

CLE, early lens extraction; LPI, laser peripheral iridotomy; SD, standard deviation; PAC, primary angle closure; PACG, primary angle closure glaucoma.

Table 2.2: Baseline demographics by responding to CLE versus LPI; optimal responder defined by IOP<21 at 36 months without any medication and no additional surgery

	CLE (n=182)		LPI (n=187)	
	Optimal responder	**Suboptimal responder**	**Optimal responder**	**Suboptimal responder**
Number (%)	120 (65.9%)	62 (34.1%)	33 (17.7%)	154 (82.4%)
Age (mean±SD)	67.6±8.1	68.6±7.9	65.6±9.2	67.6±8.3
Female [n (%)]	69 (57.5%)	38 (61.3%)	23 (69.7%)	83 (53.9%)
Chinese origin [n (%)]	38 (31.7%)	12 (19.4%)	16 (48.5%)*	40 (26.0%)*
Diagnosis (n (%))				
PAC	52 (43.3%)	21 (33.9%)	22 (66.7%)*	51 (33.1%)*
PACG	68 (56.7%)	41 (66.1%)	11 (33.3%)*	103 (66.9%)*
Spherical equivalence, Diopter (mean±SD)	+1.79±2.33	+1.43±2.36	+0.40±2.58*	+1.48±2.21*
Glaucoma medication used at baseline [n (%)]	65 (56.0%)*	42 (72.4%)*	14 (45.2%)*	104 (69.3%)*
Gonioscopy measurements				
Peripheral anterior synechiae, degree (mean±SD)	45.7±79.6	27.6±68.3	38.8±65.1	44.5±80.6
Irido-trabecular contact, degree (mean±SD)	290.1±81.9	289.1±73.4	323.4±55.3	300.3±74.8
IOLMaster (mean±SD)				
Axial length, mm	22.5±0.9	22.7±0.9	22.7±1.3	22.6±0.9
Anterior chamber depth, mm	2.51±0.34*	2.61±0.29*	2.52±0.46	2.55±0.34
Visual fields MD, dB (mean±SD)	-4.34±5.10	-5.20±5.73	-3.42±3.90	-4.87±5.35
Visual acuity, letter	78.0±10.2	74.7±16.8	73.9±15.4	75.9±13.8
Intraocular pressure, mmHg (mean±SD)	29.3±8.5	30.3±7.0	30.8±7.1	30.4±8.0
Central corneal thickness, μm (mean±SD)	550.2±38.1	552.3±38.8	560.3±38.8	550.0±40.2

CLE, clear lens extraction; LPI, laser peripheral iridotomy; SD, standard deviation; PAC, primary angle closure; PACG, primary angle closure glaucoma.

Table 3. Predictors associated with failure using Cox proportional hazards model. Failure is defined as IOP>21 or needing medication or surgery

	Univariate		Multivariate*	
	Hazard ratio (95% CI)	*p*	Hazard ratio (95% CI)	*p*
Intervention (LPI versus CLE)	**2.48 (1.89-3.25)**	**<0.001**	**2.52 (1.92-3.31)**	**<0.001**
Age (per 10 years older)	1.12 (0.97-1.30)	0.135	1.13 (0.97-1.31)	0.107
Female	1.01 (0.79-1.30)	0.945	1.01 (0.79-1.30)	0.932
Non-Chinese	**1.49 (1.11-2.00)**	**0.008**	**1.52 (1.14-2.05)**	**0.005**
PACG (versus PAC)	1.27 (0.98-1.65)	0.069	1.19 (0.92-1.55)	0.193
PAS (per 30° increase)	0.81 (0.61-1.07)	0.142	0.87 (0.65-1.16)	0.335
ACD (per 0.1 mm shorter)	0.98 (0.95-1.01)	0.309	0.99 (0.95-1.03)	0.566
Glaucoma medication at baseline	**1.37 (1.04-1.80)**	**0.024**	**1.48 (1.12-1.95)**	**0.006**
Visual field MD (per 1dB worsen)	1.01 (0.99-1.03)	0.321	1.02 (0.99-1.04)	0.166
Visual acuity (per 1 line worsen)	1.00 (0.96-1.05)	0.950	1.00 (0.96-1.05)	0.971
IOP (per 5mmHg higher)	1.07 (0.99-1.15)	0.070	**1.08 (1.01-1.16)**	**0.029**

*All multivariate analyses adjusted for intervention, age, gender and race

CI, confidence interval; LPI, laser peripheral iridotomy; CLE, clear lens extraction; PACG, primary angle closure glaucoma; PAC, primary angle closure; PAS, peripheral anterior synechiae; ACD, anterior chamber depth; MD, mean deviation; IOP, intraocular pressure.

Table 4: Multivariate analyses for baseline predictive factors of **good response (IOP<21, no additional surgery) and optimal response (IOP<21, on no medications and no additional surgery)** at long-term follow-up (36 month)

	Good response (IOP<21mmHg and no surgery)		**Optimal response (IOP<21mmHg and no medication or surgery)**	
	Odds ratio (95% CI)	*p*	Odds ratio (95% CI)	*p*
Lens extraction (versus LPI)	**4.90 (1.01-3.57)**	**0.046**	**10.13 (6.10-16.83)**	**<0.001**
Age (per 10 years older)	0.88 (0.64-1.20)	0.412	0.82 (0.61-1.10)	0.191
Female	0.66 (0.38-1.12)	0.121	1.17 (0.72-1.91)	0.531
Chinese	1.68 (0.92-3.08)	0.094	**2.26 (1.31-3.89)**	**0.003**
PAC (versus PACG)	0.93 (0.54-1.59)	0.785	**2.10 (1.26-3.49)**	**0.005**
PAS (per 30° increase)	1.18 (0.64-2.18)	0.596	1.49 (0.86-2.58)	0.156
Irido-trabecular contact (per 30°)	1.01 (0.90-1.12)	0.915	1.02 (0.93-1.13)	0.632
Axial length (per 1mm shorter)	1.23 (0.93-1.61)	0.147	1.15 (0.88-1.51)	0.297
ACD (per 0.1 mm shorter)	1.04 (0.96-1.12)	0.322	1.05 (0.97-1.13)	0.209
Spherical equivalence (+1 diopter)	1.03 (0.91-1.16)	0.673	1.01 (0.91-1.14)	0.810
No glaucoma medication	1.39 (0.79-2.44)	0.259	**2.77 (1.61-4.78)**	**<0.001**
Visual field MD (per 1dB better)	1.02 (0.97-1.07)	0.425	**1.06 (1.01-1.12)**	**0.022**
Visual acuity (per 1 line worsen)	0.96 (0.87-1.05)	0.348	0.94 (0.85-1.03)	0.190
IOP (per 5mmHg lower)	**1.21 (1.02-1.42)**	**0.026**	0.93 (0.79-1.08)	0.333

*All multivariate analyses adjusted for lens extraction, age, gender, ethnicity

CI, confidence interval; LPI, laser peripheral iridotomy; CLE, clear lens extraction; PACG, primary angle closure glaucoma; PAC, primary angle closure; PAS, peripheral anterior synechiae; ACD, anterior chamber depth; MD, mean deviation; IOP, intraocular pressure.

Table 5: Multivariate analyses for baseline predictive factors of **good response (IOP<21, no additional surgery) and optimal response (IOP<21, on no medications and no additional surgery)** at 36-month, by treatment arm.

	Clear lens extraction				**Laser peripheral iridotomy**			
	Good response		Optimal response		Good response		Optimal response	
	Odds ratio (95% CI)	*p*	Odds ratio (95% CI)	*p*	Odds ratio (95% CI)	*p*	Odds ratio (95% CI)	*p*
Age (per 10 years older)	1.22 (0.66-2.25)	0.524	0.86 (0.58-1.28)	0.455	0.77 (0.53-1.11)	0.165	0.72 (0.45-1.15)	0.173
Female	0.49 (0.17-1.44)	0.194	0.84 (0.45-1.60)	0.602	0.75 (0.40-1.40)	0.372	2.00 (0.88-4.57)	0.100
Chinese	---	---	1.89 (0.90-3.97)	0.092	1.09 (0.55-2.13)	0.812	**2.76 (1.26-6.05)**	**0.011**
PAC (versus PACG)	0.79 (0.29-2.11)	0.633	1.42 (0.73-2.75)	0.299	1.09 (0.58-2.06)	0.787	**3.80 (1.67-8.63)**	**0.001**
PAS (per 30° increase)	2.23 (0.61-8.18)	0.228	1.80 (0.85-3.82)	0.126	1.03 (0.50-2.11)	0.934	1.14 (0.48-2.67)	0.771
Irido-trabecular contact (per 30°)	1.11 (0.94-1.32)	0.212	0.98 (0.86-1.10)	0.717	0.97 (0.85-1.12)	0.715	1.15 (0.94-1.40)	0.171
Axial length (per 1mm shorter)	1.41 (0.80-2.48)	0.239	1.42 (0.97-2.07)	0.070	1.15 (0.84-1.58)	0.374	0.94 (0.63-1.40)	0.761
ACD (per 0.1 mm shorter)	**1.18 (1.02-1.36)**	**0.030**	1.09 (0.99-1.21)	0.090	1.00 (0.92-1.09)	0.926	1.00 (0.90-1.10)	0.941
Spherical equivalence (+1 diopter)	1.02 (0.83-1.25)	0.848	1.13 (0.97-1.31)	0.105	1.00 (0.86-1.15)	0.952	0.86 (0.70-1.05)	0.137
No glaucoma medication	1.09 (0.40-2.97)	0.868	**2.25 (1.12-4.54)**	**0.024**	1.44 (0.73-2.86)	0.297	**4.62 (1.86-11.48)**	**0.001**
Visual field MD (per 1dB better)	0.90 (0.78-1.02)	0.109	1.05 (0.99-1.12)	0.122	1.05 (0.99-1.12)	0.092	**1.12 (1.00-1.25)**	**0.045**
Visual acuity (per 1 line worsen)	1.00 (0.83-1.22)	0.972	**0.88 (0.77-1.00)**	**0.048**	0.96 (0.86-1.08)	0.516	1.03 (0.89-1.18)	0.712
IOP (per 5mmHg lower)	0.97 (0.71-1.34)	0.861	1.13 (0.93-1.38)	0.224	**1.30 (1.05-1.60)**	**0.017**	1.02 (0.80-1.30)	0.876

*All multivariate analyses adjusted for age, gender (and Chinese)

CI, confidence interval; LPI, laser peripheral iridotomy; CLE, clear lens extraction; PACG, primary angle closure glaucoma; PAC, primary angle closure; PAS, peripheral anterior synechiae; ACD, anterior chamber depth; MD, mean deviation; IOP, intraocular pressure.