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ARTICLE

Influence of miosis and laser peripheral iridotomy on intraocular lens power calculation in patients with primary angle closure disease

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OBJECTIVES: To evaluate the effect of miosis and laser peripheral iridotomy (LPI) on intraocular lens (IOL) power prediction and ocular biometry in eyes with primary angle closure disease (PACD).

METHODS: In this prospective observational study, primary angle closure suspects (PACS), and subjects classified with primary angle closure (PAC)/primary angle-closure glaucoma (PACG) undergoing LPI were enrolled. Ocular biometric parameters were measured with IOLMaster700 at baseline (T_0), one week after pilocarpine instillation (T_1), and another week post LPI (T_2). Biometric changes and the IOL power predicted for emmetropia using Barrett Universal II, Haigis, Holladay2, Hoffer Q and SRK/T formulae were analysed and compared among different time points.

RESULTS: 100 eyes of 50 PACS and 50 PAC/PACG patients were enrolled. Following pilocarpine-induced miosis, lens thickness (LT) increased and anterior chamber depth (ACD) decreased (all groups $p < 0.01$), while white-to-white diameter decreased and central corneal thickness increased significantly only in the PACS cohort (both $p < 0.01$). Compared to baseline, LPI induced an increase of ACD and a slight decrease of LT in PACS (both $p < 0.01$), whereas only axial length changed significantly ($p = 0.012$) in the PAC/PACG cohort. Regardless of the formula used, no significant difference to the predicted IOL power for emmetropia existed among the three time points in each group (all $p > 0.1$).

CONCLUSION: We report the changes of anterior segment parameters induced by miosis and LPI in PACD. These interventions do not significantly affect the IOL power calculation predicted for emmetropia in Chinese eyes when common third-, fourth-and new generation IOL formulae are used.

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INTRODUCTION

Primary angle closure disease (PACD) has a higher prevalence in Asian populations, with the subtype of primary angle closure glaucoma (PACG) responsible for the vast majority of glaucoma blindness in Chinese cohorts. Cataract surgery is established as an effective intervention for PACD patients, addressing multiple mechanisms in pathogeneses such as pupil block and iris crowding that stems from age-related thickening of the crystalline lens [1]. Numerous publications have highlighted the higher risk of refractive error following cataract surgery in this cohort compared to that of patients undergoing cataract surgery without anatomical features contributing to synechiae development and primary angle closure [2, 3]. It is not known whether this refractive error may be explained by interventions such as pharmacological miosis and laser peripheral iridotomy frequently employed in the management algorithm of this disease [4–6].

Anatomical and ocular biometric changes in response to pilocarpine are well known including pharmacological accommodation and forward movement of the iris-lenticular diaphragm. Conversely, LPI may deepen the peripheral ACD by reconstructing an aqueous humour outflow pathway [7, 8]. It may be hypothesized that changes related to miosis and LPI may alter ocular parameters critical to IOL prediction [9]. Additionally, modern IOL power calculation formulae and their ability to predict a target postoperative refraction may be affected to varying degrees depending on the variations of which different ocular parameters may be incorporated.

We performed this study to determine the biometric changes that pilocarpine and LPI may induce in subjects with PACD, and compared the IOL power prediction based on these parameters for emmetropia before and after these interventions. This current study clarifies whether these two interventions commonly performed for PACD would subsequently induce a change in IOL power calculated for emmetropia, which would potentially contribute to the increased refractive error frequently seen in this cohort of patients.

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METHODS

The procedures used in this study conformed to the tenets of the Declaration of Helsinki for Research Involving Human Participants and was approved by the Ethical Review Committee of Eye & ENT Hospital of Fudan University, a tertiary specialized hospital in Shanghai of China. The trial protocol was also registered at ChiCTR (www.chictr.org, Registration Number: ChiCTR2100051681). All participants were Han Chinese and provided written informed consent to participate in the study.

This prospective observational study recruited 50 eyes of 50 PACS patients and 50 eyes of 50 PAC or PACG patients diagnosed at the Eye & ENT Hospital of Fudan University from April 2020 to January 2022. Diagnoses were made by a fellow trained in glaucoma (H.Y.) and confirmed by one of the senior glaucoma consultants (Y.C. and J.W.) according to the International Society for Geographical and Epidemiological Ophthalmology (ISGEO) guidelines [10]. In brief, PACS was defined as eyes in which at least 180° of the posterior pigmented trabecular meshwork was not visible on gonioscopy in the primary position of gaze without indentation but with neither increased IOP nor glaucomatous neuropathy. People meeting gonioscopic criteria for PACS and with evidence of peripheral anterior synechia or increased IOP (greater than 22 mmHg) would be classified as primary angle closure (PAC). Those PAC who additionally demonstrated glaucomatous damage of the optic nerve were classified as primary angle closure glaucoma (PACG).

Exclusion criteria included the presence of corneal oedema, acute angle closure crisis, baseline IOP more than 30 mmHg, plateau iris, secondary angle closure, a dense cataract influencing the quality of optical biometry, severe fundus abnormalities, poor fixation, strabismus, contact lens wear, or any history of ocular trauma or prior intraocular surgery. A history of systemic or topical medication that could affect ocular accommodation was also excluded. If both eyes of one subject were eligible for enrolment, the eye with more extensive angle closure or iridotrabecular contact was selected for study inclusion.

A comprehensive medical history review and ocular examination including uncorrected visual acuity (UCVA), slit lamp examination, ophthalmoscopy, gonioscopy, ultrasound biomicroscopy (UBM), and intraocular pressure (IOP) measurement was performed. For those with normal IOP and vertical CDR ≥ 0.6, careful evaluation on the retinal nerve fibre layer was performed by one of the glaucoma consultants (Y.C., and J.W.). Patients with controversy would receive further visual field tests until final diagnoses were agreed by the three authors (H.Y., Y.C., and J.W.). All participants were prescribed with pilocarpine nitrate 0.5% (Zhenrui®, Bausch+Lomb) three times per day and scheduled for LPI one week after. LPI was routinely performed by trained doctors, under topical anaesthesia using a VOLK iridectomy laser lens with single pulsed Neodymium: Yttrium Aluminum Garnet (Nd: YAG) laser at an initial setting of 8.0–10.0 mJ to create a patent iridotomy. After the procedure, 1% Prednisolone Acetate ophthalmic suspension (Pred Forte®, Allergan) was prescribed four times a day for one week.

Optical biometry was performed using IOLMaster700® (Carl Zeiss Meditec, Jena, Germany) at the following time points: (1) at baseline (T_0), (2) one week after instillation of pilocarpine nitrate 0.5% before LPI (T_1), and (3) another 7 days post LPI (T_2). Specifically, at T_1, a horizontal pupil diameter less than 3.0 mm and the pupillary-light reflex masked completely by the pilocarpine-induced miosis were confirmed before biometry. Similarly, restoration of the pupil light reflex and pupil diameter were documented, and a patent iridotomy was confirmed before measurement at T_2.

Three biometric measurements were obtained at each time point by one experienced technician (D.Q.) to confirm reproducibility of results. The quality control criteria were applied as per manufacturer recommendations. Foveal fixation and good corneal exposure during measurement were further confirmed retrospectively (by Dr. H.Y.). The axial length (AL), the mean keratometry (average of steepest and flattest anterior keratometry, mean K), the central corneal thickness (CCT), corneal diameter (white-to-white distance, WTW), the anterior chamber depth (ACD), the lens thickness (LT) and pupil size were measured for all patients. The IOL powers predicted for emmetropia based on the TECNIS® Monofocal 1-Piece Model ZCB00 lens were calculated with multiple formulae including the Barrett Universal II, Haigis, Holladay 2, Hoffer Q and SRK/T. The lens constants were selected based on the optimized values for the IOLmaster700® and specifically for the ZCB00 lens as listed on the User Group for Laser Interference Biometry (ULIB) website (http://ocusoft.de/ulib/czm/index.htm).

Statistics

Sample size were calculated using G*Power software (version 3.0.1.9, Dusseldorf, Germany). After choosing F test and the ANOVA test with repeated measurements and within factors, required variable were set as follows: a medium effect size of 0.25 as Cohen suggested; the α level at 0.05; the power (1-β) at 0.8; number of groups = 2 and number of measurements = 3; correlation among repeated measurements set at 0 initially, and nonsphericity correction = 1/(3–1) = 0.5. The calculation results showed that the sample size required per group was 43. We enrolled 50 eyes in each group finally.

One-way repeated measures ANOVA of the General Linear Model (GLM) procedure was used to analyse the differences of each measured parameter and the IOL power prediction for emmetropia at baseline, after the usage of pilocarpine and post-LPI. The Shapiro-Wilk normality test was used to examine the normal distribution assumption, and the Mauchly's test of sphericity was used to assess whether or not the assumption of sphericity was met. When the sphericity assumption was violated (i.e., Mauchly's test $p <= 0.05$), the Greenhouse-Geisser correction was used, particularly when epsilon <0.75, and the results were interpreted from the sphericity corrections table. Significant intervention effects were tested by a Bonferroni-adjusted pairwise post hoc analysis. If the normality distribution was violated, Wilcoxon Signed rank test was conducted instead of *T* test. Fisher's exact test was used to determine if there was a significant difference of the proportion of eyes with IOL power estimation differing by greater than 0.5D between groups. Statistical significance was defined as $p < 0.05$. All statistical analysis was performed using IBM® SPSS® Statistics 26.0. Continuous data were presented as mean ± standard deviation (SD) unless otherwise stated.

RESULTS

A total of 50 PACS and 50 PAC/PACG (including 46 with PAC and 4 with PACG) patients were enrolled in the study. The mean age of all patients was 63.2 ± 8.47 years (mean ± SD) and 16% of patients were male. The clinical characteristics of the patients are shown in Table 1. Patients with PAC/PACG were prescribed intraocular pressure lowering eyedrops, i.e., brimonidine tartrate 0.15%, Brinzolamide 1% and/or Timolol Maleate 0.5%, and continued using them during the study duration. The Shapiro-Wilk normality tests showed that all the numerical parameters studied were normally distributed except IOP in the PAC/PACG group. The mean AL, ACD, LT, CCT, WTW and mean K at baseline were 22.27 ± 0.77 mm, 2.42 ± 0.26 mm, 4.88 ± 0.32 mm, 538.5 ± 28.14 μm, 11.59 ± 0.37 mm, and 44.80 ± 1.58D, respectively. There were no significant differences between the two groups on these baseline ocular biometers except ACD (2.46 ± 0.24 mm in PACS vs 2.31 mm ± 0.22 mm in PAC/PACG, $P = 0.002$).

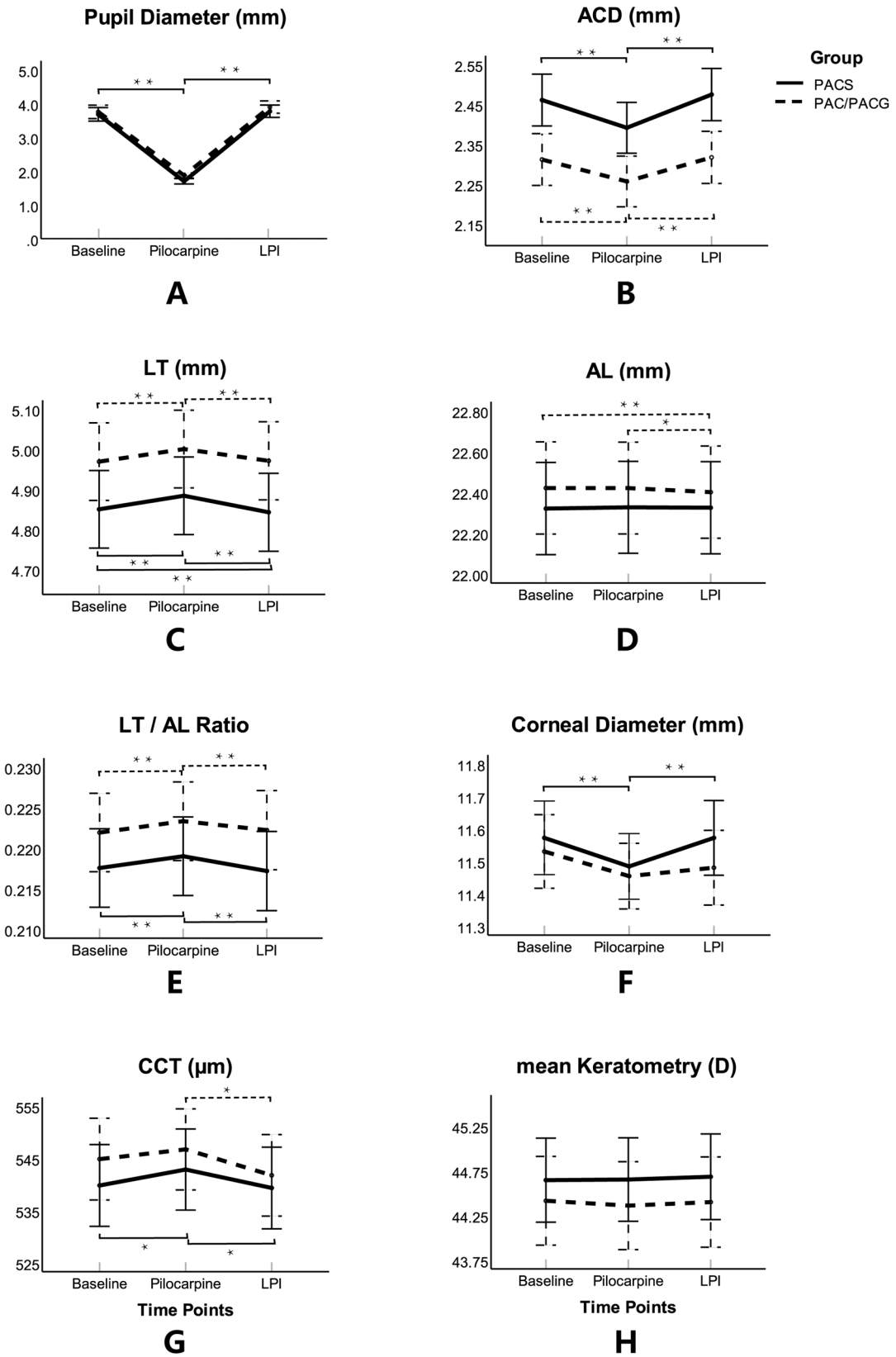
Effects of miosis and LPI on ocular biological parameters

The pupil diameter reduced from 3.71 ± 0.70 mm to 1.79 ± 0.29 mm ($p < 0.001$) after instillation of 0.5% pilocarpine nitrate three times per day for one week (T_1), and increased back to 3.84 ± 0.64 mm ($p = 0.11$ compared with baseline) one week after LPI with cessation of pilocarpine (T_2). The effect of pilocarpine and

Table 1. Clinical characteristics of enrolled patients in each group.

	PACS	PAC/PACG
Age (y)	62.82 (9.06)	62.24 (7.10)
Gender		
Male	5 (10%)	11 (22%)
Female	45 (90%)	39 (78%)
Uncorrected Visual Acuity[a]	0.25 (0.23)	0.28 (0.32)
Synechial Angle Closure (degree)[b]	0	90 (10–315)
C/D ratio[b]	0.4 (0.2–0.7)	0.4 (0.3–0.9)

Continuous variables were expressed as means (SD) and count variables as numbers (percentages).
[a]Uncorrected visual acuity was recorded in LogMAR Equivalent and expressed as means (SD).
[b]Extent of angle closure and C/D ratio were both expressed as median (range).



LPI on the ocular biometers and intraocular pressure (IOP) are shown in Fig. 1 and Table 2. There was no significant change of the IOP one week after LPI compared to the baseline IOP in either group ($p = 0.307$ for PACS, and 0.059 for PAC/PACG). The changes in all the measured parameters did not exhibit a significant time–group interaction except AL ($p > 0.05$ for pupil, ACD, LT, CCT, WTW, mean K, and $p = 0.004$ for AL, repeated-measures ANOVA), indicating similar changing trends of all the involved parameters,

Fig. 1 Comparisons of the changes in ocular parameters along three timepoints between PACS and PAC/PACG. A–H showed the variation of means of pupil diameter, central anterior chamber depth (ACD), lens thickness (LT), axial length (AL), ratio of LT/AT, mean of anterior keratometry, white-to-white (WTW) diameter and central corneal thickness (CCT) among the three time points (baseline, under miosis using pilocarpine and after LPI) in PACS (solid line) and PAC/PACG (dashed line), respectively. Error bar = +/−2SE; *indicates $p < 0.05$ and **indicates $p < 0.001$ when Bonferroni-adjusted post hoc pairwise comparisons was conducted. In PACS group: pilocarpine induced significant change of ACD, LT, WTW, and CCT, while LPI deepened ACD and thinned LT. For the PAC/PACG group, pilocarpine only reduced ACD and LT, whereas LPI shortened AL.

except AL, between PACS and PAC/PACG group along the three time points.

Generally, pilocarpine instillation induced a significant decrease of ACD by 0.07 ± 0.057 mm in PACS group and by 0.06 ± 0.055 mm in PAC/PACG (both $p < 0.001$), along with a significant increase of LT (by 0.03 ± 0.022 mm and 0.03 ± 0.023 mm in the two groups, respectively, both $p < 0.01$) and of LT/AL in both groups (by 0.0015 ± 0.00098 and 0.0014 ± 0.00120, respectively, both $p < 0.01$). Additionally, WTW decreased by 0.09 ± 0.151 mm ($p < 0.001$) and CCT increased by 3.1 ± 6.52 μm ($p = 0.006$) significantly under miosis in PACS patients but not change in PAC/PACG patients ($p = 0.06$ for WTW & $p = 0.561$ for CCT).

Compared to baseline, LPI had no effect on WTW and CCT in either group (all $p > 0.1$), but deepened the ACD by 0.01 ± 0.023 mm ($p < 0.001$), reduced the lens thickness by 0.01 ± 0.015 mm ($p = 0.004$) and reduced the LT/AL by 0.0004 ± 0.00079 ($p = 0.005$) significantly in the PACS group. LPI induced a small but significant shortening of the AL in the PAC/PACG cohort ($\triangle = -0.017 \pm 0.051$ mm, $p = 0.012$). Neither pilocarpine instillation nor LPI changed the mean keratometry of the anterior corneal surfaces significantly ($p = 0.402$ for PACS and $p = 0.105$ for PAC/PACG).

ACD and LT changes induced by either pilocarpine or LPI did not show any correlation with the ACD and LT at the baseline in both groups (Pearson's rho = −0.265, 0.212, −0.097, −0.038, all $p > 0.05$ for PACS; Pearson's rho = −0.126, −0.155, 0.024, 0.106, and all $p > 0.2$ for PAC/PACG).

Effects of miosis and LPI on the IOL power calculation

The mean IOL powers predicted for emmetropia by numerous IOL calculation formulae at baseline (T_0), under miosis (T_1) and after LPI (T_2) for each group are shown in Table 3. The predicted IOL power decreased by a mean of 0.04D~0.10D after either treatment in the PACS group, whereas it increased by an averaged 0.04D~0.08D in the PAC/PACG group (Supplementary Material 1), which demonstrated a different pattern of change between the two groups along the three time points with all the involved formulae except Holladay 2 ($p = 0.083$). Nevertheless, no statistically significant difference was detected before and after either treatment in each group (all the $p > 0.5$). (Table 3) Additionally, the proportion of eyes with a change of IOL power estimation more than 0.5D in each group was presented by formula in Supplementary Material 2. Briefly, there were 2–5 eyes (4–10%) with IOL power changing over 0.5D in each group, and the proportion did not differ neither between PACS and PAC/PACG nor among various formulas. Cumulatively, these results demonstrated that IOL power prediction by various IOL calculation formulae was not affected by the effect of pharmacological miosis or LPI in PACD patients (Fig. 2).

DISCUSSION

According to European Glaucoma Society Terminology and Guidelines for Glaucoma (5th Edition), prompt lens extraction is advisable for PAC or PACG patients with cataract [11]. LPI and pilocarpine are also important parts of the management algorithm for patients with PACD, especially among the subtypes of PACS and PAC. It has been proposed that the measurement of the phakic anterior chamber depth with pharmacological stimulation (non-physiologic state) of the ciliary muscle would induce a statistical error for IOL power calculation [5]. This study indicated that biometric changes induced by either miosis or LPI had little impact on IOL power calculation among PACD patients.

The use of pilocarpine resulted in lens thickening and shallowed anterior chamber depth in both groups of our study. In addition, our results also showed that corneal diameter decreased and CCT increased after miosis (Table 2; Fig. 1, and Supplementary Material 1). The reduction of corneal diameter during miosis was perhaps attributed to a centripetal contractive force of ciliary muscle acting on the scleral spur [7] and the peripheral cornea, whereas further investigation is warranted. As regards the CCT, Gupta and associates [12] have also observed an increased mean CCT after pilocarpine in PACS patients, although statistically insignificant. According to Kahori et al. [13], changes of corneal thickness depend on various factors, and they attributed the increased CCT observed in their study to eyelid closure after eye drops instillation before measurements. Whereas, Talajic et al. [7] imputed it to the hydrostatic pressure on the corneal endothelium secondary to the IOP changes induced by interventions. Considering that our patients did not use pilocarpine or anti-glaucoma eye drops immediately prior to measurements, Kahori's hypothesis does not apply to us. Nevertheless, since we did not measure patients' IOP after pilocarpine instillation, the cause of CCT increase in PACS patients under miosis is yet to be elucidated.

Theoretically, LPI eliminates relative pupillary block and equalizes the pressure in the anterior chamber and posterior chamber. Compared to baseline, prophylactic LPI affected neither WTW nor CCT but deepened ACD and resulted in a thinner lens measurement in our PACS group, which was consistent with findings from previous studies [12, 14–16]. This may be due to more aqueous humour flowing into the anterior chamber through the peripheral iridotomy, pushing the lens backward and flattening the anterior curvature of lens [6], resulting in reduced lens thickness. However, such subtle alterations were not detected in our PAC/PACG group. One explanation is that PACS patients arranged for LPI in our study presented with critical bowing of the iris, which resulted in a posterior shift of the iris and deepening of the ACD after LPI once pupillary block was relieved. In contrast, PAC/PACG groups may be more likely to have complicated mechanisms including a more anteriorly positioned crystalline lens, thicker and more anteriorly inserted iris, and anteriorly rotated ciliary body. This was confirmed partially by our data that PAC/PACG patients had shallower anterior chamber, thicker lens, and greater LT/AL ratio than PACS patients at baseline (Table 2), which inferred PAC/PACG participants had a more crowded anterior segment disproportionate to their AL.

Barrett Universal II, Haigis, Holladay 2, Hoffer Q and SRK/T are common IOL power calculation formulae with good performance [17, 18]. However, there are no reports about the accuracy of these formulae when influenced by pharmacological miosis or LPI. Given that TECNIS® Model ZCB00 is a standard monofocal IOL and was commonly used in many comparative

Table 2. Effect of miosis and LPI on ocular biological parameters and IOP.

Biological Parameters	Baseline [T_0]			Post-pilocarpine [T_1]			Post-LPI [T_2]			P_1 value	P_2 value	P_3 value	P_4 value
	PACS	PAC/PACG	Total	PACS	PAC/PACG	Total	PACS	PAC/PACG	Total				
IOP (mmHg)[a]	15.7 ± 3.45 [14.7, 16.7]	16.0 (11.4, 30.0)	16.3 (7.9, 30.0)	N/A	N/A	N/A	16.3 ± 3.26 [15.3, 17.2]	15.8 (8.9, 30.0)	16.0 (7.9, 30.0)	0.279	N/A	0.307	0.059
PD (mm)	3.7 ± 0.65 [3.5, 3.9]	3.7 ± 0.69 [3.5, 3.9]	3.7 ± 0.67 [3.6, 3.8]	1.7 ± 0.24 [1.6, 1.8]	1.9 ± 0.30 [1.8, 1.9]	1.8 ± 0.28 [1.7, 1.8]**	3.8 ± 0.58 [3.6, 3.9]	3.9 ± 0.70 [3.7, 4.1]	3.8 ± 0.64 [3.7, 4.0]	**<0.001**	0.725	**<0.001**	**<0.001**
ACD (mm)	2.46 ± 0.240 [2.39, 2.53]	2.32 ± 0.216 [2.26, 2.38]$^{\#\#}$	2.39 ± 0.238 [2.34, 2.44]	2.39 ± 0.231 [2.33, 2.46]**	2.26 ± 0.216 [2.20, 2.33]$^{\#\#,**}$	2.33 ± 0.232 [2.28, 2.37]**	2.47 ± 0.245 [2.41, 2.54]$^{**,\Phi}$	2.33 ± 0.213 [2.26, 2.39]$^{\#\#,\Phi}$	2.40 ± 0.241 [2.35, 0.45]**	**<0.001**	0.086	**<0.001**	**<0.001**
LT (mm)	4.85 ± 0.313 [4.76, 4.94]	4.96 ± 0.364 [4.85, 5.06]	4.90 ± 0.342 [4.84, 4.97]	4.88 ± 0.312 [4.80, 4.97]**	5.00 ± 0.363 [4.88, 5.09]**	4.94 ± 0.341 [4.87, 5.00]**	4.84 ± 0.313 [4.75, 4.93]$^{**,\Phi}$	4.96 ± 0.369 [4.85, 5.06]$^{\Phi}$	4.90 ± 0.345 [4.83, 4.97]	**<0.001**	0.075	**<0.001**	**<0.001**
CCT (μm)	540 ± 25.8 [532, 547]	545 ± 29.6 [536, 553]	542 ± 27.7 [537, 548]	543 ± 24.60 [536, 550]**	547 ± 30.25 [538, 556]	545 ± 27.5 [539, 550]*	539 ± 24.5 [532, 546]$^{\Phi}$	542 ± 30.5 [533, 551]$^{\Phi}$	541 ± 27.5 [535, 546]	**<0.001**	0.353	**0.002**	**0.005**
WTW (mm)	11.6 ± 0.38 [11.5, 11.7]	11.5 ± 0.43 [11.4, 11.7]	11.6 ± 0.40 [11.5, 11.6]	11.5 ± 0.35 [11.4, 11.6]**	11.5 ± 0.37 [11.4, 11.6]	11.5 ± 0.36 [11.4, 11.5]**	11.6 ± 0.41 [11.5, 11.7]$^{\Phi}$	11.5 ± 0.41 [11.4, 11.6]	11.5 ± 0.41 [11.4, 11.6]	**<0.001**	0.265	**0.001**	0.052
Mean K (D)	44.65 ± 1.691 [44.16, 45.13]	44.42 ± 1.609 [43.95, 44.88]	44.53 ± 1.646 [44.20, 44.86]	44.65 ± 1.683 [44.17, 45.13]	44.37 ± 1.611 [43.91, 44.84]	44.51 ± 1.645 [44.18, 44.84]	44.68 ± 1.700 [44.20, 45.17]	44.41 ± 1.658 [43.93, 44.89]	44.54 ± 1.677 [44.21, 44.88]	0.278	0.264	0.402	0.105
AL (mm)	22.32 ± 0.786 [22.10, 22.54]	22.42 ± 0.821 [22.18, 22.65]	22.37 ± 0.801 [22.21, 22.53]	22.33 ± 0.783 [22.10, 22.55]	22.42 ± 0.818 [22.18, 22.65]	22.37 ± 0.798 [22.21, 22.53]	22.32 ± 0.786 [22.10, 22.55]	22.40 ± 0.829 [22.16, 22.64]$^{*,\#,\Phi}$	22.36 ± 0.804 [22.20, 22.52]*	**0.002**	**0.004**	0.097	**0.001**
LT/AL ratio	0.22 ± 0.016 [0.21, 0.22]	0.22 ± 0.018 [0.22, 0.23]	0.22 ± 0.017 [0.22, 0.22]	0.22 ± 0.016 [0.21, 0.22]**	0.22 ± 0.018 [0.22, 0.23]**	0.22 ± 0.017 [0.22, 0.22]**	0.22 ± 0.016 [0.21, 0.22]*	0.22 ± 0.019 [0.22, 0.23]	0.22 ± 0.017 [0.22, 0.22]	**<0.001**	**0.011**	**<0.001**	**<0.001**

Measured results were presented as Mean ± Standard Deviation [95% confidence interval], except IOP of PAC/APCG group and total participants as Median (Minimum, Maximum) for their abnormal distribution.
IOP intraocular pressure, *PD* pupil diameter, *ACD* anterior chamber depth, *LT* lens thickness, *CCT* central corneal thickness, *WTW* white to white, *K* keratometry, *AL* axial length, *LT/AL* lens thickness/axial length.
P1: Significance of difference among three time points in total. Bold values indicated significant differences based on p value.
P2: Significance of changing pattern between groups. Bold values indicated significant differences based on p value.
P3: Significance of difference among three time points in group PACS. Bold values indicated significant differences based on p value.
P4: Significance of difference among three time points in group PAC/PACG. Bold values indicated significant differences based on p value.
*Indicated $p < 0.05$, while **indicated $p < 0.01$ for measurements after intervention compared with that measured at baseline.
$^{\#}$Indicated $p < 0.05$ and $^{\#\#}$indicated $p < 0.01$ when measurements compared between the two groups at each time point.
$^{\Phi}$Indicated $p < 0.05$ for measurements after LPI compared to that measured under miosis.
[a]Compared using paired samples T-test for PACS group, and related samples Wilcoxon signed rank test for PAC/PACG group for its non-normal distribution.

studies [19–21], the present study chose ZCB00 as a referenced lens to assess the IOL power calculation inconsistency with these interventions.

For the PACS group, the IOL powers predicted by the 3rd generation formulae (i.e., SRK/T and Hoffer Q) did not alter after either miosis or LPI as the variables included in these formulae (i.e., AL and mean K) did not change significantly after either intervention. Besides AL and K, ACD is another parameter incorporated into the 4th generation formula (i.e., Haigis and Holladay 2) which may improve the accuracy of estimating the postoperative lens position. An average of 0.07 mm decrease in ACD in our PACS patients corresponded to around 0.1D lower IOL power prediction according to Olsen T [22], which was consistent with the average 0.08D decreased under miosis calculated by Haigis in our study, although this was probably not a meaningful change in clinical practice. Similarly, the absolute values of the changes in all the related ocular parameters after either miosis or LPI were too small to affect any changes in subsequent IOL power calculation across all the formulae employed.

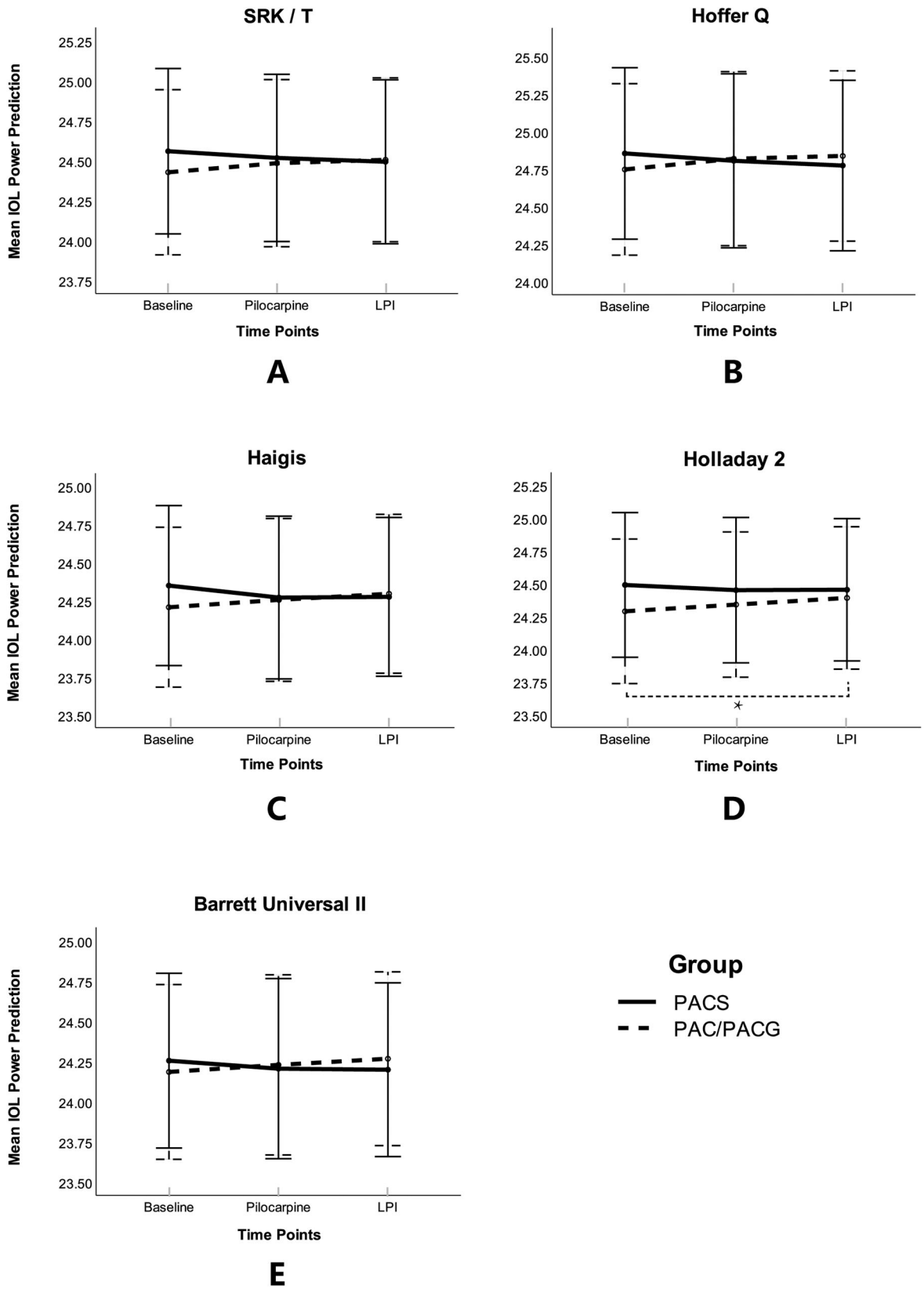
In the PAC/PACG cohort, AL shortened after LPI by 0.02 mm, with a possible mechanism relating to the significant reduction in intraocular pressure stemming from this intervention (mean reduction of 1.6 mmHg after LPI). Read et al. [23] found that a 1.6 mmHg decline in IOP might predicted a 9.44 μm reduction in AL. In any case, the significant AL reduction of 0.02 mm after LPI in our study would contribute to a negligible 0.055D increase of predicted IOL according to Gullstrand's model eye. Accordingly, no statistically significant change in IOL power prediction was suggested by various generation formulae after pilocarpine or LPI interventions, except for Holladay 2 that LPI induced an increase of the IOL power prediction by 0.1D compared with baseline. However, either 0.055D or 0.1D increase of IOL power is far from 0.5D which is meaningful to surgeon's option in clinical practice. Though the IOL power estimation reduced by more than 0.5D under miosis in 0–10% eyes and increased by more than 0.5D after LPI in 2–6% eyes in our study (Supplementary Material 2), mainly were still within a change of less than 0.5D and therefore would not affect surgeons' final decision on IOL power.

Several limitations of the present study should be mentioned. Firstly, IOP was not collected after pilocarpine instillation (T_1), so any effect of IOP changes on ocular parameters at this timepoint was unknown. However, based on clinical experience and literatures, pilocarpine or LPI reduces IOP of PACD patients no more than 4 mmHg [24–26], which is within the normal range of diurnal variation of IOP in healthy subjects [23], a range that is not expected to influence biometric parameters and the postoperative refractive outcomes significantly [27–29]. Secondly, the number of subjects with PACG in our PAC/PACG group was small. Because many PACG patients have had relative extensive angle closure, instead of benefiting from LPI, they are subjected to much higher risk of exposure to higher IOP and disease progression after LPI [30]. Since PAC and PACG have been demonstrated with similar anatomical features [31], we combined PAC and PACG into one group and compared this cohort with PACS in this study. Thirdly, several concentrations of pilocarpine eye drops are commercially available, e.g., 2%, 1.25%, 1%, and 0.5%. Quite a few studies used 2% while some used lower concentrations. Both 1% and 0.5% pilocarpine are commonly used in China and 0.5% is widely used as a maintenance option, that is why we used 0.5% in this study. Whether higher concentration would induce even more significant change of biometric parameters and subsequent IOL power estimations is yet to be elucidated. Lastly, the subjects included in this study have yet to undergo lens extraction, so that we could not assess the mean/median absolute error (MAE/MedAE) for IOL calculation formulae

Table 3. Effects of miosis and LPI on the ZCB00 IOL power calculation for emmetropia in PACS and PAC/PACG.

Formulae		IOL power predicted for emmetropia											
		Pre-intervention			Post-pilocarpine			post-LPI			Significance of changing pattern between groups	Difference among time points in PACS	Difference among time points in PAC/PACG	Total
		PACS	PAC/PACG	Total	PACS	PAC/PACG	Total	PACS	PAC/PACG	Total	*P*-value	*P*-value	*P*-value	*P*-value
Third Generation	SRK/T (Aconst = 119.3)	24.56 (1.89)	24.43 (1.77)	24.49 (1.82)	24.52 (1.93)	24.48 (1.77)	24.50 (1.84)	24.49 (1.87)	24.50 (1.75)	24.50 (1.81)	**0.006**	0.135	0.041[a]	0.942
	Hoffer Q (pACD = +5.80)	24.85 (2.12)	24.75 (1.92)	24.80 (2.01)	24.80 (2.18)	24.82 (1.92)	24.81 (2.04)	24.77 (2.11)	24.84 (1.90)	24.80 (2.00)	**0.009**	0.149	0.054	0.926
Fourth Generation	Haigis (a0 = −1.302 a1 = +0.21 a2 = +0.251)	24.35 (1.95)	24.21 (1.75)	24.28 (1.85)	24.27 (2.01)	24.25 (1.75)	24.26 (1.88)	24.27 (1.93)	24.29 (1.74)	24.28 (1.83)	**0.013**	0.12	0.076	0.731
	Holladay 2 (ACD = +5.786)	24.49 (2.01)	24.29 (1.89)	24.39 (1.94)	24.45 (2.03)	24.34 (1.88)	24.39 (1.95)	24.45 (1.98)	24.39 (1.86)*	24.42 (1.91)	0.083	0.633	**0.032**	0.522
New Generation	Barrett Universal II (LensFactor = 2.09 DesignFactor = 4)	24.25 (2.01)	24.18 (1.83)	24.22 (1.91)	24.20 (2.10)	24.23 (1.86)	24.22 (1.97)	24.20 (2.00)	24.27 (1.82)	24.23 (1.90)	**0.042**	0.366	0.07	0.829

The predicted IOL power was presneted as mean (SD). Bold values indicated significant differences based on p value.
*Indicated $p < 0.05$ for IOL power different from that predicted at baseline (T0).
[a]Repeated measures ANOVA showed there was significant differences among the IOL power predicted in PAC/PACG group using SRK/T, but Bonferroni-adjusted pairwise post hoc comparison did not reveal any significant difference between any two of the three time points.



comparison. Although our results demonstrated that neither miosis nor LPI would alter surgeons' choice of IOL power, subsequent studies in this cohort following cataract surgery would help corroborate these findings.

CONCLUSION

Both miosis and LPI induced significant changes on anterior segment parameters; but ultimately did not affect the IOL power calculations predicted for emmetropia. Other avenues which may

Fig. 2 Comparisons between PACS and PAC/PACG in terms of the changing pattern of IOL power prediction along three timepoints with various formulae. A–E showed the different patterns of IOL power predicted for emmetropia in PACS (solid line) and PAC/PACG (dashed line) group along the three time points (baseline, under miosis using pilocarpine and post LPI), calculated with various generation formulae. A and B presented results with the 3rd generation formulae (SRK/T and Hoffer Q, respectively); (**C**, **D**) showed that with the 4th generation formulae (Haigis and Holladay 2, respectively); (**E**) was the result from the new generation Barrett Universal II formula. Error bar $= +/-2$SE; solid star indicates statistical difference during pairwise comparison among the three statuses ($p < 0.05$), which means only the calculation results in PAC/APCG using Holladay2 was different between baseline and post-LPI significantly. Generally, insignificant difference was found either among different formulae or among different time points.

potentially explain postoperative refractive error warrant further investigation in the PACD cohort.

SUMMARY

What was known before

- Cataract surgery is an established treatment for PACD patients with lens opacity. However, the refractive outcomes after cataract surgery in PACD patients are not as precise compared to the general population undergoing cataract surgery.
- Pilocarpine and laser peripheral iridotomy (LPI) are two commonly used interventions in PACD patients, both of which may affect ocular biometrics.

What this study adds

- Pharmacological miosis and LPI significantly alter ocular biometrics but do not alter IOL calculation predicted for emmetropia with commonly used SRK/T, Hoffer Q, Haigis, Holladay 2 and Barrett Universal II formulae in PACD.
- Other factors accounting for increased postoperative refractive error warrant further investigation in PACD patients.

DATA AVAILABILITY

The datasets generated and analysed during the current study are available from the corresponding author, YHC, on reasonable request. The data are not publicly available due to their containing information that could compromise the privacy of research participants.

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AUTHOR CONTRIBUTIONS

XS and YC conceived and designed the work. HY and DQ majorly carried out this clinic trial and acquired data. JW, GC and HY played an important role in data analysis and results interpretation. HY, GC and YC drafted and revised the manuscript. All the authors approved the final version to be published.

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COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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