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Original Article

Capsulotomy enlargement after femtosecond laser treatment among cataract patients of different age groups: a retrospective case series

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Abstract: Purpose: Larger-than-planned capsulotomies can occur, yet their association with age and eye parameters remains poorly understood. This study aimed to assess capsulotomy enlargement after femtosecond laser treatment in cataract surgery and to explore a possible correlation of capsulotomy enlargement with age and eye parameters. Methods: This retrospective case series included consecutive patients diagnosed with cataracts between 05/2018 and 11/2019. Among them, patients within the age ranges of <18, 18-49, and ≥50 years were assigned to the childhood cataract (CC), young adult cataract (YAC), and age-related cataract (ARC) groups, respectively. The capsulotomy enlargement ratio (CER), age, degree of cataract, lens thickness (LT), axial length, and anterior chamber depth were recorded and analyzed. Results: A total of 155 participants (179 eyes) were enrolled. The CER was significantly different among the three groups (CC: 1.245 vs. YAC: 1.060 vs. ARC: 1.029, $P<0.001$). The CER was found to be independently associated with both age (β=-0.011 (0.001), $P<0.001$) and LT (β=-0.049 (0.017), $P=0.006$) in the CC group, but it was only independently correlated with age (β=-0.004 (0.001), $P=0.002$) in the YAC group and LT (β=-0.014 (0.007), $P=0.048$) in the ARC group. Conclusions: Capsulotomy enlargement can occur after femtosecond laser treatment in cataract surgery, especially in the non-adult group. Age was a determinant of the CER in CC and YAC groups, while LT was an independent determinant of the CER in CC and ARC groups. These two factors should be taken into consideration for more precise sized capsulotomy.

Keywords: Capsulotomy, femtosecond laser, cataracts, age, lens thickness

Introduction

Cataracts are the opacification of the lens, typically due to aging, resulting in altered vision [1-3]. The prevalence of cataract is 3.9% in patients aged 55-64 years and 92.6% in those aged over 80 years [3]. Cataract is the most common cause of reversible blindness worldwide [3]. Femtosecond laser technology, first introduced into ophthalmic surgery in 2001, is an important advance in cataract surgery [4-6]. Femtosecond laser-assisted cataract surgery has gained worldwide acceptance because of the high precise circularity and adjustability of the capsulotomy diameter, lens nucleus fragmentation, precise arcuate keratotomy, and multiplanar self-sealing incision [4-7]. In addition, several new types of intraocular lenses (IOLs) tailored to various needs, which are called functional IOLs, have emerged on the market. For these IOLs, accurate centration as well as precisely sized and shaped capsulotomy are considered important factors in improving refractive stability and predictability. This can help reduce the incidence of IOL movement, tilt, and decentration [8-10]. Therefore, femtosecond laser-assisted cataract surgery combined with functional IOL implantation has become the first choice for many surgeons.

IOL implantation, especially in cases of capsule-fixated IOLs, requires the attainment of a precisely planned capsulotomy. The diameter and shape of the capsulotomy are generally determined based on the shape of the IOLs [11-14]. Nevertheless, several studies reported instances where the achieved capsulotomy diameter was close but sometimes larger than the programmed capsulotomy size [12, 15, 16]. This phenomenon has been observed both in children [8, 17] and adults [18-20]. Even though it has been observed in all patient groups, it seems to be particularly associated with younger age. In pediatric cases, it is potentially attributed to greater tension release within the elastic capsule, influenced by unique characteristics of the pediatric lens. However, no study has specifically examined the association of capsulotomy enlargement with age and other factors.

Therefore, this study aimed to assess capsulotomy enlargement after femtosecond laser treatment in cataract surgery and to explore the possible correlation of capsulotomy enlargement with the patients' age, nuclear degree of cataract, lens thickness (LT), axial length (AXL), and anterior chamber depth (ACD), so as to achieve a more precise sized capsulotomy to ensure the position of the IOLs, especially functional IOLs.

Methods

Study design and subjects

This retrospective case series included consecutive patients diagnosed with cataracts at Weifang Eye Hospital between May 2018 and November 2019. This study was approved by the ethics committee of Weifang Eye Hospital, and written informed consent was obtained from all subjects.

All patients included underwent femtosecond laser-assisted cataract surgery. The inclusion criteria were 1) patients who were diagnosed with cataract and treatment-naive; 2) patients with no contraindications to femtosecond laser-assisted cataract surgery; 3) patients with complete medical records; 4) patients with no use of drugs that may affect the results of this study in the past half a year. The exclusion criteria were 1) patients whose eyes were suffered from preoperative ocular pathology such as amblyopia, corneal dystrophy, keratoconus, retinopathy, uveitis, or retinal dystrophy; 2) patients with history of eye trauma; 3) patients with complications such as posterior capsule rupture or zonulysis; 4) patients with history of ocular surgery [21].

Considering that the variability of lens elasticity with age might affect the achieved capsulotomy diameter and enlargement ratio, patients were categorized into different age groups. Patients under 18, those aged 18-49, and those above 50 years of age were assigned to childhood cataract (CC) [22], young adult cataract (YAC) [23, 24], and age-related cataract (ARC) [24, 25] groups, respectively.

Preoperative examinations

The programmed capsulotomy diameter was determined by the shape of the IOLs (4.9 mm for C-Loop IOLs, and 5.0 mm for the four-point haptic IOLs). Nuclear opalescence grading was obtained by slit-lamp microscopy according to the *Lens Opacities Classification System III* [26]. ACD and LT were measured using an IOLMaster 700 (Carl Zeiss GmbH, Oberkochen, Germany). Ultrasound A-Scan (Alcon, Hunenberg, Switzerland) was used when the data could not be obtained by optical means.

Surgical procedures

Femtosecond laser-assisted cataract surgery [27] began with local infiltration anesthesia using proparacaine hydrochloride eye drops (Alcon-Couvreur SA, Puurs, Belgium; one drop/time, three times). After capsulotomy (4.9/5.0 mm) was made, lens fragments (decussation mode; pulse energies of 10 μJ) were prepared, and a corneal incision (2.1 mm) was made using the femtosecond laser (Lensx, Alcon, Hunenberg, Switzerland). Then, microcoaxial phacoemulsification was performed with the Stellaris phacoemulsification system (Bausch & Lomb, Bridgewater, NJ, USA). The infusion bottle height was set between 90 and 110 cm, depending on the case condition and surgeons' preferred technique, especially during fragment removal. The aspiration flow rate was 40 mL/min, and the vacuum level was set at 450 mmHg.

During the early phase of the surgery, 3.0% sodium hyaluronate and 4.0% chondroitin sulfate (Viscoat®, Alcon, Hunenberg, Switzerland) were injected into the anterior chamber, followed by injection of cohesive sodium hyaluronate (Medical Hyaluronan Gel, Alcon, Hunenberg, Switzerland). During subsequent surgery phases, sodium hyaluronate was used to deepen the anterior chamber and expand the capsular bag for IOL implantation.

All surgeries were performed by the same surgeon (a chief physician with 38 years of experience) and videotaped in high resolution. All

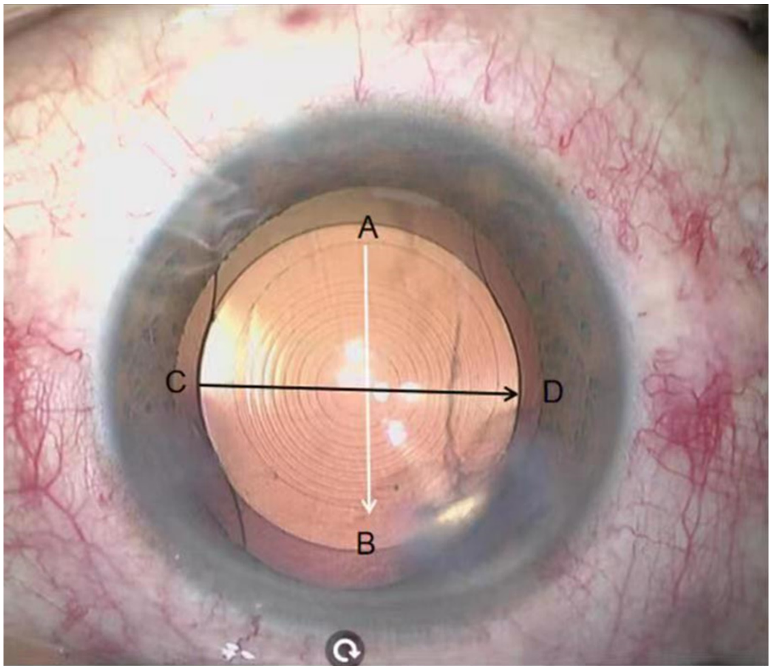

Figure 1. The calculation of the achieved diameter of the capsulotomy. The diameter of the postoperative capsule (i.e., the distance from point A to point B) was measured by three people from different directions three times. Then the average value was taken and denoted as D1. The diameter of the intraocular lens (e.g., the distance from point C to point D) was measured by the same method, and denoted as D2. Since the diameter of the intraocular lens was 6.0 mm, the achieved diameter of the capsulotomy was calculated as 6.0*D1/D2 (mm).

patients were administered 1% prednisolone acetate eye drops (Allergan, Dublin, Ireland) and 0.5% levofloxacin eye drops postoperatively, four times/day for 2 weeks, as well as 0.1% pralofen eye drops (Senju Pharmaceutical Co., Ltd., Fukusaki, Japan) four times/day for 1.5 months [28].

Data collection

Patient characteristics were collected at baseline, including age, sex, affected eye, cataract severity, visual acuity, intraocular pressure of the affected eyeball, LT, AXL, and ACD. The capsulotomy diameter, which was set as the target size for the laser system, was determined before treatment initiation. The achieved anterior capsulotomy size was horizontally and vertically measured. The capsulotomy diameter was calculated with a graphics software (GIMP, version 2.8.10, GIMP Development Team, https://www.gimp.org/) based on the diameter of the IOL implanted in the eye. For this purpose, the achieved diameter of the capsulotomy was measured on a screen capture in pixels and calculated into millimeters by cross-multiplication (**Figure 1**). Postoperatively, assessment of capsulotomy enlargement ratio (CER) was performed. We used the graphics software GIMP to measure the achieved capsulotomy diameter (programmed capsulotomy size) in pixels from a screenshot of the diameter of the implanted IOL. Subsequently, we divided the achieved capsulotomy diameter by the programmed capsulotomy size to calculate the CER. Of these parameters, the relationship between capsulotomy enlargement and patient age was the primary outcome measure, while cataract severity, visual acuity, and intraocular pressure of the affected eyeball, LT, AXL, ACD, CER and affected side were the secondary ones. The flow chart of this study is shown in **Figure 2**.

Statistical analysis

Continuous data were tested for normality using the Shapiro-Wilk test. The data meeting a normal distribution were expressed as means ± standard deviations and analyzed using ANOVA and the Tukey post-hoc test; otherwise, they were expressed by medians (25th percentile, 75th percentile) and analyzed using the Kruskal-Wallis H-test. Categorical data, expressed as n (%), were analyzed using the chi-square test or Fisher's exact probability test. Pearson correlation analysis was used for bivariable correlation analysis of normally distributed variables, while the Spearman correlation analysis was used for bivariate correlation analysis when at least one variable was non-normally distributed. Multivariable regression analysis (Logistic regression) was performed to explore the independent influencing factors of the enlargement ratio of the capsular incision. The factors with *P*-values <0.05 in the univariable analyses and the clinically relevant factors were included in the multivariable analysis. All statistical analyses were performed using

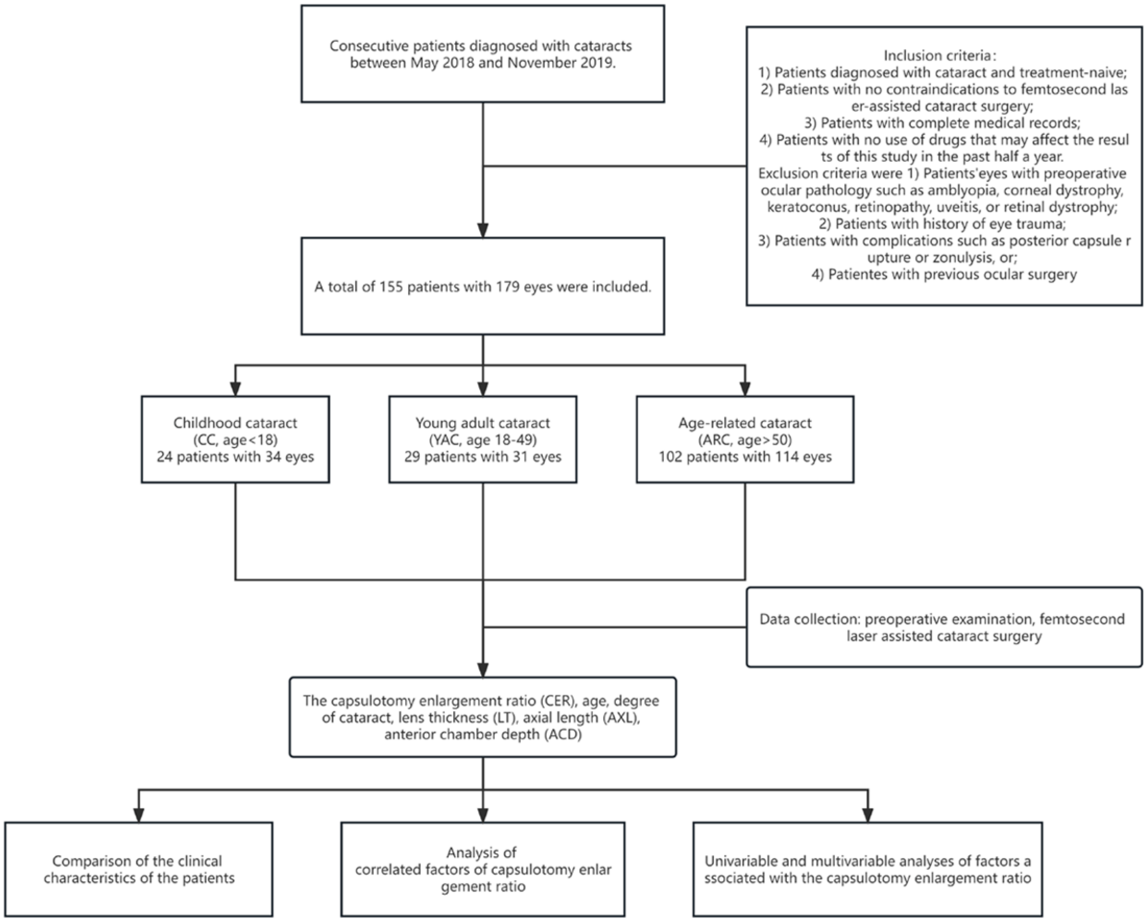

Figure 2. Flow chart of this study.

SPSS (Version 22.0, IBM, Armonk, NY, USA). *P*-values <0.05 were considered significant.

Results

Characteristics of the participants

A total of 155 participants (179 eyes) were enrolled (**Table 1**). There were 24 participants (34 eyes) in the CC group, with a mean age of 6 (3.5-10) years. The YAC group consisted of 29 participants (31 eyes), with an average age of 44 (39-48) years. There were 102 participants (114 eyes) in the ARC group, aged 66 (58-73) on average. Bilateral involvement was more frequent in the CC group (58.8%) than in the YAC (12.9%) and ARC (21.1%) groups (P<0.001). The cataracts were more severe in the ARC group (P<0.001). LT displayed an age-related increase (P<0.001). AXL was observed to be shorter in the CC group (P<0.05), while ACD was shallower in the ARC group (P<0.05). The sex, visual acuity, and intraocular pressure were not significantly different among the three groups (all P>0.05) (**Table 1**).

CER

The CER was significantly different among the three groups (CC: 1.245 vs. YAC: 1.060 vs. ARC: 1.029, P<0.001) (**Table 1**). As shown in **Table 2**, the CER was correlated with age (r=-0.95, P<0.001), cataracts severity (r=-0.55, P=0.001), visual acuity (r=-0.70, P<0.001), LT (r=-0.56, P=0.001), and AXL (r=-0.65, P<0.001) in the CC group. In the YAC group, the CER was correlated with age (r=-0.43, P=0.016) only. In the ARC group, the CER was correlated with LT (r=-0.21, P=0.027) only.

Factors independently associated with the CER

Table 3 presents the multivariable analysis results in the three groups. In the CC group, age

Table 1. Characteristics of the participants

Characteristic	CC	YAC	ARC	P
Number of cases	24	29	102	
Number of eyes	34	31	114	
Age, years, median (P25, P75)	6 (3.5, 10)	44 (39, 48)	66 (58, 73)	
Sex, N (%)				0.543
Male	15 (62.5)	15 (51.7)	51 (50.0)	
Female	9 (37.5)	14 (48.3)	51 (50.0)	
Affected eyeball, n (%)				<0.001
Unilateral	14 (41.2)	27 (87.1)	90 (78.9)	
Bilateral	20 (58.8)	4 (12.9)	24 (21.1)	
Severity of the cataracts, n (%)				<0.001
N0	19 (55.9)	4 (12.9)	0 (0.0)	
N1, 2	15 (44.1)	21 (67.7)	66 (57.9)	
N3, 4, 5	0 (0.0)	6 (19.4)	48 (42.1)	
Visual acuity, median (P25, P75)	0.3 (0.2, 0.5)	0.2 (0.08, 0.275)	0.25 (0.1, 0.5)	0.039
Intraocular pressure (mmHg), medians (P25, P75)	16 (14, 18)	16 (14.5, 17.5)	16 (14, 18)	0.771
LT (mm), median (P25, P75)	3.115 (2.87, 3.22)	4.11 (3.72, 4.26)	4.425 (4.08, 4.75)	<0.001
AXL (mm), median (P25, P75)	21.58 (20.34, 23.17)	24.45 (23.505, 26.445)	23.73 (23.03, 24.57)	<0.001
ACD (mm), median (P25, P75)	3.27 (3.14, 3.46)	3.45 (3.23, 3.655)	3.175 (2.83, 3.36)	<0.001
Capsulotomy enlargement coefficient, median (P25, P75)	1.245 (1.191, 1.300)	1.060 (1.039, 1.084)	1.029 (1.000, 1.069)	<0.001

N: number of patients; n: number of affected eyeballs; CC: childhood cataract; YAC: young adult cataract; ARC: age-related cataract; LT: lens thickness; AXL: axial length; ACD: anterior chamber depth. Data are presented as medians (25th percentile, 75th percentile) or N/n (%). *P*-values <0.05 were considered statistically significant.

Table 2. Correlated factors of capsulotomy enlargement ratio

Index	CC		YAC		ARC	
	r	P	r	P	r	P
Age	-0.949	<0.001	-0.429	0.016	-0.098	0.299
Severity of nuclear cataract	-0.554	0.001	-0.319	0.081	-0.061	0.516
Visual acuity	-0.704	<0.001	0.245	0.185	0.010	0.917
Intraocular pressure	0.038#	0.832	0.305	0.095	-0.053	0.574
LT	-0.564#	0.001	-0.062	0.739	-0.207	0.027
AXL	-0.649	<0.001	-0.144	0.439	-0.014	0.884
ACD	-0.136	0.459	-0.190	0.306	0.116	0.234

CC: childhood cataract; YAC: young adult cataract; ARC: age-related cataract; LT: lens thickness; AXL: axial length; ACD: anterior chamber depth. #Pearson's correlation coefficient; otherwise, Spearman's correlation coefficient if unmarked. The severity of the nuclear cataract was analyzed as 0-5 degrees in this table. *P*-values <0.05 were considered significant.

(β=-0.011 (0.001), P<0.001) and LT (β=-0.049 (0.017), P=0.006) were independently associated with the CER. In the YAC group, only age (β=-0.004 (0.001), P=0.002) was independently associated with the CER. In the ARC group, only LT (β=-0.014 (0.007), P=0.048) was independently associated with the CER. Accordingly, the formula for the CER was CER=1.483 - 0.011 × age - 0.049 × LT, 1.224 - 0.004 × age, 1.111 - 0.014 × LT in CC, YAC, and ARC group, respectively.

Discussion

Larger-than-planned capsulotomy can occur [8, 17-20], but its association with age and ocular measurements needs further exploration. The results of this study suggest that the capsulotomy enlarges after femtosecond laser treatment in cataract surgery, especially in the non-adult patient group. In both CC and YAC groups, age was a factor independently associated with the CER. LT was a factor independently associated with CER in the CC and ARC groups. Although the relationship between age and capsule rigidity is well-known, this study further quantified this relationship and provided a mathematical formula.

Aging of the human anterior lens capsule appears to be associated with a progressive loss of mechanical strength. The tissue on the

Table 3. Univariable and multivariable analyses of factors associated with the capsulotomy enlargement ratio

Variables	CC				YAC				ARC			
	Univariable		Multivariable		Univariable		Multivariable		Univariable		Multivariable	
	β (SE)	p	β (SE)	p	β (SE)	p	β (SE)	p	β (SE)	p	β (SE)	p
Age	-0.013 (0.001)	<0.001	-0.011 (0.001)	<0.001	-0.004 (0.001)	0.002	-0.004 (0.001)	0.002	0.000 (0.000)	0.418	0.000 (0.000)	0.744
Sex (0= female, 1= male)	-0.016 (0.023)	0.481	-0.011 (0.009)	0.269	-0.014 (0.014)	0.304	-0.010 (0.012)	0.422	-0.008 (0.009)	0.367	-0.006 (0.009)	0.504
Affected eyeball (0= Unilateral, 1= Bilateral)	-0.014 (0.023)	0.532			0.002 (0.021)	0.918			0.016 (0.011)	0.143		
Severity of nuclear cataract (0= N0, 1= N1, 2)	-0.071 (0.019)	0.001	-0.004 (0.011)	0.704								
Visual acuity	-0.257 (0.044)	<0.001										
LT	-0.121 (0.031)	0.001	-0.049 (0.017)	0.006					-0.015 (0.007)	0.027	-0.014 (0.007)	0.048
AXL	-0.024 (0.005)	<0.001										

In the CC group, age was collinear with preoperative visual acuity and AXL; therefore, preoperative visual acuity and AXL were not included in the multivariable analysis. CC: childhood cataract; YAC: young adult cataract; ARC: age-related cataract; LT: lens thickness; AXL: axial length; ACD: anterior chamber depth. *P*-values <0.05 were considered significant.

central anterior surface of the lens capsule changes with age [29, 30]. As the lens capsule thickens over time, this outermost layer of the capsule may experience increased tensile forces that alter its pore structure. The highest CER was found in the CC group in our study, which might be related to the lower tensile forces in the lenses of children and the increased tensile forces in the lenses of older adults. Fisher [31] studied the elastic properties of the human anterior lens capsule in relation to accommodation using a volumetric strain method. His finding revealed that the extensibility of the anterior lens capsule was only 29%, regardless of age. In a study performed on human donor eyes, Thim et al. [32] observed that the extensibility of a continuous circular capsulotomy edge could be as high as 60%, which was to the results of Lee et al. [21] who found a negative association between extensibility of the capsulotomy edge and age. Krag et al. [33] reported that the extensibility was as high as 100% in the young age group, while it was reduced to approximately half in the old age group. The present study observed significant differences in the CER across different age groups. These results are supported by the previous studies presented above. Age was found to be correlated with the CER in the CC and YAC groups only. This suggests a progressive stiffening of the lens structure until a certain age, elucidating the weaker correlation in the YAC group and the lack of significance in the ARC group.

Another factor that might be involved in capsulotomy enlargement is the zigzag shape of the laser-made capsulorhexis. Indeed, capsulotomy created by a femtosecond laser is more tear-resistant than a manual capsulorhexis, which may be related to capsular expansion [34]. Sandor et al. [35] found that femtosecond laser capsulotomy resulted in a mildly serrated capsule edge, while the opening formed by continuous curvilinear capsulorhexis exhibited a smooth edge upon scanning electron microscopy observation. Microheterogeneity of the capsule edge after femtosecond laser capsulotomy essentially expands the overall surface area of the capsule edge, compared with the manual technique [34]. A study of Packer et al. [16] showed that the stress at rupture and extension capability of the anterior lens capsule edge depended on the initial diameter of the femtosecond laser capsulotomy. At a diameter ≥5.0 mm, the elasticity and extensibility of the capsule edge after femtosecond laser capsulotomy were higher than that after manual capsulotomy [16]. Thus, it is hypothesized that in older patients, postoperative capsule expansion is primarily related to the extension of the jagged edge. However, in younger patients, the extensibility of the thinner and more elastic anterior capsule itself also plays an important role in postoperative capsule expansion, in addition to jagged edge extension. Still, these possible mechanisms require further investigation.

Previous studies have reported larger-than-planned capsulotomy in children [8, 17], possibly due to the tensile properties of the eye tissues as discussed above, but these findings can be difficult to apply to adults. Nevertheless, this phenomenon has also been observed in adults [36]. Hollick et al. [19] did not examine the factors associated with capsulotomy enlargement. Hu et al. [18] showed that capsulotomy enlargement was not associated with IOP, ACD, spherical equivalent, refractive astigmatism, keratometric astigmatism, or residual astigmatism. Joo et al. [20] reported that age, sex, IOL haptic length, IOL haptic material, and capsulotomy size were not related to changes in capsulotomy enlargement. In the present study, the factors associated with capsulotomy enlargement varied among different age groups. The factors independently associated with the CER were identified to be age and LT in the CC group, age in the YAC group, and LT in the ARC group. The differences might be attributed to varying factors. Indeed, the elasticity of the anterior capsular membrane in children is very high [8, 17], so there is a significant difference in the process of intraoperative capsular avulsion compared with that in the ARC group. The younger the age, the greater the elasticity of the anterior capsule. Therefore, it is highly probable that age is an important influencing factor in CC and YAC groups, continuing to the expansion of the capsule. Regarding the influence of LT on anterior capsular dilatation in the CC group, our perspective is that this phenomenon could be attributed to the diverse crystal development patterns observed in different types of congenital cataracts. These variations might lead varying degrees of capsule development abnormalities, subsequently affecting capsule elasticity to different extents. Of course, this hypothesis needs to be tested further in the future. Finally, in the ARC group, many cataract patients had thickened lenses, but the size of the capsule was fixed and the capsule remained tense. Constant stretching of the fibers inside the capsule membrane may cause elasticity degeneration, resulting in differences in the expansion ratio.

The Bochum formula for pediatric laser capsulotomies is applicable to children [17] but not to adults, because the Bochum formula was not developed using data from adults. The present study showed that the correlation ratio of age in the YAC group was about half that in the CC group. In addition, different factors were found to be associated with the CER in CC and YAC groups. The regression analysis showed that the CER could be calculated as 1.483 - 0.011 × age - 0.049 × LT, 1.224 - 0.004 × age, 1.111 - 0.014 × LT in CC, YAC, and ARC group, respectively. Obviously, the present equations cover a wider age range than that reported previously, and thus have better clinical application potential [17]. Unlike the formula obtained in this study, the Bochum formula (1.34 - 0.009 × age) only considers age as an independently associated factor when calculating the CER in children [17], which may be caused by ethnic differences and needs further research. Liao et al. [36] proposed the formula 1.177 - 0.052 × ACD + 0.009 × AL for the calculation of the enlargement ratio for anterior capsulorhexis in children aged 2-6 years. Since the determination of such formulas depends upon the study population, validation using a large sample size is necessary. Nevertheless, three different formulas for CC, YAC, and ARC groups were proposed in this study, allowing for better personalization of the procedure.

This study also has the following limitations. First, this is a single-center study with limited number of samples included. Since ARCs were more frequent than CCs or YACs, there was a big difference in the number of cases across the age groups. Second, only routine eye parameters were analyzed. Some correlations were marginally significant, and it is unclear whether they remain significant after adjustment for confounders. Unfortunately, the sample size was too small for meaningful adjustments. More patients should be included in future studies, and the type of IOL should be limited to a single type and size for further in-depth study. Third, nomogram analysis should be supplemented to visually evaluate the prediction value of CER.

In conclusion, capsulotomy enlargement can occur after femtosecond laser treatment in cataract surgery, especially in CC. Age was a determinant of the CER in the CC and YAC groups, while LT was an independent determinant of the CER in the CC and ARC groups. The CER could be calculated as 1.483 - 0.011 × age - 0.049 × LT, 1.224 - 0.004 × age, and 1.111 - 0.014 × LT in CC, YAC, and ARC, respectively. For the application of the femtosecond laser in cataract surgery, the precise size of the anterior capsule is very important. Future studies should focus on identifying corrective factors for more precise capsulotomies, especially in younger patients.

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Written informed consent was obtained from all participants.

Disclosure of conflict of interest

None.

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