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Addressing the unmet needs of cataract patients: When quality of vision can make the difference in quality of life

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Addressing the unmet needs of cataract patients: When quality of vision can make the difference in quality of life

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Editorial: Addressing the unmet needs of cataract patients: when quality of vision can make the difference in quality of life

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KEYWORDS

cataract surgery, presbyopia correction, enhanced monofocal intraocular lenses, intraocular lens, multifocal intraocular lens, extended depth of focus (EDOF), quality of vision

Editorial on the Research Topic
Addressing the unmet needs of cataract patients: when quality of vision can make the difference in quality of life

"Senectus ipsa morbus est" Terentius highlighted already in the second century BC that aging can have a significant impact on the quality of life. This is particularly true for vision, one of the most important among the five senses, together with hearing, for the closest relationship with social life. Even though quality of life and quality of vision are not real synonyms, both can contribute to "wellness" in aging.

A cataract is one of the main causes of visual impairment in old age. Even though clinical interventional studies on these research topics are lacking, it has been suggested that cataract surgery may decrease fall risk, reduce depression, and limit the risk of cognitive impairment (Mencucci et al.). In the narrative review published on this Research Topic (Mencucci et al.), we also emphasize the need to move from the concept of visual acuity to functional vision, especially in the context of the older adult patients. Further studies are necessary in order to evaluate the impact on the cited outcomes of different cataract treatment strategies, such as systematic bilateral vs. monolateral surgery and the use of different intraocular lenses (Mencucci et al.).

In addition to aging, environmental factors, such as UV exposure, diabetes, smoking, and some prescription drugs, can contribute to cataract formation. In particular, the study by Carlson et al. shows how drug-induced cataract represents a poorly addressed source of cataract.

In this context, choosing the right timing of cataract surgery is crucial, and new parameters have been proposed: beyond visual acuity, an objective scatter index can be a helpful early indicator of subjective visual function impairment (Li Y. et al.).

Cataract surgery is a highly successful and cost-effective procedure, even though various factors such as diabetic retinopathy, glaucoma, and at-risk surgery, can affect its outcome (AlRyalat et al.). In the majority of cases, the implantation of conventional monofocal intraocular lenses (IOLs) allows restoration of distance vision, with a very good quality of vision. Nevertheless, these IOLs do not provide spectacle independence in terms of near and intermediate vision, which are involved in many common daily tasks. Therefore, this has led to a growing interest in multifocal IOLs, trifocal IOLs, and extended depth of

focus (EDOF) IOLs (1, 2). Although these are good options (Pedrotti et al.), there are possible drawbacks related to photic phenomena, reduced contrast sensitivity (Wang et al.), and reduced stereopsis when a blended or monovision approach is chosen (Zhu et al.).

An important factor that can influence the quality of life after cataract surgery is corneal astigmatism, and among the correction methods (Ding et al.), toric IOLs are the most used and the most successful approach during cataract surgery (3). This strategy has also been applied to multifocal/trifocal/EDOF intraocular lenses (Li Z. et al.).

In recent years, intermediate vision has gained importance, since many daily activities, such as cooking, performing hobbies, and using digital devices may not correlate with far best corrected visual acuity (4). The study by Ribeiro et al. (5) revealed that patients primarily dedicated their time to near (42.53%) and intermediate (30.23%) visual tasks and confirmed the significance of the range of distances between 1 m and ∼30–40 cm for the daily life activities.

To reduce the visual disturbances related to trifocal and EDOF IOLs, enhanced monofocal IOLs that give optimal far vision with functional intermediate vision have been introduced. These IOLs demonstrated excellent visual performances, especially at intermediate distances while maintaining good quality of vision, contrast sensitivity, and overall patient satisfaction (6).

Cataract surgery and different IOL options may have a critical influence on visual function, mental and systemic health, and quality of life. Future directions not only in terms of different IOLs but also in determining appropriate instruments to measure the challenge related to different tasks are needed.

Author contributions

All authors contributed to the conception and design of the editorial, wrote the first draft of the manuscript, manuscript revision, and read and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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ORIGINAL RESEARCH
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Comparison of Visual Outcomes Between Toric Intraocular Lenses and Clear Corneal Incisions to Correct Astigmatism in Image–Guided Cataract Surgery

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Purpose: To compare the astigmatism correction effects of toric intraocular lenses (IOL) and clear corneal incisions during image-guided cataract surgery.

Methods: All patients with regular corneal astigmatism of 0.75–1.5 D underwent cataract surgery and astigmatism correction using the Callisto eye image-guided system. One group had implantation of an AcrySof toric IOL. Another group had implantation of aspheric IOL with 3.0 mm single clear corneal incision (SCCI) on the steep axis. Uncorrected and best-corrected spectacle visual acuity, refraction, and toric IOL axis were evaluated at 1, 4, and 12 weeks postoperatively.

Results: Sixty-eight eyes of 68 patients were included. The mean residual refractive cylinder was 0.34 ± 0.40 D in the toric group and 0.64 ± 0.57 D in the SCCI group. There were no significant differences in residual refractive cylinder, spherical equivalent, uncorrected distance visual acuity (UDVA), and best-corrected spectacle visual acuity (BCSVA) between groups. The percentage of the residual cylinder within ± 0.50 D was 75 and 56% for toric and SCCI cases, respectively ($p > 0.1$). The mean surgical induced astigmatism vector was 0.61 ± 0.29 D in the SCCI group and 1.04 ± 0.38 D in the toric group. The mean magnitude of error was negative (−0.54 ± 0.48 D) and the correction index was < 1.0 ($p < 0.05$) in SCCI group. At 3 months, all toric IOL alignment errors were within 5 degrees from the intended axis.

Conclusions: Both toric IOL and SCCI can correct low and medium astigmatism effectively with the help of a precise image-guided system.

Keywords: single clear corneal incision, corneal astigmatism, cataract surgery, image-guided surgery, toric IOL, Callisto eye image-guided system

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INTRODUCTION

Corneal astigmatism is one of the important factors affecting visual quality after cataract surgery. It is estimated that 67.7% of eyes had corneal astigmatism between 0.25 and 1.25 diopters (D), and 27.5% of eyes had astigmatism at 1.25 D or higher in the cataract population (1). Another study showed that corneal astigmatism in the range

of 0.50–0.99 D was the most common (30.08%), followed by 1.00–1.49 D (22.15%) (2). A simple, accurate, effective, and safe method to correct astigmatism is the pursuit of surgeons.

Preoperative marking is an important step in astigmatism correction, whether using toric intraocular lenses (IOLs) or corneal incisions. Previous studies have usually used conventional manual marking with an ink pen. However, the application of an intraoperative image-guided system can improve the accuracy of IOL alignment and incision location. It has been shown that digital marking is more reliable than manual marking using a slitlamp (3). Therefore, we compared the astigmatism-reducing effect during Callisto eye image-guided cataract surgery using toric IOLs or non-toric IOL combined with 3.0 mm single clear corneal incision (SCCI) on the steep meridian in the correction of low-to-moderate regular corneal astigmatism.

PATIENTS AND METHODS

The study was approved by the Ethics Committee of Beijing Tongren Hospital, Capital Medical University, and conforms to the tenets of the Declaration of Helsinki (as revised in 2013) and good clinical practice.

A total of 68 eyes with cataracts and preoperative anterior corneal astigmatism with optical biometry (IOL Master 700, Carl Zeiss Meditec AG, Jena, Germany) of 0.75–1.5 D were enrolled in the study. The inclusion criteria were as follows: regular and symmetric astigmatism shape on the corneal topographic map, pupil dilation >6.00 mm, and no obvious ocular and systemic diseases. The exclusion criteria were as follows: undergoing pterygium surgery within 1 month, a history of intraocular surgery, irregular corneal astigmatism (corneal scar, corneal degeneration, keratoconus), and other ocular diseases (lens subluxation, uveitis, glaucoma, traumatic cataract, retinopathy, macular disease, or optic neuropathy).

All included patients underwent phacoemulsification and IOL implantation for astigmatism correction, including 36 eyes with toric IOL implantation and 32 eyes with aspheric monofocal IOL implantation with corneal astigmatic incisions. In the toric group, AcrySof Toric IOL (Alcon Laboratories, Inc., Fort Worth, TX, USA) power and orientation were calculated using the Barrett toric calculator (http://calc.apacrs.org/toric_calculator20/Toric%20Calculator.aspx). A 2.4 mm clear corneal incision was made on a 160° axis and surgical induced astigmatism vector (SIA) was calculated as 0.3. In the SCCI group, a 3.0 mm clear corneal incision was made at 1 mm inside limbus on the steep meridian. The IOL implanted was a MI60 (Bausch and Lomb, USA). Both groups' biometry data were obtained by IOL Master 700 and exported into the Callisto eye system (version 3.5.1.116555, Carl Zeiss Meditec AG). Results of the above calculations were preset in the Callisto eye system and the intraoperative overlay was displayed under OPMI Lumera 700 microscope (Carl Zeiss Meditec AG, Germany) to serve as a guide for the surgeon of toric IOL intended axis for the toric group and position and size of incision for SCCI group (**Figure 1**). All surgeries were performed by the same experienced surgeon. No complications occurred.

Participants were evaluated preoperatively and followed up 1 day, 1 week, 1 month, and 3 months postoperatively. Preoperative assessment included uncorrected distance visual acuities (UDVA), slitlamp examination, and intraocular pressure. A comprehensive evaluation of IOL Master 700, pentacam HR (Oculus Optikgerate GmbH, Wetzlar, Germany) and OPD scan III (Nidek Inc., Tokyo, Japan) was made to determine the regularity of the cornea and the suitability of toric IOL. Patients with regular central corneal topography and similar results of these three examinations were considered suitable for toric IOL implantation. Comparing the results of three examinations, if the difference of steep axis was greater than 10° or if the difference between simulated keratometry (SimK) and total corneal refractive power (TCRP) was >0.75D, then it was considered that the cornea is not regular and excluded from the study. This same process was repeated for the SCCI group. The UDVA, manifest refraction, best-corrected spectacle visual acuity (BCSVA), and toric IOL orientation were recorded at each postoperative visit. Among these, the toric IOL orientation was measured at the retro image by OPD scan III at every follow-up (**Figure 2**).

The residual refractive astigmatism, spherical equivalent (SE) refraction, UDVA, and BCSVA were compared in both groups at 3 months after surgery. The toric IOL orientation (intended vs. actual) at 1 and 3 months postoperatively were also evaluated.

The vector analysis of astigmatic correction was performed using the Alpins method (4, 5). The refractive astigmatism values were converted to the corneal plane for calculation. All statistical analyses were performed by Excel file (Microsoft Corp., Redmond, WA, USA) and SPSS software (version 22.0.0.0, IBM Corp., Armonk, NY, USA). *T*-test or chi-square (χ^2) test was used for the difference between the groups when appropriate. A *p*-value of < 0.05 was considered statistically significant.

RESULTS

The statistical characteristics of patients at the preoperative stage and 3 months postoperatively are shown in **Table 1**. Preoperative astigmatism in the eyes was measured with the optical biometer. There were 72.22% with the rule (WTR) (26 eyes), 25% against the rule (ATR) (9 eyes), and 2.78% Oblique (OB) (1 eye) eyes in the toric group and 43.75% WTR (14 eyes), 50% ATR (16 eyes), and 6.25% OB (2 eyes) eyes in the SCCI group. At 3 months after surgery, the mean residual refractive cylinder was 0.34 ± 0.40 D (0–1.00 D) in the toric group and 0.64 ± 0.57 D (0–1.25 D) in the SCCI group. The mean residual astigmatism in the toric group was ∼0.3 D lower than that of SCCI group, but with no difference between the 2 groups ($p = 0.24$). The mean SE refraction was 0.17 ± 0.28 D (−0.21 to 0.59 D) in the toric group and 0.13 ± 0.45 D (−0.43 to 0.90 D) in the SCCI group ($p = 0.83$). At 3 months, the average UDVA was 0.17 ± 0.22 logarithm of the minimum angle of resolution (logMAR) (0 to 0.52 logMAR) in the toric group and 0.12 ± 0.11 logMAR (−0.08 to 0.30 logMAR) in SCCI group ($p = 0.57$, *t*-test of independent samples). The mean BCSVA was

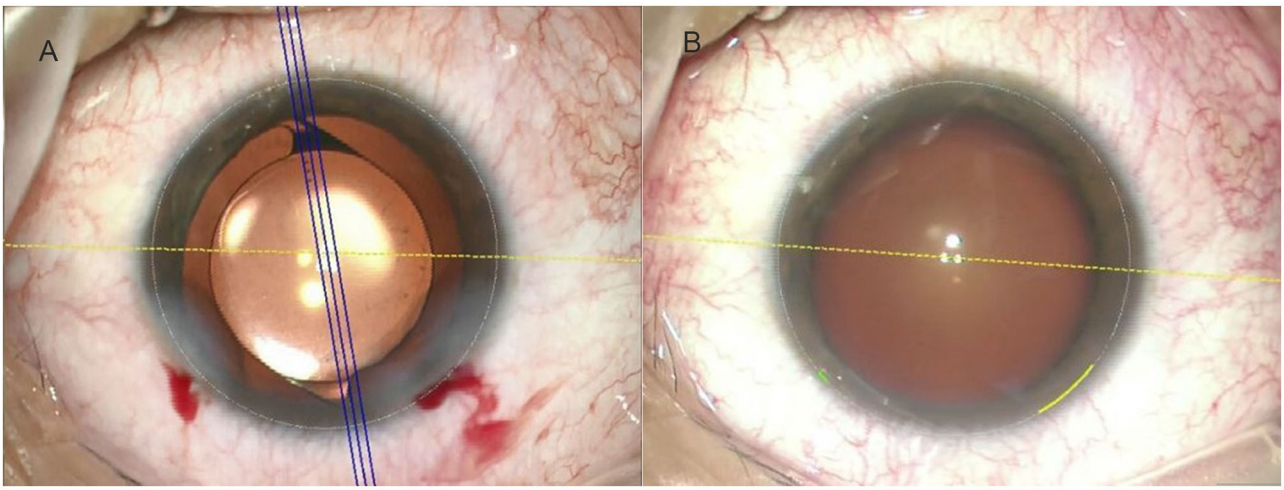

FIGURE 1 | The Callisto eye image-guided system was used to determine digital markers with the Lumera microscope. **(A)** The toric intraocular lens (IOL) target axis (3 parallel blue lines indicate the intended axis, and the yellow dots indicate a 0–180-degree axis). **(B)** The yellow arc indicates a corneal incision of the steep meridian with a length of 3.0 mm.

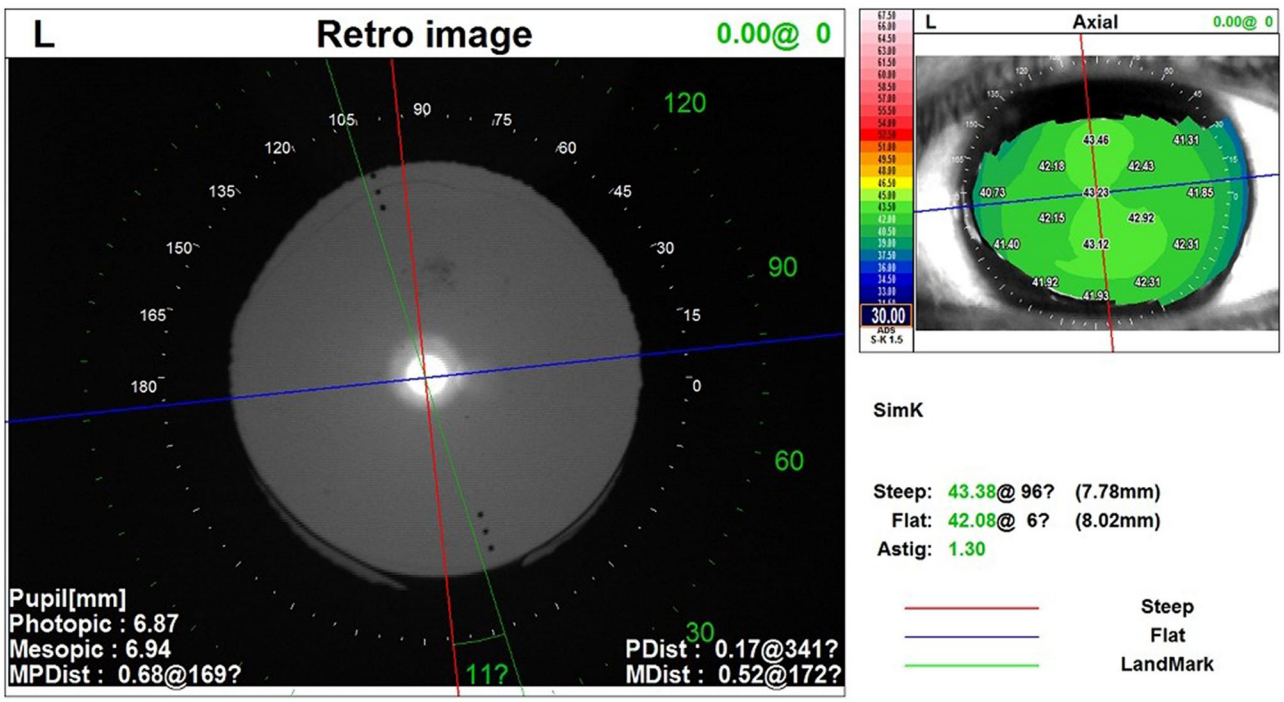

FIGURE 2 | The OPD scan III was used to evaluate the toric IOL orientation using the retro image. The red line indicates the steep axis of the cornea and the blue line indicates the flat axis. The green line indicates the toric IOL orientation. The included angle degrees are displayed between the red and green lines. IOL, intraocular lens.

0.04 ± 0.09 logMAR (−0.08 to 0.22 logMAR) in the toric group and 0.03 ± 0.07 logMAR (−0.08 to 0.10 logMAR) in SCCI group ($p = 0.92$, *t*-test of independent samples).

Table 2 lists the toric IOL models implanted in surgery.

The Standard Graphs for Cataract Surgery are used to show refractive outcomes at 3 months after image-guided cataract surgery in **Figure 3**. The percentages of postoperative UDVA and postoperative BCSVA were significantly improved in both groups. For UDVA, 92% of toric cases and 100% of SCCI cases were < 0.3 logMAR ($p = 0.24$). For BSCVA, 92% of toric cases and 100% of SCCI cases were < 0.1 logMAR ($p = 0.24$) (**Figure 3A**). In postoperative UDVA, about 47% of eyes in the

TABLE 1 | Comparison of outcomes before and 3 months after surgery (mean ± SD).

	Toric IOL group	SCCI group	*P* value
Age (y)(range)	65.00 ± 8.03 (46 to 71)	59.22 ± 13.80(32 to 82)	0.32
Gender (M/F)	13/23	10/22	–
Eyes (R/L)	16/20	17/15	–
Axial length (mm)(range)	23.64 ± 0.82 (22.34 to 24.47)	24.27 ± 1.05(22.38 to 25.59)	0.19
Preop corneal cylinder (D)	1.28 ± 0.18	1.15 ± 0.27	0.26
WTR	26	14	–
ATR	9	16	–
OB	1	2	–
Keratometry 1(range)	43.21 ± 1.16 (41.97 to 45.56)	44.09 ± 1.59(42.1 to 47.47)	0.22
Keratometry 2(range)	44.49 ± 1.16 (43.27 to 46.74)	45.24 ± 1.64(42.91 to 48.76)	0.30
Residual refractive cylinder (D)(range)	0.34 ± 0.40 (0.00 to 1.00)	0.64 ± 0.57(0.00 to 1.25)	0.24
SE refraction (D)(range)	0.17 ± 0.28 (−0.21 to 0.59)	0.13 ± 0.45(−0.43 to 0.90)	0.83
Preop UDVA (logMAR)(range)	0.55 ± 0.38 (0.15 to 1.30)	0.87 ± 0.70(0.22 to 2.00)	0.26
Postop UDVA (logMAR)(range)	0.17 ± 0.22 (0.00 to 0.52)	0.12 ± 0.11(−0.08 to 0.30)	0.57
Postop BCSVA (logMAR)(range)	0.04 ± 0.09 (−0.08 to 0.22)	0.03 ± 0.07(−0.08 to 0.10)	0.92

The clear corneal incision was made on the steep axis. Range is minimum to maximum points.
SD, standard deviation; D, diopters; Toric IOL, toric intraocular lens; SCCI, single clear corneal incision. ATR, against the rule; WTR, with the rule; OB, Oblique; SE, spherical equivalent; UDVA, uncorrected distance visual acuity; BCSVA, best-corrected spectacle visual acuity.

TABLE 2 | Toric IOLs power at corneal plane.

IOL model	Cylinder power (D)	Number (%)
SN6AT2	0.69	4 (11.11)
SN6AT3	1.03	21 (58.33)
SN6AT4	1.55	11 (30.56)

IOL, intraocular lens.

toric group and 38% in the SCCI group were in the same lines as BCSVA, while 75% in the toric group and 85% in the SCCI group were within 1 line of BCSVA (**Figure 3B**). About 89% of the toric cases and 91% of the SCCI cases were within ± 0.50 D ($p = 1.00$) in postoperative SE refraction, and all eyes in the two groups were within ± 1.00 D (**Figure 3C**). About 75% of toric cases and 56% of the SCCI cases were within ± 0.50 D in the residual refractive cylinder ($\chi^2 = 2.661$, $p = 0.103$). All toric cases were within ± 1.00 D, with the difference not being statistically significant ($p = 0.10$) (**Figure 3D**). Angle-of-error analysis for refraction showed that the AE (angle of error) of most eyes in both groups was between −5 and 15 degrees. The arithmetic mean was 4.6 degrees counterclockwise (CCW) in the toric group and −1.6 degrees slightly clockwise (CW) in the SCCI group, while the absolute means were 10.1 degrees in the toric group and 10.9 degrees in the SCCI group (**Figure 3E**; **Table 3**).

Figure 4 shows preoperative corneal astigmatism and residual postoperative refractive astigmatism for each group over 3 months. The proportion of astigmatism reduction would be an average of 73.44 and 44.35% for the toric and SCCI, respectively, at 3 months after surgery.

The vector analysis results using the Alpins method are shown in **Table 3**. The mean SIA in SCCI group (0.61 ± 0.29 D) was less than in the toric group (1.04 ± 0.38 D) ($p < 0.05$), and it was lower than its target induced astigmatism vector (TIA) (1.15 ± 0.27 D), indicating under correction. The mean magnitude of error (ME) in the toric group was closer to 0, while the negative value (−0.54 D) in the SCCI group indicates under correction ($p < 0.05$). The correction index (CI) is preferably 1.0, but it was < 1.0, which also confirmed that there was an under correction in SCCI group ($p < 0.05$). The results in the difference vector (DV) were not large in both toric (0.34 ± 0.39 D) and SCCI (0.62 ± 0.56 D) cases. The best result for index of success (IOS) is 0, and it was less in the toric group (IOS = 0.39) than in the SCCI group (IOS = 0.48). There were no statistically significant differences in TIA, DV, angle of error (AE), and IOS between the two groups.

The toric IOL orientation (intended vs. actual) was evaluated by OPD scan III and changes are shown in **Table 4**, including the changes at the time of surgery and 3 months postoperatively,as well as the changes from 1 to 3 months after surgery. The absolute difference of all toric IOLs from the intended axis was within 5 degrees until 3 months after surgery. No eye underwent a secondary alignment to reorient the IOL.

DISCUSSION

Modern cataract surgery brings expectations of clearer vision, greater visual quality, and less dependence on spectacles. Meanwhile, more attention has been paid to the necessity of astigmatism correction. Mild astigmatism can cause significantly decreased vision, even as low as 1.00 D. If not corrected, it has a significant effect on patients' independence, quality of life, and well being (6). Postoperative residual astigmatism of < 0.5 D is recommended to achieve better visual function and patient satisfaction after cataract surgery. However, how to

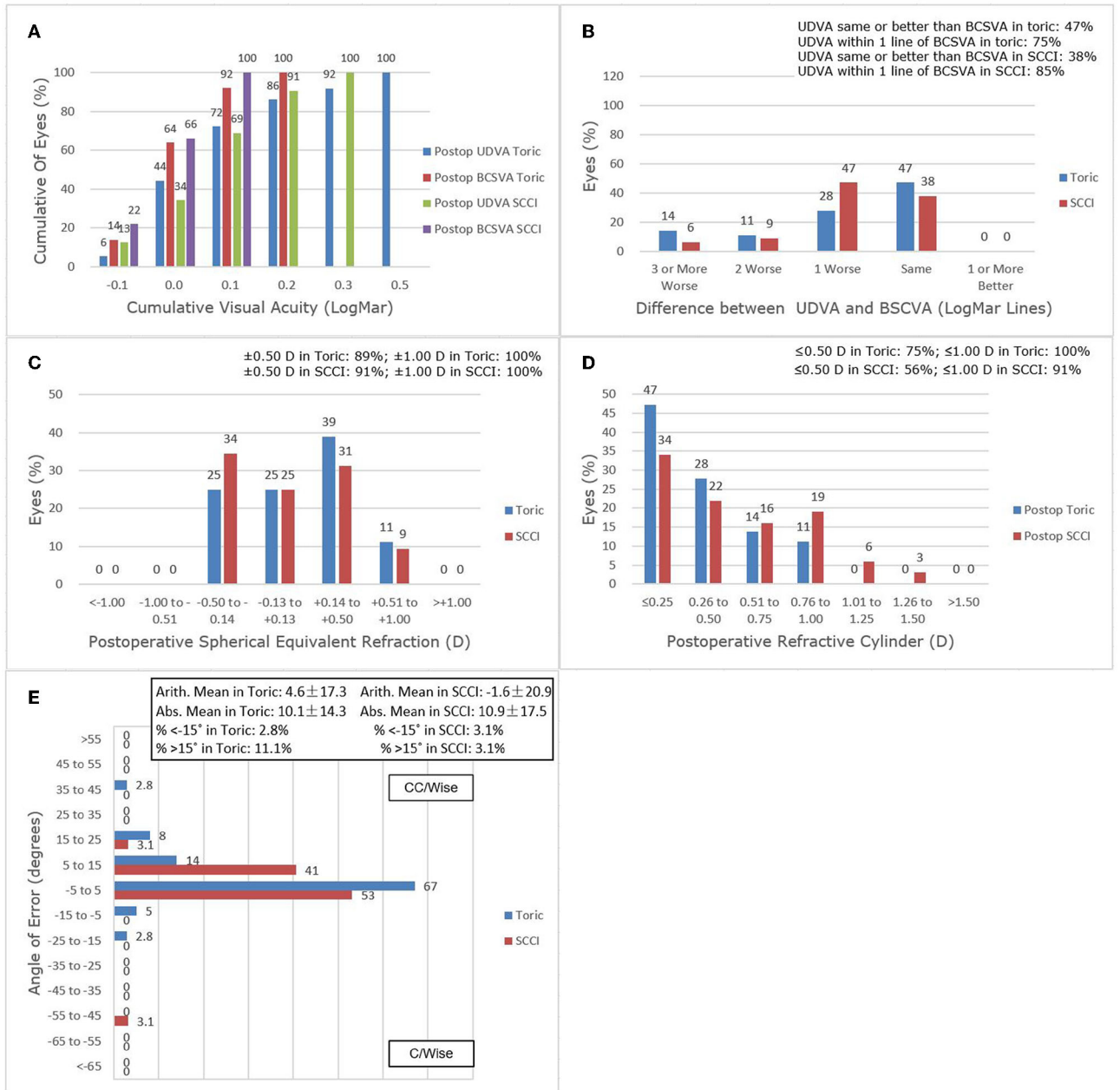

FIGURE 3 | Refractive outcomes at 3 months postoperatively. **(A)** Uncorrected distance visual acuity. **(B)** Uncorrected distance visual acuity vs. best-corrected spectacle visual acuity. **(C)** Spherical equivalent refraction accuracy. **(D)** Postoperative refractive cylinder. **(E)** Refractive Astigmatism Angle of Error.

suitably correct astigmatism during surgery is a big challenge for ophthalmologists.

There are various ways to correct astigmatisms in cataract surgery, such as toric IOL implantations (7, 8), astigmatic keratotomy (9), limbal relaxing incisions (LRI) (10), SCCI, or opposite clear corneal incision (OCCI) on the steep meridian (11–13), excimer laser *in situ* keratomileusis (14), and photorefractive keratectomy (15). Surgeons need to choose appropriate methods according to the amount of corneal astigmatism and the equipment of the operating room.

Toric IOLs have been widely used in cataract patients with regular astigmatism over the past few years, with good effectiveness and predictability especially in the effective correction method of medium and high astigmatism (16, 17). However, it is possible that due to inaccurate marking and the rotation of toric IOL (18), a second intraocular procedure may have to be performed to reposition the IOL, increasing the risk for infection. As a step of cataract surgery, SCCI is a simple technique that requires no additional skills or equipment. It is an easy, safe, and inexpensive method for astigmatic correction

TABLE 3 | Vector analysis for treatment and error at 3 months after surgery (mean ± SD).

	Toric IOL group	SCCI group	*P* value
TIA, D(range)	1.02 ± 0.23 (0.78 to 1.31)	1.15 ± 0.27 (0.81 to 1.50)	0.320
SIA, D(range)	1.04 ± 0.38 (0.40 to 1.59)	0.61 ± 0.29 (0.31 to 0.96)	0.02
DV, D(range)	0.34 ± 0.39 (0 to 0.98)	0.62 ± 0.56 (0 to 1.46)	0.25
AE, degrees			
arithmetic mean	4.63 ± 17.25	−1.56 ± 20.93	0.52
(range)	(−22 to 39)	(−56 to 12)	
absolute mean	10.13 ± 14.32	10.89 ± 17.53	0.92
(range)	(0 to 39)	(0 to 56)	
ME, D(range)	0.02 ± 0.22 (−0.40 to 0.43)	−0.54 ± 0.48 (−1.19 to 0)	0.01
CI(range)	1.00 ± 0.24 (0.50 to 1.37)	0.58 ± 0.35 (0.21 to 1.00)	0.01
IOS(range)	0.39 ± 0.47 (0 to 1.26)	0.48 ± 0.41 (0 to 1.12)	0.67

Range is minimum to maximum points.
SD, standard deviation; TIA, Target induced astigmatism; SIA, Surgically induced astigmatism; DV, Difference vector; AE, angle of error; ME, magnitude of error; CI, correction index; IOS, index of success.

that is effective for low to moderate astigmatism. It has been reported that the size, shape, and location of a clear corneal incision (CCI) can affect corneal astigmatism (14). Corneal factors can also affect astigmatism correction, such as the size and meridian of preoperative corneal astigmatism (19), thickness and elasticity of cornea, and the extent of incision scarring after surgery (11). The main disadvantage of CCI is that it is difficult to predict accurately and the long-term correction effect may decrease. However, previous studies showed that surgically induced astigmatism was stable for a long time after operation in 3.0 mm SCCI and OCCI cases. Nemeth et al. (12) observed that the amount of astigmatism reduction is not related to the position of incisions and its effect remains unchanged during the postoperative period in the SCCI and OCCI cases. Other studies have revealed that the average astigmatism corrected by CCI may remain stable for 12 weeks (20) or even 1 year (21) after surgery.

It is widely known that accurate alignment of toric IOL is crucial for astigmatism correction, and the location of the corneal incision is the same. Precise preoperative marking is the basis of exact alignment. With the help of new technologies, the preoperative marking procedure is simplified and the patient's discomfort is greatly alleviated. Meanwhile, the astigmatism-reducing effect is improved. The image-guided system is objective and easy to use. Without requiring subjective estimation and contact with the patient's eyes during the whole surgery, it can project real-time digital image guidance on the eye to identify the target meridian on the operating microscope, reducing the patient's psychological and eye discomfort. A prospective study in India showed that using the slit-lamp marking method about 28% of toric cases had an alignment error of more than 5 degrees (17). Another study showed that marking under a slit lamp using a marker pen or toric marker caused an average axis misalignment of 3.4 to 6.9 degrees. As a result, the astigmatism correction effect is reduced by 10 to 20% on average (22). Several image-guided modalities have been used in clinical practice for precise and contactless alignment in order to decrease the subjectivity of manual marking (3, 23–25) and the technical dependence on the operator. Research has shown that image-guided marking is superior to manual marking, with more precise alignment, less axial misalignment, and better refractive outcomes (23, 24, 26). Other studies have found that although visual acuity is similar between the image-guided group and manual group, the former has better visual quality and the difference is clinically significant (27). Moreover, both the mean toric IOL alignment time and total operation time are significantly shorter in the digital group (23).

We compared toric IOLs with 3.0 mm SCCI. The results showed that the mean residual astigmatism of the toric group was ∼0.3 D less than that of SCCI, but with no difference between the 2 groups ($p > 0.05$). With the corneal wound healing process, we found that residual astigmatism was postoperatively stable in both groups over 3 months. The residual refractive cylinder was 0.64 ± 0.57 D on average in the SCCI group at 3-month follow-up, which was slightly lower than the finding of previous research. Ren et al. reported the mean corneal astigmatism was reduced to 0.82 ± 0.68 D in 3.0 mm SCCI group at 3 months after surgery (28). Though it has been shown that OCCI is better than SCCI of the same size (28) in reducing astigmatism, OCCI adds one corneal incision, prolongs the operation time, and has greater potential damage to the cornea. In the current study, there were no significant differences in the residual refractive cylinder, SE, UDVA, and BCSVA between the groups. The proportion of residual astigmatism within ± 0.5 D was higher in the toric IOL group compared with SCCIs ($p > 0.1$). As is well known, the effect of posterior corneal astigmatism on postoperative manifest refractive astigmatism would differ according to the meridian of the anterior steep axis. This will reduce with the rule astigmatism and increase against the rule astigmatism. The proportion of WTR in the toric group (72.22%) was higher than that of SCCI group (43.75%). Hence, it is possible to underestimate the astigmatism reduction in the SCCI group. Furthermore, our results showed that all of the toric IOL alignment errors were within 5 degrees from the intended axis at 3 months, and the mean error in alignment was −0.50 ± 3.12 degrees. This alignment error is lower than what is reported in other studies. Farooqui et al. (16) showed that 6% of toric cases had a misalignment of more than 10 degrees by slit-lamp method. Webers et al. (24) found that the mean misalignment of toric IOL was 1.7 ± 1.5 degrees in the image-guided group at 3 months. Emesz et al. (29) stated that less effective correction in the low toric IOL group may be caused by slight misalignment and measurement errors. However, our findings suggest that by using a new digital navigation technique, the alignment of the IOL during surgery is more accurate. Accurate alignment, skilled surgical technique, and good IOL rotation stability will bring the better effect of astigmatism correction.

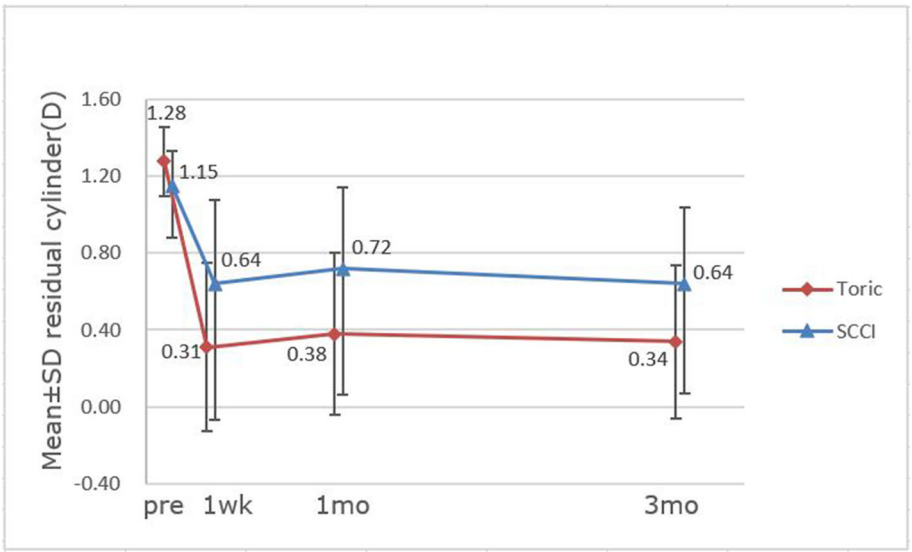

FIGURE 4 | Astigmatism changes over time between toric IOL and single clear corneal incision (SCCI) groups.

TABLE 4 | Toric intraocular lens alignment error changes over time.

Change	1 month to 3 months	Surgery to 3 months
0 to 2 degrees (eyes)	32	19
3 to 5 degrees (eyes)	4	17
6 to 10 degrees (eyes)	0	0
>10 degrees (eyes)	0	0
Mean ± SD (degrees)	−0.63 ± 1.85	−0.50 ± 3.12
Median (degrees)	0	−1
Range (degrees)	−5,1	−5,4

Range is minimum to maximum points.
SD, standard deviation.

Meanwhile, we performed vector analysis by Alpins method. It can be seen that the correction effect of the toric group is better, while that of SCCI group is slightly under corrected (**Table 3**). In the current study, as the SCCI group cannot accurately predict TIA like the toric group. For the convenience of calculation, TIA of the SCCI group was set as full correction for calculation, possibly causing errors and affecting the statistical results. In addition, there are other factors at work, such as posterior corneal astigmatism. However, the trend of under correction for the SCCI group is evident. IOS suggested that the postoperative astigmatic status was better in the toric group (0.39 = 61%) than in the SCCI group (0.48 = 52%), but the difference was not statistically significant.

Moreover, the image-guided system had some limitations. Although the computer-assisted markerless system provided better outcomes than using manual marking, it should be noted that the intraoperative factors (e.g., conjunctival edema or hemorrhages) might affect the real-time identification of limbal and scleral vessels, resulting in deviation either at the beginning of the procedure or during the operation. Sometimes, anterior segment photos of sufficient quality were not available by IOL Master 700 due to dry eyes or poor coordination. These patients still need to be manually marked and excluded from the study.

In summary, combined use of 3.0-mm SCCIs on the steep meridian with the Callisto eye image-guided system can effectively correct mild to moderate corneal astigmatism in cataract surgery. In eyes with up to 1.50 D of regular corneal astigmatism, according to respective surgical conditions, both 3.0 mm SCCIs or toric IOL implantations can be selected combined with accurate alignment, which can achieve a good effect of astigmatic correction at the time of cataract surgery.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary materials, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

This retrospective study was approved by the Ethics Committee of Beijing Tongren Hospital, Capital Medical University (TRECKY2020-124). Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

ND designed the study, examined patients, analyzed and interpreted results, and wrote the manuscript. XS performed the cataract surgery with intraocular lens (IOL) implantation and astigmatism correction and reviewed the manuscript. XW analyzed results. WW reviewed the manuscript. All authors contributed to the article and approved the submitted version.

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Drugs associated with cataract formation represent an unmet need in cataract research

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Decreased light transmittance through the ocular lens, termed cataract, is a leading cause of low vision and blindness worldwide. Cataract causes significantly decreased quality of life, particularly in the elderly. Environmental risk factors, including aging, UV exposure, diabetes, smoking and some prescription drugs, are all contributors to cataract formation. In particular, drug-induced cataract represents a poorly-addressed source of cataract. To better understand the potential impact of prescription drugs on cataract, we analyzed publicly-available drug prescriptions data from the Australian Pharmaceutical Benefits Scheme. The data was analyzed for the 5-year period from July 2014 to June 2019. Analyses included the number of prescriptions for each drug, as well as the associated government and total prescription costs. The drugs chosen for analysis belonged to any of four broad categories—those with known, probable, possible or uncertain association with cataract in patients. The analyses revealed high prescription rates and costs for drugs in the Known category (e.g., steroids) and Possible category (e.g., psychotropic drugs). Collectively, these data provide valuable insights into specific prescription drugs that likely contribute to the increasing annual burden of new cataract cases. These data highlight the need—as well as new, stem cell-based opportunities—to elucidate molecular mechanisms of drug-induced cataract formation.

KEYWORDS

prescription drug, dexamethasone, human pluripotent stem cell, micro-lens, cataracts, bioinformatics, lens

Introduction

Cataracts disrupt light transmission through the lens of the eye. Excluding uncorrected refractive errors, cataracts are the leading cause of blindness and low vision worldwide—with over 65 million (M) patients affected in 2015 (1). Current cataract treatment involves removal of the cataractous lens tissue and replacement of lens function with a synthetic intra-ocular lens. Where access to treatment is available,

cataract surgery is a relatively simple and effective approach to restoring vision. However, despite continued advances in cataract surgery, the number of patients affected by cataract continues to increase (1).

Over 70 drugs have been associated with a known or suspected increased risk of cataract formation (2). These drugs can be grouped into four distinct categories based on the evidence underpinning their association with cataract formation: (i) Known category drugs are known to increase the risk of cataract in patients; (ii) Probable category drugs are likely to cause increased risk of cataracts; (iii) Possible category drugs, and (iv) Uncertain category drugs may increase cataract risk but the data is inconclusive (**Supplementary Table 1**). A collective analysis of the prescribing rates for the cataract-associated drugs in these four categories is yet to be performed.

In Australia, the Federal Government manages two programs that provide universal healthcare to citizens, permanent residents, and some international travelers. The Medicare scheme provides access to health and hospital services, including cataract surgery, at low or no cost. The Pharmaceutical Benefits Scheme (PBS) subsidizes the cost of prescription medicines approved for inclusion in the scheme. Among the PBS-listed medicines are drugs known or suspected to increase the risk of cataract. To investigate the number of prescriptions and associated costs for these drugs in Australia, we examined publicly available, PBS drug prescriptions data for the 5-year period from July 2014 to June 2019.

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval; LEC, lens epithelial cell; M, million; PBS, Pharmaceutical Benefits Scheme; RR, relative risk.

Results

Known category drugs dominated by high and increasing glucocorticoid prescriptions

Of the 31 drugs known to increase the risk of cataract (**Supplementary Table 1**), analysis of the PBS data revealed 17 were prescribed over the 5-year period analyzed (**Table 1**). The top 3 most prescribed Known category drugs averaged more than 1 M prescriptions per year, and cost from $18 M to $53 M a year each (**Table 1**).

Most notable among the Known category drugs prescribed over the 5 years were 11 steroids, of which 8 were in the top 10 most prescribed Known drugs (**Table 1**). On average, each year over 9 M total steroid prescriptions were supplied at a combined average annual cost of > $175 M (**Figure 1**). Prednisolone (>3 M prescriptions and > $50 M per year) and betamethasone (>1.7 M prescriptions and > $53 M per year) were the most prescribed and also the most costly drugs in the Known category.

Over the 5-year period, 8 Known category drugs showed increasing annual prescriptions (5 steroids) and 9 showed increasing annual costs (**Supplementary Figure 1**). The total number of annual steroid prescriptions increased 7.7% over the 5 years (9,031,988 in 2014/15 to 9,725,044 in 2018/19), and the

TABLE 1 PBS data (2014–2019) showing prescription numbers and costs for members of the known category of drugs associated with cataract (gray background = steroids).

Drug name	Total prescriptions (2014–2019)	Total cost (2014–2019)	Total government cost (2014–2019)	Trend
Prednisolone	16,390,059	$253,257,180	$96,718,235	Up
Betamethasone	8,616,640	$266,088,884	$159,901,957	Up
Allopurinol	6,625,962	$89,269,641	$37,871,101	Up
Triamcinolone	4,905,834	$70,161,998	$29,960,557	Up
Methylprednisolone	3,911,183	$92,643,240	$40,556,629	Up
Prednisone	3,687,206	$48,707,232	$19,615,930	Stable
Dexamethasone	3,666,197	$63,549,170	$30,930,017	Stable
Hydrocortisone	2,436,800	$41,382,170	$19,657,190	Down
Amiodarone	1,987,962	$33,713,930	$21,184,186	Up
Fluorometholone	1,408,451	$23,797,616	$8,842,284	Stable
Tamoxifen	877,558	$26,296,362	$10,981,787	Up
Raloxifene	506,690	$24,104,552	$18,996,743	Down
Haloperidol	451,204	$7,660,017	$5,089,181	Stable
Beclomethasone	280,818	$8,992,458	$4,729,624	Down
Cortisone	205,460	$4,539,133	$2,355,101	Stable
Fludrocortisone	162,601	$6,578,401	$4,403,161	Up
Busulfan	1,768	$148,476	$132,684	Stable

FIGURE 1
Average annual prescription numbers **(A)** and costs **(B)** for members of the Known category of drugs associated with cataract, together with typical conditions for which they are prescribed.

TABLE 2 PBS data (2014–2019) showing prescription numbers and costs for members of the probable category of drugs associated with cataract.

Drug name	Total prescriptions (2014–2019)	Total cost (2014–2019)	Total government cost (2014–2019)	Trend
Methotrexate	1,671,826	$58,958,809	$33,952,887	Up
Pilocarpine	201,535	$3,389,391	$2,168,548	Down

associated costs increased 42.9% $142M in 2014/15 to $203M in 2018/19).

Overall, these data indicate that numerous Known cataract-inducing drugs are being increasingly used. At a combined average annual cost of >$212 M per year, of which the direct government cost is > $102 M, it is clear a large investment is being made to treat patients using drugs known to increase the rate of cataract formation.

Probable cataract-inducing drugs largely involves methotrexate

Of the 9 drugs classified as having a probable association with cataract formation (Supplementary Table 1), only two were prescribed over the 5-year period analyzed–methotrexate and pilocarpine (Table 2). These drugs are prescribed for conditions including cancer and rheumatoid arthritis (methotrexate), or glaucoma (pilocarpine). Methotrexate averaged > 330,000 annual prescriptions (Figure 2), with prescriptions increasing ~28% over the 5 years (from 298,589 in 2014/15 to 398,799 in 2018/19). Average methotrexate costs were > $11 M/yr (Figure 2), having increased 49% over the 5 years ($9.9M to $14.7M; Supplementary Figure 2). In contrast, pilocarpine, averaged > 40,000 prescriptions/year at an average annual cost of $677,000/year (Figure 2). The prescribing rate for pilocarpine steadily decreased over the 5 years (Supplementary Figure 2).

Possible cataract-inducing drugs dominated by psychotropic drugs

Of the 23 drugs having a possible association with increased risk of cataract (Supplementary Table 1), 14 were prescribed over the 5 years (Table 3). These drugs are typically prescribed for conditions from depression to diabetes mellitus. Notably, 8 psychotropic drugs were in the top 10 most prescribed drugs in this category (Table 3). The top 6 most prescribed Possible category drugs averaged more than 1 M prescriptions

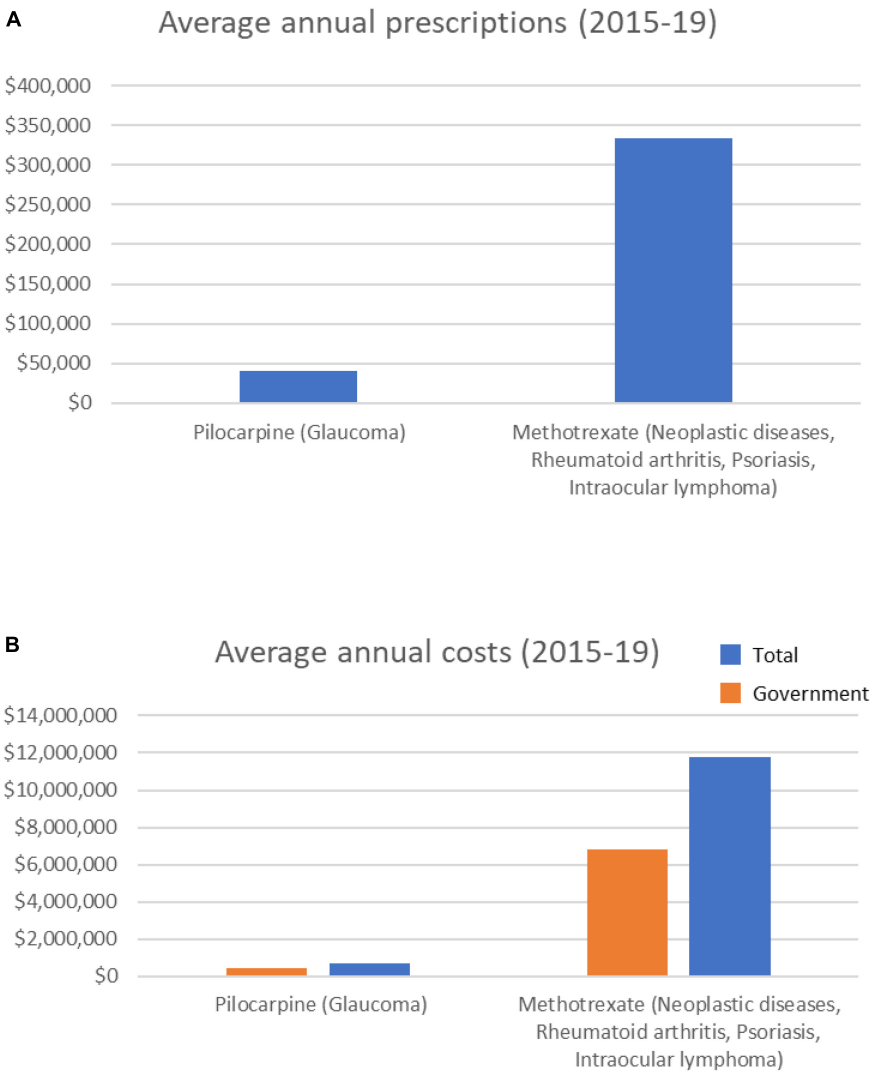

FIGURE 2
Average annual prescription numbers **(A)** and costs **(B)** for members of the probable category of drugs associated with cataract, together with typical conditions for which they are prescribed.

TABLE 3 PBS data (2014–2019) showing prescription and cost data for drugs that have a probable association with cataract; drugs with gray background are psychotropic drugs (gray background = psychotropic drugs).

Drug name	Total prescriptions (2014–2019)	Total cost (2014–2019)	Total government cost (2014–2019)	Trend
Escitalopram	19,668,355	$267,239,697	$77,242,077	Up
Sertraline	19,621,073	$250,805,008	$75,720,013	Up
Fluoxetine	9,175,210	$159,591,755	$56,952,481	Up
Citalopram	8,757,519	$107,923,398	$36,708,280	Stable
Quetiapine	5,208,959	$250,578,382	$199,228,874	Up
Paroxetine	5,186,599	$84,724,396	$33,597,402	Stable
Fluvoxamine	2,181,096	$47,293,012	$21,200,592	Stable
Glimepiride*	1,111,627	$13,956,211	$6,955,193	Down
Phenytoin	636,940	$21,170,351	$14,014,774	Down
Glibenclamide*	562,997	$9,342,018	$5,090,815	Down
Glipizide*	139,061	$2,416,335	$1,464,987	Down
Cyclophosphamide	57,541	$4,683,890	$3,760,884	Stable
Benzalkonium	6,913	$156,968	$134,716	Down
Verteporfin	391	$940,222	$932,472	Down

*Sulphonylurea drug category.

per year and cost from $16 M to $53 M annually (Figure 3). Psychotropic drug prescriptions averaged > 14 M annually, at a combined average annual cost of >$237 M. Escitalopram (>3.9 M prescriptions and > $53 M per year) and sertraline (>3.9 M prescriptions and >$50 M per year) were the most prescribed and most costly drugs.

Of the 14 drugs in the Possible Category, 4 (all psychotropic drugs) increased in annual prescriptions, government cost and total cost, including 4 of the top 5 drugs (Supplementary Figure 3). The other 4 psychotropic drugs showed relatively stable prescribing rates over the past 5 years. Overall, the number of annual psychotropic prescriptions increased by 19.7% over the 5 years (from 12.8 M in 2014/15 to 15.4 M in 2018/19), with an associated increase in costs 7% (from $230 M in 2014/15 to $246 M in 2018/19).

The other drugs having a Possible association with cataracts were the sulfonylureas (Table 3) typically used to treat diabetes mellitus. Sulfonylureas were prescribed at an annual rate of > 360,000 prescriptions a year (Figure 3), costing ∼$5 M/year, and with a steadily decreasing prescribing rate over the 5 years (Supplementary Table 2).

Statins dominate the drugs with uncertain effects on cataract: Statins

Of the 15 drugs in the Uncertain category (Supplementary Table 1), the PBS data revealed 11 were prescribed over the 5-year period (Table 4). These drugs are prescribed for conditions ranging from hypercholesterolemia to endometriosis. The top three most prescribed averaged > 3 M annual prescriptions, and cost from $107 M to $260 M a year each (Figure 4). Most notable among these Uncertain category drugs were 5 statins, 3 of which were in the top five most prescribed (Table 4). Atorvastatin (> 12 M prescriptions and > $224 M per year) and rosuvastatin (>10 M prescriptions and > $260 M per year) were the most prescribed and most costly over the 5-year period. On average each year > 27 M statin prescriptions were filled in total at a combined average annual cost of over $604 M.

The prescribing rates of statins were mixed, with some trending up and others trending down over the 5 years (Supplementary Figure 4). Statins were the highest prescribed and most costly drugs in this study (>138 M prescriptions and > $3 billion over 5 years). Overall, the number of annual statin prescriptions increased by 11.8% over the 5 years (from 26,064,117 in 2014/15 to 29,127,562 in 2018/19), though the total costs decreased by –33% (from $775M in 2014/15 to $516M in 2018/19). The annual governments costs decreased by 51% (from ∼$510M in 2014/15 to ∼$249M in 2018/19).

Discussion

The analysis of PBS data presented here shows tens-of-millions of prescriptions are filled every year in Australia for drugs known to or suspected of inducing cataract. The most prescribed and costly of these drugs are glucocorticoids, psychotropic drugs, and statins.

Glucocorticoids

Glucocorticoids—a class of drug known to cause posterior subcapsular cataract, particularly in people above the age of 40 (3)—are prescribed for a variety of diseases including ocular conditions (e.g., macula edema), asthma, arthritis and

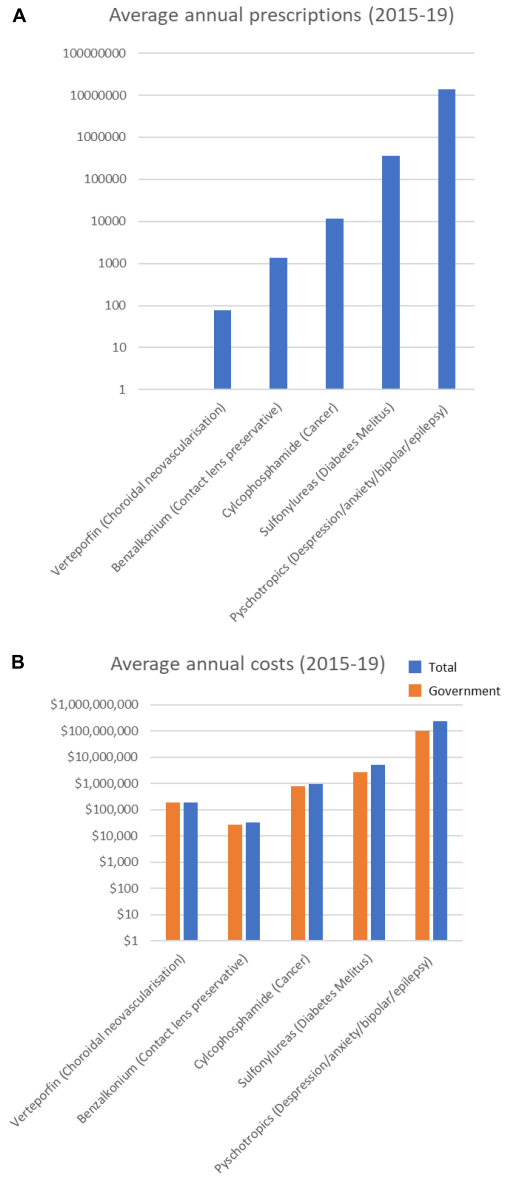

FIGURE 3
Average annual prescription numbers **(A)** and costs **(B)** for members of the Possible category of drugs associated with cataract, together with typical conditions for which they are prescribed.

inflammatory bowel disease (4, 5). The data here showed an average of ∼9 M annual steroid prescriptions in Australian over the 5 years from 2014 to 2019. Over that period, the annual number of steroid prescriptions increased 7.7% to 9,725,044 in 2018/19, and the associated costs increased by 42.9% to $203M. A UK trial found, on average, patients require 6.5 glucocorticoid prescriptions (6), and approximately 50% of these patients were 45 years and above (7). Using this as a guide, this equates to ∼1.5 M Australians using prescription steroids in 2018/19 with approximately 750,000 patients 45 years or older. In Australia, the increased risk of PSC due to glucocorticoids is OR 2.5 for inhaled and OR 4.1 for oral corticosteroids. Glucocorticoids were also associated with an increase in nuclear cataracts, with an OR of 2.0 for inhaled and 3.5 for oral corticosteroids (mean age 63 years) (3).

As discussed below, minimizing drug-induced cataract could help offset the burden of cataract in Australia and elsewhere. The large number and cost of cataract surgeries likely arising from prescription steroids provides a strong argument for better understanding the molecular mechanisms of steroid-induced cataract. Application of such molecular knowledge could lead to early identification of at-risk patients, and potentially to development of alternative treatment strategies. For example, folate is recommended as a co-therapy with methotrexate prescribed for rheumatoid arthritis, to mitigate risks associated with methotrexate-induced folate deficiency (8).

Clinically, the cataracts caused by glucocorticoid steroids are centrally-located, posterior subscapular cataracts with vacuoles (9, 10)—suggesting they relate to aberrant migration of lens epithelial cells (LECs) along the posterior capsule. At present, there is little data describing the molecular mechanisms of steroid-induced cataracts in human lenses. While steroids can bind to lens proteins, this is generally discounted as a mechanism for cataract formation as they do so with lower affinity than other proteins that do not induce cataract (11).

Primary human LECs transfected with firefly luciferase (controlled by glucocorticoid response elements) showed increased luciferase activity when exposed to dexamethasone (12)—demonstrating the ability of primary human LECs to activate the glucocorticoid receptor. In the same study, microarray analysis of the immortalized human LEC line, HLE B-3, after dexamethasone treatment revealed altered expression of various genes (136 and 86 genes after 4 and 16 h of treatment, respectively).

Analysis of primary human LECs from patients with steroid-induced cataract showed a small increase in mRNA expression and protein activity for the matrix metalloproteinases, MMP2 and MMP-9 (13). Additional studies using primary and immortalized human LECs showed dexamethasone treatment led to phosphorylation of the glucocorticoid receptor, altered expression of MAPK and PI3K/AKT regulators, decreased phosphorylation of MAPK- and AKT-related proteins (14), and altered expression of cell adhesion molecules (15). No detectable effect of dexamethasone on proliferation or apoptosis of the human LEC line (HLE B-3) was observed, though some dexamethasone-induced apoptosis in human lens cells has been reported elsewhere (16, 17).

Overall, these studies provide initial insights into steroid-induced effects in human lens cells. However, their clinical relevance remains unclear due to differences (abnormalities) in behavior of immortalized lens cells compared to normal primary human LECs, and also the short timeframes being analyzed (i.e., typically < 24 h). Notably, none of these *in vitro* studies

TABLE 4 PBS data (2014–2019) showing prescription numbers and costs for members of the uncertain category of drugs associated with cataract (gray background = statins).

Drug name	Total prescriptions (2014–2019)	Total cost (2014–2019)	Total government cost (2014–2019)	Trend
Atorvastatin	60,343,650	$1,122,411,672	$613,870,024	Stable
Rosuvastatin	54,192,851	$1,301,723,120	$699,934,742	Stable
Simvastatin	19,661,920	$536,558,720	$375,715,069	Down
Diazepam	12,410,290	$136,617,166	$55,009,989	Stable
Aspirin	7,058,298	$159,273,025	$111,798,669	Down
Pravastatin	3,926,680	$56,291,429	$29,753,960	Down
Carbamazepine	1,503,278	$48,796,399	$29,920,620	Stable
Fluvastatin	179,164	$7,182,544	$5,010,457	Down
Clomifene	149,657	$5,227,406	$745,483	Down
Finasteride	21,424	$2,066,376	$1,979,100	Down
Danazol	7,362	$525,664	$355,747	Stable

involving human LECs or lens cell lines were able to assess the effects of dexamethasone on critical lens functional properties of transparency or focusing.

Psychotropic drugs

In Australia, one in five people experienced a mental disorder in a 12-month period (18), with many of them prescribed psychotropic drugs. The PBS data show eight psychotropic drugs from the possible category were prescribed in Australia, with most averaging > 1 M prescriptions a year. The average annual number of psychotropic drug prescriptions was > 14 M, with an associated cost of > $237 M per year. Annual prescriptions increased 19.7% over the 5 years to 15.4 M in 2018/19, at a cost of $246 M (a 7% increase over the 5 years).

Published health record analyses have shown significant positive associations between risk of cataract formation and use of psychotropic drugs, including: citalopram (OR = 1.53, 95% CI, 1.33–1.77; $P < 0.001$) and fluvoxamine (RR, 1.39; 95% CI, 1.07–1.80) (19, 20); fluoxetine (AOR: 1.21; 95% CI, 1.01–1.46, $p = 0.042$) (21), fluvoxamine (AOR: 1.47; 95% CI: 1.01–2.12, $p = 0.043$) and sertraline (AOR: 1.29; 95% CI, 1.12–1.48, $p < 0.001$); sertraline (AOR: 1.29; 95% CI, 1.12–1.48, $p < 0.001$) and fluvoxamine (AOR: 1.37; 95% CI, 1.07–1.76, $p = 0.012$) (21). A recent meta-analysis also identified an association between cataract and use of fluoxetine (RR 1.08, 95% CI, 1.03–1.12) and fluvoxamine (RR 1.22, 95% CI, 1.06–1.40) (22).

These studies also showed many working-age patients (e.g., 50–64) who have taken these psychotropic drugs have required cataract surgery, with direct implications for labor force productivity (discussed below) as well as direct medical costs. In some studies, the average time to cataract diagnosis while on SSRI (Selective Serotonin Reuptake Inhibitor) therapy was relatively short, ∼656 days (20). The large annual number of psychotropic prescriptions in Australia may lead to sizeable numbers of drug-induced cataract.

At present, it is not clear how psychotropic drugs could lead to cataract formation in patients. It is possible selective serotonin reuptake inhibitors (such as citalopram, escitalopram, fluoxetine, fluvoxamine and sertraline all prescribed in Australia) could lead to elevated levels of serotonin, as detected in the aqueous humor of patients having undergone cataract surgery (23). In rats, application of serotonin *via* injection or eyedrops led to rapid development of dense cataracts thought to be related to reduced aqueous (24). These findings suggest an indirect mechanism for cataract formation *via* selective serotonin reuptake inhibitors. However, rabbit lenses express serotonin receptors (e.g., 5-HT_{1A} and 5-HT_7) (25) and exposure of rabbit LECs to serotonin led to phosphoinositide turnover (26). A more comprehensive analysis of the effects of psychotropic drugs on human cataract formation is needed.

Statins

Statins are prescribed to reduce blood cholesterol levels in order to reduce the risk of cardiovascular disease. Statins are effective inhibitors of 3-hydroxy-3-methyl-glutaryl-CoA reductase, a key enzyme in cholesterol biosynthesis. Statins can also increase expression of low density lipoprotein (LDL) receptors, enabling liver cells to capture cholesterol-containing LDL particles from the blood (27). The PBS data revealed the average annual number of statin prescriptions in Australia is > 27 M, with an average annual cost of > $604 M. Approximately 44% of Australians were prescribed and used statins in 2016 (28). Statins are listed in the Uncertain category of cataract-inducing drugs. In the lens, it appears cholesterol levels need to be maintained within a relatively narrow range to avoid cataract formation (29). Increased cholesterol levels in the lens–for example, 25-hydroxycholesterol–have been associated with cataract (30). Conversely, the cholesterol-lowering drug, triparanol, also causes irreversible cataract

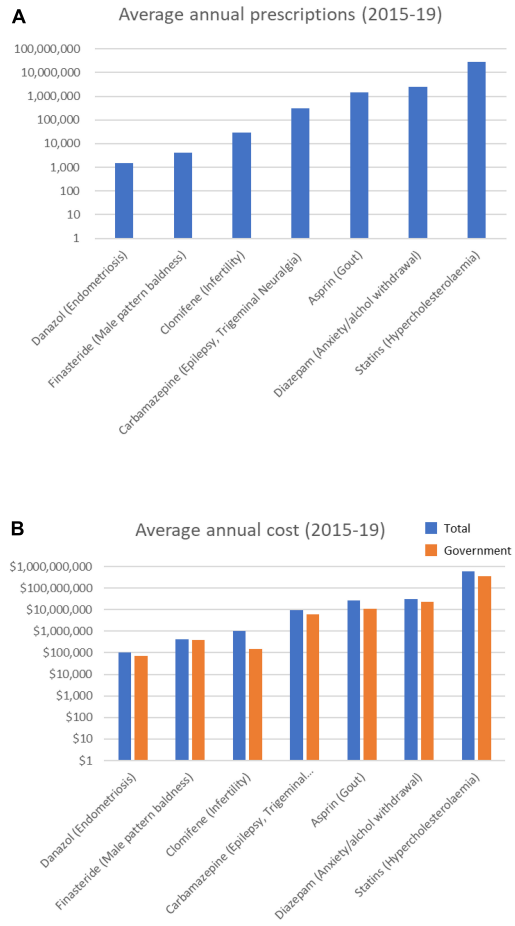

FIGURE 4
Average annual prescription numbers **(A)** and costs **(B)** for members of the Uncertain category of drugs associated with cataract, together with typical conditions for which they are prescribed.

(31). Triparanol inhibits cholesterol synthesis downstream of lanosterol production, leading to accumulation of lanosterol in lenses (32, 33). While recent reports suggest cataracts can be dissolved with intermediates of cholesterol biosynthesis–lanosterol or 25-hydroxycholesterol (34, 35) (that increase the chaperone activity of α-crystallin)–other studies have failed to replicate these effects anti-cataract effects (30, 36, 37). Perhaps unsurprisingly, the evidence relating to statins and cataract formation has been contradictory. Outcomes from systematic reviews have been mixed–with positive, negative and no associations all identified (38–41). A recent meta-analysis encompassing 313,200 patients found no association with cataract. However, given the heterogeneity in the studies underpinning the meta-analysis, it was recommended that large, multicenter, pragmatic, prospective observational studies or registries be performed to assess the risk of cataracts arising from statin use (41).

Elucidating mechanisms of drug-induced cataracts in humans

Worldwide, cataracts are a large and increasing cause of blindness. The number of people with low vision or blindness due to cataracts increased from 50.5 M in 1990 to 65.2 M in 2015 (1), because of the increasing size and age of populations worldwide. The PBS data analysis presented here indicates prescription drugs could be a significant source of cataracts in Australia. In the United States, outpatient services are used annually by 1.6 M cataract patients aged 40-64 years, and 8.9 M aged 65 and older (42). Direct medical costs attributed to these two groups are $2.14 billion/year and $4.66 billion/year, respectively. US cataract patients also contributed to $11.2 billion in other annual direct costs (e.g., care programs); and $8 billion in annual productivity losses (e.g., lower participation and lower wages). Worldwide, the economic, employment and social consequences of cataracts cost $tens-of-billions annually. It is possible a significant proportion of annual cataract cases arise due to prescription drug use in both working-aged people and retirees. However, cataractous human lens tissue is difficult to obtain, and transparent/light-focusing human lens tissue is essentially impossible to reliably obtain in meaningful amounts for research during the early stages of cataract formation.

Human pluripotent stem cells offer the ability to generate large numbers of human LECs and light-focusing micro-lenses (43, 44). These stem cell-derived human LECs share morphological, transcriptional and proteomic profiles similar to fetal human LECs (43, 44). Light-focusing micro-lenses derived from these human LECs share similar anatomical and molecular characteristics with human lenses, including expression of a broad range of crystallin proteins associated with the focusing ability of primary human lenses (43, 44). Notably, exposing human stem cell-derived micro-lenses to a cystic fibrosis drug suspected of causing cataract in human patients (43, 44), or to dexamethasone (45), resulted in decreased light focusing in the treated micro-lenses. Together, these data suggest human stem cell-derived micro-lenses may provide a useful new tool for investigating the initiating molecular mechanisms of drug-induced cataract. Consistent with this, the human micro-lens system is amenable to detailed analyses including imaging (light, confocal and electron microscopy), transcriptomics and proteomics. Thus, the human micro-lens system provides a novel and potentially powerful approach to time-course cataract studies *in vitro*, with lens transparency and light-focusing as functional end-points. This includes new opportunities to elucidate the molecular mechanisms through which prescription drugs cause cataracts. Such new knowledge could provide opportunities to decrease the annual global burden of cataract through improved identification of at-risk patients, prescription of co-therapies, or identification of candidate anti-cataract drugs. Such studies would address the

large, unmet need for a reduction in the amount of drug-induced cataract that currently occurs worldwide. Use of human stem cell-derived micro-lenses could also provide a functional human lens system to reduce reliance on animal-based lens models for investigating molecular mechanisms of cataract formation (46, 47).

Materials and methods

Public PBS drug prescription data from Australia was analyzed for the period 2014 to 2019, to identify the prescribing rates for drugs associated with cataract formation. Categories of drugs that have different associations with cataract formation were obtained from Drug-Induced Ocular Side Effects, 7th Edition. Australian PBS data supply records were downloaded from PBS and RPBS Section 85 Date of Supply Data (48). This data was divided into financial years from July to June based on the month of supply on the PBS per item. Item codes for drugs of interest were matched with the item codes in the PBS prescription record data. Total frequency of prescriptions, cost and government cost for the July–June financial years from 2014 to 2019. The frequency of total prescriptions, average annual prescription rates, total cost, average annual cost and total government cost were calculated for each potential cataract causing agent.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found here: Health AGD of Pharmaceutical Benefits Scheme (PBS) and PBS and RPBS Section 85 Date of Supply Data.

Author contributions

MO'C: conceptualization, resources, project administration, and funding acquisition. MO'C and KM: methodology and supervision. JC and MO'C: validation and visualization. JC: formal analysis, investigation, and writing—original draft preparation. JC, MO'C, and KM: writing—review and editing. All authors have read and agreed to the published version of the manuscript.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2022.947659/full#supplementary-material

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Predictors of visual acuity improvement after phacoemulsification cataract surgery

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Purpose: This study aimed to assess preoperative predictors of visual outcome after phacoemulsification cataract surgery in Jordan, a Middle Eastern country.

Methods: This was a retrospective longitudinal study of adult patients who underwent phacoemulsification cataract surgery from January 2019 to July 2021. For each patient, we included only the first operated eye. We obtained pre-operative ocular history, cataract surgery complication risk based on a predesigned score, visual acuity, best correction, and best corrected visual acuity. We recorded intraoperative complications. We also obtained postoperative best corrected visual acuity and refractive error for correction after 1–3 months.

Results: A total of 1,370 patients were included in this study, with a mean age of 66.39 (± 9.48). 48.4% of patients achieved visual acuity ≥ 0.8, and 72.7% achieved visual acuity ≥ 0.5. The mean visual acuity improvement after phacoemulsification cataract surgery was 0.33 (95% CI 0.31–0.35). In the regression model, significant predictors that affected visual acuity improvement included the presence of diabetic retinopathy, glaucoma, and complication risk factors (i.e., high-risk surgery).

Conclusion: Predictors of visual acuity improvement vary between studies. This study was conducted in a developing country; we defined predictors of visual acuity improvement. We also provided a new preoperative phacoemulsification cataract surgery complication risk score.

KEYWORDS

cataract, phacoemulsification, risk score, visual acuity, developing country

Introduction

Cataract extraction is considered one of the most beneficial procedures in medicine, with its outcome rapidly observed subjectively and objectively (1). According to the Global Health Commission on Global Eye Health report (2), cataract extraction is considered a "highly cost-effective vision-restoring intervention" in modern medicine. Cataract extraction *via* phacoemulsification surgery largely replaced older techniques with a high safety profile (3). Its main outcome is primarily measured by visual acuity improvement, which is translated by considerable gains in real-life activities and emotional and social life components (4). Despite the provided visual acuity improvement after phacoemulsification surgery, such improvement might not be sufficient to improve the quality of life of certain populations (5). Several studies tried to predict visual acuity improvement after phacoemulsification surgery and to provide preoperative risk factors for poor visual acuity improvement, which varied for different populations and countries and were generally of low-quality evidence (6–8). Most such studies were performed in developed countries, where surgical training and available technologies are more advanced than in developing countries. Studies from developing countries, including Jordan, are generally limited to small-size studies and cross-sectional designs (9), despite the high volume of cataract surgery performed. In this study, we aimed to analyze predictors of visual acuity gain after phacoemulsification cataract surgery in the major referral center in Jordan. This was the first study from Jordan to assess the outcome of phacoemulsification cataract surgery, where we included a relatively homogenous sample from Jordan's largest tertiary referral center. We assessed preoperative predictors of visual outcome after phacoemulsification cataract surgery in a large cohort from the largest referral center in Jordan.

Materials and methods

This was a retrospective longitudinal study for patients who underwent phacoemulsification cataract surgery at Jordan University Hospital, the largest tertiary referral hospital in Jordan. The patients were followed up for at least 3 months after surgery. We obtained institutional review board (IRB) committee approval from Jordan University Hospital IRB (IRB 5439/2021/67). Due to the retrospective data collection method, patients' consent was waived, and the data were analyzed anonymously. The study was conducted in accordance with the latest declaration of Helsinki.

Participants

We reviewed all phacoemulsification surgeries performed at Jordan's largest tertiary referral center for 31 months, from January 1st, 2019, to July 30th, 2021. We included the first operated eye for patients who had both eyes operated on in the specified period to avoid correlated data analysis bias (10). We excluded patients with congenital cataracts or aged below 40 years (36 patients) and cataract surgeries done as part of pars plana vitrectomy (24 patients).

We reviewed the patient's pre-operative clinic assessment, operative notes, and post-operative clinic visits. Each included patient had a pre-operative assessment visit, where visual acuity, refraction, anterior segment, and fundus exams were performed. Diabetic patients with diabetic retinopathy also underwent macular optical coherence tomography exams to exclude co-existent diabetic macular edema. Phacoemulsification surgery details obtained from each case's operative note are detailed in the next section. Post-operatively, our institution's standard regimen includes eye patching until the next day's morning visit and movement restrictions for 3 days post-operatively. The next day, the eye patch was removed, and the eyes were examined, including visual acuity, wound leak, and intraocular pressure, along with an anterior segment exam. The postoperative regimen included topical fluoroquinolone antibiotics and topical steroid eye drops.

Phacoemulsification surgery

All patients signed informed consent before entering the theater room. The eye undergoing surgery was marked, and dilating eye drops were applied 15 min before surgery. Intraoperatively, patients underwent topical, retrobulbar, or general anesthesia, depending on the patient's factors. Each operator had an operative technique for dividing the nucleus and cortex aspiration. Stop and chop was the most commonly used technique. Otherwise, other steps were usually performed according to a standard protocol. The standard protocol intraoperatively after draping and scrubbing included paracentesis creation, injection of intracameral adrenaline and lidocaine, the use of trypan blue dye, cohesive viscoelastic to form the anterior chamber, standard up to 3 mm superior limbal clear corneal incision, capsulorhexis creation, nucleus division, aspiration, and cortex aspiration according to the surgeon's training and preference, acrylic single-piece monofocal intraocular lens (IOL) injection in most patients (the IOL which was covered by insurance), viscoelastic aspiration, wound hydration, followed by subconjunctival moxifloxacin and steroid injection. No intracameral antibiotic is usually given per our institutional protocol.

All surgeries were performed either using R-Evolution Optikon (Italy), Geuder (Germany), or DORC (Germany) phacoemulsification machines.

Cataract surgery complication risk scoring

We performed a literature review on cataract surgery risk for intraoperative complications and their associations with postoperative outcomes. Based on previous literature (5, 11–26), we identified several pre-operative factors that have the potential to increase surgery difficulty and complication risk. Further details about each risk score are provided in **Supplementary Table 1**. In regard to combining factors for a final risk score, previous studies varied from a dichotomous classification into high and low risk, which can be simpler and advantageous in statistical models; other studies used an ordinal classification scale from no risk, low risk, moderate risk, and high risk.

In our study, we classified cataract surgery complication risk into either high risk or low risk, where high-risk surgeries are those with any of the following pre-operative risk factors: Pseudoexfoliation or phacodenesis; proliferative diabetic retinopathy; previous vitrectomy; a 4 + dense, white, or brunescent cataract; age above 88; central or paracentral corneal opacity; previous penetrating keratoplasty or radial keratotomy; history of uveitis or synechia; and posterior polar cataract; high myopia (above −6); or high hyperopia (above + 3).

Variables

We obtained demographic characteristics for each patient, including pre-operative medical history, ocular history, best corrected visual acuity, and refractive error for correction. We also obtained intraoperative data regarding the operator (senior resident or consultant), surgical notes, and any intra-operative complications, including posterior capsular rupture, dropped nucleus, or IOL, and the use of sutures to secure the wound. Finally, we obtained follow-up data for best corrected visual acuity and refractive error for correction after 1–3 months. Based on the operator, we classified surgeries into teaching cases done by senior ophthalmology residents under the supervision of consultants or cases done by consultants alone.

Visual acuities were measured on a standard E-chart at a 6-meter distance, with acuities measured in decimals. For visual acuities worse than 0.05, we converted counting fingers, hand motion, light perception, and no light perception into 0.014, 0.005, 0.0016, and 0.0013, respectively (27). Based on minimal important difference improvement, we further categorized visual acuity improvement into either improved by more than 0.1, 0.1 or less improvement or worsening in visual acuity (28, 29).

Statistical analysis

We used SPSS version 26.0 (Chicago, USA) in our analysis. We used the mean (± standard deviation) to describe continuous variables. We used count (frequency) to describe other nominal variables. We performed linear regression analysis to assess predictors of visual acuity changes between pre-operative and post-operative visual acuity after phacoemulsification cataract surgery. We adopted a model-building strategy, where we first performed a univariate analysis, and then we only included in the regression analysis significant variables from the univariate analysis. For the univariate analysis, we performed an independent sample *t*-test and one-way ANOVA to analyze the mean difference between visual acuity and each nominal measurement (e.g., gender, operator, risk factors) and presented the data as a mean difference and 95% confidence interval (CI). We performed Pearson correlation to analyze the relationship between visual acuity difference and age, preoperative visual acuity, and refractive error. On univariate analysis, the following pre-operative predictors achieved a significance level above the pre-specified threshold: age (0.001), diabetic retinopathy (<0.001), pre-operative visual acuity (<0.001), spherical pre-operative refractive error (0.001), cylindrical preoperative refractive error (0.038), presence of glaucoma (0.003), history of intravitreal injections (<0.001), age-related macular degeneration (0.019), and cataract surgery complication risk (0.039). However, the following variables did not reach the threshold, including gender (0.666), a teaching case (0.936), laterality (0.789), and cylindrical axis of preoperative refractive error (0.762). We presented regression analysis results in B value and its 95% CI, along with model prediction accuracy, representing the model's ability to explain the variance in the outcome. All the underlying assumptions were met. We adopted a *p*-value of 0.05 as a significant threshold.

Results

A total of 1,370 patients were included in this study, with a mean age of 66.39 (± 9.48). They were 673 (49.1%) men and 698 (50.9%) women. Of the total cases, 312 (22.8%) were teaching cases. 48.4% of patients achieved visual acuity of ≥ 0.8, and 72.7% achieved visual acuity of ≥ 0.5. **Table 1** details the characteristics of the included sample.

Predictors of visual acuity improvement

The mean visual acuity improvement after phacoemulsification cataract surgery was 0.33 (95% CI 0.31–0.35), from a mean best corrected visual acuity

TABLE 1 The characteristics of included sample.

		Mean (Standard deviation)	Count	Column *N*%
Age		66.39 (9.48)		
Gender	Male		673	49.1%
	Female		698	50.9%
Operator	Consultant		1,055	77.2%
	Resident		312	22.8%
Laterality	Right		699	51.1%
	Left		669	48.9%
Cataract surgery complication risk	Low risk		1,021	74.5%
	High risk		350	25.5%
Ocular history	Diabetic retinopathy		254	18.6%
	Glaucoma		99	7.3%
	Age-related macular degeneration		39	2.8%
Pre-operative best corrected visual acuity		0.32 (0.26)		
Post-operative best corrected visual acuity		0.65 (0.32)		
Intra-operative complications	Posterior capsular rupture		146	10.6%
	Wound suturing		251	18.3%
	Dropped nucleus or IOL		10	0.7%

TABLE 2 Predictors of visual acuity improvement.

Factor	Impact on visual acuity improvement	95.0% confidence interval		*P*-value
Presence of diabetic retinopathy	−0.095	−0.182	−0.007	0.034
Presence of glaucoma	−0.123	−0.220	−0.026	0.013
High-risk cataract surgery	−0.071	−0.138	−0.004	0.037
Each 0.1 increase in pre-operative vision	−0.0653	−0.0772	−0.0534	0.000
A dioptric increase in spherical refractive error	−0.010	−0.018	−0.002	0.011
A dioptric increase in cylindrical refractive error	−0.051	−0.081	−0.021	0.001

preoperatively of 0.32 (*SD* 0.26) to 0.65 (*SD* 0.32) postoperatively. The regression model predicted 35.7% of the visual acuity change after cataract surgery based on pre-operative characteristics. The significant predictors that affected visual acuity improvement included the presence of diabetic retinopathy, glaucoma, and a complication risk factor (i.e., high-risk surgery). Moreover, increased pre-operative visual acuity, spherical refractive error, or cylindrical refractive error were also significant predictors of decreased visual acuity improvement after cataract surgery (Table 2).

The model building strategy and included variables were detailed in the statistical analysis section.

Cataract surgery complication risk factors

A total of 350 (25.5%) surgeries were high-risk surgeries. They had a total of 382 risk factors, whereas 39 surgeries had more than one risk factor. The most common risk factor was pseudoexfoliation (23.56%), followed by high myopia (22.25%) and proliferative diabetic retinopathy (19.9%). Figure 1 shows the frequency of each risk factor for cataract surgeries.

We found a significant difference in visual acuity improvement between high-risk and low-risk surgeries (p = 0.039), where the mean visual acuity improvement in

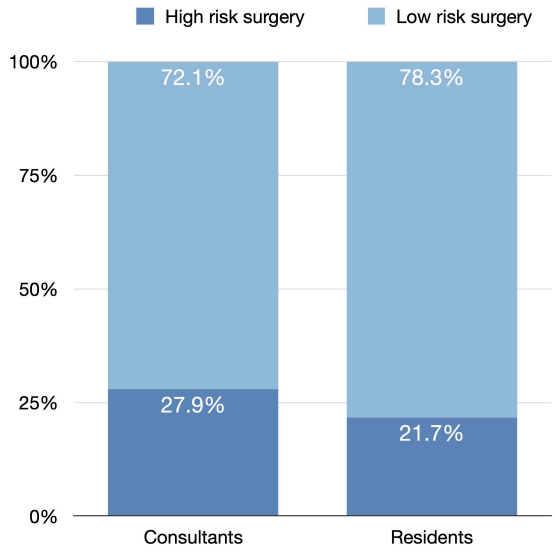

FIGURE 1
The frequency of each risk factor studies for cataract surgeries.

low-risk surgeries was 0.355 (*SD* 0.31), compared to 0.301 (*SD* 0.33) for high-risk surgeries (mean difference 0.054, 95% CI 0.003–0.105). No significant difference was found in the intra-operative complication rate between both groups ($p = 0.523$).

Teaching cases

Teaching cases operated by senior residents under the supervision of consultants comprised 312 (22.8%) cases. The majority of these cases were of low risk (78.8%), with only 66 (21.2%) cases of high risk compared to 283 (26.8%) non-teaching cases, a frequency that differed significantly ($p = 0.025$). No significant difference in visual acuity gains after cataract surgery ($p = 0.940$) or frequency of complications ($p = 0.336$) between teaching and non-teaching cases. **Figure 2** compares consultants and residents who performed surgeries regarding surgery difficulty.

Refractive error change after cataract surgery

Upon comparing refractive error change after cataract surgery, we found a significant difference in spherical refractive error ($p < 0.001$), with a mean increase in spherical refractive error by a mean of 2.18 (95% CI −2.74 to −1.62). No significant difference was found in cylindrical refractive errors or their axes (**Table 3**).

Clinically meaningful visual acuity change

After categorizing patients into three categories, we found that most patients had an improvement of > 0.1 in visual acuity (69.4%), while 20% of patients had 0.1 or less visual acuity improvement, and only 10.6% had a worsening in visual acuity. Baseline visual acuity was significantly associated with each category of visual acuity improvement ($p < 0.001$). In addition, the visual acuity worsening group had a higher cataract surgery complication risk. **Table 4** compares the mean baseline visual acuity and complication risk among the three categories.

Discussion

This study was the largest to define predictors of visual acuity improvement after phacoemulsification cataract surgery. The mean improvement expected after phacoemulsification cataract surgery was 0.33 (95% CI 0.31–0.35); this magnitude of improvement would decrease if the eye had glaucoma, diabetic retinopathy, pre-operative complication risk factors, higher pre-operative visual acuity, or refractive error. We also performed a literature review to find factors that increase the risk of surgical complications, and we classified phacoemulsification into high- and low-risk surgeries accordingly. We found that surgeries classified as high-risk had significantly lower visual acuity improvement compared to low-risk surgeries. Almost 23% of included cases were teaching cases operated by senior ophthalmology residents, and we did not find a higher complication rate or worse visual acuity in teaching cases. Regarding refractive error change after phacoemulsification cataract surgery, we found an improvement in spherical error. A European Registry of Quality Outcomes for Cataract and Refractive Surgery study found that ocular comorbidities were the most important predictor of visual acuity improvement, where ocular comorbidities included macular degeneration, glaucoma, diabetic retinopathy, and amblyopia, among others (7). Another US-based study also found pre-operative comorbidities to be predictors of poor visual acuity, which included diabetes mellitus, chronic pulmonary disease, and age-related macular degeneration (30).

Among the factors that affect the outcome of cataract surgery is the difficulty and complexity of the surgery itself, which can be predicted by preoperative factors (31). The complexity of cataract surgery was one of the most commonly appearing predictors of poorer visual acuity improvement (13, 32). Considering preoperative risk scoring in surgery, decision-making and planning should also be included during the surgery decision-making process (5). Studies used different scores to classify surgeries into high-risk (aka. complex surgery) and low-risk surgeries. In the study by Lundström et al. complex surgery

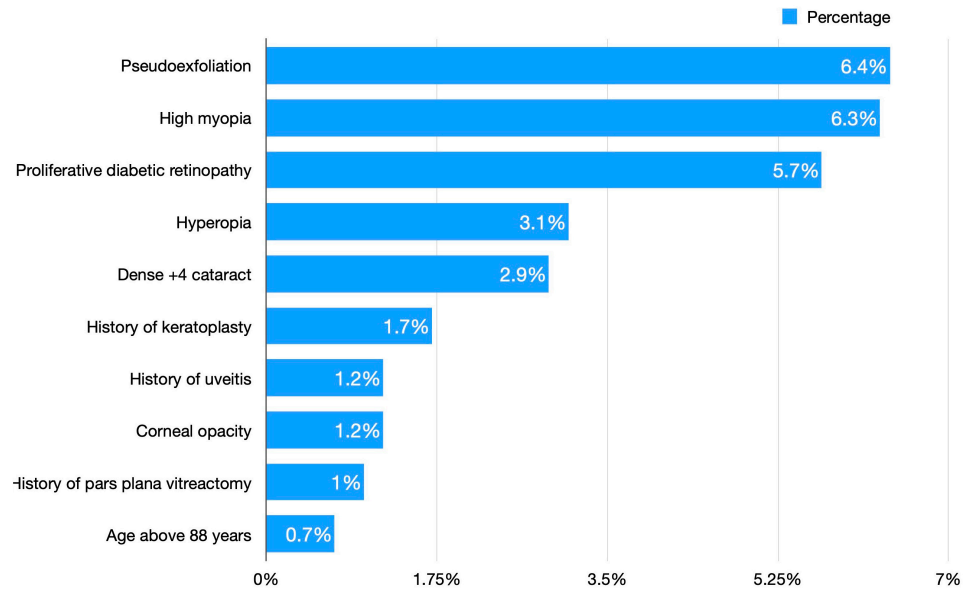

FIGURE 2
A comparison of surgery difficulty between consultants and residents who performed phacoemulsification surgeries.

TABLE 3 Refractive error change after cataract surgery.

		Mean	Std. deviation	Mean difference (95% CI)	*P*-value
Spherical equivalence change	Pre-op	−0.98	1.17156	−0.23 (−0.48 to 0.02)	0.075
	Post-op	-0.75	1.32752		
Spherical refractive error change	Pre-op	−1.99	3.71822	−2.18 (−2.74 to −1.62)	<0.001
	Post-op	0.19	1.00916		
Cylindrical refractive error change	Pre-op	1.55	1.08636	−0.09 (−0.36 to 0.18)	0.514
	Post-op	1.64	1.31116		
Cylinder axis change	Pre-op	92.64	38.831	1.25 (−6.41 to 8.92)	0.746
	Post-op	91.39	33.733		

TABLE 4 Comparison between best corrected visual acuity (BCVA) improvement by > 0.1, ≤0.1, and worsening in terms of mean baseline visual acuity and complication risk among the three categories.

	> 0.1 BCVA improvement	≤ 1 BCVA improvement	BCVA worsening	*P*-value
Mean (95% CI) baseline visual acuity	0.28 (95% CI 0.29–0.32)	0.34 (95% CI 0.28–0.39)	0.42 (95% CI 0.35–0.49)	<0.001
High risk for complication	25.7%	35.4%	41.7%	0.002

is defined by the presence of previous vitrectomy, previous corneal refractive surgery, miosis, white/brown cataract, corneal opacities, pseudoexfoliation, and others (7). Another negative predictor factor of visual acuity improvement was glaucoma. The relationship between cataract extraction and glaucoma is complex. Although it has been established that cataract extraction has a beneficial intraocular pressure lowering effect and improves the quality of life (33, 34), phacoemulsification

cataract extraction surgery might sometimes be challenging in these patients. Patients with glaucoma usually also have other ocular co-morbidities, both diagnosed and undiagnosed, along with frequent topical medication use (35, 36). After surgery, glaucoma patients experience increased intraocular pressure, severe corneal edema, endothelial cell damage, and poor vision (37, 38). A study performed on a European registry of 15 European countries found that preoperative ocular co-morbidity was the strongest negative predictor for visual outcome, where comorbidities included glaucoma and other retinal diseases (7). A previous study in several African developing countries found that pre-operative refractive error was the leading cause of poor visual outcomes (39). Consultants operated at a higher frequency of high-risk surgeries compared to residents, a finding also found in a UK-based national study (40). A recent systematic review found that the previous history of intravitreal injection can be regarded as a risk factor for PCR and should be considered when planning cataract surgery. However, the magnitude of this risk is generally small (41). The complexity of preoperative risk score discussion increases when we consider protective factors that might decrease surgery difficulty or complication rate (42), which should be considered in future studies.

In our study, no significant difference in complication rates was found between teaching cases operated by residents and non-teaching cases operated by specialists. Our results were consistent with previous studies done in other countries, including the USA (43), the UK (40), Canada (44), and Australia (45). On the other hand, a recent study on surgeries performed in Europe found higher complication rates for surgeries performed by residents (46). Higher complication rates for residents were also found in studies done in Hungary (47). It is important to note that these studies differed in settings, countries, and teaching methods. A future review investigating surgical factors and teaching methods might reveal the reason behind these differences. While we did not measure the duration of surgery, a previous study found that the duration of surgery significantly differed according to experience, with the longest duration for trainees and the shortest duration for experienced specialists (48).

Our study is the first in Jordan and the Middle East to assess the visual outcome and predictors of visual acuity in a large cohort; its main limitation is the use of a retrospective design for data collected from university hospital-based ophthalmology clinics. As a result, we could not include certain factors that may be considered pre-operative risk factors due to under-reporting by patients' records.

Conclusion

In our cohort from Jordan, a developing country, we found that the mean improvement expected after phacoemulsification cataract surgery was 0.33 (95% CI 0.31–0.35), where the mean best corrected visual acuity after cataract surgery was 0.65 (*SD* 0.32) postoperatively, which is above the limit for driving in most countries. The majority of patients had visual acuity improvement in more than one line. Patients with higher baseline visual acuity would be expected to improve less than patients with lower baseline visual acuity. Poor visual acuity improvement predictors include glaucoma, diabetic retinopathy, pre-operative complication risk factors, higher pre-operative visual acuity, and refractive error. We provided a literature-based new preoperative phacoemulsification cataract surgery complication risk score.

What was known

- Phacoemulsification has revolutionized the management of cataracts in recent years. However, there has been wide variation in its outcome and predictors of outcome between different studies in different countries.
- Most such studies were performed in developed countries, where surgical training and available technologies are more advanced than in developing countries.

What this paper adds

- Our study is the first in Jordan, a developing country, and the Middle East to assess the visual outcome and predictors of visual acuity in a large cohort.
- We also provided a literature-based new preoperative phacoemulsification cataract surgery complication risk score.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by we obtained institutional review board (IRB) committee approval from Jordan University Hospital IRB (IRB 5439/2021/67). Due to the retrospective data collection method, patients' consent was waived, and the data were analyzed anonymously. The study was conducted in accordance with the latest declaration of Helsinki.

Author contributions

SA, DA, and MA-A contributed to research conception, protocol development, manuscript writing, and data analysis. AA, MH, RT, and RA contributed to data collection and manuscript writing. TA contributed to research conception and manuscript writing. All authors approved final manuscript.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2022.894541/full#supplementary-material

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Stereopsis and visual acuity: Bilateral trifocal versus blended extended depth of focus and diffractive bifocal intraocular lenses

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Purpose: To compare stereopsis and visual acuity (VA) between bilateral implantation of trifocal intraocular lenses (IOL) and blended implantation of an extended depth of focus (EDOF) IOL with a bifocal IOL.

Methods: This is a non-randomized, prospective comparative study included 74 eyes of 37 patients who underwent phacoemulsification and bilateral implantation of AT LISA tri 839MP IOL (bilateral group; 21 patients) or blended implantation of Tecnis Symfony ZXR00 and Tecnis ZLB00 IOL (blended group; 16 patients). The primary outcomes were stereoacuity and binocular VA. The secondary outcomes were visual defocus curve, quality of life, and patient satisfaction. Follow-up was performed 3 months after the surgery.

Results: The mean near stereoacuity was 49.76 ± 22.67 and 120.63 ± 90.94 seconds of arc (arcsec) in the bilateral and blended groups, respectively ($P < 0.001$). Near stereoacuity was positively correlated with VA difference of two eyes (r = 0.896, $P < 0.001$). The mean binocular uncorrected visual acuity at 40 cm, 80 cm, 5 m, and corrected distance visual acuity at 5 m of the bilateral and blended groups was not statistically significant different. The bilateral group had better VA at a vergence from −2.5 to −4.0 D. Both groups obtained high quality of life and patient satisfaction scores.

Conclusion: The bilateral and blended groups achieved good binocular VA, quality of life, and high patient satisfaction. However, the near stereoacuity of the blended group was worse.

KEYWORDS

stereopsis, visual acuity, trifocal intraocular lens, extended depth of focus intraocular lens, multifocal intraocular lens, cataract

Introduction

Since the widespread use of mobile devices, many people have shown an increased need for near and intermediate vision, and patients have hoped to obtain a full range of vision after cataract surgery. Multifocal intraocular lenses (IOL) can provide multiple foci, enabling patients to obtain high spectacle independence (1). There are several ways to achieve a good whole range of visual acuity (VA), such as bilateral implantation of trifocal IOL or blended implantation of different multifocal IOL (also called contralateral implant strategy) (2–4). The contralateral implant strategy aims to combine the advantages of different multifocal IOL to achieve good binocular visual performance. Previous research has shown that the Tecnis Symfony ZXR00, which is the most widely used extended depth of focus intraocular lenses (EDOF IOL), can provide good distance and intermediate vision but has some limitations in near vision performance (5, 6). The blended implantation of an EDOF IOL with a low-add power bifocal IOL is an effective method to realize good VA from far to near distance (7–9).

Stereopsis is an important part of binocular vision. It is the awareness of the relative distance of objects from the observer through binocular vision only and is based on retinal disparity (10). Although people possess good vision, they also need stereopsis to lead normal lives or work, especially people who perform operations, use microscopes, or conduct other fine activities (11, 12). For cataract patients, surgery is the best solution to their diseases and optical correction, as an IOL after cataract extraction can restore stereopsis (13). Many studies have confirmed that patients can restore normal stereopsis after multifocal IOL implantation, the pseudoaccommodation and multifocality-induced retinal blur do not worsen stereopsis (14, 15). Previous studies have shown that patients who used contralateral implant strategy could achieve good stereoacuity (9, 16), but one study has shown the worse stereoacuity after blended implantation of different add power bifocal IOL compared to bilateral implantation (17). In recent years, there has been growing concern about whether using the contralateral implant strategy would impair stereopsis. The current study aims to assess visual outcomes after bilateral implantation of a trifocal IOL (Carl Zeiss Meditec AT LISA tri 839MP) and blended implantation of an EDOF IOL (Tecnis Symfony ZXR00) with a bifocal IOL (Tecnis ZLB00), and compare the main clinical outcomes in stereoacuity and visual acuity.

Materials and methods

Study design

This was a non-randomized, prospective comparative study involving patients who underwent bilateral cataract surgery at the Xiamen Eye Center affiliated with Xiamen University, Xiamen, Fujian, China, from July 2021 to May 2022. Ethical clearance was obtained from the Ethics Committee of Xiamen Eye Center of Xiamen University, this study adhered to the tenets of the Declaration of Helsinki. The informed consent had been obtained from all patients participating in the study.

The type of lens to be implanted was determined by the patient individual choice. Patients were divided into two groups: bilateral group or blended group. The bilateral group consisted of patients who had bilateral implantation of trifocal IOL (Carl Zeiss Meditec AT LISA tri 839MP). The blended group consisted of patients who had implantation of an EDOF IOL (Tecnis Symfony ZXR00) in the dominant eye and a bifocal IOL (Tecnis ZLB00) in the non-dominant eye. We used the pinhole test to determine the dominant eye. Patients were excluded if they had any of the following: (1) angle kappa greater than 0.5 mm, (2) any ocular or systemic disease that could influence postoperative VA, (3) previous refractive surgery and/or any other ocular surgery history, and 4) intraoperative or postoperative complications.

Lenses

The AT LISA tri 839MP (Carl Zeiss Meditec AG, Inc.) is single-piece, aspheric (−0.18 asphericity), diffractive trifocal lens. It has a 6.0 mm optic bench with a central trifocal zone over a diameter of 4.34 mm and a peripheral bifocal zone from 4.34 to 6.0 mm. The light distribution is 50, 20, and 30% for distance, intermediate, and near foci, respectively. The additions are + 3.33 D for near and + 1.66 D for intermediate at the IOL plane; in addition, it has a + 3.75 D add in its outer bifocal area.

The Tecnis Symfony ZXR00 (Johnson & Johnson Vision, Santa Ana, Inc.) is a single-piece, aspheric (−0.27 asphericity) EDOF IOL. The optical zone is 6.0 mm. It has a patented diffractive echelette design to form an elongated focal zone with an addition of + 1.75 D at the IOL plane. The posterior achromatic diffractive surface has an echelette design for correction of chromatic aberrations and contrast sensitivity enhancement, which forms a step structure whose modification of height, spacing, and profile of the echelette extends the depth of focus.

The Tecnis ZLB00 (Johnson & Johnson Vision, Santa Ana, Inc.) is a single-piece, aspheric (−0.27 asphericity), diffractive bifocal lens. The optical zone is 6.0 mm. The IOL incorporates a posterior diffractive multifocal optic pattern designed to provide both near and distance vision, with a near power of + 3.25 D.

Surgical technique

Phacoemulsification was performed by a single experienced surgeon. The temporal clear corneal incision

TABLE 1 Descriptive measures for preoperative ocular characteristics of bilateral and blended groups.

Measurement	Bilateral group(AT LISA tri 839MP)	Blended group(ZXR00/ZLB00)	*P* value
UDVA (logMAR)			0.016
Mean ± SD	0.49 ± 0.41	0.67 ± 0.41	
Range	0.00 to 1.70	0.10 to 2.00	
CDVA (logMAR)			0.005
Mean ± SD	0.22 ± 0.33	0.41 ± 0.44	
Range	0.00 to 1.70	0.10 to 2.00	
Corneal astigmatism (D)			0.312
Mean ± SD	0.65 ± 0.39	0.56 ± 0.30	
Range	0.00 to 1.61	0.00 to 1.30	
Corneal spherical aberration (μm)			0.282
Mean ± SD	0.29 ± 0.12	0.32 ± 0.10	
Range	0.09 to 0.57	−0.03 to 0.55	
Axial length (mm)			0.027
Mean ± SD	23.50 ± 1.15	24.08 ± 1.02	
Range	21.30 to 26.04	22.33 to 26.24	
Pupil diameter (mm)			0.201
Mean ± SD	2.90 ± 0.38	2.73 ± 0.66	
Range	2.10 to 3.86	1.64 to 4.08	
Angle kappa (mm)			0.802
Mean ± SD	0.26 ± 0.13	0.23 ± 0.11	
Range	0.05 to 0.50	0.03 to 0.46	
IOL power (D)			0.158
Mean ± SD	21.25 ± 2.69	20.66 ± 2.35	
Range	14.50 to 25.00	15.00 to 24.50	
Target refraction (D)			0.078
Mean ± SD	−0.04 ± 0.10	−0.08 ± 0.10	
Range	−0.17 to 0.17	−0.24 to 0.16	

CDVA = corrected distance visual acuity; D = diopters; logMAR = logarithm of the minimum angle of resolution; SD = standard deviation; UDVA = uncorrected distance visual acuity.

was 2.2 mm. Continuous curvilinear capsulorhexis was performed in surgery, and the size of the capsulorhexis was approximately 5.5 mm. Surgery was performed using a standard technique on an active-fluidic torsional phacoemulsification machine (Centurion Vision System, Alcon Laboratories, Inc.).

Preoperative examination

A complete preoperative ophthalmological examination was performed, including biomicroscopy, fundoscopy, uncorrected distance visual acuity (UDVA) at 5 m, corrected distance visual acuity (CDVA) at 5 m, pupil diameter and corneal spherical aberration (Pentacam; Oculus, Inc.), angle kappa (iTrace; Tracey Technologies Corp., Inc.), axial length and corneal astigmatism (IOLMaster 700; Carl Zeiss Meditec AG, Inc.). The IOL power was calculated using the Barrett Universal II formula. All eyes were targeted for emmetropia.

Postoperative examination

The postoperative examinations included uncorrected near visual acuity (UNVA) at 40 cm, uncorrected intermediate visual acuity (UIVA) at 80 cm, UDVA and CDVA at 5 m, manifest refraction. The defocus curve from + 1.0 D to −4.0 D in decrements of 0.5 D were evaluated under distance correction. The stereoacuity at near distance (40 cm), intermediate distance (80 cm), and far distance (5 m). Subjective outcomes included quality of life and patient satisfaction.

A Binoptometer 4P was used to assess the stereoacuity of the patients. The measuring method was designed based on the principle of polarized light, similar to that of Titmus. This stereotest has been proven to be a reliable method for measuring stereoacuity (18), and has been used to evaluate the stereoacuity of patients (19). A stereoacuity level of 60 seconds of arc (arcsec) or better is considered good stereoacuity (20), and 100 arcsec is the lowest limit of normal stereoacuity (13).

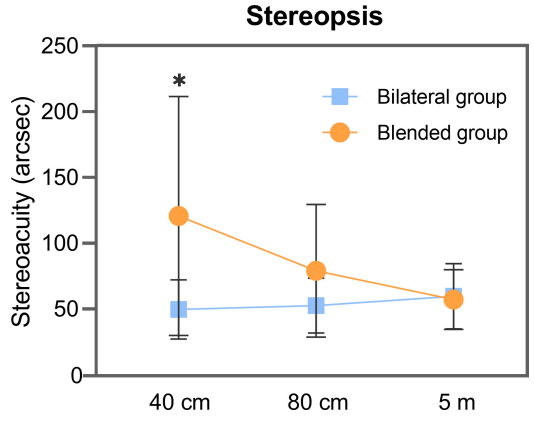

FIGURE 1
Stereoacuity measured by Binoptometer 4P of bilateral and blended groups at 40 cm, 80 cm, and 5 m distance. arcsec = seconds of arc. *Statistically significant difference between two groups.

Quality of life was evaluated based on the Chinese version of the visual function index-14 (VF-12-CN), and some minor adjustments were made according to current living habits (21). The difficulty scale was graded as not difficult (100 score), slight (75 score), moderate (50 score), difficult (25 score), and inability to read due to vision problems (0 score). The questionnaire had 12 items, and the average score for each item was calculated separately (excluding the "not applicable" responses).

Patient satisfaction was assessed with a five-point Likert scale: very satisfied (100 score), satisfied (75 score), neither satisfied nor dissatisfied (50 score), dissatisfied (25 score), and very dissatisfied (0 score).

Statistical analysis

Statistical analysis was performed using SPSS for Windows software (v. 26.0, IBM Corp). The normal distribution of variable was evaluated using the Shapiro-Wilk test. Normally distributed variables were compared between the two groups using an independent-sample *t* test. Non-normally distributed variables were compared between the two groups using the Mann-Whitney *U* test. Pearson's correlation test was used to evaluate the correlation between the VA difference of two eyes and stereoacuity at near distance. A *P* value of less than 0.05 was considered statistically significant.

Results

A total of 37 patients were enrolled. Follow-up was performed 3 months after the surgery. The bilateral group included 42 eyes of 21 patients, the mean age was 59.33 ± 5.89 years. The blended group included 32 eyes of 16 patients, the mean age was 61.69 ± 7.20 years. No statistically significant difference was found in age of the two groups ($P = 0.281$). The preoperative ocular characteristics are shown in Table 1.

Stereoacuity

For the bilateral group, the mean stereoacuity at near distance, intermediate distance, and far distance was 49.76 ± 22.67 (range 15 to 100), 52.62 ± 20.77 (range 30 to 100), and 59.76 ± 24.92 (range 30 to 100) arcsec, respectively. For the blended group, the mean stereoacuity at near distance, intermediate distance, and far distance was 120.63 ± 90.94 (range 45 to 400), 79.06 ± 50.41 (range 45 to 200), and 57.19 ± 22.66 (range 30 to 100) arcsec, respectively. No statistically significant difference was found between far and intermediate distance stereoacuity ($P = 0.844$, far distance; $P = 0.083$, intermediate distance), but a statistically significant difference was observed in near distance stereoacuity ($P < 0.001$) (Figure 1).

At far distance, good stereoacuity was achieved in 13 of 21 (62%) and 12 of 16 (75%) patients in the bilateral and blended groups, respectively. At intermediate distance, good stereoacuity was achieved in 17 of 21 (81%) and 11 of 16 (69%) patients in the bilateral and blended groups, respectively; all patients in the bilateral group had normal stereoacuity, whereas two patients in the blended group had abnormal stereoacuity (both 200 arcsec). At near distance, good stereoacuity was achieved in 17 of 21 (81%) and 4 of 16 (25%) patients in the bilateral and blended groups, respectively; all patients had normal stereoacuity in the bilateral group, whereas four patients had abnormal stereoacuity (three patients had 200 arcsec and one patient had 400 arcsec) in the blended group.

In near distance, the VA difference of two eyes of the bilateral and blended groups was 0.04 ± 0.06 and 0.18 ± 0.15 logMAR, respectively ($P < 0.001$). The correlation analysis indicated that the VA difference of two eyes was positively correlated with stereoacuity (correlation coefficient, $r = 0.896$, $P < 0.001$; Figure 2).

Binocular visual acuity and manifest refraction

The mean binocular UNVA of the bilateral and blended groups was 0.08 ± 0.07 and 0.12 ± 0.05 logMAR ($P = 0.101$), respectively. The mean binocular UIVA of the bilateral and blended groups was 0.10 ± 0.07 and 0.09 ± 0.06 logMAR ($P = 0.660$), respectively. The mean binocular UDVA of the bilateral and blended groups was −0.01 ± 0.05 and 0.00 ± 0.04

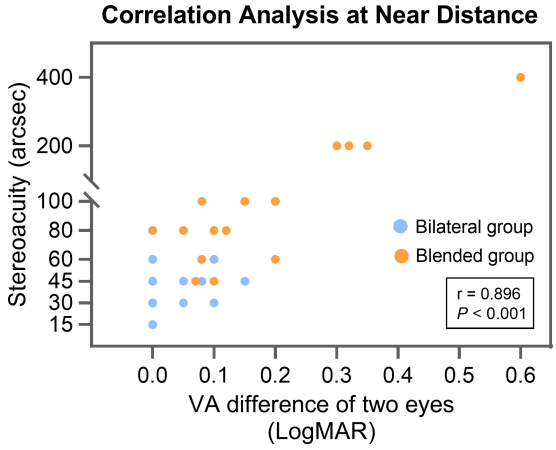

FIGURE 2
The correlation analysis between VA difference of two eyes and stereoacuity for all patients at near distance (40 cm).
arcsec = seconds of arc; LogMAR = logarithm of the minimum angle of resolution; VA = visual acuity.

logMAR (P = 0.868), respectively. The mean binocular CDVA of the bilateral and blended groups was −0.03 ± 0.05 and −0.02 ± 0.04 logMAR, respectively (P = 0.639). The proportion of patients in bilateral group with binocular UNVA, UIVA, UDVA, and CDVA of 0.1 logMAR (Snellen 20/25) or better was 86%, 76%, 100%, and 100%, respectively (Figure 3A). The proportion of patients in blended group with binocular UNVA, UIVA, UDVA, and CDVA of 0.1 logMAR (Snellen 20/25) or better was 75, 87, 100, and 100%, respectively (Figure 3B).

The mean spherical equivalent of the bilateral and blended groups was −0.05 ± 0.38 D and 0.00 ± 0.26 D, respectively (P = 0.450). The postoperative spherical equivalent was within ± 0.50 D in 89% of patients in the bilateral group and in 94% of patients in the blended group (Figure 4A). The mean postoperative cylinder of the bilateral and blended groups was −0.16 ± 0.40 D and −0.11 ± 0.35 D, respectively (P = 0.204; Figure 4B).

Monocular and binocular defocus curves

Figure 5A illustrates the monocular defocus curves of eyes implanted with AT LISA tri 839MP, ZXR00, and ZLB00 IOLs. Among the three IOLs, no statistically significant difference was found at the defocus curves of + 1.0, + 0.5, and 0 D. At a defocus curve of −0.5, −1.0, and −1.5 D, AT LISA tri 839MP and ZXR00 were significantly better than ZLB00 (−0.5 D: P = 0.005 vs. AT LISA tri, < 0.001 vs. ZXR00; −1.0 D: P = 0.002 vs. AT LISA tri, < 0.001 vs. ZXR00; −1.5 D: P = 0.024 vs. AT LISA tri, 0.002 vs. ZXR00). No statistically significant difference was found between AT LISA tri 839MP and ZXR00. At a defocus curve of −2.0 D, ZLB00 was significantly better than AT LISA tri 839MP and ZXR00 (P = 0.006 vs. AT LISA tri, 0.048 vs. ZXR00). No statistically significant difference was observed between AT LISA tri 839MP and ZXR00. At a defocus curve of −2.5 D, AT LISA tri 839MP and ZLB00 were significantly better than ZXR00 (P < 0.001 both). No statistically significant difference was found between AT LISA tri 839MP and ZLB00. At a defocus curve of −3.0 D, AT LISA tri 839MP maintained good visual performance, but ZLB00 (P = 0.016) and ZXR00 (P < 0.001) were significantly poor. Additionally, ZLB00 had significantly better VA than ZXR00 (P = 0.030). At the defocus curve of −3.5 and −4.0 D, AT LISA tri 839MP remained significantly better than ZXR00 and ZLB00 (−3.5 D: P < 0.001 vs. ZXR00, 0.011 vs. ZLB00; −4.0 D: P < 0.001 vs. ZXR00, 0.005 vs. ZLB00). No statistically significant difference was found between ZXR00 and ZLB00.

Figure 5B illustrates the binocular defocus curves of the bilateral and blended groups. The defocus VA from + 1.0 to −2.0 D was not statistically significantly different between the groups. At the defocus of −2.5, −3.0, −3.5, and −4.0 D, the VA of the bilateral group was significantly better than that of the blended group (−2.5 D: P = 0.029; −3.0 D: P < 0.001; −3.5 D: P < 0.001; −4.0 D: P < 0.001).

Quality of life and patient satisfaction

All patients filled out the questionnaire for this study. Table 2 shows the questionnaire used in this study. For the bilateral group, the mean near, intermediate, and far distance activities scores were 93.95 ± 10.18, 96.33 ± 7.06, and 99.11 ± 2.24, respectively. For the blended group, the mean near, intermediate, and far distance activities scores were 94.66 ± 8.30, 97.14 ± 6.54, and 100.00, respectively. No statistically significant difference was found between the two groups (P = 0.964, near distance activities; P = 0.820, intermediate distance activities; P = 0.476, far distance activities). The mean patient satisfaction score was 91.67 ± 14.43 for the bilateral group and 92.19 ± 11.97 for the blended group. Patient satisfaction score of the bilateral and blended groups was not statistically significantly different (P = 0.964).

Discussion

The contralateral implant strategy is used to achieve a full range of binocular VA, as bilateral implantation of a trifocal IOL (2, 8). However, this method has shortcomings. Eyes implanted with different multifocal IOLs would cause a VA difference between eyes at some visual distance, it could reduce the stereoacuity (13, 22). Hayashi et al. (17) reported that the stereoacuity of patients who had implantation of bifocal IOL with different near addition was worse than that of patients

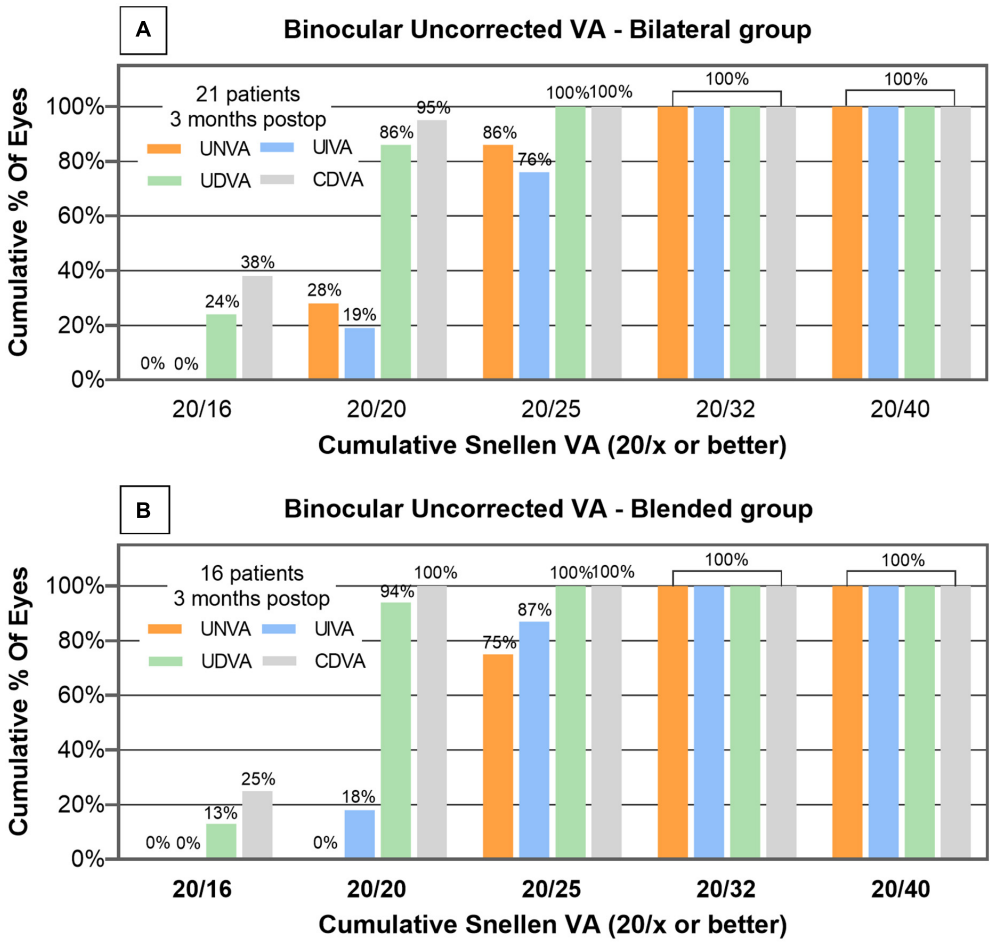

FIGURE 3
Distribution of postoperative binocular UNVA, UIVA, UDVA and CDVA of bilateral group **(A)** and blended group **(B)** measured 3 months after cataract surgery. corrected distance visual acuity = CDVA; uncorrected distance visual acuity = UDVA; uncorrected intermediate visual acuity = UIVA; uncorrected near visual acuity = UNVA; VA = visual acuity.

who had bilateral implantation of a trifocal IOL. As studies on whether the contralateral implant strategy could affect stereopsis are lacking, this topic should be studied further. In the present study, we set up two groups (the bilateral implantation of trifocal IOL group and the blended implantation of EDOF IOL with a bifocal IOL group) and compared their visual outcomes. Furthermore, we used an identical stereotest to evaluate near, intermediate, and far distance stereoacuity after cataract surgery, thus making the stereoacuity of different distances more comparable.

In our study, the bilateral and blended groups achieved good binocular VA in near, intermediate, and far distance. Aside from VA measured at fixed distance, the binocular defocus range (defined as VA greater than 0.2 logMAR) of the bilateral group reached nearly 3.5 D, and that of the blended group reached nearly 3.0 D. Both groups achieved satisfactory binocular VA from far to near distance. The bilateral group showed better VA at a vergence of −2.5, −3.0, −3.5, and −4.0 D. Previous study has reported a better VA at a vergence of −3.0 and −3.5 D of patients implanted with ZXR00 and ZMB00 IOL than trifocal IOL (8). It is worth noting that ZMB00 had an addition power of + 4.0 D at the IOL plane, this design enhanced near vision. In the present study, we used ZLB00 to compensate for near vision, and it still provided good near vision. For patients with a strong demand for near vision, a bifocal IOL with higher addition power is feasible.

In terms of stereopsis, most patients of the bilateral and blended groups achieved good far and intermediate distance stereoacuity. By contrast, the near stereoacuity of the bilateral group was still at a good level, but that of the blended group was significantly poor (only 25% patients achieved good stereoacuity). Patients implanted with trifocal IOL bilaterally showed excellent stereoacuity at various distances after the surgery, but implantation of an EDOF IOL with a bifocal IOL did not achieve similar outcomes.

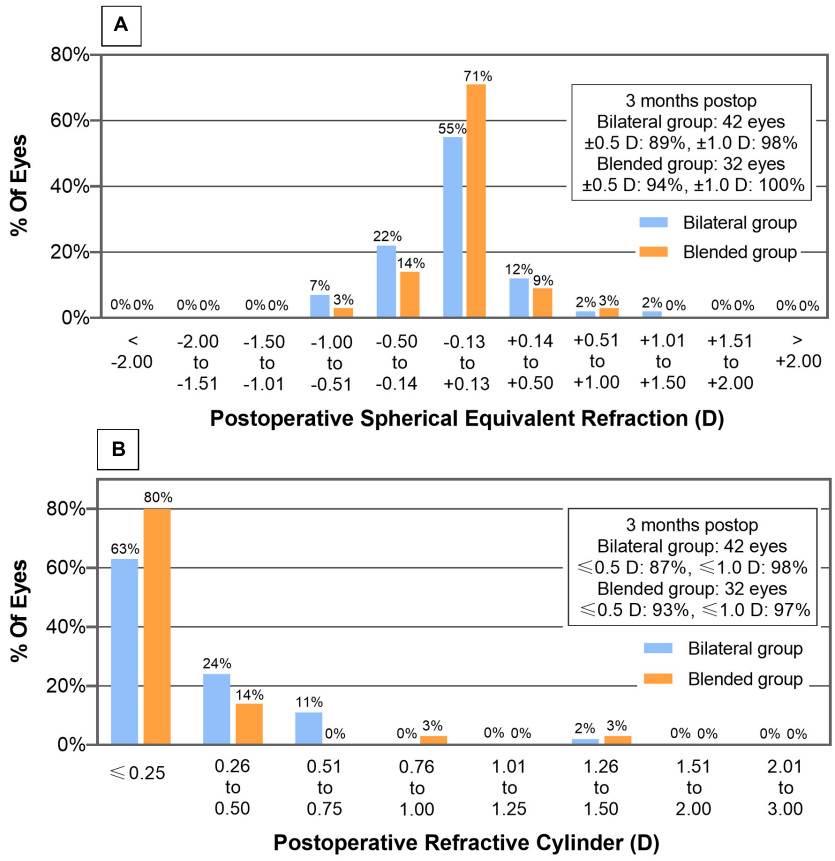

FIGURE 4
Distribution of postoperative spherical equivalent **(A)** and refractive cylinder **(B)** of bilateral and blended groups.

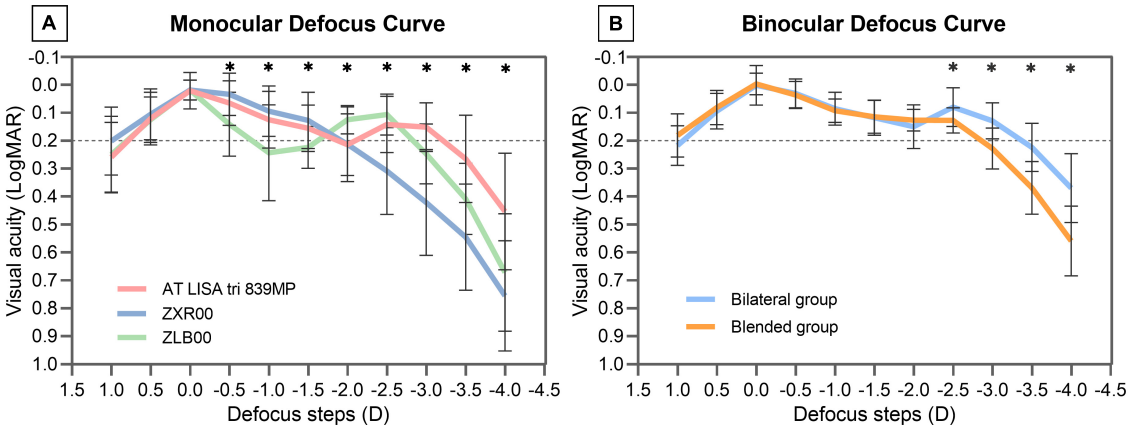

FIGURE 5
Monocular defocus curves of eyes implanted with AT LISA tri 839MP, ZXR00, and ZLB00 IOLs **(A)**. Binocular defocus curves of patients in bilateral and blended groups **(B)**. LogMAR = logarithm of the minimum angle of resolution. Results are shown in logMAR notation, with reference to the 0.2 logMAR thresholds; *Statistically significant difference between two groups.

As shown in previous study, the stereopsis is not affected by measuring distance, as it depends on the binocular disparity of the patient (23). However, in this study, the mean far and intermediate distance stereoacuity of blended group was normal, but the mean near distance stereoacuity was abnormal. It is worth noting that the VA difference between

TABLE 2 Questionnaire used in this study to evaluate the quality of life and patient satisfaction.

Question	Answer
Near distance activities	
Do you have difficulty reading small print, such as labels on medicine bottles?	1-5 scale[a]
Do you have difficulty reading newspaper or a book?	1-5 scale[a]
Do you have difficulty using mobile phone and identify the content?	1-5 scale[a]
Do you have difficulty filling out forms or signing names?	1-5 scale[a]
Intermediate distance activities	
Do you have difficulty using computer?	1-5 scale[a]
Do you have difficulty playing games such as mahjong, chess?	1-5 scale[a]
Do you have difficulty cooking?	1-5 scale[a]
Do you have difficulty doing fine handwork, such as sewing, crocheting?	1-5 scale[a]
Far distance activities	
Do you have difficulty watching television?	1-5 scale[a]
Do you have difficulty recognizing people when they are close to you?	1-5 scale[a]
Do you have difficulty going down stairs at night?	1-5 scale[a]
Do you have difficulty reading street signs?	1-5 scale[a]
Patient satisfaction	
How satisfied are you with your surgery outcomes?	1- 5 scale[b]

[a] Difficulty of doing daily activities was rated on a scale of 1 to 5: 1 = not difficult; 2 = slight; 3 = moderate; 4 = difficult; 5 = inability to read due to vision problems.
[b] Patient satisfaction was rated on a scale of 1 to 5: 1 = very satisfied; 2 = satisfied; 3 = neither satisfied nor dissatisfied; 4 = dissatisfied; 5 = very dissatisfied.

two eyes of the blended group was 0.18 ± 0.15 logMAR. When one eye received a blurred image, it would become difficult to fuse the images received by both eyes and affect the formation of a three-dimensional image (24, 25). The decrease in stereoacuity was greater when the VA difference between two eyes exceeded 0.1 logMAR (25). In the current study, we also found a positive correlation between the VA difference of two eyes and stereoacuity at near distance, and the results showed a strong positive correlation of the two variables. Aside from visual acuity, age also affects stereopsis, and it tends to deteriorate after 65 years (26). The mean age of the bilateral and blended groups is no more than 65 years, and no statistically significant difference was found between the two groups.

To assess the subjective experience of the patients, we used the Chinese version of the Visual Function Index-14 (VF-12-CN) questionnaire to evaluate quality of life, and this questionnaire is a reliable and valid tool to assess the visual function of Chinese patients (27). The bilateral and blended groups achieved high quality of life and the patients encountered no difficulty performing daily activities at various distances. Regarding patient satisfaction, the patients in the bilateral and blended groups achieved high satisfaction, and no patient in this study was dissatisfied with the postoperative visual performance.

Notably, the patients in the blended group had significantly worse near stereoacuity than the bilateral group, but no significant difference was found in the near distance activities and patient satisfaction scores between the two groups. The interpretation may be many of the near distance items in the VF-12-CN are directly dependent on VA, such as filling out forms, signing names, reading newspaper, and using mobile phone. In this study, both the bilateral and blended groups obtained good near binocular VA, and the uncorrected VA had a direct impact on visual quality and influence patient satisfaction (28). Additionally, stereopsis not only depend on binocular cues to perceive depth, but also can obtain from monocular depth cues (such as use of shadows, compare relative size, and relative defocus blur), and patients can compensate for loss of stereopsis by using these monocular depth cues (10).

This study has some limitations. One limitation is the absence of reading acuity and reading speed. Reading ability plays an important role in work and life. We did not evaluate reading ability in this study, so we are unable to conduct a comprehensive assessment of functional vision. Another limitation is we cannot examine the stereoacuity of patients with cataract preoperatively. Currently, there is no stereotest designed for cataract patients. Decreased contrast sensitivity due to cataracts and different degrees of cataract in both eyes may affect the accuracy of a clinically available stereotest. Therefore, we are unable to compare stereoacuity before and after the surgery.

In conclusion, the bilateral and blended groups achieved excellent binocular VA at all ranges of distance, all patients had high quality of life and patient satisfaction. Bilateral implantation of trifocal IOL restored good stereopsis at near, intermediate, and far distance after cataract surgery, but the near stereopsis of patients who underwent blended implantation of an EDOF IOL with a bifocal IOL was impaired. Further studies on the effect of contralateral implant strategy on stereopsis should be performed.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Ethics Committee of Xiamen Eye Center of Xiamen University. The patients/participants provided their written informed consent to participate in this study.

Author contributions

MZ: conceptualization, methodology, validation, formal analysis, investigation, data curation, writing-original draft, writing-review and editing, and visualization. WF: conceptualization, data curation, and investigation. GZ: conceptualization, methodology, resources, supervision, and project administration. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Evaluation value of subjective visual quality examination on surgical indications of the early cataracts based on objective scatter index values

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Aim: To evaluate the subjective visual functions of early cataracts patients and assess their surgical indications.

Methods: Eyes were separated into a control group (Group A without cataract) and two early cataracts groups (Group B with $2.0 \leq \text{OSI} < 3.0$ and Group C with $3.0 \leq \text{OSI} < 4.0$). The objective scatter index (OSI), modulation transfer function cut-off frequency (MTF cut-off), and Strehl ratio (SR) values were applied to measure objective visual functions. The contrast sensitivity (CS) and scores of the questionnaires (QOL and VF-14) characterized subjective visual functions. Above visual functions were compared among three groups. Postoperative visual functions in Group B and C were analyzed to assess the outcome of surgery.

Results: Ninety two subjects (126 eyes) were included in the study. All objective visual function in Group B were significantly better than Group C (all $P < 0.01$), but worse than Group A (all $P < 0.01$). Except for 1.5 c/d CS, subjective visual function in Group A were significantly better than Group B and C (all $P < 0.05$), but there was no significant differences between Group B and C. As for eyes that underwent surgery in Group B and C, all visual functions significantly improved after surgery ($P < 0.05$), except for 1.5 c/d CS in Group C. There were no significant differences among the three groups after surgery.

Conclusion: The subjective visual function can be impaired in early cataracts patients with $\text{OSI} < 3.0$, whose objective visual functions were statistically better than patients with $\text{OSI} \geq 3.0$. These patients can benefit equally from surgery as patients with $\text{OSI} \geq 3.0$. Subjective visual functions can be used as surgical indications for these patients.

KEYWORDS

early cataracts, surgical indications, subjective visual function, objective visual function, the objective scatter index

Introduction

Cataract is a common eye disease that causes visual function loss due to opacity in the lens. So far, surgery is the only effective way to treat cataracts (1). At present, low visual acuity (VA) is no longer the only indication for cataract surgery. Especially for early cataracts, they still often complain of impaired visual function, even with the good corrected distance visual acuity (CDVA) and only slight lens opacity. In the latest Preferred Practice Pattern (PPP), the visual function is emphasized in the interpretation of cataract surgical indications (2). The analysis of visual function includes two parts, subjectively and objectively. Many studies have found that objective examinations are more reliable and sensitive than subjective examinations (3–5).

Recently, the application of Objective Quality Analysis System II (OQAS II) in guiding surgery for cataract has been widely used (6–9). OQAS II directly collects the retinal images of point light sources through the double-pass system and analyzes their point spread function (PSF) (10). The objective scatter index (OSI) values is calculated by PSF. The OSI values refers to the ratio of the peripheral light intensity to the central peak light intensity of the retinal image, that is, the ratio between the light intensity of the ring area between 12 arc minutes and 20 arc minutes to the light intensity of 1 arc minute (11). The OSI values can be influenced not only by the lens opacities, but also by the tear film instability. And the tear film-related OSI values (TF-OSI) is a quantitative and objective measure of tear-film related vision quality. TF-OSI can excludes the effect of the tear film on the OSI values and it can be calculated by the OSI values and the Mean OSI values. OQAS II provides excellent stability, repeatability, and minimal interference to better assess the actual visual quality of patients (12). A previous study has concluded that OSI $\geq$ 3.0 may be an objective threshold for preoperative decision-making for cataract surgery (8, 9). According to another research, the OSI equaling to 3.2 was considered as the critical value for surgical treatment (7).

However, there were lots of early cataract patients with CDVA $\leq$ 0.22 (LogMAR) and OSI $<$ 3.0 that still complained of poor visual quality. This study aimed to explore the visual qualities of such patients and evaluate whether their visual quality could be improved after surgery.

Materials and methods

Subjects

The study was a prospective, cross-sectional, and self-comparative research. 94 eyes (45 right and 49 left eyes) of 70 patients (24 males and 46 females) diagnosed as early cataracts by the same experienced ophthalmologists from November 2020 to June 2021 at Union Hospital, Tongji Medical College, Huazhong University of Science and Technology were involved. 32 eyes without cataracts (14 right and 18 left eyes) of 22 volunteers (13 males and 9 females) were also enrolled. The main inclusion criteria of early cataract eyes were as follows: early age-related cataracts, age between 45 and 80 years, CDVA of 0.22 (LogMAR) or less, 2.0 $\leq$ OSI $<$ 4.0, and complaint of impaired visual function. The early cataracts patients with 2.0 $\leq$ OSI $<$ 3.0 were enrolled in Group B, and the early cataracts patients with 3.0 $\leq$ OSI $<$ 4.0 were in Group C. The main inclusion criteria of control eyes were as follows: age between 45 and 80 years, CDVA of 0.22 (LogMAR) or less, no lens opacification with OSI $<$ 2.0. The control eyes were in Group A. Patients with glaucoma, corneal, retinal diseases, refractive errors (over $\pm$ 3.0 D spherical or over $\pm$ 2.0 D cylinder), severe dry eye disease, and any other disease likely to affect visual function were excluded. 29 eyes of 22 patients (17 eyes in Group B and 12 eyes in Group C) underwent cataract surgery (**Figure 1**). All postoperative evaluations were performed 1 month after surgery until the patients recovered steadily.

This study was approved by the Institutional Review Board of the Ethics Committee of the Union Hospital, Tongji Medical College, Huazhong University of Science and Technology (UHCT20257). All patients have provided written informed consent before participating in this study, and they were examined and treated following the tenets of the Declaration of Helsinki. The clinical trial accession number is NCT04757350.[1]

Preoperative examinations

Each patient was evaluated by the same ophthalmologist with slit-lamp microscopy to assess the severity of cataracts. Everyone enrolled in this study had refraction, CDVA, intraocular pressure (IOP), and fundus examination. Besides, all people finished the objective and subjective visual function evaluation. Ocular biological parameters and endothelial cell count examination were measured to implant intraocular lens. Each parameter was measured at least three times by the same well-trained doctor.

OQAS II (Visiometrics SL, Spain) test is based on the system setting of the pupil size of 4 mm to ensure consistency. The test was carried out in the darkroom to ensure suitable size of the pupil. And refractive errors are fully corrected during these evaluations: spherical errors are corrected by OQAS II automatically, and cylindrical errors sections are corrected using external lens (12, 13). The double-pass provides three parameters: OSI, Mean OSI, MTF cut-off, and Strehl ratio (SR) (12). Each test was repeated three times for accuracy.

There were two types of CS testing, contrast visual acuity (CVA) and spatial frequency CS. We evaluated the CVA using Binoptometer 4 p (OCULUS, Germany) in a darkroom. By fixing the visual table size (0.4 visual table) and distance (3

1 http://www.clinicaltrials.gov

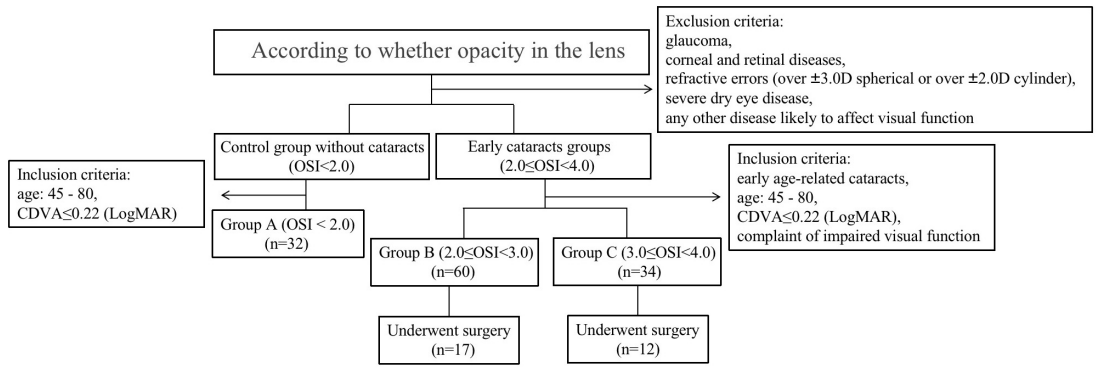


FIGURE 1
The flow diagram of the overall the study design, including inclusion and exclusion criteria's as well as participants distribution in each groups.

m), the operator adjusted the different contrast (80, 40, 25, 20, 15, 10, 7.5, 5%) to measure the CVA of patients, reflecting the ability to distinguish the edges of an object requiring the level of black-and-white contrast. Patients were required to identify the direction of the "E" letter by adjusting the contrast until patients could not recognize the word to achieve the critical value of the CVA. The spatial frequency CS test (SHIQI visual check end) measures the discrimination and physiological function of the human visual system by different spatial frequencies and contrast gratings. This was an important index of ophthalmological disease, which had a weak correlation with visual acuity, and an index of disease progression. It can also help predict visual function (14). Patients were required to identify the direction of the stripe by adjusting the different spatial frequencies and contrast until not being able to recognize the strip. We measured 1.5, 3, 6, 12, and 18 c/d CS. Each measurement was repeated three times per patient.

The Visual Function-14 (VF-14) and Quality of Life (QOL) questionnaires were designed by the American Eye Institute and Aravind Eye Hospital in India. They were often used as an evaluation tool for QOL associated with visual function in cataract patients (15). The VF-14 questionnaire quantifies subjectively the visual function impairments caused by cataracts. This study used the Visual Function Index-14 of Chinese Revision to assess the QOL which is related to subjective visual function of patients (16). QOL questionnaire is also based on daily activities to reflect the QOL affected by the visual function. The patients complete the questionnaire independently under guidance of a same ophthalmologist. Patients first determine whether the daily actions in the questionnaire were limited by the visual function, even with glasses. The degree of difficulty in completing these projects was scored (no difficulty, slightly difficult, very difficult, unable to complete) if the difficulty was caused by decreased visual function. If patients were unable to carry out these activities for other reasons, the item was excluded. Higher scores indicate better visual function (17).

Surgical technique

All surgeries were done by the same skilled surgeon. Before surgery, the pupil was dilated to 7 mm with 0.5% tropicamide drops (Santen, Osaka, Japan). Phacoemulsification was accomplished under local anesthesia using 0.4% Oxybuprocaine Hydrochloride Eye Drops (Santen, Osaka, Japan). According to preoperative examination results, the 3.0 mm clear corneal incision was located at different positions of corneal limbus in different patients. Continuous circular capsulorhexis was performed, and the hydrodis section and phacoemulsification cataract extraction were performed. Finally, the intraocular lens (ZMB00) was implanted into the capsular bag.

Postoperative examinations

Postoperative examinations and follow-up visit were routinely performed at 1 day, 1 week, 1 month, 3 month, and 6 month after the surgery. The results of postoperative subjective and objective visual function indexes at 1 month were used for analysis.

Statistical analysis

SPSS 22.0 and Prism 8 software were used to analyze all data. Continuous variables were expressed as mean ± standard deviation (SD). When parametric analysis was available, ANOVA was performed using Bonferroni *post hoc* analysis to determine significant differences among the three groups. The Kruskal-Wallis tests were used for non-parametric data. Nominal variables were expressed as absolute frequency (*n*) and relative frequency (%). As for sex, eye laterality, and the number of normal CVA eyes, the chi-square test or Fisher test was used to compare the differences among the three groups. Paired *t*-test was performed to compare the continuous

variables between preoperative and postoperative parameters in each group if data accords with normality, otherwise Wilcoxon test were used. *P*-values less than 0.05 were considered to be statistically significant.

Results

Baseline population data

Total 32 eyes (14 right and 18 left eyes) of 22 volunteers without cataracts (13 males and 9 females) were enrolled in Group A, 60 eyes (28 right and 32 left eyes) of 51 patients (16 males and 35 females) in Group B, and 34 eyes (15 right and 19 left eyes) of 30 patients (11 males and 19 females) in the Group C. The demographics and baseline characteristics of the three groups were similar. No statistically significant differences were found in sex, eye laterality, age, CDVA, and TF-OSI values among the three groups (Table 1, all $P > 0.05$).

Objective visual function

The OSI, MTF cut-off, and SR values in the three groups were listed in Table 2. Group B demonstrated lower OSI, higher MTF cut-off and SR values than Group C, meanwhile higher OSI, lower MTF cut-off and SR values than Group A. The differences among the three groups were statistically significant (all $P < 0.01$).

Subjective visual function

There were 21, 17, and 4 eyes with normal CVA (contrast $\leq$ 25%) in Group A, Group B, and Group C. Accordingly, there are 11, 43, and 30 eyes with impaired CVA (contrast > 25%) in the three groups, respectively (Table 2). The differences among the three groups were statistically significant ($P < 0.01$), but there was no significant difference between Group B and Group C ($P > 0.05$).

As demonstrated in Table 2, the CS at 1.5 c/d spatial frequencies were 51.81 ± 12.61, 45.90 ± 18.27, and 47.56 ± 18.50 in Group A, Group B, and Group C, respectively. But the three groups did not show significant difference in the CS at 1.5 c/d ($P > 0.05$). As for CS at 3, 6, 12, and 18 c/d spatial frequencies, the control group demonstrated significantly higher CS than the two early cataracts groups (Figure 2A, all $P < 0.01$). But there were no significant differences between the two early cataracts groups in CS at five spatial frequencies ($P > 0.05$).

The scores of the QOL and the VF-14 questionnaires in the three groups were listed in Table 2. There was significant difference in scores of QOL and VF-14 among the three groups (both $P < 0.01$), but not between the two early cataracts groups.

TABLE 1 Demographics information.

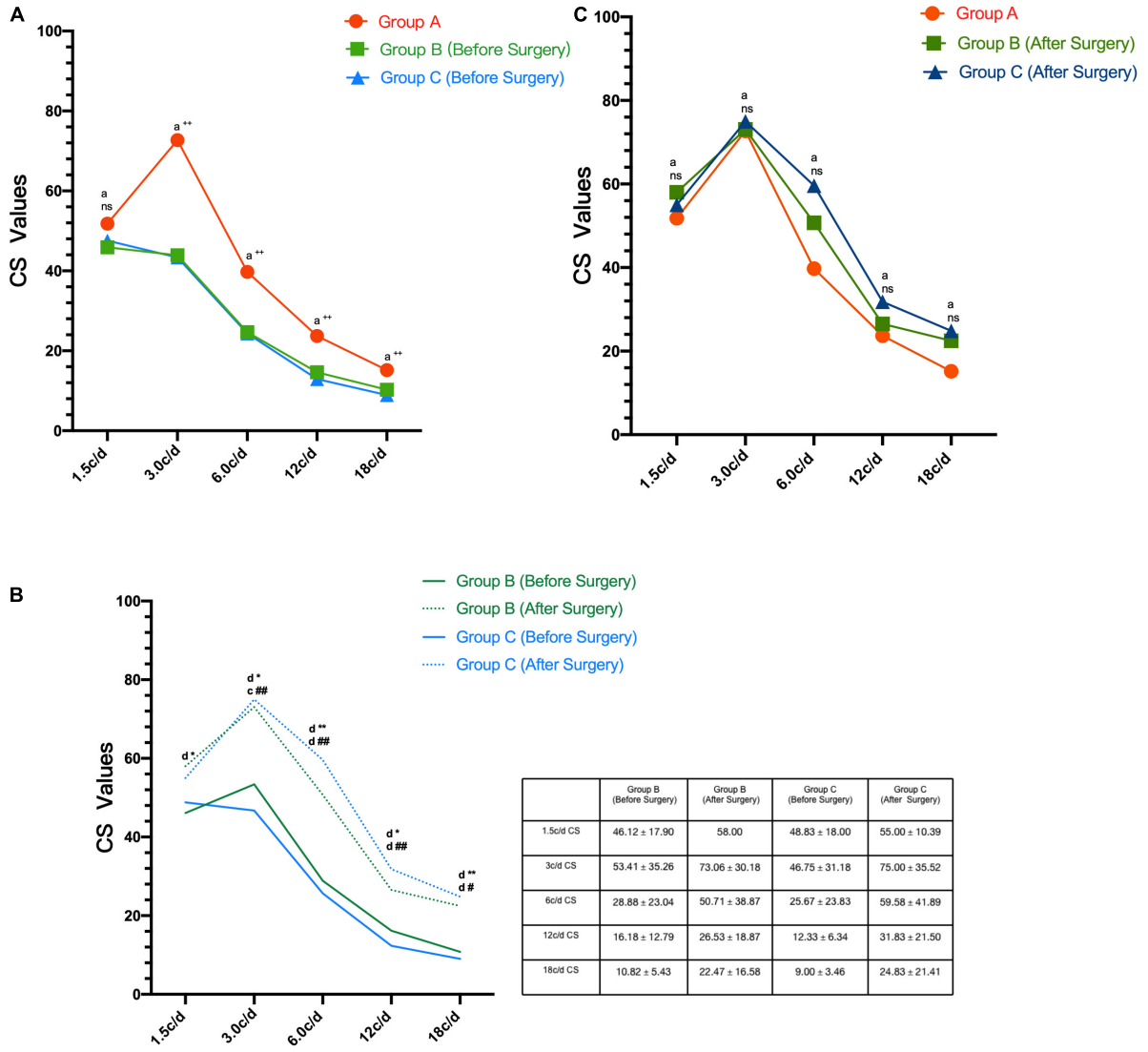
	Group A	Group B	Group C	*P*-value
Age (mean ± SD, years) (range)	66.67 ± 8.90 (51–78)	67.83 ± 7.52 (45–80)	68.03 ± 7.03 (49–80)	>0.05[c]
Laterality (R/L) (relate frequency%)	14/18 (43.8%/56.2%)	28/32 (46.7%/53.3%)	15/19 (44.1%/55.9%)	>0.05[b]
Sex (male/female) (relate frequency%)	13/9 (59.0%/41.0%)	16/35 (31.4%/68.6%)	11/19 (36.7%/63.3)	>0.05[b]
CDVA (LogMAR)	0.07 ± 0.08	0.09 ± 0.08	0.10 ± 0.05	>0.05[a]
TF-OSI (range)	0.38 ± 0.10 (0.20–0.56)	0.38 ± 0.11 (0.10–0.57)	0.38 ± 0.15 (0.11–0.59)	>0.05[a]

CDVA, corrected distance visual acuity; TF-OSI, tear film objective scattering index; LogMAR, logarithm of the minimum angle of resolution.
[a]Kruskal-Wallis test; [b]Chi-square test; [c]ANOVN test.

TABLE 2 Objective and subjective visual function indexes of the three groups.

	Group A	Group B	Group C	*P*-value
OSI (mean ± SD) (range)	1.0 ± 0.5^{+} (0.2–1.90)	2.3 ± 0.3$^{+,\#}$ (2.0–2.9)	3.6 ± 0.3$^{\#}$ (3.1–4.0)	<0.01**[a]
MTF cut-off (mean ± SD) (range)	29.14 ± 9.31^{+} (15.63–48.45)	20.55 ± 7.55$^{+,\#}$ (4.23–39.29)	13.89 ± 4.93$^{\#}$ (8.75–33.48)	<0.01**[a]
SR (mean ± SD) (range)	0.161 ± 0.048^{+} (0.110–0.301)	0.124 ± 0.037$^{+,\#}$ (0.050–0.249)	0.098 ± 0.026$^{\#}$ (0.071–0.189)	<0.01**[a]
CVA (normal/impaired eyes)(relate frequency%)	21/11^{+} (65.6%/34.4%)	17/43^{+} (28.3%/71.7%)	4/30 (11.8%/88.2%)	<0.01**[b]
1.5 c/d CS (mean ± SD) (range)	51.81 ± 12.61 (22.00–58.00)	45.90 ± 18.27 (9.00–58.00)	47.56 ± 18.50 (9.00–58.00)	>0.05[a]
3 c/d CS (mean ± SD) (range)	72.69 ± 30.72^{+} (7.00–100.00)	43.92 ± 31.98^{+} (5.00–100.00)	43.35 ± 25.65 (5.00–100.00)	<0.01**[a]
6 c/d CS (mean ± SD) (range)	39.72 ± 31.42^{+} (8.00–125.00)	24.68 ± 20.67^{+} (8.00–125.00)	24.35 ± 18.49 (8.00–76.00)	<0.01**[a]
12 c/d CS (mean ± SD) (range)	23.69 ± 14.14^{+} (8.00–62.00)	14.65 ± 8.69^{+} (8.00–58.00)	12.94 ± 7.59 (8.00–40.00)	<0.01**[a]
18 c/d CS (mean ± SD) (range)	15.16 ± 8.43^{+} (1.00–40.00)	10.27 ± 4.85^{+} (8.00–28.00)	8.94 ± 2.42 (8.00–20.00)	<0.01**[a]
Scores of QOL (mean ± SD) (range)	99.05 ± 2.07^{+} (91.67–100.00)	94.53 ± 9.06^{+} (69.44–100.00)	92.50 ± 9.29 (69.44–100.00)	<0.01**[a]
Scores of VF-14 (mean ± SD) (range)	90.76 ± 9.44^{+} (62.50–100.00)	78.56 ± 16.55^{+} (4.17–100.00)	78.98 ± 11.87 (50.00–100.00)	<0.01**[a]

CVA, contrast visual acuity; c/d, cycle per degree; CS, contrast sensitivity; MTF cut-off, modulation transfer function cut-off frequency; OSI, objective scatter index; QOL, Quality of Life; SR, Strehl ratio; VF-14, Visual Function-14.
[a]Kruskal-Wallis test; [b]Chi-square test; **$P < 0.01$: compare among the three groups; $^{+}P < 0.01$: compare between Group A and Group B; $^{\#}P < 0.01$: compare between Group B and Group C.



	Group B (Before Surgery)	Group B (After Surgery)	Group C (Before Surgery)	Group C (After Surgery)
1.5c/d CS	46.12 ± 17.90	58.00	48.83 ± 18.00	55.00 ± 10.39
3c/d CS	53.41 ± 35.26	73.06 ± 30.18	46.75 ± 31.18	75.00 ± 35.52
6c/d CS	28.88 ± 23.04	50.71 ± 38.87	25.67 ± 23.83	59.58 ± 41.89
12c/d CS	16.18 ± 12.79	26.53 ± 18.87	12.33 ± 6.34	31.83 ± 21.50
18c/d CS	10.82 ± 5.43	22.47 ± 16.58	9.00 ± 3.46	24.83 ± 21.41

FIGURE 2
(A) CS values at each spatial frequency (1.5, 3.0, 6.0, 12, 18 c/d) in Group A, Group B (Before Surgery), and Group C (Before Surgery) **(B)**. Preoperative and postoperative CS values at each spatial frequency (1.5, 3.0, 6.0, 12, 18 c/d) in Group B and Group C **(C)**. CS values at each spatial frequency (1.5, 3.0, 6.0, 12, 18 c/d) in Group A, Group B (After Surgery), and Group C (After Surgery). (CS, contrast sensitivity; c/d, cycle per degree; [a]Kruskal-Wallis test; [c]Paired *t*-test; [d]Wilcoxon test; $^{ns}P > 0.05$: compare among the three groups; $^{++}P < 0.01$: compare between Group A and Group B; $^{**}P < 0.01$:compare before and after surgery in the Group B; $^{*}P < 0.05$:compare before and after surgery in the Group B; $^{\#\#}P < 0.01$:compare before and after surgery in the Group C; $^{\#}P < 0.05$: compare before and after surgery in the Group C).

Comparison of visual quality before and after surgery and postoperative parameters among groups

Seventeen eyes in Group B and 12 eyes in Group C undergone cataract surgery, and all postoperative evaluations were performed 1 month after surgery until the patients recovered steadily. No adverse event occurred.

Figure 3 shows the mean preoperative and postoperative OSI, MTF cut-off, and SR values in Group B and C. After the phacoemulsification cataract surgery, objective indexes OSI, MTF cut-off, and SR values improved significantly in the two groups (all $P < 0.01$). There were no statistically significant differences among postoperative parameters in the two early cataracts groups and the control group as for OSI, MTF cut-off, and SR values (Table 3, all $P > 0.05$).

Figure 4 shows the preoperative and postoperative related frequencies (%) of eyes with normal CVA in Group B and C, and the preoperative and postoperative scores of QOL and VF-14 in Group B and C. The relate frequencies (%) of eyes with normal CVA and the scores of QOL and VF-14 increased

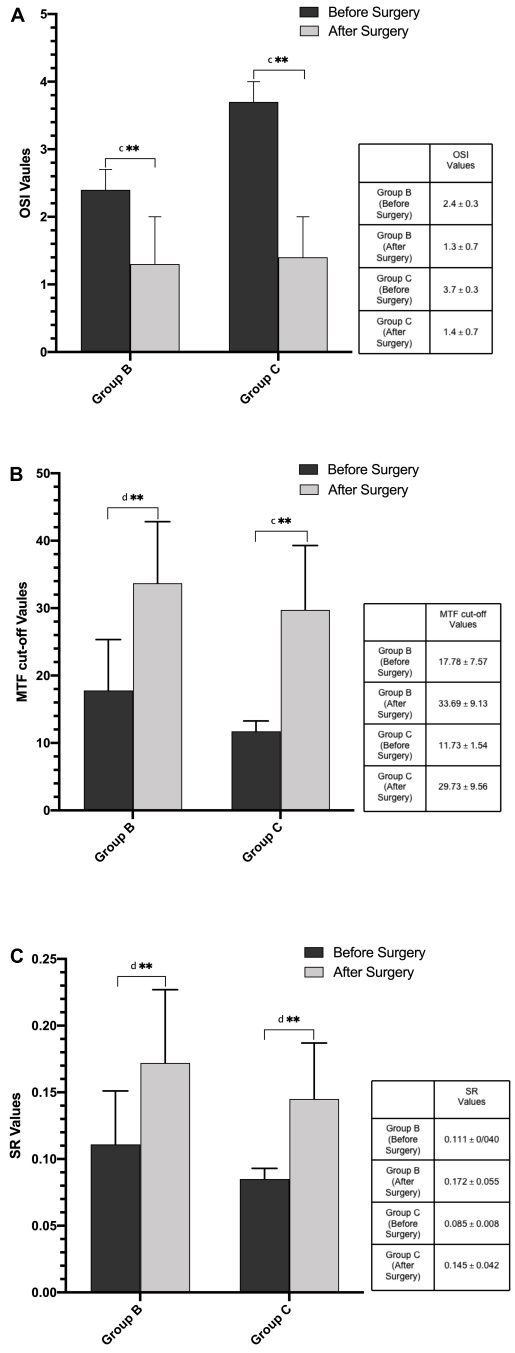


FIGURE 3
(A) Preoperative and postoperative OSI values in Group B and Group C. **(B)** Preoperative and postoperative MTF cut-off values in Group B and Group C. **(C)** Preoperative and postoperative SR values in Group B and Group C. (MTF cut-off, modulation transfer function cut-off frequency; OSI, objective scatter index; SR, Strehl ratio; [c]Paired *t*-test; [d]Wilcoxon test; $^{**}P < 0.01$: compare between the preoperative and postoperative values).

significantly after phacoemulsification cataract surgery in the two early cataracts groups ($P < 0.05$). And there were no significant differences between the postoperative CVA and scores of questionnaires in the two groups and these parameters in the control group (Table 3, all $P > 0.05$).

As shown in Figure 2B, the postoperative CS at five spatial frequencies were better than preoperative CS. After the phacoemulsification cataract surgery, the CS at five spatial frequencies improved significantly in the two groups (all $P < 0.05$), except for 1.5 c/d spatial frequency CS in Group C ($P > 0.05$). And there were no significant differences in the postoperative CS at five spatial frequencies between the two groups and the CS in the control group (Table 3 and Figure 2C).

Discussion

The main discovery of this study is that patients with both impaired objective and subjective visual functions (except for the 1.5 c/d CS), whose OSI was less than 3.0, could benefit from significant visual function improvement after cataract surgeries. Meanwhile, there was no statistically significant differences in the outcomes of surgery between the two groups of early cataract patients with different OSI values. Except for 1.5 c/d CS, subjective visual qualities can be used as a surgical indication for early cataract patients with OSI < 3.0.

The OSI values is currently recognized as a diagnostic parameter capable of discerning surgical cataracts objectively, and as a highly reproducible tool for evaluating optical quality based on the cataract degrades (6, 18–21). Furthermore, more and more researchers proved that the OSI values is the most effective parameter for decision-making in surgery which is approximately 3.0 (9–11). Clinically, many cataract patients with good VA and low OSI values (i.e., less than 3.0), often complained of deterioration of visual quality. As for these patients, the surgical decision-making is more complicated for clinicians.

This research compares the OSI, MTF cut-off, SR, CVA, spatial frequencies CS, QOL and, VF-14 questionnaire together between two groups with early cataracts and the control group without cataracts to evaluate the visual function of early cataracts patients with OSI < 3.0. Moreover, the surgical effects on the two groups with early cataracts were compared to assess surgical indications of early cataracts patients with OSI < 3.0.

We found that MTF cut-off and SR values have significant differences in the three groups, and that there was the highest MTF cut-off and SR values in the control group and the lowest in the group of early cataracts with $3.0 \leq$ OSI < 4.0. The MTF cut-off values is the frequency at which the MTF reaches a value of 0.01. SR values is defined as the ratio between the MTF area of the eye to the diffraction-limited MTF area. According to previous studies, the MTF cut-off and SR values decreased significantly with the increase of OSI values (11, 22, 23). This result indicates that

TABLE 3 Postoperative objective and subjective visual function indexes of the two groups with early cataracts and these parameters in control group.

	Group A	Group B (after surgery)	Group C (after surgery)	*P*-value
OSI (mean ± SD) (range)	1.0 ± 0.5 (0.2–1.9)	1.3 ± 0.7 (0.3–2.8)	1.4 ± 0.6 (0.4–2.8)	>0.05[c]
MTF cut-off (mean ± SD) (range)	29.630 ± 9.500 (15.630–48.450)	33.690 ± 9.134 (18.620–48.720)	29.730 ± 9.564 (14.890–45.100)	>0.05[c]
SR (mean ± SD) (range)	0.161 ± 0.047 (0.105–0.301)	0.172 ± 0.055 (0.095–0.290)	0.145 ± 0.042 (0.108–0.269)	>0.05[a]
CVA (normal/impaired eyes) (relate frequency%)	21/11 (65.6%/34.4%)	15/2 (88.24%/11.64%)	11/1 (91.67%/8.33%)	>0.05[b]
1.5 c/d CS (mean ± SD) (range)	51.81 ± 12.61 (22.00–58.00)	58.00	55.00 ± 10.39 (22.00–58.00)	>0.05[a]
3 c/d CS (mean ± SD) (range)	72.69 ± 30.72 (7.00–100.00)	73.06 ± 30.18 (14.00–100.00)	75.00 ± 35.52 (7.00–100.00)	>0.05[a]
6 c/d CS (mean ± SD) (range)	39.72 ± 31.42 (8.00–125.00)	50.71 ± 38.87 (10.00–125.00)	59.58 ± 41.89 (8.00–125.00)	>0.05[a]
12 c/d CS (mean ± SD) (range)	23.69 ± 14.14 (8.00–62.00)	26.53 ± 18.87 (8.00–66.00)	31.83 ± 21.50 (8.00–58.00)	>0.05[a]
18 c/d CS (mean ± SD) (range)	15.16 ± 8.43 (1.00–40.00)	22.47 ± 16.58 (8.00–66.00)	24.83 ± 21.41 (8.00–58.00)	>0.05[a]
Scores of QOL (mean ± SD) (range)	99.05 ± 2.07 (91.67–100.00)	99.67 ± 0.92 (97.22–100.00)	99.07 ± 3.21 (88.89–100.00)	>0.05[a]
Scores of VF-14 (mean ± SD) (range)	90.76 ± 9.44 (62.50–100.00)	92.40 ± 7.33 (81.25–100.00)	90.43 ± 9.15 (77.08–100.00)	>0.05[a]

CVA, contrast visual acuity; c/d, cycle per degree; CS, contrast sensitivity; MTF cut-off, modulation transfer function cut-off frequency; OSI, objective scatter index; QOL, Quality of Life; SR, Strehl ratio; VF-14, Visual Function-14.
[a]Kruskal-Wallis test; [b]Chi-square test; [c]ANOVA test.

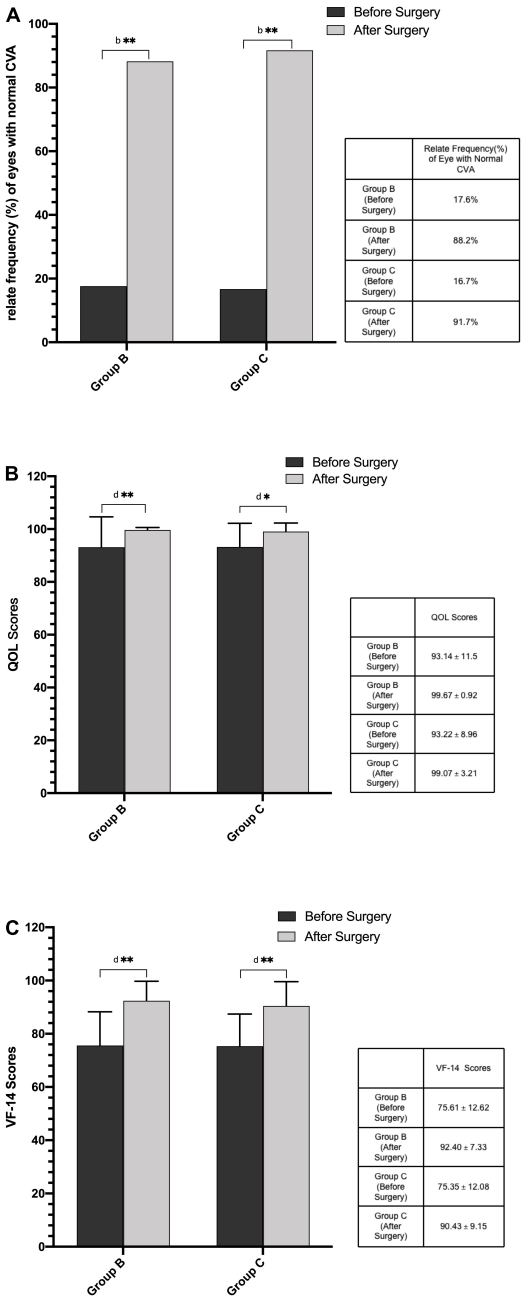


FIGURE 4
(A) Preoperative and postoperative relate frequency (%) of eyes with normal CVA in Group B and Group C. **(B)** Preoperative and postoperative scores of QOL questionnaire in Group B and Group C. **(C)** Preoperative and postoperative scores of VF-14 questionnaire in Group B and Group C. (CVA, contrast visual acuity; QOL, Quality of Life; VF-14, Visual Function-14; [b]Chi-square test; [d]Wilcoxon test; $^{**}P < 0.01$: compare between the preoperative and postoperative values; $^{*}P < 0.05$: compare between the preoperative and postoperative values).

the MTF cut-off and SR are equally sensitive based on the OSI grading.

Interestingly, there was a significant difference in CVA among the three groups in the study. However, there was no significant difference between the two early cataracts groups. The result indicated that the early cataract patients with OSI < 3.0 may be affected by the visual disturbance of gray and blurry. In our study, the low spatial frequency CS had no significant difference among the three groups. It is reported that the CS decreased with the increase of scattering for different spatial frequencies (24). This study agrees with the results of the researches, which have concluded that the low spatial frequency CS is of little value in early-stage cataract assessment (25), and that low spatial frequency CS reduced increasingly with late-stage cataract (26). The results of the research showed that the medial and high spatial frequencies CS were better in the

control group than the two early cataracts groups, but there were no differences between the two early cataracts groups. This study indicated that the CS at medial and high spatial frequencies had been impaired even though the CDVA and light-scatter were not affected at the earlier cataract stage with OSI < 3.0. Similar to the other studies, the medial and high spatial frequencies CS may be more sensitive than traditional VA tests in quantifying the level of visual damage in early cataract patients (27). Elliott et al. also concluded that CS at high spatial frequency is more sensitive (28). In daily life, light intensity and light contrast are variable. At the same time, we need to identify objects with clear or blurred boundaries. The measurement of central vision underestimates the extent of visual impairment (29). In this study, we measured CS at all spatial frequencies (low, medial, and high) in all subjects with early cataracts and without cataracts. We found that the CS at medial and high spatial frequencies may significantly decrease in early cataracts. The finding suggests that we need to test all spatial frequencies CS, especially the medial and high spatial frequencies CS, to assess the comprehensive visual function of early cataract patients.

The result of our study was that the scores of QOL and VF-14 were the highest in the control group, the lowest in the group of cataracts with 3.0 ≤ OSI < 4.0, which was consistent with the conclusions of previous studies that high OSI levels corresponded with lower VF-14 scores (11, 21, 30). Cataracts in our study were at an early stage with OSI < 3.0, but the scores of VF-14 had decreased. The visual function reflected by QOL and VF-14 questionnaire were critical in understanding and explaining the complaint of patients, and the visual function evaluated by VF-14 had been reported to be a strong indicator of visual quality (31). Although QOL and VF-14 questionnaire is time-consuming and affected by subjective nature, it can also be a decisive test in some uncertain cases, such as early cataracts with good VA and apparent visual disturbances.

In this study, the postoperative objective visual function in the two groups with early cataracts patients were significantly improved. Except for the 1.5 c/d CS in Group C, all postoperative subjective visual function in the two groups with early cataracts were significantly improved. Postoperative parameters of the two groups of cataracts reached a normal level. The results indicated that in the early-stage cataracts patients with good baseline VA, even though the OSI values was less than 3.0, their visual function can be significantly improved through cataract surgeries. Furthermore, the surgical effect on them was the same as cataracts patients with 3.0 ≤ OSI < 4.0.

The OQAS II has recently been used to evaluate the opacity of lens (8, 10, 32). The OSI is an appropriate parameter to objectively distinguish between transparent lens and cataracts, facilitating the decision-making process, particularly in early-stage cataracts (8, 21, 32), with OSI from 3.0 to 7.0 as an indication for surgery (10, 11). In this study, we found that only OSI values cannot explain complaints about the impaired visual quality of early cataract patients or help doctors to decide the timing of surgery. Subjective visual function can verify the symptoms of early cataract patients and guide doctors to decide the timing of surgery.

In this study, our aim was to evaluate the subjective and objective visual functions of early cataracts patients and assess their surgical indications. And we concluded that subjective visual functions can be used as surgical indications for these patients. We have discussed the problems that puzzled many ophthalmologists and patients and reached corresponding conclusions about surgical indications for early cataracts. Therefore this study is of great practical significance. In additions, the samples in the study were examined by slit lamp and divided into early cataracts group and no cataract control group. The devices we used, such as OQAS II, contrast sensitivity, contrast visual acuity tests, as well as VF-14 and QOL questionnaires are common examination in ophthalmology. Therefore, the conclusions of our research can be applied to the ophthalmology departments in other hospitals to a large extent.

There are two limitations to this study. Firstly, large sample size should be provided to obtain more accurate results for reference. Further studies are required to expend the sample size. Secondly, we followed up at 1 week, 1 month, 3 month, and 6 month postoperatively for patients who chose surgical intervention, but only adopted data of 1 month after operation for statistical analysis. In further research, we should conduct statistical analysis of the long-time postoperative data to obtain the change trend of patients' various visual functions after surgery and judge the long-term effect.

Conclusion

In conclusion, a combination of current methods, including objective and subjective parameters, should be used for early-stage cataract visual quality evaluating and surgery planning. Subjective visual function indexes can also be used as a meaningful indicator of cataract surgery even the OSI value is less than 3.0.

Data availability statement

The original contributions presented in this study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

Ethics statement

The studies involving human participants were reviewed and approved by the Institutional Review Board of the Ethics Committee of the Union Hospital, Tongji Medical College, Huazhong University of Science and Technology (UHCT20257). The patients/participants provided their written informed consent to participate in this study.

Author contributions

YL, LJ, MW, and YH were responsible for study design. YL, LJ, and MW were involved in date collection and date analysis. YL drafted and wrote the manuscript. YH revised the manuscript. All authors have read and approved the manuscript.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Effect of larger corneal spherical aberration in improving the near visual acuity of eyes implanted with the TECNIS Symfony

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Purpose: To explore the effect of corneal spherical aberration on the visual acuity and visual quality of eyes implanted with the TECNIS Symfony intraocular lens (IOL).

Methods: A total of 43 patients with age-related cataract (60 eyes) undergoing phacoemulsification and TECNIS Symfony IOL implantation were enrolled in this study. The uncorrected distance (UDVA), intermediate (UIVA), near visual acuity (UNVA), corrected distance visual acuity (CDVA), contrast sensitivity, and ocular spherical aberration were recorded 3 months after surgery. Preoperative and postoperative corneal spherical aberration were also measured using the iTrace device. Objective scattering index (OSI), modulation transfer function cut-off frequency (MTF cut-off), and Strehl ratio (SR) were measured by the Optical Quality Analyzing System. Catquest-9SF questionnaire were applied too. Spearman's correlation analysis was used to evaluate the relationship between spherical aberration and visual quality parameters.

Results: Patients were satisfied with their postoperatively visual quality. And the postoperative logMAR UDVA, UIVA, UNVA, and CDVA was 0.05 ± 0.07, 0.04 ± 0.06, 0.15 ± 0.07, and 0.03 ± 0.05, respectively. The mean preoperative corneal spherical aberration was 0.24 ± 0.10 μm, which is the only factor influencing postoperatively UNVA, and it was negatively correlated with UNVA and glare contrast sensitivity under 18 cpd (cycle/degree, cpd) spatial frequency (r = −0.403, −0.300, −0.360; all $P < 0.05$). Additionally, the greater the residual spherical aberration of the cornea, the better the near vision after operation. The mean postoperative ocular spherical aberration was −0.03 ± 0.07 μm, it was not correlated with visual acuity, contrast sensitivity, and visual quality (all $P > 0.05$).

Conclusion: Preoperative positive spherical aberration can benefit near vision while decrease contrast sensitivities at high spatial frequencies when implanted with the TECNIS Symfony IOL.

KEYWORDS

corneal spherical aberration, ocular spherical aberration, visual quality, near vision quality, contrast sensitivities

Introduction

With the advent of refractive cataract surgery, ophthalmologists and patients have higher expectations of visual quality after cataract surgery. Multifocal aspherical intraocular lenses (IOLs) have greatly decreased spectacle dependence and created to compensate for the spherical aberration of the cornea and to lessen total ocular spherical aberration in pseudophakic eyes. However, even after the monofocal aspherical IOLs implantation, the optimal value of target ocular spherical aberration remains controversial. Previous studies have revealed that implantation with aspherical IOLs can improve the visual quality (1, 2). Denoyer et al. (3) reported that bilateral implantation of an IOL with no aberration resulted in better quality of near vision. Other researchers though that completely correcting spherical aberration will damage depth of field and near acuity (4–6). Rocha et al. (5) found that the reduction of total spherical aberration after aspheric IOL implantation may degrade distance-corrected near and intermediate visual acuity. Nochez et al. (7) reported that some residual positive spherical aberrations (0. 07–0.10 μm) can increase the depth of focus and improve the near visual acuity in eyes implanted with aspherical monofocal IOLs.

TECNIS Symfony IOL (Johnson & Johnson Vision, Santa Ana, CA, USA) is a single-piece, hydrophobic acrylic extended depth-of-focus (EDOF) IOL with an asphericity of −0.27 μm (8). As a hybrid EDOF IOL, it provides excellent far, intermediate visual acuity and good visual quality. But the near visual acuity is not always good enough (9, 10). Interestingly, we found that in the clinic some patients had good near vision, while some had poor near vision despite having the same TECNIS Symfony IOL implantation. Does the spherical aberration play a role in improving near vision? In addition, how does the spherical aberration affect the visual quality after surgery?

Therefore, this study aimed to explore the influence of spherical aberration on the visual acuity and visual quality, especially the near vision, after TECNIS Symfony IOL implantation.

Patients and methods

Patients

This prospective study was conducted at the Eye Hospital of Wenzhou Medical University from January 2019 to October 2021. Sixty eyes of 43 age-matched cataract patients who underwent uneventful phacoemulsification and TECNIS Symfony IOL implantation were enrolled. All surgeries were performed by the same surgeon (Z.Y.E.) using topical anesthesia. Patients with other ocular diseases (such as keratopathy, glaucoma, uveitis, and fundus disease), history of intraocular or corneal surgery, and any complications intra- and post-operative were excluded. All procedures were conducted following the tenets of the Declaration of Helsinki, and the study design was approved by the Institutional Ethics Committee of Wenzhou Medical University, Zhejiang Province, China. All study participants provided informed consent.

Examinations and measurements

All patients underwent a comprehensive ophthalmological examination. The preoperative examination data included uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), intraocular pressure, axial length, and corneal astigmatism measured by the IOL Master 700 (Carl Zeiss, Jena, Germany) and corneal spherical aberration measured by the iTrace aberrometer (Tracey Technologies, Houston, TX, USA) in a 6-mm range. The Barrett Universal II formula was used to determine the IOL power, and the postoperative target diopter was set to mild myopia (0–0.5D).

Postoperative examinations were conducted 3 months after cataract surgery. The data included UDVA, CDVA, uncorrected intermediate visual acuity (UIVA) at a distance of 80 cm, uncorrected near visual acuity (UNVA) at a distance of 40 cm, using Snellen visual charts and then converted into logarithm of the minimum angle of resolution (logMAR) notation. Astigmatism, and postoperative ocular spherical aberration, coma, trefoil in a 4-mm range was also recorded. After correcting refractive errors, CSV-1000HGT (Vector Vision, Dayton, OH, USA) was applied to measure the contrast sensitivity (CS) with and without glare after adapting the patient to scotopic conditions. Spatial frequencies of 3, 6, 12, and 18 cpd (cycle/degree, cpd) were used, which were then converted into base 10 logarithmic units for statistical analysis. Objective visual quality parameters, that is, the objective scatter index (OSI), modulation transfer function (MTF), and Strehl ratio (SR) using an optical quality analysis system (OQAS, Visiometrics SL, Terrassa, Spain) were recorded. Subjective visual quality was evaluated using the Catquest-9SF questionnaire with four response options for perceived difficulty in vision (4 = very great difficulty; 3 = great difficulty; 2 = some difficulty; 1 = no difficulty), and the Quality of Vision (QoV) questionnaire wherein the patients rated 10 visual symptoms with four response levels (0, 1, 2, 3; higher scores indicated worse photic phenomena).

Statistical analyses

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) (version 22.0; SPSS, Inc., Chicago, IL, USA). The normality of the evaluation data was tested by the Shapiro–Wilk test. If the data followed a normal distribution, parametric analysis was performed, and if not, non-parametric statistical analysis was used. Categorical data, such as halos and glares, were expressed as frequencies with percentages (n%). Spearman's correlation was used to evaluate the influence of preoperative corneal spherical aberration and postoperative ocular spherical aberration on the visual quality and visual acuity of eyes implanted with TECNIS Symfony IOL, and factors with $P < 0.2$ were included in the further multiple linear regression. The multiple linear regression was used to analyze the impact of eye parameters on postoperative UNVA. Statistical significance was set at $P < 0.05$. The sample size calculation suggested that a sample of 55 would achieve a power of 80% and a level of significance of 5% for the detection of a significant correlation between preoperative corneal spherical aberration and postoperative UNVA.

Results

Sixty eyes from 43 patients (16 men and 27 women) were enrolled. Of these, 17 eyes had bilateral cataracts, and 26 had unilateral cataracts. The mean patient age was 66 ± 10 years. Before the operation, the mean corneal spherical aberrations of 6-mm measurement were 0.24 ± 0.10 μm (ranging from 0.07 to 0.47 μm), the mean logarithmic values of CDVA and UDVA were 0.35 ± 0.44 and 0.54 ± 0.40, respectively. The axial length and corneal astigmatism were 23.56 ± 0.99 mm and −0.47 ± 0.30 diopter, respectively. After the operation, the ocular spherical aberrations of 4-mm measurement were −0.03 ± 0.07 μm (ranging from −0.23 to 0.14 μm) (Table 1). There were no intraoperative or postoperative complications. The capsule was transparent at the end of the follow-up.

Visual acuity

Postoperatively, the mean logarithmic values of UDVA, UIVA, UNVA, and CDVA were 0.05 ± 0.07, 0.04 ± 0.06, 0.15 ± 0.07, and 0.03 ± 0.05, respectively (Table 1). All UDVA and UIVA values were 0.2logMAR or above; 93% (56/60) of UNVA values were 0.2logMAR or above, and all of them were 0.3logMAR or above (Figure 1). The sphere and cylinder were −0.23 ± 0.49D and −0.59 ± 0.49D, respectively.

Contrast sensitivity

The mean logarithmic value of contrast sensitivity at spatial frequencies of 3, 6, 12, and 18 cpd without glare were 1.37 ± 0.21, 1.58 ± 0.20, 1.11 ± 0.34, and 0.68 ± 0.37, respectively. The mean logarithmic value of contrast sensitivity at spatial frequencies of 3, 6, 12, and 18 cpd with glare were 1.40 ± 0.26, 1.54 ± 0.30, 1.09 ± 0.37, and 0.68 ± 0.37, respectively. All values of the mean contrast sensitivity with and without glare were within the normal range except at a spatial frequency of 12 cpd (Figure 2) (11).

TABLE 1 Pre- and post-operative data of patients.

	Pre-operative	Post-operative
Age (year)	66 ± 10 (37, 85)	–
Axial length (mm)	23.56 ± 0.99 (21.92, 25.89)	–
Corneal astigmatism (D)	−0.47 ± 0.30 (−1.54, 0)	–
Corneal spherical aberration (6 mm)	0.24 ± 0.10 (0.07, 0.47)	–
Ocular spherical aberration (4 mm)	–	−0.03 ± 0.07 (−0.23, 0.14)
UDVA (log MAR)	0.54 ± 0.40 (0.10, 2.30)	0.05 ± 0.07 (−0.1, 0.2)
CDVA (log MAR)	0.35 ± 0.44 (0, 2.30)	0.03 ± 0.05 (0, 0.2)
UIVA (log MAR)	–	0.04 ± 0.06 (−0.10, 0.2)
UNVA (log MAR)	–	0.15 ± 0.07 (0, 0.3)

UDVA, uncorrected distance visual acuity; CDVA, corrected distance visual acuity; UIVA, intermediate visual acuity; UNVA, uncorrected near visual acuity.

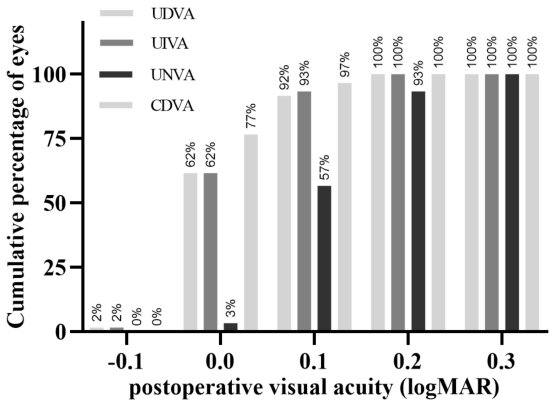

FIGURE 1
Cumulative percentage of eyes that achieved a cumulative value of monocular uncorrected distance (5 m), intermediate (80 cm), and near (40 cm) visual acuity, and corrected-distance visual acuity in logarithmic units. UDVA, uncorrected distance visual acuity; UIVA, intermediate visual acuity; UNVA, uncorrected near visual acuity; CDVA, corrected distance visual acuity.

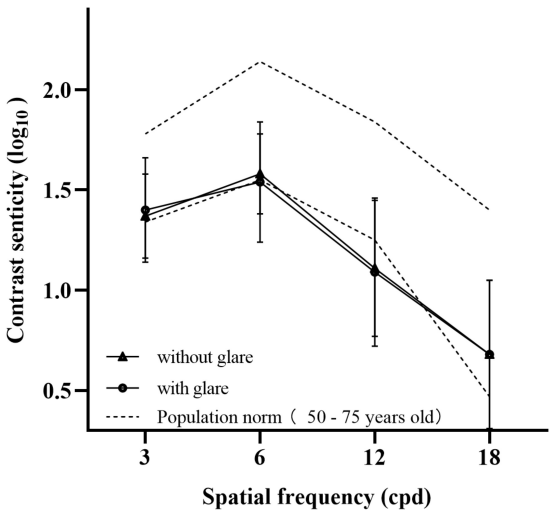

FIGURE 2
Mean value of contrast sensitivity without glare (triangle) and contrast sensitivity with glare (circle) at spatial frequencies of 3, 6, 12, and 18 cpd. The results were compared with the normal value defined previously (dotted line).

Visual quality

According to the results of this subjective visual quality questionnaire survey, all the patients were very satisfied with their current vision. Approximately 65.1% (28/43) of them never wear glasses, and 34.9% (15/43) occasionally wear glasses (Figure 3A). The visual symptoms of the operative eyes, if any, were mainly glare, halos, and starbursts. However, these had no significant effect on daily life and work (Figure 3B).

The objective visual quality values of OSI, MTF cutoff, SR were 1.01 ± 0.65, 38.92 ± 10.52, 0.20 ± 0.07, respectively. All these values suggested that the patients had excellent objective visual quality after the operation.

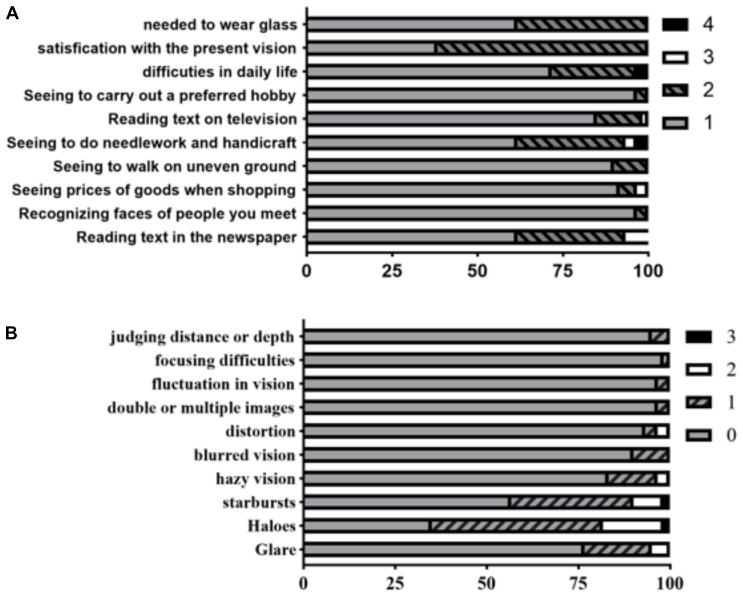

FIGURE 3
The Catquest-9SF questionnaire perceived difficulty scores in performing daily-life activities. There are four (summary scoring value) response options for the perceived difficulty levels as follows: 4 = very great difficulty; 3 = great difficulty; 2 = some difficulty; 1 = no difficulty **(A)**. The Quality of Vision (QoV) questionnaire were asked to rate 10 dysphotopsia items with 4 response levels (0, 1, 2, 3; higher score means worse photic phenomena) **(B)**.

TABLE 2 The relationship between preoperative corneal spherical aberration and some postoperative parameters of visual quality using Spearman's correlation analysis.

	Preoperative corneal spherical aberration (6 mm)		Postoperative ocular spherical aberration (4 mm)	
Parameters	*r* value	*P*-value	*r* value	*P*-value
UDVA	0.114	0.387	−0.089	0.498
UIVA	0.035	0.791	−0.170	0.195
UNVA	−0.403	0.001*	−0.129	0.327
CDVA	0.141	0.283	−0.010	0.938
OSI	0.050	0.704	0.076	0.565
MTF cutoff	−0.088	0.505	−0.078	0.551
SR	−0.087	0.511	−0.088	0.503
3 cpd	−0.083	0.527	−0.114	0.386
6 cpd	−0.054	0.681	−0.110	0.404
12 cpd	−0.096	0.463	−0.199	0.127
18 cpd	−0.300	0.020*	−0.055	0.676
3 cpd (with glare)	−0.085	0.520	−0.072	0.584
6 cpd (with glare)	−0.146	0.266	−0.171	0.192
12 cpd (with glare)	−0.225	0.084	−0.124	0.346
18 cpd (with glare)	−0.360	0.005*	−0.162	0.216

UDVA, uncorrected distance visual acuity; UIVA, intermediate visual acuity; UNVA, uncorrected near visual acuity; CDVA, corrected distance visual acuity; OSI, objective scatter index; MTF, modulation transfer function; SR, Strehl ratio; cpd, cycle/degree; *r*, correlation coefficient. *$P < 0.05$.

Higher-order aberration

The mean corneal spherical aberrations of 6-mm measurement range before and after the operation were 0.24 ± 0.10 μm (ranging from 0.07 to 0.47 μm) and 0.22 ± 0.12 μm (ranging from 0.01 to 0.51 μm), respectively, with no significant difference between them ($P > 0.05$). The mean postoperative ocular spherical aberration of 4-mm measurement range was −0.03 ± 0.07 μm, ranging from −0.23 to 0.14 μm. The mean postoperative ocular coma, trefoil, and secondary astigmatism were 0.15 ± 0.10 μm (range:

TABLE 3 Spearman correlation (A) and multiple linear regression (B) were used to analyze the impact of preoperative corneal spherical aberration, age, axial length, corneal astigmatism, postoperative sphere, cylinder, ocular coma, trefoil, and secondary astigmatism on UNVA.

A. Spearman's correlation analysis was used to analyze the factors affecting UNVA		
	r value	*P*-value
Preoperative corneal spherical aberration	−0.403	0.001**
Age	−0.091	0.491
Axial length	−0.162	0.216
Preoperative corneal astigmatism	−0.096	0.465
Postoperative sphere	0.320	0.013**
Postoperative cylinder	−0.038	0.772
Postoperative ocular coma	0.092	0.483
Postoperative ocular spherical aberration	−0.129	0.327
Postoperative ocular trefoil	0.137	0.296
Postoperative ocular secondary astigmatism	−0.205	0.116**

B. After the spearman's correlation analysis, factors with $P < 0.2$ were included in the further multiple linear regression					
Parameters	*b*	Standard error	β	*t* value	*P*-value
Preoperative corneal spherical aberration	−0.223	0.087	−0.316	−2.549	0.014
Postoperative ocular secondary astigmatism	−0.131	0.125	−0.127	−1.053	0.297
Sphere	0.028	0.017	0.202	1.634	0.108

UNVA, uncorrected near visual acuity. **$P < 0.2$.

0.01–0.44 μm), 0.21 ± 0.10 μm (range: 0.05–0.50 μm), and 0.09 ± 0.07 μm (range: 0.01–0.26 μm), respectively.

The relationship between spherical aberration and visual quality parameters

Spearman's correlation analysis was used to evaluate the relationship between preoperative corneal spherical aberration and postoperative ocular spherical aberration with the postoperative parameters of visual quality (UDVA, UIVA, UNVA, CDVA, OSI, MTF cutoff, SR, and CS). Preoperative corneal spherical aberration was negatively correlated with postoperative UNVA and contrast sensitivity at a spatial frequency of 18 cpd under non-glare and glare ($r = -0.403$, -0.300, -0.360; all $P < 0.05$). This meant that an increase in preoperative corneal spherical aberration resulted in better postoperative UNVA (the logarithmic value of UNVA was lower), while the contrast sensitivity at 18 cpd became worse. There was no correlation between preoperative corneal spherical aberration and all the other parameters (all $P > 0.05$). Additionally, no correlation between postoperative ocular spherical aberration and any of the visual quality parameters was present (all $P > 0.05$) (Table 2).

Factors affecting near vision

Spearman's correlation analysis was used to analyze the factors affecting UNVA. The influencing factors included preoperative corneal spherical aberration, age, axial length, corneal astigmatism, postoperative sphere, cylinder, ocular coma, trefoil, and secondary astigmatism. After the spearman's correlation analysis, factors with $P < 0.2$ were included in the further multiple linear regression, namely preoperative corneal spherical aberration ($r = -0.403$; $P = 0.001$), postoperative sphere ($r = 0.302$; $P = 0.013$), and secondary astigmatism ($r = -0.205$; $P = 0.116$). Lastly, the preoperative corneal spherical aberration was the only factor influencing UNVA after multiple linear regression analysis (Tables 3A,B).

Discussion

In this study, patients obtained satisfactory UDVA and UIVA values, but their UNVA was slightly insufficient, similar to previous studies (9, 10). The present study was first found that preoperative corneal spherical aberration was the only factor influencing UNVA after implanted with the TECNIS Symfony IOL, and it was negatively correlated with postoperative UNVA (logMAR visual acuity), which indicates that the greater the preoperative corneal spherical aberration, the better the UNVA. It was thought that this was caused by the larger corneal spherical aberration retaining more positive ocular spherical aberration after cataract surgery, which provided synergistic depth of focus. The depth of focus then extended to the front of the retina, compensating for the poor near vision. This result can partly explain the clinical doubts, why some patients have excellent near visual acuity, and why some have poor near visual acuity.

We also found that preoperative corneal spherical aberration was negatively correlated with contrast sensitivity at a spatial frequency of 18 cpd, indicating that the larger the corneal spherical

aberration, the worse the contrast sensitivity under 18 cpd spatial frequency. This characteristic is similar to that of the visual quality of a monofocal pseudophakic eye. After implantation of negative-aberration IOLs in pseudophakic eyes, the ocular spherical aberration decreases, and the contrast sensitivity becomes better than that of no-aberration IOLs (3, 12). Therefore, we summarized that large preoperative corneal spherical aberration and residual positive ocular spherical aberration can improve near vision but impair contrast sensitivity at high spatial frequencies. This finding can guide clinicians to select appropriate IOLs based on the patient's preoperative corneal spherical aberration and vision requirements. For patients with large preoperative plus spherical aberration, better near vision could be expected. On the contrary, if the preoperative spherical aberration is relatively small, the postoperative refraction should be targeted more myopic to achieve better near vision, or a multifocal IOL with high near-add as an alternative.

In addition, it was found in this study that preoperative corneal spherical aberration did not correlate with contrast sensitivity under 3, 6, 12 cpd spatial frequency and objective visual quality parameters, as measured by OQAS. This explains why there are no correlations between preoperative corneal spherical aberration and postoperative ocular spherical aberration with subjective visual quality parameters measured by the two questionnaires. A majority of our patients were satisfied with their visual acuity and visual quality in their daily lives. Son et al. (13) and Xu et al. (14) have found that EDOF-IOL is more tolerant to decentration and refractive errors than bifocal and monofocal IOLs. Therefore, when cataract patients want to take off their glasses after surgery and are sensitive to photic symptoms, EDOF-IOLs may be a better choice. Besides, Ruiz-Alcocer et al. (15, 16) assessed that the EDOF-IOL optical properties were more stable when a myopic ablation is introduced.

This study has some limitations. First, including both eyes from some patients may have biased the results. However, the measured parameters were analyzed individually in each eye, which mitigated this shortcoming to some extent. Second, only a type of intraocular lens was enrolled. Whether this result can be extended to other types of multifocal intraocular lenses needs further research. Lastly, although the −0.27 μm asphericity of the TECNIS Symfony IOL was designed based on a corneal spherical aberration in the range of 6 mm, it can be assumed that the measured value of ocular spherical aberration in the 4-mm range is valid because the pupils of elderly individuals become smaller over time, so the ocular spherical aberration better reflects the real-life state (17).

In summary, positive spherical aberration will benefit near-visual acuity by reducing contrast sensitivity at high spatial frequency when implanted with the TECNIS Symfony IOL.

Data availability statement

The original contributions presented in this study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by the Institutional Ethics Committee of Wenzhou Medical University, Zhejiang Province, China. The patients/participants provided their written informed consent to participate in this study.

Author contributions

DW participated in the topic selection, design, data analysis, interpretation, and wrote the manuscript. CL, WG, ZL, and YiZ participated in data collection and data analysis. YuZ participated in topic selection, design, data analysis, interpretation, and manuscript revision. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Quality of vision and outcomes after bilateral implantation of pseudo-non diffracting beam IOL

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Purpose: To analyze the objective and subjective visual performances of a new hybrid refractive/aspheric extended depth of focus (EDOF) intraocular lens (IOL).

Methods: In this monocentric prospective study patients with bilateral cataracts underwent cataract surgery and were implanted with a Lucidis IOL (SAV-IOL SA, Neuchâtel, Switzerland) in both eyes, 1 week apart from each other. At 3months from implantation postoperative evaluations included monocular and binocular uncorrected and distance-corrected distant (4m), intermediate (80cm, 67cm) and near (40cm) visual acuities (UDVA/DCVA, UI80-67VA/DCI80-67VA, UNVA/DCNVA), binocular defocus curves, halometry, contrast sensitivity and objective quality-of-vision measurements. Also, patients were also asked to complete the national eye institute refractive error quality of life (NEI-RQL-42) questionnaire.

Results: Twenty-five patients (50 eyes) were included. The mean postoperative binocular UDVA, UI80VA, UI67VA and UNVA were-0.02±0.13, 0.05±0.09, 0.05±0.08 and 0.03±0.1 LogMar, and did not significantly differ from their corrected counterparts. On binocular defocus curves a VA ≥0.05LogMar was found between +0.50 and−2.50 D of vergence, whereas the mean distance from the central stimulus on halometry was 1.23±0.01. Mean ocular and corneal radical mean square at 4mm were 0.31±0.28 and 0.19±0.07, respectively; whereas the mean Strehl ratio was 0.2±0.09.

Conclusion: Lucidis IOLs demonstrated excellent visual performances, especially at close distances while maintain good quality of vision, contrast sensitivity, and overall patient-satisfaction.

KEYWORDS

cataract, spectacle independence, near vision, premium IOLs, extended depth of focus IOL

1. Introduction

In the last decades premium multifocal intraocular lenses (MFIOL) have been designed to meet the patients' need for spectacle independence, however, these lenses frequently led to a bad quality of vision, especially at near and/or far distances. Other issues that have emerged through the years with these lenses consisted in the decrease of both contrast sensitivity and night vision, as well as in the frequent manifestation of visual phenomena such as halos, glare and starburst (especially with diffractive MFIOLs) (1–4). Recently, the need to overcome these concerns has

led to the development of new technologies able to generate a single focal point with an extended depth of focus (EDOF). While improving far- and intermediate-distance spectacle independence, EDOF-IOLs are also said to be able to induce fewer visual phenomena (5, 6). However, these lenses are also known for the need of a small amount of positive spectacle correction at close distances (7).

The Lucidis IOL (Swiss Advanced Vision, SAV-IOL SA, Neuchâtel, Switzerland) is a new special hybrid refractive/aspheric EDOF IOL that has been created to overcome the limitation of near vision. However, until now only few studies have analyzed the outcomes of this lens and none of these has examined neither the defocus curve, nor the objective visual quality (8–10). The aim of this study was to examine the visual performances of the Lucidis IOL focusing on near vision, defocus curves, subjective and objective quality of vision and on the patient's satisfaction 3 months after the surgery.

2. Patients and methods

This prospective interventional monocentric study adhered to the tenets of the Declaration of Helsinki and was approved by the local Ethics Committee (protocol 54,139). A written informed consent was obtained from all participating subjects after thorough explanation of the benefits and the risks related to the implantation of the IOL in study.

Inclusion criteria were the presence of significant bilateral cataracts, defined by a preoperative corrected distance visual acuity (DCVA) of 0.20 logMAR (20/32 Snellen) or worse, availability to undergo both surgeries 1 week apart from each other, an axial length between 22 and 23 mm and a preoperative regular corneal astigmatism of less than 1.00 diopter (D). We excluded patients younger than 18, those with any other concomitant or previous ocular disease, irregular astigmatism and those who had undergone previous ocular surgeries. Patients that had experienced intraoperative complications were excluded from the final analysis.

3. Clinical protocol

All patients underwent a thorough ophthalmological examination before surgery and 3 months after IOL implantation. The preoperative evaluation included measurement of monocular and binocular uncorrected and distance-corrected distant and near visual acuity (UDVA/DCVA at 4 m and UNVA/DCNVA at 40 cm, respectively) using the CSO Vision Charts V14.0 (CSO, Florence, Italy), measurement of the subjective refractive error, corneal tomography (MS-39, CSO, Firenze, Italy), optical biometry (Lenstar 900; Haag-Streit Diagnostics, Koeniz, Switzerland), Goldmann applanation tonometry, slit-lamp anterior segment examination, fundus examination under dilation and optical coherence tomography at the retinal plane (Spectralis OCT Heidelberg Engineering Inc., Heidelberg, Germany). Biometric values were used as inputs in the Kane formula to calculate the lens power, which in turn was selected targeting emmetropia (11).

Besides the binocular and monocular UDVA and DCVA at 4 m and the UNVA and DCNVA at 40 cm, the 3 months-postoperative visit, also included the uncorrected and best distance corrected intermediate visual acuity at 80 cm and 67 cm (UI80VA, DCI80VA, UI67VA and DCI67VA), binocular defocus curves, contrast sensitivity (CS) testing under photopic (80 cd/m2), mesopic (6 cd/m2), and scotopic (3 cd/m2) light conditions (CSV 1000 HGT; Vector Vision, Greenville, OH), ocular optical quality analysis by Pyramidal WaveFront-based sensor aberrometer (Osiris T Aberrometer, CSO, Firenze, Italy) and the halo test (Aston Halometer). After a slit lamp examination (to exclude the presence of posterior capsular opacity - PCO), patients were also asked to complete the National Eye Institute Refractive Error Quality of Life Instrument 42 (NEI-RQL-42) questionnaire.

Binocular defocus curves were obtained between +1.50 to −3.50 D using regular shifts of 0.50 D with respect to the 4 m DCVA and recording the best visual acuity for each step. To avoid memory effects, presenting letter sequences were randomized and patients' eyes were occluded between each lens presentation (12). To analyze the ocular optical quality we used the Osiris T Aberrometer studying the ocular Root Means Square (RMS) and the Point-Spread-Function Strehl ratio (PSF Strehl ratio), which is defined as the ratio between the peak image intensity of the patient's eye and that of an ideal eye (i.e., maximal intensity), limited only by diffraction (13). On the other hand, the purpose of the halo test is to measure in degrees how much a glaring source of light clouds a target. The halometer consisted of a light source (LED, Golden Dragon Pluc LCW W5AM.PC, 5000 K color temperature; Osram Licht AG, Munich, Germany) located in the center of an iPad4 tablet on which 0.3 logMAR (Snellen 20/40) letters were presented and moved toward the light source in 0.05-degree steps (14). To identify the halo area, patients stayed at 2 meters from the halometer in a dark room and were asked to recognize in succession the letters in six directions of orientation and separated by 60°. The cut-off value was collected for each direction. On slit lamp examination, if a grade 3 or higher PCO (According to Congdon's study), (15) was detected, this was treated by YAG-laser capsulotomy and the 3 months evaluation was postponed 10 days thereafter. Finally, patients completed the NEI RQL-42 questionnaire to evaluate their quality of life in relation to their refractive error correction and visual acuity recovery (16). The questionnaire consists of 13 subscales with 42 items in 16 different question/response category formats.

3.1. Surgery

All cataract surgeries were performed by the same surgeon (E.P.) under topical anesthesia. A 2.2 mm corneal tunnel was created on the steepest meridian and was followed by a standard phaco-chop technique-surgery using the Stellaris phaco-platform (Bausch & Lomb Inc., Rochester, NY). The 12.4 mm Lucidis IOL was then placed in the capsular bag. The second surgical procedure was performed within 7 days from the first one. Prophylaxis consisted of an antibiotic and a nonsteroidal anti-inflammatory eye drop whereas the postoperative therapy also included topical steroid drops.

3.2. IOL

The Lucidis lens (Swiss Advanced Vision, SAV-IOL SA, Neuchâtel, Switzerland)is a single-piece foldable hydrophilic acrylic lens with an optical diameter of 6.0 mm and a total diameter of 10.8 mm or 12.4 mm. The IOL has square edges with closed loop haptics and is

designed to be implanted in the capsular bag. Its hybrid refractive/aspheric design, where a 1-mm aspheric central zone is surrounded by a 6-mm refractive ring (Figure 1), allows for a + 3.0 D addition power on top of the normal distance power, which ranges from +5.0 D to +30.0 D. In this study only the 12.4 mm-IOL was implanted in order to avoid IOL decentration.

3.3. Statistical analysis

Statistical analysis was performed using the IBM SPSS software version 24 for MacIntosh (IBM-SPSS). The Shapiro–Wilk test was used to determine data distribution. All quantitative results are reported as mean ± standard deviation for parametric distribution and as median ± interquartile range for non-parametric distribution. The t test for parametric distribution and the Mann–Whitney test for non-parametric distribution were used to compare the data. A p value lower than 0.05 was considered statistically significant.

The sample size was calculated based on monocular and binocular DCNVAs obtained from previous studies. With an estimated standard deviation of 0.13, a sample size of 50 patients produces a 95% confidence interval in DCNVA of 0.037. When the estimated standard deviation is 0.14, a sample size of 25 gives a 95% confidence interval of 0.06 (17). Postoperative data are presented at 3 months from implantation.

4. Results

Twenty-five patients (50 eyes) with a mean age (±SD) of 68 ± 10 years were included. Thirty-six percent of patients were male and 64% were female. The average spherical dioptric power of the implanted IOLs was 19.01 ± 4.29 D (median: 19.0 D, range: 12.5 to 26.5 D).

There were no major postoperative or intraoperative complications.

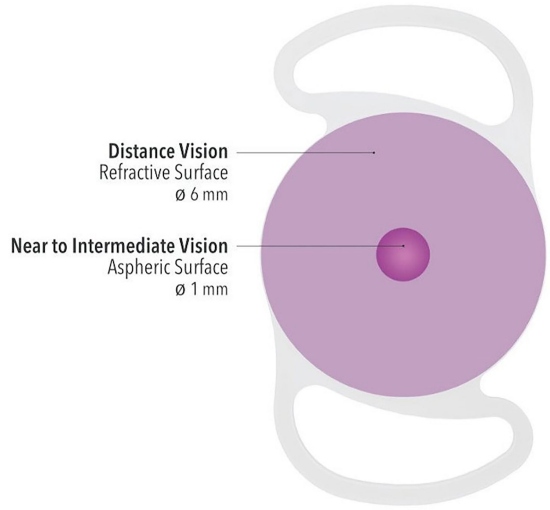

FIGURE 1
Schematic graph of the optic technology of Lucidis IOL with a central aspheric surface for near to intermediate vision and a larger refractive surface for distance vision.

At 3-months from implantation, a grade 3 PCO was found in 1 eye (2.1%) and a YAG-laser capsulotomy was performed.

4.1. Visual outcomes

The mean postoperative subjective refractive spherical equivalent was −0.36 ± 0.39 D and laid within ±0.51 D in 58% of eyes and within ±1.00 D in 100% of cases.

Table 1 summarizes both the monocular and binocular uncorrected and distance corrected VA-results.

The differences between the mean binocular and monocular UDVA and UI80VA, UI67VA and UNVA were not statistically significant ($p = 0.26$, $p = 0.24$ and $p = 0.24$ and $p = 0.31$, $p = 0.83$ and $p = 0.84$, respectively).

4.2. Defocus curve

Figure 2 shows the mean binocular defocus curve at 3 months after surgery. Visual acuity was found to be higher than or equal to 0.05 logMar between +0.50 and − 2.50 D of vergence, showing the deepest point at −1.50 D. However, neither the difference in VA between 0.00 and − 1.5 D, nor that between −1.5 and − 2 D, were statistically significant ($p = 0.08$ and $p = 0.11$, respectively).

TABLE 1 Postoperative monocular and binocular visual acuities.

	Monocular VA	p	% of patients reaching a VA>20/40	% of patients reaching a VA>20/25
UDVA	0.04 ± 0.13	0.17	93	54
DCVA	−0.04 ± 0.08		100	89
UI80VA	0.07 ± 0.09	0.53	98	46
DCI80VA	0.09 ± 0.09		98	37
UI67VA	0.08 ± 0.11	0.44	87	41
DCI67VA	0.11 ± 0.11		83	43
UNVA	0.07 ± 0.12	0.82	91	41
DCNVA	0.07 ± 0.11		89	46
	Binocular VA	**p**	**% of patients reaching a VA>20/40**	**% of patients reaching a VA>20/25**
UDVA	−0.02 ± 0.13	0.87	100	70
DCVA	−0.07 ± 0.09		100	87
UI80VA	0.05 ± 0.09	0.75	96	52
DCI80VA	0.06 ± 0.07		100	42
UI67VA	0.05 ± 0.08	0.89	96	52
DCI67VA	0.04 ± 0.09		96	57
UNVA	0.03 ± 0.1	0.99	100	65
DCNVA	0.00 ± 0.08		100	74

p values show no statistical differences between distance corrected and uncorrected visual acuities.

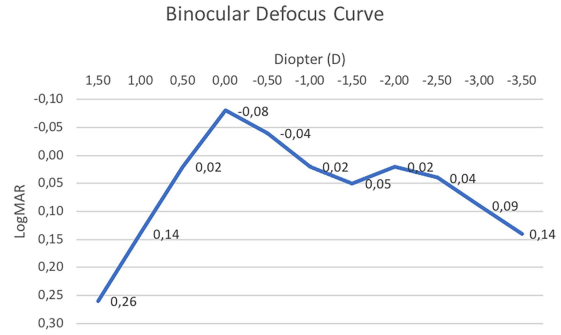

FIGURE 2
Mean binocular defocus curve.

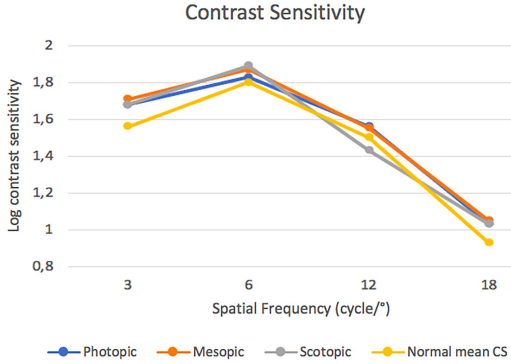

FIGURE 3
Postoperative contrast sensitivity function measured under scotopic, mesopic and photopic conditions.

4.3. Contrast sensitivity outcomes

Figure 3 presents the binocular CS function measured under scotopic, mesopic, and photopic light conditions. There were no statistically significant differences among the three conditions at any of the studied spatial frequencies (e.g., in the scotopic vs. photopic condition at 12 cpg the p value was 0.26). Mean CS values of a population ranging from 50 to 75 years of age were also taken into account and the performance of this IOL was statistically significant better at 3 cpd in photopic, mesopic and scotopic condition $p = 0.01$, $p = 0.004$ and $p = 0.03$, respectively (18).

4.4. Halometry

The mean distance from the central stimulus was 1.23 ± 0.01. Figure 4 presents the mean halometric cut-off values for each of the six axes.

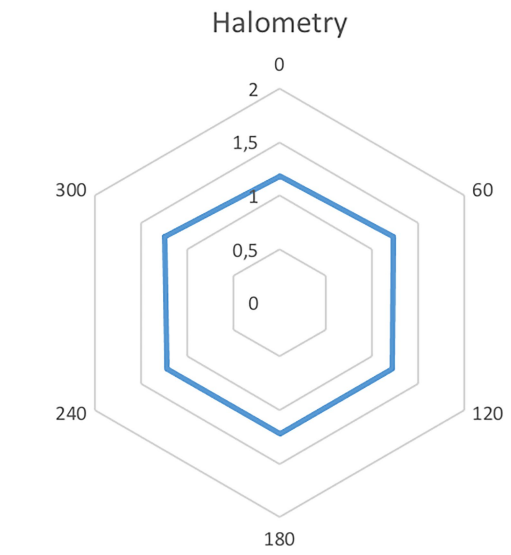

FIGURE 4
Six-vertex mean halometry for the hybrid refractive/aspheric Lucidis IOL.

4.5. Quality of vision parameters

At 3 months from the operation the mean ocular and corneal RMS at 4 mm were 0.31 ± 0.28 (range: 0.09–1.5) and 0.19 ± 0.07 (range: 0.07–0.5), respectively; whereas the mean PSF Strehl ratio was 0.2 ± 0.09 (range: 0.03–0.41).

4.6. Quality of life outcomes

The NEI RQL-42 evidenced high subjective satisfaction results for all the items, especially for suboptimal correction, activity limitations, glare, appearance, far vision, dependence on correction and satisfaction with correction (Table 2).

5. Discussion

Extended depth of focus technology is among the most effective proposed methods to enhance spectacle independence after cataract surgery. Nevertheless, when it comes to near vision, these lenses are usually outperformed by MFIOLs, which, however, are often burdened by annoying light phenomena (1, 2).

In this study, the Lucidis IOL has shown to be able to strengthen the near-distance VA at the expense of a slight decrease in the intermediate vision. Indeed, 74, 57 and 42% of patients reached a binocular VA higher than 20/25 at 40, 67 and 80 cm, respectively. This result was confirmed by the trend of the defocus curve and seems to be in accordance with the current literature (4–6). Authors would like to underline that these results appear to be in agreement with the available literature on Lucidis IOLs, as to our knowledge currently no study has ever reported the DCIVA, but only the UIVA (without specifying how many cm it was run) and none performed defocus curves.

Although a direct comparison was not performed, when considering the results of other EDOF IOLs, it is striking how these are usually characterized by a regular downslope in the myopic portion of the defocus curve, reaching the lowest performances

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TABLE 2 Postoperative QoL scores on the 13 subscales of the NEI-RQl-42.

Parameter	
Clarity of vision	
Mean ± SD	78.50 ± 26.97
Median (range)	100 (0.00 to 100.00)
Expectations	
Mean ± SD	52.94 ± 44.28
Median (range)	50.00 (0.00 to 100.00)
Near vision	
Mean ± SD	78.57 ± 24.19
Median (range)	75.00 (0.00 to 100.00)
Far vision	
Mean ± SD	81.74 ± 25.75
Median (range)	100.00 (0.00 to 100.00)
Diurnal fluctuations	
Mean ± SD	76.61 ± 28.09
Median (range)	87.50 (0.00 to 100.00)
Activity limitations	
Mean ± SD	91.67 ± 23.36
Median (range)	100.00 (0.00 to 100.00)
Glare	
Mean ± SD	86.76 ± 21.86
Median (range)	100.00 (50.00 to 100.00)
Symptoms	
Mean ± SD	70.15 ± 28.51
Median (range)	75.00 (0.00 to 100.00)
Dependence on correction	
Mean ± SD	72.38 ± 36.21
Median (range)	100.00 (0.00 to 100.00)
Worry	
Mean ± SD	52.18 ± 35.40
Median (range)	50.00 (0.00 to 100.00)
Suboptimal correction	
Mean ± SD	93.75 ± 13.86
Median (range)	100.00 (50.00 to 100.00)
Appearance	
Mean ± SD	84.19 ± 30.15
Median (range)	100.00 (0.00 to 100.00)
Satisfaction with correction	
Mean ± SD	78.89 ± 18.75
Median (range)	80.00 (40.00 to 100.00)

around −2.50 D; indeed, patients often need a spherical addition of 1 D in order to achieve the optimal near-distance VA (7, 19, 20). Meanwhile, in our study, at −2.50D of vergence, the defocus curve showed a mean VA of little less than 0.05 LogMar. With regards to intermediate VAs, on the other hand, our results do not significantly differ with those of other EDOF IOLs.

When considering an extended range of vision (ERV) IOL (21) such as the TECNIS Symphony, it seems like Lucidis IOLs perform better at far and near distances, whereas the former performs better at intermediate distances (22, 23).

Surprisingly, the Lucidis IOL showed comparable performances to the tri-quadrifocal Enlighten Panoptix IOL at the 40 cm distance (0.14 ± 0.04 and 0.00 ± 0.08 for Enlighten and hybrid IOLs, respectively) and performed even better than this IOL at intermediate distances (0.10 ± 0.03 and 0.04 ± 0.09 for Enlighten and Lucidis IOL, respectively) (22).

This outstanding performance is probably related to the special hybrid design of these lenses. The main optical propriety is due to the central aspheric portion of this IOL which is able to create a peak of light *via* constructive light wave interference, whereas the periphery maintains a refractive surface. The lens therefore acts as an axicon (Bessel like ray of light). The system altogether results in the formation of a pseudo non diffracting beam which starts to diverge after some distance from the lens itself, therefore covering the whole range of vision (i.e., from near-intermediate to far distances). An axicon lens is an optical element first introduced in 1954 by McLeod, (24) able to transform a laser beam into a ring-shaped distribution, resulting in a beam of focal fields that allow a continuous vision from intermediate to short distances.

Interestingly, these visual performances are achieved while preserving a good quality of vision. Indeed, the ocular RMS was 0.31 ± 0.28, with corneal component of 0.19 ± 0.07 and a mean internal RMS of 0.12 (i.e., ocular RMS – corneal RMS). The RMS is closely related to Zernike polynomials and its minimum value is 0, which represents the ideal wavefront condition. Even though the measurement was taken using different instruments, the internal RMS of the Lucidis IOL results to be lower than both the ZXR00s-TECNIS Symphony's (0.15 ± 0.06) and the tri-quadrifocal Enlighten Panoptix's (0.18 ± 0.06), measured in a previous study of ours (22). The RMS results of the current study differ from those found by Rabinovich et al. (10) on Lucidis IOLs. However, the latter study has several limitations, such as its retrospective design and the absence of a precise description of what RMS evaluation had been carried out and what instrumentation was used, so a reliable comparison between our results is not feasible. Nonetheless, the total RMS found in this study (i.e., 0.18 ± 0.1) seems to be better than that obtained with aberrometric EDOFs, multifocal diffractive and refractive IOLs (13).

Lucidis IOLs however, showed worse performances than the aberrometric EDOF Mini Well IOL (SIFI S.p.A., Catania, Italy) and the Enlighten IOL in terms of mean PSF Strehl ratio and CS at the lower spatial frequencies (3, 22).

In addition, halometry results show that the Lucidis IOL performs very similarly to monofocal IOLs for all mean cut-off values (17). Even though no direct comparison has been performed, the NEI RQL-42 questionnaire-results seem to show higher subjective satisfaction with the Lucidis IOL than with aberrometric EDOF, ERV and Enlighten IOLs with regards to "glare" evaluation. Despite patients reporting good levels of satisfaction after bilateral implantation of this hybrid lens, all other items in the questionnaire seem to show better results with aberrometric EDOF IOLs (17, 22).

Among the limitations of this study it is worth mentioning its limited number of patients and the absence of a direct comparison with the other type of IOLs.

To conclude, Lucidis IOLs demonstrated a good safety profile and excellent visual performances at all distances, but especially at near distances, while also allowing a good quality of vision.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by Comitato etico per la Sperimentazione Clinica (CESC) delle Province di Verona e Rovigo. The patients/participants provided their written informed consent to participate in this study.

Author contributions

All authors made substantial contributions to conception and design, acquisition of data, analysis, and interpretation of data. They all took part in drafting the article or revising it critically for important intellectual content and agreed to submit it to the current journal. All authors gave final approval of the version to be published and agreed to be accountable for all aspects of the work.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Beyond vision: Cataract and health status in old age, a narrative review

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Cataract is a leading cause of visual impairment in old age. Lens opacification is notoriously associated with several geriatric conditions, including frailty, fall risk, depression and cognitive impairment. The association is largely attributable to visual impairment, while other mechanisms, associated with extraocular comorbidity and lifestyle, might partly explain this correlation. Available literature suggests that cataract surgery may be effective in decreasing fall risk, improving depressive symptoms and limiting the risk of cognitive impairment and dementia incidence, although intervention studies on these outcomes are still limited. In this review we also emphasize the need to move from the concept of visual acuity to functional vision, especially in the context of the geriatric patient. Research is needed regarding the effect on the cited outcomes of different cataract treatment strategies, such as systematic bilateral versus monolateral surgery and use of different intraocular lenses.

KEYWORDS

cataract, cataract surgery, functional vision, quality of vision, elderly, frailty, intraocular lenses, accidental falls

Introduction

Cataract is the partial or total opacification of the lens, usually progressive and irreversible, leading to loss of vision with medical, social and economic implications. Typically occurring with advancing age, it is a frequent cause of age-related blindness and it is reversible through surgery (1).

It is estimated that 95 million people worldwide are affected by cataract (2). In 2020, the leading worldwide causes of blindness in patients aged 50 years and older were: cataract, followed by glaucoma, under-corrected refractive error, age-related macular degeneration, and diabetic retinopathy (3). To underline the importance of the disease, cataract is responsible for 50% of cases of blindness in middle- and low-income countries, which have poor access to primary care compared to 5% in developed countries (2, 4). The World Health Organization has estimated that with population growth and progressive aging in future years there will be an increase of visual impairment attributable to cataract (5). Furthermore, up to two-thirds of adults with visually significant cataract have been estimated to be undiagnosed, and half of these cases have bilateral visual impairment, often resulting in significant functional impairment (6). Overall, the cited data underline the huge and probably underestimated impact of cataract on visual functioning of older adults. The present narrative review is aimed at assessing the association of

cataract with different aspects of health status of aging population, including frailty, falls, fracture, depressive symptoms, and cognitive impairment. Accordingly, we describe potential impact of cataract surgery in old age, and discuss synergies between ophthalmologic and geriatric care possibly resulting in a reduced burden of the disease.

Cataract, frailty, falls and fractures

Cataract and frailty

Frailty is defined as a clinical state in which there is an increase in an individual's susceptibility to developing negative health-related events when exposed to endogenous or exogenous stressors (7). Two main models have been established to define frailty: the *physical frailty phenotype* proposed by Linda Fried and the *deficit accumulation index* elaborated by Kenneth Rockwood (8).

However it is defined, frailty is associated with an increased risk of adverse events, including mortality, disability, and hospital admission. Falls are included among frailty-associated adverse events and, in turn, are associated with fragility fractures, head trauma, disability and mortality risk.

The possible role of cataract as a global frailty biomarker is underlined by data which shows an association with mortality risk (9). Nevertheless, data regarding the association between cataract surgery and mortality are not consistent. In fact, some results suggest a reduced mortality risk after cataract surgery (10), other works show a reduced mortality risk only among the patients who gained better visual acuity (11); on the contrary, some studies suggest a neutral effect after adjusting for confounders (12). Finally, a cohort study has also documented a greater mortality risk among patients that underwent cataract surgery (13).

As a matter of fact, cataract and frailty are both correlated with aging and often coexist. Beyond the parallelism due to demographic factors, an association has been identified between visual impairment and incident physical frailty, independently of coexistent diseases and possible confounders (14); in this work, visual impairment was correlated with a future development of frailty after a 4-year follow-up among non-frail older patients, placing cataract as the most common reversible cause of visual impairment.

On the other hand, a specific association has been detected between cataract and physical frailty in cross-sectional studies, also independently of visual impairment (15), suggesting shared biological mechanisms which include similar age-associated biochemical alterations involving the lens and skeletal muscle protein structures. The cited authors found an association between nuclear cataract in men and a slower gait time ($p = 0.01$) as well as a poorer frailty index score ($p = 0.01$); however cortical and posterior subcapsular cataract in women was correlated with a lower peak expiratory flow rate ($p < 0.01$). Consistently, in a different sample of community-dwelling older patients, there was a significant difference in cataract risk between non-frail (31%), prefrail (37%), and frail groups (42%) (16).

In specific conditions the association between cataract and frailty has known biological explanation. For example, pseudoexfoliation (PEX) syndrome is associated both with an increased risk of nuclear cataract and cataract surgery and with a higher prevalence of cardio- and cerebrovascular disorders, sensorineural hearing loss and Alzheimer-related dementia (17–21). Moreover, posterior subcapsular cataracts may be associated with diabetes mellitus and with steroid treatment, which in turn may correlate with frailty risk independently of lens opacification (22). Other mechanisms, including similar protein aging in lens and in muscle, have been suggested to explain the potential role of cataract as frailty biomarker independently of low vision (15). Further research in this field is needed.

Cataract and fall risk

Several observational and some randomized studies have examined the association between cataract surgery and fall risk (23–28). Table 1 summarizes the main studies cited in this review.

Normal aging is accompanied by visual dysfunctions that correlate with fall risk, including reduced visual acuity, reduced contrast sensitivity, reduced depth perception, visual field contraction and prolonged glare recovery (29). Similarly, several specific age-associated ocular diseases have a well-established correlation with recurring fall events, with cataract being both the most prevalent, as previously discussed, and one of the most easily treatable, at least in economically-stable countries.

Vision contributes not only to the detection of tripping hazards on the ground, but also to a patient's posture and balance through visual-sensory inputs modulated at the cerebellar level, where they are integrated with a proprioceptive signal. Good vision is also associated with high levels of physical activity, thus suggesting its enabling effect on health through the biomechanical benefits of physical exercise on the musculoskeletal system, resulting in a lower fall risk (30). Consistent with these data, a large multinational study has observed a graded association between vision impairment severity and sarcopenia (i.e., loss of muscle mass in old age) (31).

Most literature shows that first-eye cataract surgery reduces the risk of falls in older people, but the effect of second-eye cataract surgery is less clear (25, 27, 32).

Some studies have been summarized in a recent meta-analysis, which documented that fall risk could be reduced by one third after cataract extraction (in comparison with the pre-surgery period), although a significant between-study heterogeneity was observed (27). These data are consistent with the single randomized controlled trial that reported a significant reduction of rate of falls among randomized patients undergoing expedited surgery compared with a postponed-list group, in a 12-month follow-up (25). Moreover, the treatment group showed a better outcome with regard to anxiety, depression and quality of life. Conversely, no significant fall rate decrease was observed after second-eye surgery, both in observational studies and in a single, although underpowered, randomized clinical trial, in spite of a decrease in visual disability and increase in quality of life observed in the latter study (23, 27). Somehow at odds with the cited data, a large Australian observational study found an increase in fall rate during the 2 years following first-eye cataract surgery, while waiting for the second-eye surgery, with a relative decrease only after the treatment of the second eye (28). These data are consistent with a US population-based study showing that, after a 2-year follow-up, older patients undergoing monolateral cataract surgery had a greater decline in motor function in comparison with a general older population without severe visual impairment, while this decline was not observed in the subgroup undergoing bilateral surgery (33). A recent cohort Australian study on patients referred for bilateral cataract surgery, confirmed an

TABLE 1 Summary of the studies regarding age-related cataract and main health outcomes.

Cataract and frailty							
Study design	First Author	Ref	Country	Publication year	Sample size	Main findings	Limitations
Cross-sectional							
	Klein BEK	15	United States	2006	2,370	Nuclear and cortical cataract in men are significantly associated with a poorer frailty index score, independently of visual acuity and systemic comorbidities. All cataract subtypes are associated with specific frailty indicators.	No standardized frailty measures. Exclusion of subjects with cataract surgery.
	Chen CY	16	Taiwan	2010	2238	Cataract prevalence is significantly different among non-frail, pre-frail and frail subjects.	Subjective assessment of frailty. No multivariate analysis. No significant difference between pre-frail and frail subjects.
Longitudinal							
	Zhu Z	9	China	2020	1,405	Age-related cataract is a predictor of a poorer 10-year survival independently of visual impairment, therefore representing a possible frailty biomarker	No formal frailty assessment. Limited statistical adjustment.
Cataract and falls							
Study design	First Author	Ref	Country	Publication year	Sample size	Main findings	Limitations
Longitudinal							
	Meuleners LB	28	Australia	2014	28,396	Risk of injurious falls is increased between first- and second-eye cataract surgery, and relatively decreased after second-eye surgery	Lack of a control group. Exclusion of subjects with unilateral surgery. Only severe falls recorded.
	Keay L	26	Australia	2022	409	Fall incidence is significantly decreased only after second-eye, not first-eye surgery.	Lack of a control group. Selected sample at enrollment.
Randomized controlled trial							
	Harwood RH	25	United Kingdom	2005	306	First eye cataract surgery reduces 1-year risk of recurrent fall, rate of falling and risk of fractures.	No effect on the risk of a first fall. Selected sample at enrollment.
	Foss AJE	23	United Kingdom	2006	239	Second-eye cataract surgery is followed by a non-significant decrease of 1-year fall rate, in spite of improved visual disability.	Underpowered study. No effect on the risk of a first fall.
Meta-analysis							
	Gutiérrez-Robledo LM	27	Mexico	2021	1,014	First-eye cataract surgery is followed by a decreased fall rate, second-eye surgery does not have significant impact.	Both clinical trials and before-after studies included. Few studies on second-eye surgery. Heterogeneous fall assessment.

(Continued)

TABLE 1 (Continued)

Cataract and fractures							
Study design	First Author	Ref	Country	Publication year	Sample size	Main findings	Limitations
Case series							
	Cox A	39	United Kingdom	2005	537	Older subjects with hip fracture have poorer vision than that documented in other older population, with cataract representing the most frequent cause.	Lack of a control group. No multivariate assessment.
Cohort							
	Tseng VL	42	United States	2012	1,113,640	Among older subjects with cataract, surgical treatment is associated with a lower adjusted 1-year hip fracture risk in comparison with no treatment.	Analysis based on administrative data. Treated group is sicker and has a higher absolute risk compared with non-treated, and a higher risk after surgery compared with the year before. No distinction between first-and second-eye surgery.
	Huang H-K	40	Taiwan	2019	115,944	Cataract is independently associated with an increased 6-year risks of osteoporosis and fractures.	Analysis based on administrative data, possible under-diagnosis of osteoporosis.
	Lim J-Y	41	Korea	2022	558,147	Older subjects treated with cataract surgery have a lower 10-year incidence of hip and vertebral fracture than non-treated ones.	No information on non-operated cataract. Analysis based on administrative data. Groups differ for covariates. No distinction between first-and second-eye surgery.
Cataract and depression							
Study design	First Author	Ref	Country	Publication year	Sample size	Main findings	Limitations
Case series							
	Mylona I	55	Greece	2021	150	Greater improvement in visual acuity is associated with greater decrease of depressive symptoms after cataract surgery.	Few subjects with depressive symptoms, mild in severity.
Cross-sectional							
	Kang MJ	47	Korea	2023	4,122	Older subjects with cataract have a greater risk of major depression than those without.	Self-reported diagnosis.
Longitudinal							
	Chen PW	48	Taiwan	2020	233,258	Cataract is associated with increased 7-year risk of incident depression. Within cataract subjects, surgery is associated with a decreased risk of depression compared with no treatment.	Analysis based on administrative data, possible under-recognition of mild depressive symptoms. No distinction between first-and second-eye surgery.
Randomized controlled trial							
	Harwood RH	25	United Kingdom	2005	306	First eye cataract surgery is associated with a decrease of depression and anxiety symptoms.	Psychological status was an ancillary outcome. Selected sample at enrollment.

(Continued)

TABLE 1 (Continued)

Cataract and dementia							
Study design	First author	Ref	Country	Publication year	Sample size	Main findings	Limitations
Longitudinal							
	Yu W-K	58	Taiwan	2015	491,226	Among older subjects with cataract, surgery is associated with a decreased 10-year incidence of dementia	Analysis based on administrative data. No distinction between first-and second-eye surgery.
	Lee CS	60	United States	2022	3,038	Among older subjects with cataract or glaucoma, cataract surgery is associated with a decreased 8-year dementia incidence, glaucoma surgery is not.	Ophthalmic diagnoses based on administrative data.
Meta-analysis							
	Kuźma E	51	Germany	2021	6,659	In a meta-analysis of longitudinal, observational studies, cataract is associated with an increased risk of incident dementia.	Not all studies designed to assess dementia incidence. High heterogeneity (sampling, adjustment strategy, exposure and outcome assessment).

absolute decrease in the fall rate only after the second intervention (26). This is consistent with data that show an association between stereopsis and fall risk, which is even more important than that observed for visual acuity, thus suggesting that good binocular vision, which can be attained with bilateral surgery, may be needed to minimize fall risk (23, 34). On the whole, cited data suggest that cataract is a marker of increased risk of motor impairment and fall risk, possibly beyond vision impairment, and that a bilateral correction is probably needed to achieve a substantial risk reduction, while patients undergoing monolateral surgery may show a paradoxical increase in fall risk.

Yet more research is needed to support a systematic policy of bilateral surgery to decrease fall risk in an aging population (35).

Cataract and hip fractures

Approximately one in three community-dwelling individuals over the age of 65 reports at least one fall event per year, with this risk proportionally increasing with age, determining in 5–10% of cases fragility fractures and 1–2% of cases hip fractures, also due to the frequent coexistence of osteoporosis (36).

Nevertheless, the role of osteoporosis over the years has been downplayed. Siris et al., using data from NORA (National Osteoporosis Risk Assessment), examined a population of almost 150.000 white, postmenopausal women aged 50 to 104 years (mean age 64.5 years) and observed that 82% of postmenopausal women with fractures had T-scores higher than −2.5, the threshold value below which osteoporosis is diagnosed (37). This makes it clear that reduced bone mineral density (BMD) is not actually as decisive as we might think in hip fracture development. The most recent literature points out that BMD and risk of falling independently increase fracture risk, with a need for multifactorial interventions for primary and secondary prevention of fragility fractures (36).

One area for further study is represented by the relationship between visual impairment, including cataract and fractures, with the aim of identifying effective prevention strategies. It has been clearly demonstrated that blindness (defined as a best corrected visual acuity ≤20/500 in the better eye) increases the risk of hip and vertebral fractures (38). Among conditions of visual impairment, untreated cataract has been identified as the main cause of hip fracture in a UK sample (39). In a Taiwanese matched cohort study cataract was associated with an increased risk of hip and vertebral fractures over a 6.4-year follow-up (40). To note, patients with cataract had a greater baseline comorbidity and an increased risk of osteoporosis incidence during follow-up, suggesting it may represent a frailer population, beyond visual impairment (40). Little data, and no specifically designed intervention studies, are available regarding the association between cataract surgery and hip fractures. In the previously cited Taiwanese study, patients undergoing cataract surgery showed a decreased fracture risk in comparison with those with non-operated cataract. A recent nationwide Korean cohort study confirmed that older patients who underwent cataract surgery showed a lower incidence of hip and vertebral fragility fractures than those who did not (41). In a previous Medicare cohort study, patients that underwent surgery in comparison with patients with non-operated cataract had similar hip fracture rates in a 12-month follow-up period. However, patients in the surgery group were older, had more severe comorbidity and disability and were more frequently affected by severe cataract and, after adjusting for these covariates, hip fracture rate was significantly lower in the surgery group, with an absolute risk difference of about 0.2% per year, and more beneficial effects observed among older patients, more advanced cataract and greater comorbidity (42). Overall, these studies suggest that cataract surgery in elderly patients may reduce and prevent the incidence of hip and vertebral fragility fractures. No study has compared fracture risk associated with first- and second-eye cataract surgery.

Cataract, depression and cognitive impairment

Depression is common in old age and is typically associated with chronic disease and multimorbidity, psychosocial adversity, cognitive impairment and disability (43).

Several studies have shown an association between depression in old age and visual disturbances, including cataract. The association between low vision and depression may be explained by reduction in daily activity, such as reading, loss of autonomy, difficult social interaction and loss of self-esteem (44). A recent metanalysis has identified a huge 25% prevalence of depression in samples of patients referred to eye clinics and low vision rehabilitation centers. The prevalence of depression was even higher, estimated as 33%, in the subgroup of studies that did not adopt exclusion criteria, and dropped to 18% when patients with comorbidity, mainly cognitive impairment, were excluded (45). A French cohort study has shown that patients with low vision have a threefold increase of depression risk in a 10-year follow-up, but that patients with depression have a 60% increased risk of vision impairment incidence (46). Regarding the specific effect of cataract, its diagnosis has been recently associated with a 65% increase of major depression risk in the cross-sectional analysis of a representative sample of older Korean citizens (47). Moreover, cataract was specifically associated with a 78% increase of depression risk after a 7.8-year follow-up in a propensity score matched cohort study in Taiwan (48).

Several studies have recently examined the association between vision impairment and risk of cognitive decline. A recent metanalysis has observed an association of low vision with an increased risk of cognitive impairment and dementia incidence (49). A dose–response association has been observed in a large UK cohort, with dementia risk being greatest among patients with severe vision impairment (50). In a meta-analysis that compared the risk of cognitive impairment between different causes of low vision, cataract and diabetic retinopathy were associated with an increased risk of dementia and Alzheimer's disease (51).

Regarding cataract surgery, some studies suggest that it can improve depressive symptoms and anxiety and may be associated with a decreased risk of cognitive impairment (52–54). In a previously cited cohort study, subjects with cataract undergoing surgery had a 25% less depression risk in comparison with untreated ones over a 7.8-year follow-up (48). Moreover, data from the previously-cited randomized controlled study on expedited cataract surgery have shown a significant decrease in depression and anxiety in the early treatment group (25). Of notice, an association has been observed between visual acuity improvement and depressive symptoms decrease after phacoemulsification, thus highlighting the importance of successful surgery for this specific outcome (55).

Data have been less consistent over the years regarding the association between cataract surgery and risk of cognitive impairment, as older studies reported no significant effects on neuropsychological functions (56, 57), while more recent ones showed a protective association on cognitive impairment and dementia risk (58). A small study conducted using functional magnetic resonance imaging suggested functional and morpho-structural improvements in visual and cognitive-related brain areas after cataract surgery (59). In a large US cohort including older patients (mean age 74) with a diagnosis of cataract and glaucoma, cataract surgery was independently associated with a significant decrease in dementia risk in a 7.8-year follow-up, while glaucoma surgery was not (60).

A recent systematic review and meta-analysis focusing on psychiatric and neuropsychological assessments provided further evidence that cataract surgery has a positive effect not only on depressive symptoms but also on cognitive function in older patient (61).

Discussion

Visual acuity is the main parameter evaluated in ophthalmology to monitor visual progress of a medical or surgical treatment. The term "visual acuity" refers to the ability of the human eye to detect and perceive the smallest details of an object at a given distance (62, 63). Normal visual acuity depends on the transparency of the eye's dioptric media, the correction of any refractive defect, and the integrity of the macula and optic pathways. However, it is now well established that visual acuity provides only raw data on the overall functioning of sight, indeed it does not consider a patient's ability to use his or her visual apparatus within a complex and dynamic socio-cultural environment (64, 65). The visual acuity test with Snellen tables is a high-contrast test: recognizing black letters on a white background allows even a patient with low contrast sensitivity to achieve 20/20 (66). Moreover, high visual acuity can be found in patients with severe peripheral visual field deficit: despite high performance using Snellen's table, a patient with visual field defect may have difficulty relating to the outside world and is potentially limited in a large number of daily activities, implying reduced quality of life and poor social and occupational functioning (67).

Concerning the cataract patient, visual acuity is used to address surgical indication. In Europe, for example, it is customary to advise patients with visual acuity of 6/12 or less in one or both eyes to undergo surgery (68). However, this advice has clear limits: a patient with preserved visual acuity but affected by a posterior subcapsular cataract may experience bothersome nighttime glare at the sight of traffic lights, therefore for a nighttime driver, even with high VA, a subcapsular cataract can severely limit his or her functioning and merit expedited surgery. Indeed, the National Institute of Health and Care Excellence guidelines for the management of cataracts established that the assessment of visual acuity as an indication for cataract surgery fails to recognize other visual impairments that may limit the activities of daily living and hence require intervention (69).

Nevertheless, cataract surgery can have intraoperative or postoperative complications, such as endophthalmitis, posterior capsular ruptures, IOL (intra-ocular lens) dislocations, refractive errors, endothelial damage and dry eye (70–73). Even though nowadays these complications are rare, they can affect the postoperative visual outcomes and quality of life. Therefore, the patients should be informed of these risks, but it has to be pointed out that the benefits of surgery very often overcome the possible complications in visually-impaired individuals.

It is also necessary to consider the visual system as binocular. Precise correction of 1 eye by an IOL (intra ocular lens) while

waiting for the contralateral eye to be treated could lead to non-negligible anisometropia and sometimes diplopia. This phenomenon could partly explain the increased incidence of falls and fractures after cataract surgery that is documented in some studies, although it cannot be ruled out that phacoemulsification induces patients to consider themselves freer, thus leading them to perform more activities and expose themselves to the risk of falling.

Regarding fall risk, it is reported that multiple "fallers" usually have decreased vision, as indicated by all visual tests, with impaired depth perception, contrast sensitivity and low-contrast visual acuity being the strongest risk factors (74).

There are a few older studies in literature that have found that visual impairment is not a predictor for the risk of falling in old age (75–78). However, most of these studies only assessed a limited aspect of the global visual functioning, that it to say visual acuity. Other studies showed a lack of association between fracture risk and visual impairment when only visual acuity was evaluated (79).

Lastly, patients' necessities in relation to his or her daily activities must be taken into account when choosing which IOL to implant. For example, a classic monofocal IOL may provide perfect distance visual acuity but limit the range of action at intermediate and close distances. In the context of fall risk and femur fracture, the intermediate distance is perhaps the most impactful. Recognizing an obstacle requires good contrast sensitivity (especially at night), sense of depth, color perception, motion perception, good visual processing speed as well as an optimal binocular field of view. All these factors fall under the concept of *functional vision,* and should be evaluated synergistically to develop a "cataract frailty index" that could select patients at risk of falling, on whom preventive action can be taken with tailored surgical strategies (80).

Comparison of different intraocular lenses regarding visual impairment, visual function and patient satisfaction are becoming available (81, 82). Similar studies addressing outcomes which are specifically relevant to older populations, such as fall incidence, depressive symptoms and cognitive impairment, are needed to guide clinicians' choice.

To summarize what has been said so far, cataracts increase the risk of developing frailty, falls, fractures, depression and cognitive impairment, and reduce the percentage of functional reserve of an individual over time. *Functional reserve* refers to a patient's residual capacity to perform his or her physiological activities (83). It is conceivable that by assessing functional vision instead of visual acuity, surgery should be planned within an early "window of opportunity" to prevent the aforementioned geriatric adverse events.

A limitation of our review is the narrative design: further systematic reviews are necessary in order to better describe the current knowledge on the different aspects of this topic.

Conclusion

Cataract is a primary cause of visual impairment worldwide and, among older subjects, is associated with frailty, fall risk, depressive symptoms, and neurocognitive decline. Due to the high prevalence and the frequent lack of recognition of lens opacification, a systematic screening of visual impairment with a timely referral to the ophthalmologist is advised to prevent progression to bilateral visual impairment and possibly prevent negative health outcomes. In particular, it is necessary to include visual performance in comprehensive geriatric assessment, in order to identify subjects at risk and to develop questionnaires or clinical indices to assess the impact of *functional vision* on daily activities. The introduction of visual assessment in geriatric clinical practice would allow an appropriate referral to the ophthalmologists, with the aim to decide, with a greater clinical awareness, whether cataract extraction is indicated.

On the other hand, ophthalmologists should adopt a comprehensive approach to older subjects, keeping a focus on individual priorities, global autonomy and cognitive difficulties, and tailoring the IOL choice beyond visual function. Indication for surgery should be considered in relation not only to *visual acuity*, but also to the *functional vision* assessment, daily needs and individual priorities. A geriatric referral may be helpful for the ophthalmologist to decide regarding surgery in complex cases, including those with cognitive decline and multimorbidity. After surgery a joint geriatric and ophthalmologic follow-up may allow the assessment of treatment effects on different domains of health status, and may possibly help decision regarding second-eye surgery in frail older subjects.

Generally speaking, cataract surgery should be encouraged for both visual recovery and prevention of negative health-related events in frail patients or those with neurocognitive impairment. However, several research areas remain to be addressed with the aim of identifying the most effective strategies to reduce the global health impact of cataract. In particular, it is conceivable that the protective effect of cataract treatment on functional impairment, falls incidence and dementia risk may be time-dependent, with the need to identify a "window of opportunity" for surgery, before the frailty process becomes irreversible. Therefore, valid and easy-to-use screening instruments of visual impairment, focusing on the impact on daily activities, are needed in primary care and routine geriatric practice. Moreover, the specific role of different intervention strategies, such as systematic bilateral versus unilateral surgery or use of different intraocular lenses, deserves further studies. Most important, future intervention studies should increasingly include global health outcomes, such as disability and quality of life, falls and fracture incidence, depressive symptoms and cognitive impairment.

Author contributions

RM, SS, and EM wrote the first draft of the manuscript. EF, MC, and CV wrote sections of the manuscript. All authors contributed to conception, design of the review, manuscript revision, read, and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Comparison of cataract patients with regular corneal astigmatism after implantation of extended range-of-vision and bifocal toric intraocular lenses

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Purpose: To compare the postoperative visual acuity and visual quality between extended range-of-vision and multifocal toric intraocular lens (IOLs) after implantation in cataract patients with regular corneal astigmatism.

Setting: Department of Ophthalmology, the Second Hospital of Jilin University, Changchun, Jilin Province, China.

Design: Retrospective and single-center study.

Methods: The study involved implanting the Tecnis Symphony (ZXR00IOL) or the bifocal toric (ZMTIOL) in patients undergoing cataract surgery. Three months after surgery, lens performance was evaluated using distance, intermediate, and near visual acuity tests, defocus curves, the modulation transfer function (MTF), a visual function index questionnaire (VF-14), and the adverse optical interference phenomena.

Results: The 3-month postoperative follow-up found that both groups had good corrected distance vision. The ZMT group had better-uncorrected distance visual acuity and near visual acuity ($p<0.05$). However, the ZXR group showed better uncorrected intermediate visual acuity ($p<0.05$) and visual continuity. Overall astigmatism in the postoperative ZMT group was significantly lower than that in the pre-operative group ($p<0.05$). The ZMT group had lower total high-order aberrations (tHOs), higher MTF values, and higher VF-14 scores ($p<0.05$). Finally, the ZXR group exhibited reduced halo and glare phenomena ($p<0.05$).

Conclusion: We found that ZMT can effectively correct a corneal astigmatism of 1.0–1.5 D and ZXR can improve patient outcomes regarding subjective optical quality and range of vision. These findings have the potential to improve future astigmatism treatment options.

KEYWORDS

refractive cataract surgery, astigmatism, extended range-of-vision IOLs, high-order aberration, visual quality

1. Introduction

Cataract surgery has entered the era of refractive surgery. Multifocal intraocular lens (MIOLs) can replace the opaque lens of cataract patients and solve the problem of ametropia (1). Among these lens, the diffractive IOL uses a diffraction ring to split incident light into 2–3 focal points. Furthermore, the continuous-range diffracted IOL provides a power of 1.75 diopters (D), which causes ladder diffraction to allow for extended vision. However, while multifocal IOL technology offers high visual acuity, it can also produce adverse optical interference phenomena, such as glare and halos (2). Another limitation is that they cannot correct corneal astigmatism for patients, a common type of ametropia. Approximately 40 and 20% of cataract patients exhibit astigmatism greater than 1.0 D and 1.5 D, respectively, prior to surgery (3). Studies have established that pre-operative astigmatism above 1.0 D can significantly impact the patient's postoperative visual acuity, contrast sensitivity, and quality of life (4, 5). Thus, it is crucial to address pre-operative astigmatism when using multifocal IOLs to correct farsightedness and myopia.

The toric IOL has been in clinical use since 1992. A meta-analysis study by Kaur et al. (6) indicated that, for patients with pre-operative astigmatism, the toric IOL offered improved uncorrected distance vision, a higher spectacles independence, and lower residual astigmatism compared to the non-toric IOL. The complex surface design of Tecnis ZMT (Abbott Medical Optics, United States) diffraction bifocal toric IOL is used to correct hyperopia, myopia, and astigmatism. Although the bifocal IOL distributes light to two points, some light energy loss occurs, resulting in glare and halo phenomena (7). However, the Tecnis Symphony (ZXR00, Johnson & Johnson, United States) extended depth of focus (EDoF) IOLs extend the depth of focus and increase the tolerance of residual astigmatism, due to their unique diffraction grating design (8, 9). Unfortunately, there is a lack of studies on the effects of toric bifocal IOLs on postoperative visual quality (10, 11). Previous research has described several aspects of visual outcomes, including visual acuity, defocus curve, contrast sensitivity, rotation, subjective optical phenomenon, and use of spectacles. However, to our knowledge, research involving objective visual quality measurement has not yet been published, which is a crucial factor in assessing the patient's visual outcome after IOL implantation. Thus, the objective of this study is to provide further insight into this vital subject matter. In this study, the visual quality of EDoF IOL ZXR00 and toric bifocal IOL ZMT in patients with pre-operative astigmatism between 1.0 D ~ 1.5 D were compared and analyzed. Through the comparison of the postoperative visual acuity, visual quality, spectacles independence, and questionnaire results of the two groups, our aim is to offer essential information to guide refractive cataract surgery for clinicians.

2. Methods

2.1. Research objective

This retrospective study was approved by the institutional review board of The Second Hospital in Jilin University, Changchun, China and underwent ethical review at our hospital. The ethics review number is 2022–229. The study was performed in accordance with the tenets of the Declaration of Helsinki. The patients provided written informed consent to participate in this study.

2.2. Inclusion and exclusion criteria, grouping, and pre-operative examination

Patients underwent uneventful cataract surgery with the implantation of a Tecnis ZMT (Abbott Medical Optics, United States) or a Tecnis Symphony (ZXR00, Johnson & Johnson, United States) IOL. The surgeries took place from January 2021 to July 2022 at our hospital.

The inclusion criteria were as follows: (1) pre-operative diagnosis of cataract and age > 50 years; (2) regular corneal astigmatism in the range of 1.0–1.5 D; (3) angle of kappa and alpha <0.5; and (4) photopic pupil >2.0 mm and mesopic pupil <6.0 mm. The exclusion criteria were as follows: (1) history of ophthalmic surgery, trauma, uveitis, retinopathy, glaucoma, high myopia, or severe dry eyes; (2) irregular corneal astigmatism; (3) intraoperative complications; and (4) severe diabetes, immune diseases, and systemic diseases.

All patients underwent the following examinations before operation: uncorrected distance visual acuity (UDVA, 5m), best-corrected distance visual acuity (CDVA, 5 m), intraocular pressure (IOP), tear secretion, biological measurement (IOL Master 700, Carl Zeiss Meditec AG), corneal topography (OPD-ScanIII, NIDEK), slit lamp examination, binocular ultrasound, optical coherence tomography (SPECTRALIS OCT, HEIDELBERG), and corneal endothelial count and morphology.

2.3. Calculation of IOLs and labeling method for toric IOLs

Refractive parameters were measured using an IOL Master 700 (Zeiss, Germany). IOL power was calculated using the Barrett TK Universal II formula, and the target refractive diopter was 0 ± 0.5 D.

An online calculation platform[1] was used to calculate the ZMT models and determine the position of the operative incision and IOLs loop axis. Before surgery, we marked the axial and operative incision positions on the patients.

2.4. Operation method

The same surgeon operated on all patients. Before each operation, the operative eyes were fully anesthetized using 0.4 ml:2 mg procaine hydrochloride. A 2.2 mm main corneal incision, 0.8 mm side-port corneal incision, and 5.5 mm diameter circular continuous capsulorhexis were performed. Lens extraction was accomplished using a standard phacoemulsification technique. The IOL was implanted into the capsule bag, and the toric IOLs were rotated to align with the axial position of the pre-operative marker. Both the toric and EDoF IOLs were centered. No complications occurred during the operations.

2.5. Intraocular lenses

The EDoF TECNIS ZXR00 has a one-piece posterior surface diffractive design with an EDoF IOL. It has nine grating diffraction

1 https://www.Tecnistoriccalc.com

apertures on the rear surface, and the Echelette diffraction grating technology achieves a continuous field of view; chromatic achromatic technology is used to further enhance the image contrast (9, 12, 13). A large central optic design with a diameter of 1.6 mm increases tolerance, has a strong anti-deviation ability, and can accommodate astigmatism <1.5 D.

ZMT IOL integrates aspheric, diffractive multifocal, and toric designs, and has an all-optical rear surface diffraction design, with +4.0 D attached to the near side. ZMT IOL is a pupil-independent IOL with the same ratio of far and near focus under photopic or mesopic photometry. It can correct different degrees of astigmatism of the cornea according to the different cylinders (9).

2.6. Postoperative visual quality assessment

2.6.1. Visual acuity

Three months after the operation, a standard logarithmic visual acuity chart was used to measure uncorrected distant, intermediate and near visual acuity (UDVA, UIVA, and UNVA) at 5 m, 80 cm, and 40 cm, and corrected distant visual acuity (CDVA) at 5 m. All patients were assessed in an environment of equal luminance.

2.6.2. Defocus curve

The defocus curve was drawn using a comprehensive optometer and performed with uncorrected visual acuity. The optometer adjusted the degree of the spherical lens in front of the operated eye. The defocus curve ranged from +2.0 D to −4.0 D (by decreasing the spherical degree by +0.5 D for each reading).

2.6.3. High-order aberration and MTF

Total high-order aberrations (tHOs) [including spherical aberrations (SA), coma, and trefoil aberrations] and the MTF values were measured at a pupil diameter of 3 mm using an iTrace visual quality analyzer (Tracy Technologies, United States).

2.6.4. Spectacles independence, questionnaire, and subjective adverse optical interference phenomenon

A visual function index questionnaire (VF-14) was used to evaluate visual function in patients (14). There were 14 items, all divided into five grades according to their degree of difficulty. Adverse optical interference (glare and halo) and the spectacle independence of the postoperative patients were also evaluated.

2.6.5. Refractive state

The iTrace visual quality analyzer was used to measure (i) the pre-operative and postoperative corneal astigmatism (*D*) and the whole total astigmatism (D); (ii) the postoperative residual astigmatism (*D*) of the two groups; and (iii) the axial deviation (*D*) of the ZMT IOL with the toric check function.

2.7. Statistical analysis

SPSS25 (IBM, Armonk, NY, United States) was used for the statistical analysis. First, the Kolmogorov–Smirnov test was used to test for a normal distribution of data. When a normal distribution was found, two independent samples Student's t-test was used; the results are expressed as mean ± standard deviation. If the data did not follow a normal distribution, a nonparametric rank-sum (Wilcoxon) test was used to test the difference between two independent samples. The ratio of the two groups was compared using Fisher's chi-square test. All tests were double-tailed statistics, and statistical significance was set at a *p*-value of <0.05.

3. Results

3.1. Pre-operative parameters

Based on the inclusion and exclusion criteria, 95 patients (103 eyes) were included. ZXR00 IOL was implanted in those who required intermediate vision and ZMT IOL in those who required near vision. There were no significant differences in age, eye difference, sex, corneal astigmatism, axial length, intraocular pressure, etc., between the two groups ($p > 0.05$) (Table 1).

3.2. Postoperative visual acuity

There was no significant difference in the best CDVA between the two groups 3 months after surgery ($p > 0.05$); the UDVA in the ZMT group was better than that in the ZXR group ($p < 0.005$), the UIVA in the ZXR group was better than that in the ZMT group ($p < 0.001$), and the UNVA in the ZMT group was better than that in the ZXR group ($p < 0.001$) (Table 2).

TABLE 1 Comparison of general data between the two groups before surgery.

Preoperative parameter	Mean±SD		*p*-value
	ZXR	ZMT	
No. of eyes (patients)	53 (46)	50 (49)	
Age (*y*)	58.77 ± 11.29	61.30 ± 7.15	0.310
Sex (*n*)			0.738
Male	29	29	
Female	24	21	
Eyes (*n*)			0.896
OD, ocular sinister	29	28	
OS, ocular sinister	24	22	
Astigmatic (*D*)	−1.27 ± 0.14	−1.29 ± 0.14	0.380
Anterior chamber depth (mm)	2.99 ± 0.41	3.02 ± 0.50	0.709
Axial length (mm)	23.13 ± 1.38	23.09 ± 1.43	0.140
IOL power (*D*)	22.16 ± 2.33	21.69 ± 2.20	0.190
Corneal endothelial cell count (/mm)	2731.11 ± 312.30	2773.80 ± 250.64	0.448
Intraocular pressure (mmHg)	15.81 ± 2.81	15.12 ± 2.84	0.240
UDVA (logMAR)	0.76 ± 0.56	0.78 ± 0.61	0.786

OD, ocular dexter; OS, ocular sinister; IOL, intraocular lens; UDVA, uncorrected distance visual acuity.

3.3. Defocus curve

In the ZXR group, visual acuity was in a plateau ranging from 0 to −1.5 D. The initial average visual acuity was >0.2logMAR which gradually decreased to −1.5–−4.0 D. The curve of the ZMT group showed a bimodal shape and an average visual acuity above 0.1logMAR. A visual acuity of 0 D (5 m distance) and −3.0 D (approximately 33 cm) were the best findings. The defocus curve of the ZXR group was better than that of ZMT at 0–−2.5 D and intersected at −2.5–−3.0 D. However, the visual acuity of the ZMT group was better than that of ZXR at −2.5-−4.0 D, as shown in Figure 1.

3.4. Refractive state

(i) *Corneal Astigmatism Diopter*: The absolute value difference of the corneal cylinders between the ZXR and ZMT groups pre- and post-operation were 0.18 ± 0.23 and 0.18 ± 0.12, respectively. There was no significant difference between the two groups ($z = -1.373$, $p = 0.175 > 0.05$).

(ii) *Residual Astigmatism Diopter*: There was no significant difference between the postoperative cylinder (−1.23 ± 0.31 D) and the pre-operative cylinder (−1.27 ± 0.14 D) in the ZXR group. The postoperative astigmatism in the ZMT group (−0.35 ± 0.15 D) was less than pre-operation astigmatism (−1.29 ± 0.14 D). The postoperative cylindrical diopter in the ZMT group was smaller than that in the ZXR group, and the difference was statistically significant (Table 2).

(iii) *Rotation Stability of the ZMT Group*: The rotation degree of ZMT IOL implanted 3 months after the operation was 2.50 ± 1.66 D (Table 2).

TABLE 2 Comparison of visual acuity and diopter 3months after the operation.

Parameter	Mean±SD		*p*-value
	ZXR	ZMT	
UDVA (logMAR)	0.13 ± 0.09	0.05 ± 0.07	0.001**
CDVA (logMAR)	0.01 ± 0.05	0.02 ± 0.05	0.813
UIVA (logMAR)	0.15 ± 0.09	0.30 ± 0.12	$p < 0.001$***
UNVA (logMAR)	0.35 ± 0.17	0.08 ± 0.08	$p < 0.001$***
IOL rotation (*D*)		2.50 ± 1.66	
Sphere (*D*)	−0.17 ± 0.50	0.03 ± 0.40	0.065
Cylinder (*D*)	−1.23 ± 0.31	−0.35 ± 0.15	<0.001***

IOL, intraocular lens; UDVA, uncorrected distance visual acuity; CDVA, corrected distance visual acuity; UIVA, uncorrected intermediate visual acuity; UNVA, correct near visual acuity (**$p < 0.01$, ***$p < 0.001$).

3.5. High order aberration and the MTF

The tHOA, coma, and trefoil in the ZMT group were lower than those in the ZXR group ($p < 0.05$), but there were no significant differences in SA ($p > 0.05$) (Table 3). There was no significant difference in the MTF of the cornea between the two groups; however, the mean MTF of the whole eye under a pupil size of 3 mm was significantly lower than that of the ZMT group ($p < 0.05$) (Table 3). There were also significant differences in the MTF values between the two groups at different spatial frequencies ($p < 0.05$), as shown in Figure 2.

3.6. Questionnaire

The postoperative VF14 score was higher in the ZMT group than in the ZXR group (Table 4). Comparing the subjective adverse optical interference between the two groups, the number of patients with glare and halo in the ZMT group was significantly higher than that in the ZXR group ($p < 0.05$), as shown in Figure 3. There was no significant difference in spectacle independence.

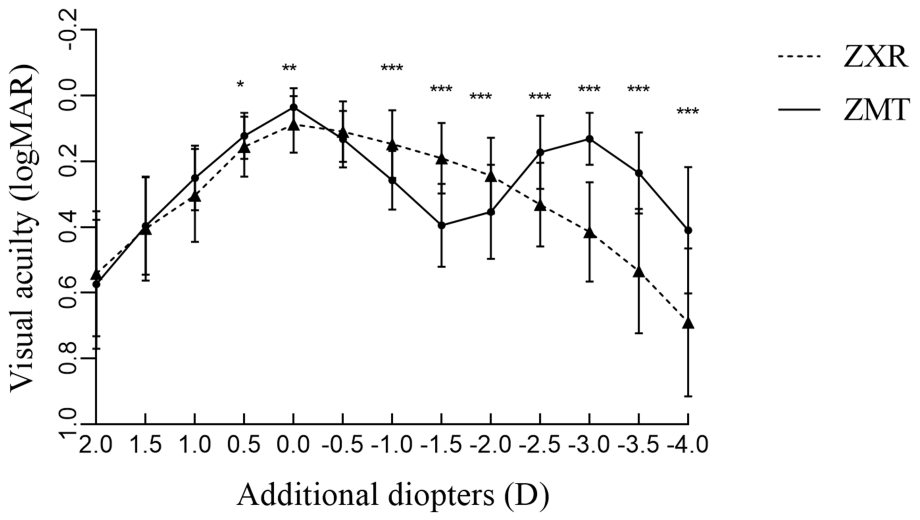

FIGURE 1
Comparison of defocus curves of patients 3months after surgery (*p<0.05, **p<0.01, and ***p<0.001).

4. Discussion

In order to improve the postoperative visual function and quality of life for cataract patients, it is crucial to correct excessive astigmatism. Various methods, such as main corneal incision (PI), excimer laser *in situ* keratectomy (LASIK), astigmatic keratectomy (AK/FSAK), limbal release keratectomy (LRIS), femtosecond laser non-penetrating interlamellar astigmatism keratectomy (ISAK), and astigmatism correction intraocular lens implantation, can be employed (15–18). However, when taking into consideration the cost of surgery, complications, and the accuracy of astigmatism correction, toric intraocular lens implantation stands as a more suitable option for cataract patients. In this study, we provided a comparative analysis of Tecnis ZMT and Symphony ZXR00 IOLs to assess the visual quality of two different types of intraocular lens following cataract surgery with astigmatism. As far as we know, this is the first comparative analysis of its kind.

The uncorrected distance visual acuity in the ZMT group was found to be better than that in the ZXR group. The uncorrected astigmatism found in the ZXR group had a perceptible impact on the UDVA, whereas the ZMT group showed effective correction of astigmatism yielding good UDVA. The UIVA of the ZXR group was better, fully demonstrating the advantages of the EDoF IOLs extended visual range (19). Our findings revealed a naked near visual acuity (UNVA) of less than 0.2logMAR in the ZMT group, with the ZMT IOL near addition +4.0 D design enabling comfortable and clear near vision. Other studies have also observed comparable findings concerning the UNVA of ZMT (10, 11).

The defocus curve can be used to simulate the vision of the patient at different distances, and the accommodative range of the intraocular lens can be evaluated (20). Both lens provided good recovery of postoperative distant visual acuity. ZXR allowed for a more continuous distant and intermediate visual acuity from +0.5D to −2.0D, of a value above 0.2logMAR. The bimodal defocus curve also provided better near vision. The defocus curve shape is similar to that of Chang et al. (13, 21). Carones et al. found that the ZXR00 IOL has a higher tolerance for astigmatism than other types of bifocal and trifocal intraocular lens, which is related to the design of the ZXR00 IOL 1.6 mm large central apertures (22). Cylindrical lens of varying diopters were added in front of the patients' eyes post-cataract implantation with ZXR00 IOL, and uncorrected distance vision was observed. Results demonstrated that postoperative residual astigmatism impacted distance vision (22).

High-order aberrations have a significant impact on the visual quality of patients, and MTF serves as a well-established standard for reflecting objective visual imaging. ZMT IOL effectively tackled the astigmatism, but residual astigmatism persisted after ZXR00 IOL surgery. We found that astigmatism may increase high-order aberrations (23, 24), mainly coma and trefoil (25), aligning with previous study findings. Additionally, the rotational stability design principle of ZMT IOL played a role in optimizing its objective visual quality. Ruiz-Alcocer et al. (26) previously highlighted that IOL rotation beyond 5D could impede overall visual quality. Based on our analysis, it is plausible to posit that the variations observed in objective visual quality indicators can be attributed to the combined effects of ZMT IOL correction for astigmatism and rotational stability.

TABLE 3 Comparison of aberrations and MTF values under 3mm pupil at 3 months after the operation.

Parameter	Mean±SD		*p*-value
	ZXR	ZMT	
tHO (μm)	0.19 ± 0.13	0.13 ± 0.06	0.014*
SA (μm)	−0.00 ± 0.04	0.00 ± 0.02	0.343
Coma (μm)	0.07 ± 0.05	0.05 ± 0.03	0.043*
Trefoil (μm)	0.11 ± 0.08	0.08 ± 0.06	0.030*
Corneal MTF	0.50 ± 0.16	0.50 ± 0.13	0.947
Mean MTF	0.32 ± 0.11	0.41 ± 0.13	0.001**

tHO, total high-order; SA, spherical aberration; MTF, modulation transfer function (*p<0.05, **p<0.01).

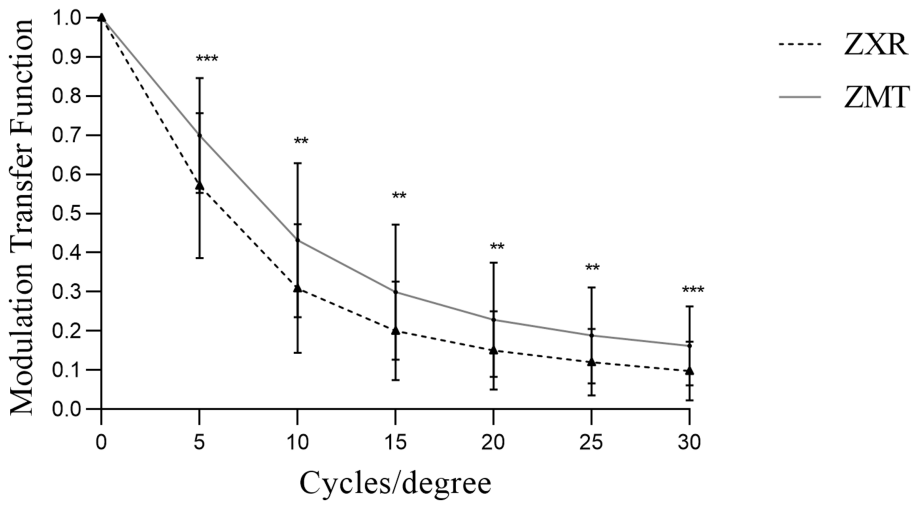

FIGURE 2
Comparison of the modulation transfer function (MTF) values under 3mm pupil of patients 3months after the operation (*p<0.05, **p<0.01, and ***p<0.001).

TABLE 4 Comparison of questionnaires and spectacle independence at 3 months after the operation.

Parameter	Mean±SD		*p*-value
	ZXR	ZMT	
VF14	89.02 ± 4.46	91.57 ± 3.46	0.002**
Spectacles independence	52 (98.11%)	50 (100%)	
Glare			0.037*
None (*n*/%)	46 (86.8%)	34 (68.0%)	
Light (*n*/%)	6 (11.3%)	9 (18.0%)	
Medium (*n*/%)	0 (0%)	5 (10.0%)	
Heavy (*n*/%)	1 (1.9%)	2 (4.0%)	
Halo			0.025*
None (*n*/%)	50 (94.3%)	38 (76.0%)	
Light (*n*/%)	3 (5.7%)	8 (16.0%)	
Medium (*n*/%)	0 (0%)	2 (4.0%)	
Heavy (*n*/%)	0 (0%)	2 (4.0%)	

IOL, intraocular lens; VF14, visual function; QoV, quality of vision (*p<0.05, **p<0.01).

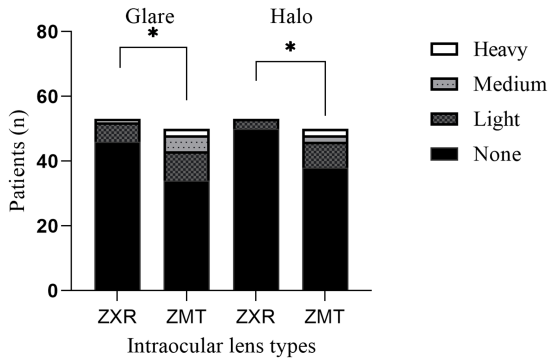

FIGURE 3
Comparison of adverse optical interference in postoperative patients in 3 months (*p<0.05, **p<0.01, and ***p<0.001).

During the postoperative follow-up, we found that the halo and glare phenomenon in the ZMT group was more serious than that in the ZXR group. As per our previous research, it has been observed that ZXR00 portrays a diminished occurrence of halos when compared to ZMB00, which is a diffractive bifocal IOL that shares similar design attributes with ZMT IOL (27). The ZXR00 IOL has a wide central optical zone (1.6 mm in diameter) and a large central step diameter, resulting in a reduced number of diffraction apertures and refraction of light. Additionally, ZXR00's achromatic technology and low additional diopter incorporated in its echelette diffraction grating can reduce the occurrence of glare and halos while minimizing the loss of contrast sensitivity (28). The ZXR00 IOL also displays a light energy utilization rate of 92%, whereas bifocal IOLs employ a light-splitting design principle that limits the light allocated to each focus. Despite the potential for increased aberration with a larger pupil, the ZXR00 IOL's large central ring design maintains excellent visual function with a pupil size of 4.5 mm (29). While postoperative glare can significantly impact visual cortex activation during the early stages of recovery, studies indicate that such disturbances typically dissipate over time (30, 31).

The VF14 score was higher in the ZMT group, which is presumably a result of the lens's ability to correct astigmatism and provide better near vision correction for presbyopia in a single operation (14). Extensive research has shown that the ZMB00 IOL provides good near vision, and the addition of astigmatism correction with the ZMT IOL offers further benefits (32–35). Liu et al. (21) found higher VF-14 scores for the ZXR00 IOL group than the ZMB00 group, which differs from our findings. We speculate that the uncorrected astigmatism of ZXR00 caused lower scores in this study. Wolffsohn et al. (5) found that levels of uncorrected astigmatism as low as 1.00 D can significantly impact visual function and quality of life. In contrast, correction of astigmatism can effectively improve the quality of life of patients (36).

The limitations of our study are as follows: firstly, given the varying aberrations across different pupil sizes, it is advisable to undertake a broader visual quality analysis for larger pupils. Secondly, further examination on the astigmatism tolerances of the ZXR00 IOL lens can be done by grouping astigmatism degrees. Lastly as our study measured near visual acuity at a distance of 40 cm, we suggest that 33 cm, the habitual distance of Asian eyes, could be adopted as the distance of near visual acuity for future studies.

5. Conclusion

The ZMT IOL exhibited proficient near and distant vision, effectively correcting astigmatism, while the ZXR00 IOL provided an extended visual range and was found to be reasonably tolerant to astigmatism, primarily regarding its subjectively evaluated optical quality and range of vision. These findings offer essential information to guide refractive cataract surgery for clinicians and improve the future of eye health.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

ZL: conceptualization, methodology, data curation, formal analysis, and writing—original draft. RG: methodology and data curation. XH, XY, ZW, and YL: data curation. HZ: funding acquisition, project administration, resource, and writing—review and editing. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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