Journal of Ophthalmology

Cataract Surgery in Complex Anterior Segment Pathology

Lead Guest Editor: Zisis Gatzioufas
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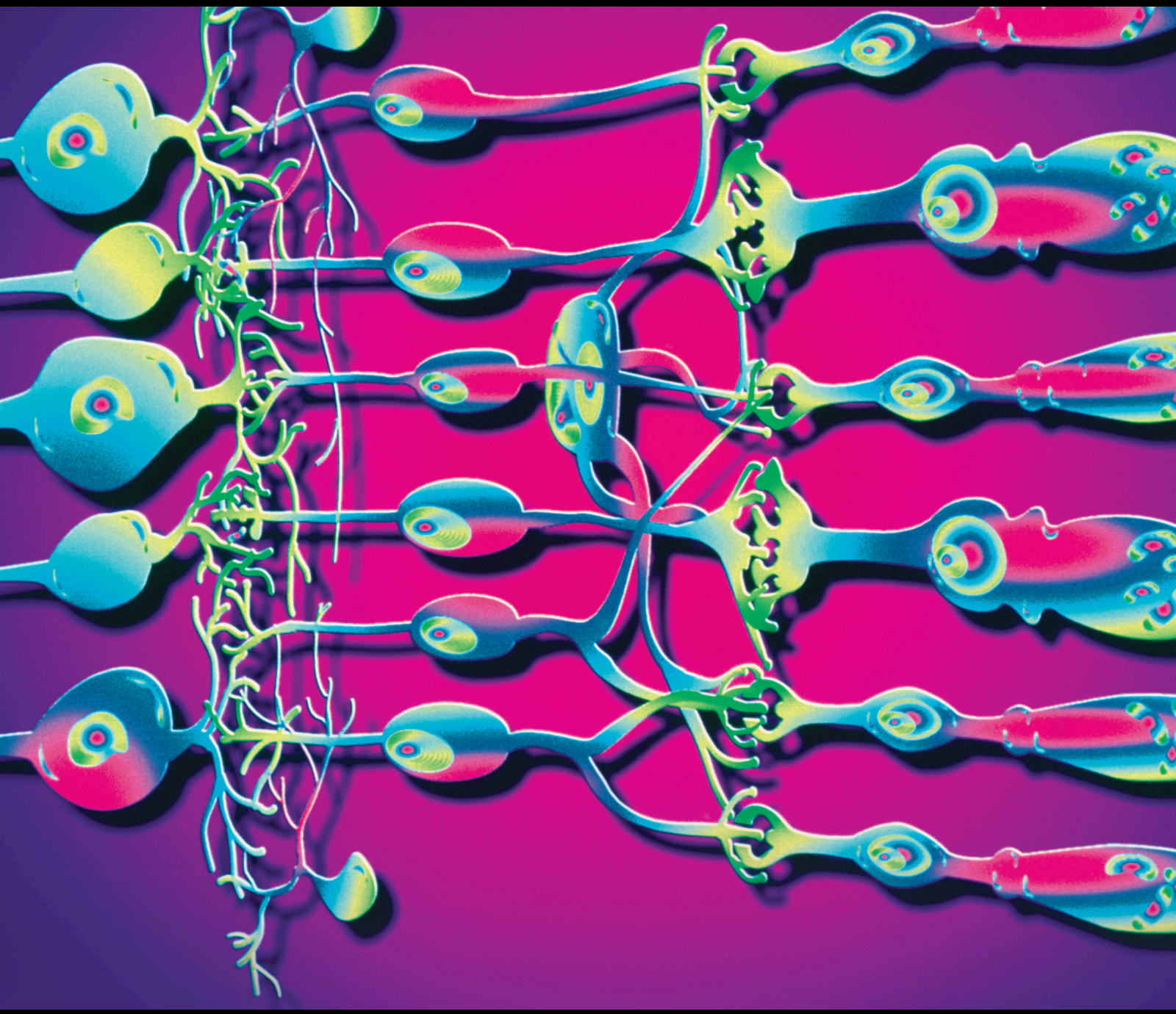

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Editorial

Cataract Surgery in Complex Anterior Segment Pathology

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Modern cataract surgery provides a high level of efficacy and safety, incorporating numerous technological innovations, such as femtosecond laser technology or 3D visualization, as well as advances in intraocular lens (IOL) technology with the development of special or premium IOLs, such as aniridia IOLs, toric IOLs, or multifocal IOLs. As a result, unparalleled visual outcomes can be achieved for patients by using customized solutions for each individual patient.

However, there are an increasing number of anterior segment pathologies, which could complicate cataract surgery and compromise the expected visual outcomes. Cataract surgery in the presence of these complex conditions requires a special approach, including modification of surgical techniques and/or the use of special IOLs.

In this special issue, Schmidt et al. provide a systematic review on the results of comparative studies of modern cataract surgery in pediatric uveitis with or without intraocular lens (IOL) implantation and perform comparative meta-analyses to compare visual acuity outcomes and complication rates. Takai et al. compare the refractive status between eyes implanted with toric and nontoric IOLs during combined cataract surgery and microhook ab interno trabeculotomy, a minimally invasive glaucoma surgery. Tsakiris et al. elaborate on surgical and perioperative considerations for the treatment of cataract in eyes with glaucoma. Ahmadzadeh et al. systematically review the literature to compare the efficacy and safety of phacotrabeculectomy and trabeculectomy either alone or followed by later phacoemulsification.

Moreover, Hu et al. describe a flapless/grooveless technique for four-point refixation of a dislocated IOL with four fenestrated haptics, as well as a minimally invasive suture fixation technique for four-point fixation of IOLs in the treatment of aphakic eyes, namely, the intrascleral suture anchoring technique. Wu et al. evaluate the efficacy of a modified four-point fixation technique for the repositioning of a dislocated IOL with four eyelets in the absence of capsule support. Finally, Iyer et al. highlight the nuances of performing cataract surgery in various ocular surface disorders and emphasize the need to have a comprehensive stepwise approach in such cases. In addition, they report the retrospective analysis of cataract surgery outcomes in 73 eyes of 57 patients with Stevens–Johnson syndrome.

Conflicts of Interest

The guest editors declare that there are no conflicts of interest regarding the publication of this special issue.

Miltos Balidis
Miguel Rechichi
Rajesh Fogla
Zisis Gatzioufas

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Review Article

Cataract Surgery with or without Intraocular Lens Implantation in Pediatric Uveitis: A Systematic Review with Meta-Analyses

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Purpose. To systematically review the results of comparative studies of modern cataract surgery in pediatric uveitis with or without intraocular lens (IOL) implantation and to perform comparative meta-analyses to compare visual acuity outcomes and complication rates. *Methods*. On 12 November 2020, we systematically searched the Cochrane Central, PubMed/MEDLINE, EMBASE, ClinicalTrials.gov, and all affiliated databases of the Web of Science. Two authors independently reviewed studies and extracted data. Studies were reviewed qualitatively in text and quantitatively with meta-analyses. Outcome measures were preoperative and postoperative best-corrected visual acuity (BCVA), inflammation control, and rates of postoperative complications. *Results*. Ten studies of 288 eyes were eligible for review of which the majority were eyes with juvenile idiopathic arthritis-associated uveitis. Summary estimates revealed that the BCVA was better in pseudophakic eyes vs. aphakic eyes (1-year postoperative: −0.23 logMAR, 95% CI: −0.43 to −0.03 logMAR, $P = 0.027$; 5-year postoperative: −0.35 logMAR, 95% CI: −0.51 to −0.18 logMAR, $P = 0.000036$). Pseudophakic eyes had more visual axis opacification (OR 6.76, 95% CI: 2.73 to 16.8, $P = 0.000036$) and less hypotony (OR 0.19, 95% CI: 0.04 to 0.95, $P = 0.044$). *Conclusions*. In modern era cataract surgery on eyes with pediatric uveitis with IOL implantation leads to satisfactory and superior visual outcomes and no differences in complication rates apart from an increased prevalence of visual axis opacification and a decreased prevalence of hypotony when compared to aphakia. However, limitations of the retrospective design and the presence of selection bias necessitate a careful interpretation.

1. Introduction

Pediatric uveitis is a challenging condition with an annual incidence of 4.3–6.9 per 100.000 children under the age of 16 years [1–3]. The condition often has an asymptomatic course and children tend to underreport visual changes resulting in advanced disease at the time of diagnosis [4, 5]. Complications such as cataract, ocular hypertension/glaucoma, amblyopia, cystoid macula edema (CME), posterior synechiae, band keratopathy, vasculitis, vitreous haze, and papillitis can be seen in case of delayed referral [6, 7]. These complications of pediatric uveitis lead to severe visual impairment in 18–38% of the patients [8–10]. Cataract is seen in up to 2/3 of patients with pediatric uveitis and is a complication related to chronic inflammation, prior surgical procedures (such as trabeculectomy or vitrectomy for retinal detachment), or prolonged treatment with glucocorticoids [5, 9, 11–13]. In these patients, it may be necessary to remove the cataract if it causes significant visual impairment, to prevent amblyopia, or to ensure adequate monitoring of the inflammation and the retina.

Cataract surgery in pediatric uveitis is technically challenging due to higher rates of ocular comorbidities, inflammatory sequelae, and structural abnormalities [14]. Intraocular lens (IOL) implantation in pediatric uveitis has been controversial and aphakia after cataract surgery has previously been practiced as a rule of thumb. Historically, early studies reported poor visual acuity after IOL

implantation as well as a high rate of complications such as posterior synechiae, retrolental membranes, CME, secondary glaucoma, hypotony, and phthisis bulbi [15, 16]. This was ascribed to challenges in the surgical technique, increased ocular inflammation with IOL implantation, and lack of sufficient management of inflammation [17]. Recent technological advancements in the IOL design, biocompatible IOL materials, and modern surgical techniques, as well as immunomodulatory therapy, have improved inflammatory control pre- and postoperatively, all of which leads to better outcomes with IOL implantation according to more recent studies [18–21]. Despite the positive results reported in recent studies, IOL implantation remains controversial [22, 23].

The purpose of this study was to systematically review the results of comparative studies of modern cataract surgery in pediatric uveitis with or without IOL implantation and conduct meta-analyses to summarize and compare important outcomes.

2. Materials and Methods

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [24]. For all aspects of this study, we followed the recommendations of the Cochrane Handbook [25]. Institutional review board approval was not relevant for systematic reviews according to Danish law.

2.1. Eligibility Criteria. We defined eligible studies as those fulfilling the following criteria.

Population. Studies of a pediatric population (individuals below 18 years of age) with any uveitis who undergo cataract surgery. We restricted to studies that only considered a pediatric population or studies that included such individuals as a subset of the study sample where data from such individuals could be extracted.

Intervention. Posterior chamber IOL implantation in the bag.

Comparator. Aphakia.

Outcomes. Short-term (1 year) and long-term (5 years) results of best-corrected visual acuity (BCVA) were defined as the primary outcome. Secondary outcomes were defined as specific incidence of the following within 5 years: anterior chamber inflammation, need for topical steroids, need for systemic immunosuppressive treatment, glaucoma (using the authors definition) or ocular hypertension, hypotony, need for resurgery for any reason, need for IOL explantation, visual axis opacification (posterior capsular opacification (PCO) and pupillary membrane formation), synechiae, phthisis bulbi, cystoid macular edema (CME), and retinal detachment.

Study Types. Eligible studies could be prospective or retrospective. We did not restrict based on randomization, blinding, or any other initiative to reduce bias. We included relevant abstracts, but not studies without original data or case reports. We did not restrict studies based on geography or journal. We only considered studies disseminated in English language. Since we want to focus on outcomes of modern cataract surgery, we only considered publications from year 2000 and onwards.

2.2. Information Sources, Search, and Study Selection. We searched the literature databases the Cochrane Central, PubMed/MEDLINE, EMBASE, Web of Science Core Collection, BIOSIS Previews, Current Contents Connect, Data Citation Index, Derwent Innovations Index, KCI-Korean Journal Database, Russian Science Citation Index, SciELO Citation Index, CINAHL, and ClinicalTrials.gov. The search was conducted on 12 November 2020. Details of the search strategy across databases are available as Supplementary file 1. One author (Y. S.) examined title and abstracts of all identified records, removed duplicates, and obviously irrelevant reports. Two authors (Y. S. and A. R.) independently screened remaining references in full text to evaluate eligibility of studies. Disagreements were discussed between the two authors and if consensus could not be reached, a third author (L. K.) would be invited for final decision. All reference lists were reviewed for identification of further relevant studies.

2.3. Data Extraction and Risk of Bias Assessment. We extracted data regarding study design, participant characteristics, and outcomes using predesigned data extraction forms. Two authors (Y. S. and D. C. S.) extracted all data independently. Based on our a priori knowledge of the literature, we anticipated nonrandomized comparative studies. Therefore, quality of eligible studies was assessed using the Risk of Bias in Nonrandomized Studies of Interventions (ROBINS-I) tool as recommended by Cochrane Methods [25, 26]. Two authors (Y. S. and M. A-B.) evaluated risk of bias independently. Disagreements between the authors were discussed and if consensus could not be reached, a third author (L. K.) would be invited for final decision.

2.4. Data Analysis and Synthesis. Eligible studies were described in text and tabulated for a qualitative synthesis. Due to the nonrandomized nature of available studies, we summarized and compared preoperative demographic and clinical characteristics of the intervention and the comparison group. All BCVA data were converted to logMAR for analyses [27]. For very low vision, we used the following conversion: no light perception = 2.9 logMAR, light perception = 2.6 logMAR, hand motion = 2.3 logMAR, and counting fingers = 1.9 logMAR [27]. For BCVA, we compared preoperative values as well as the postoperative results at short-term (1 year) and at long-term (5 years). Where no data was available specifically for 1 or 5 years, measures closest to these dates were used. All meta-analyses were performed using MetaXL 5.3 (EpiGear International,

Sunrise Beach, QLD, Australia) for Microsoft Excel 2013 (Microsoft, Redmond, WA, USA). We used the random-effects model for our meta-analyses. Heterogeneity was assessed with Cochran's Q and quantified with I2 [28]. A Funnel plot was used to investigate for skewed results (risk of bias across studies) [29]. However, acknowledging the small number of studies potentially available, heterogeneity and risk of bias across studies were interpreted with caution. Sensitivity analyses were made to explore robustness of the estimates. All summary estimates are presented with 95% confidence intervals (CI) and P values. P values below 0.05 were interpreted as statistically significant.

3. Results

3.1. Study Selection. The literature search identified 185 records. Of these, 77 were duplicate records, 76 records were obviously irrelevant, and 18 records were not published in English language. One study known *a priori* to us was added to the reference list. The remaining 15 records were read in full text. One additional eligible study was identified by reviewing reference lists. Finally, 10 studies were eligible for the qualitative review and nine for quantitative synthesis (Figure 1).

3.2. Study Characteristics. The 10 studies collectively summarized data on 202 patients (Table 1). Three studies were only available as conference abstracts [30–32]. All were nonrandomized studies comparing groups obtained through retrospective chart reviews. Studies were from the USA ($n = 4$), Europe ($n = 4$), India ($n = 1$), and Israel ($n = 1$). Mean age of uveitis diagnosis ranged from 4 to 8 years. Mean age of cataract surgery ranged from 5 to 11 years. All studies had at least 1 year of follow-up and four studies had at least 5 years of follow-up.

Study populations were predominantly of eyes with juvenile idiopathic arthritis- (JIA-) associated uveitis (Table 2). Non-JIA-associated uveitis included Behçet's disease, herpes zoster virus uveitis, HLA-B27 associated uveitis, ocular tuberculosis, pars planitis, sarcoidosis, toxocariasis, Vogt-Koyanagi-Harada disease, and idiopathic uveitis (Table 2). Three studies reported that the uveitis was quiescent 3 months prior to surgery in all eyes [21, 35, 36], one study reported that the uveitis was inactive in 6 months prior to surgery [34], and one study reported absence of inflammation in 3 months prior to surgery except one eye with absence of inflammation for 2 months [33]. Three studies do not report on the degree of preoperative inflammation [30, 31, 37] and two studies operated all eyes despite active inflammation [16, 20].

Across the 10 studies, a total of 288 eyes underwent cataract surgery, of which 166 eyes had posterior chamber IOL implantation in the bag and 122 eyes were left aphakic. Four studies reported data on a very small number (3 or below) of aphakic eyes while no such small numbers were observed in the group of eyes with IOL implantation. Demographic and clinical factors differed in three studies [16, 21, 35] without any clear trend across studies (Table 3). In BenEzra and Cohen [16], the aphakic group differed by better preoperative BCVA [16]. In Quinones et al. [35], more cases of JIA-associated uveitis were in the left aphakic eyes [35]. Yangzes et al. [21] had more cases of panuveitis and poorer preoperative BCVA in left aphakic eyes [21]. None of the studies had a significant difference in age at cataract surgery between the study groups.

4. Results of Individual Studies and Risk of Bias within Studies

Artigas et al. [30] did not report visual acuity but found that IOL implantation leads to more frequent visits due to PCO and glaucoma development compared to aphakia [30]. The authors conclude that these visits should be taken into consideration when planning surgery [30]. Beal and Wang [31] found a nonsignificant trend towards better visual acuity in pseudophakic patients compared to the BCVA in aphakic patients and no differences were found in subsequent glaucoma development [31]. BenEzra and Cohen [16] described a practice where a choice of primary IOL implantation or aphakia was presented for cases with unilateral disease or young children with markedly unequal bilateral disease and the presence of dense cataract in one eye, whereas aphakia was the only presented option for children with bilateral disease and similar affection in both eyes [16]. They found that cataract surgery benefitted patients and improved visual acuity regardless of being pseudophakic or aphakic but that contact lenses were poorly tolerated especially among the young children [16]. Guindolet et al. [32] presented results of cataract surgery with either hydrophobic primary IOL implantation or aphakia [32]. Here, primary IOL implantation lead to good and prompt visual rehabilitation, but in comparison to aphakic patients, patients with IOL implantation had a higher postoperative oral corticosteroid use [32]. Kemp et al. [33] found cataract surgery with primary IOL implantation to yield satisfactory outcomes as all eyes achieved visual acuity of 20/30 or better, and no differences were found in use of medications after surgery between pseudophakic and aphakic patients [33]. Kotaniemi and Penttilä [20] investigated outcomes after change in practice from aphakia to primary IOL implantation [20]. Primary IOL implantation improved visual acuity and visual acuity of ≥0.5 Snellen was achieved in 64% of eyes with IOL [20]. In this study, comparison could only be made to the few patients with contralateral eye who had cataract surgery with aphakia prior to the implementation of new practice [20]. O'Rourke et al. [34] found that IOL implantation leads to excellent visual acuity (defined as >6/9.5 Snellen) but that comorbidities such as glaucoma, band keratopathy, and CME all required a tight postoperative care and that 80% of eyes had uveitis flare-ups [34]. They left one eye aphakic due to preexisting advanced uveitic glaucoma and difficulties in satisfactory immunosuppression; this eye did not improve in BCVA [34]. Sijssens et al. [36] compared cataract surgery with aphakia to primary IOL implantation, in which the latter had presurgical history of a higher rate of glaucoma history, trabeculectomy, and treatment with methotrexate [36]. In this comparative study, the authors found that the

BCVA improved significantly more in the pseudophakic eyes than in the aphakic eyes [36]. Yangzes et al. [21] found that cataract surgery improved vision in eyes regardless of IOL implantation or not, the rate of glaucoma development was comparable between the groups, but PCO leads to more secondary procedures in the pseudophakic eyes [21]. Taken together, studies found that cataract surgery, regardless of IOL implantation, generally improved vision. Nearly all studies specifically highlighted the need for intensive immunosuppressive treatment and control of uveitis after cataract surgery, but it was unclear whether it was a question of sustaining preexisting regimen or based on a change in the need for controlling the uveitis [16, 20, 21, 32–36].

Risk of bias assessment was challenged in three studies since we only had access to conference abstracts with limited information [30–32]. Remaining studies had moderate-to-serious risk of bias (Table 4), in which the key source of bias was the baseline confounding from the fact that the allocation to either IOL implantation or aphakia across studies was based on the individual surgeon's estimation of whether or not pseudophakia or aphakia would benefit the patient best.

4.1. Synthesis of Results in Meta-Analyses and Risk of Bias across Studies. Nine studies provided eligible and comparable data for the meta-analyses [16, 20, 21, 30, 32–36]. These studies collectively summarized data on 256 eyes: 153 eyes underwent IOL implantation and 103 eyes were aphakic.

Primary outcomes: short-term and long-term results on best-corrected visual acuity.

Eight studies provided relevant data for the primary outcome [16, 20, 21, 32–36]. O'Rourke et al. [34] provided only data on a single eye with aphakia, which leads to SD = 0, and therefore this study was ineligible for the meta-analysis for analytical reasons [34]. Thus, seven studies were included for the meta-analyses of the primary outcome [16, 20, 21, 32, 33, 35, 36].

For preoperative BCVA, the random-effects pooled weighted mean difference between those with primary IOL implantation and aphakia was −0.23 logMAR (95% CI: −0.55 to 0.08 logMAR, $P = 0.15$), i.e., the preoperative BCVA did not differ significantly between the two populations (Figure 2). Cochran's Q of 20.95 and I^2 of 71% were both indicative of a large heterogeneity across studies, and the Funnel plot appeared symmetrical apart from the outlier from BenEzra and Cohen [16] (Supplementary file 2). Our sensitivity analysis revealed that excluding BenEzra and Cohen [16], which unlike the other studies had significantly better preoperative BCVA in the aphakia group, would completely change the conclusions from our initial calculations. Excluding BenEzra and Cohen [16] leads to a random-effects pooled weighted mean difference of −0.36 logMAR (−0.52 to −0.20 logMAR, $P = 0.000014$); i.e., the preoperative BCVA was significantly better in eyes planned for primary IOL implantation compared to those planned for aphakia (Figure 2). This analysis had much less heterogeneity across studies: Cochran's $Q = 4.59$ and $I^2 = 0\%$. A separate sensitivity analysis of this subanalysis showed strong robustness of the analysis as excluding studies in turn did not significantly change the size (range −0.30 to −0.44 logMAR), the direction (all in favor of primary IOL implantation), or the statistical significance of the findings (Supplementary file 2).

For short-term results on postoperative BCVA, the random-effects pooled weighted mean difference between primary IOL implantation and aphakia was −0.23 logMAR (95% CI: −0.43 to −0.03 logMAR, $P = 0.027$); i.e., primary IOL implantation leads to significantly better BCVA on the short-term (Figure 3). A Cochran's Q of 8.34 and I^2 of 28% were indicative of small heterogeneity across studies. The Funnel plot appeared symmetrical (Supplementary file 3). Sensitivity analysis revealed that excluding either Quinones et al. [35], Sijssens et al. [36], or Yangzes et al. [21] would lead to loss of the statistical significance of the findings; hence short-term differences did not show robustness in the sensitivity analysis (Supplementary file 3).

For long-term results on postoperative BCVA, the random-effects pooled weighted mean difference between primary IOL implantation and aphakia was −0.35 logMAR (95% CI: −0.51 to −0.18 logMAR, $P = 0.000036$); i.e., primary IOL implantation leads to significantly better BCVA on the long-term (Figure 3). A Cochran's Q of 5.74 and I^2 of 0% were indicative of a small-to-none heterogeneity across studies. The Funnel plot appeared symmetrical (Supplementary file 4). Sensitivity analysis demonstrated robustness of the findings as excluding studies in turn did not significantly change the size (range −0.30 to −0.38 logMAR), the direction (all in favor of primary IOL implantation), or the statistical significance of the findings (Supplementary file 4).

Secondary outcomes: presence of inflammation (anterior chamber inflammation and cystoid macular edema) and the need for immunosuppression (topical steroids and systemic immunosuppressive treatment).

BenEzra and Cohen [16], Kemp et al. [33], and O'Rourke et al. [34] reported postoperative anterior chamber inflammation in terms of uveitis flares [16, 33, 34]. These outcomes were not reported sufficiently homogenous for a meaningful meta-analysis. In the BenEzra and Cohen study [16] two pseudophakic eyes (out of 10 eyes) and one aphakic eye (out of 10 eyes) experienced chronic intraocular inflammation after surgery [16]. In the Kemp et al. study [33], five pseudophakic eyes (out of six eyes) and none of the three aphakic eyes experienced uveitis flares [33]. In the O'Rourke et al. study [34], the only aphakic eye had three flare episodes, while the remaining nine pseudophakic eyes had three flare episodes in two eyes, in six eyes a single flare episode, and in two eyes no flare episodes [34].

Quinones et al. [35] reported anterior chamber cells in a grading system (<1+, 1+, 2+, >2+) during the postoperative follow-up period [35]. At final visit, eight pseudophakic eyes (62%) and 23 aphakic eyes (82%) had <1+ anterior chamber cells, which was not statistically significant [35].

Postoperative CME during the follow-up period in specific study groups was reported in five studies [16, 20, 21, 32, 36]. The random-effects risk estimate for postoperative CME between IOL implantation and aphakia was OR 0.70 (95% CI: 0.15 to 3.29, $P = 0.65$) (Supplementary file 5), i.e., no significant

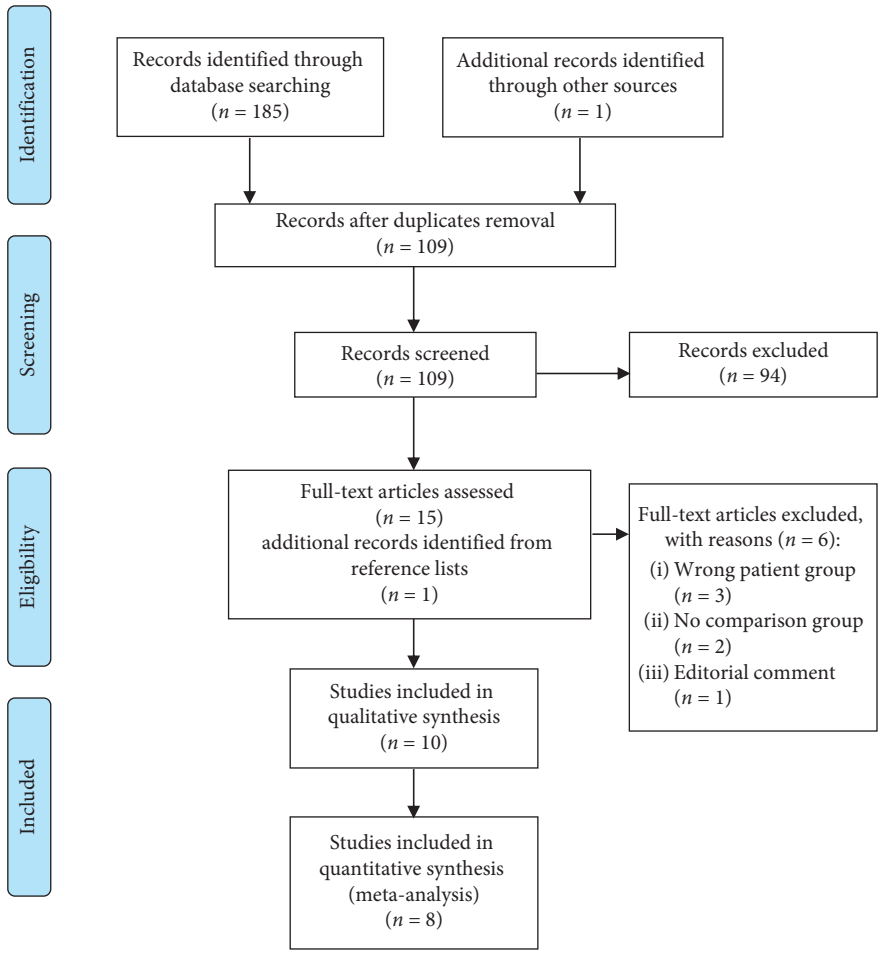

Figure 1: Flow diagram of study selection.

difference in risk of postoperative CME between IOL implantation and aphakia. The Funnel plot appeared symmetrical and the sensitivity analysis demonstrated robustness of the findings (Supplementary file 5).

Kemp et al. [33], Kotaniemi and Penttilä [20], O'Rourke et al. [34], and Yangzes et al. [21] reported on the postoperative need for topical steroids and systemic immunosuppressive treatment [20, 21, 33, 34]. These outcomes were not reported sufficiently homogenous for a meaningful meta-analysis. Kemp et al. [33] reported that, postoperatively, all patients continued their preoperative immunomodulatory medications, which were different combinations of systemic prednisone, methotrexate, infliximab, adalimumab, and topical prednisolone acetate 1% [33]. Kotaniemi and Penttilä [20] reported that, at the end of follow-up (3.3 ± 3.2 years), topical corticosteroid treatment was ongoing in 33 (92%) pseudophakic eyes and 3 (100%) aphakic eyes [20]. Here, systemic immunomodulatory medications were either single treatment or a combination treatment of the following: prednisolone (17 patients), methotrexate (15 patients), and cyclosporine A (14 patients); in 9 patients, infliximab or etanercept were introduced but withdrawn in two patients due to inefficacy or allergy [20]. Further, the authors also tried other disease-modifying antirheumatic drugs (sulfasalazine, leflunomide, azathioprine, hydroxychloroquine, and chlorambucil) [20]. For all these systemic immunomodulatory medications, Kotaniemi and Penttilä [20] did not provide comparative data on pseudophakic vs. aphakic eyes [20]. O'Rourke et al. [34] reported that eight cases of uveitis flare-ups were managed with augmented topical treatment in three cases, dexamethasone intravitreal implant in one case, and Adalimumab in four cases of which Mycophenolate mofetil was added in two [34]. This study did not specify how the immunomodulatory treatments were distributed in pseudophakic vs. aphakic eyes [34]. Yangzes et al. [21] reported that systemic prednisolone was given in all cases in the postoperative period, that 23 patients (62%) received additional immunosuppressive treatment (methotrexate in 6, azathioprine in 7, and combination of methotrexate and azathioprine in 10), and that four eyes (8%) received dexamethasone intravitreal implant [21]. However, whether or not some of these medications were reduced or intensified during the follow-up period was not described [21].

Table 1: Characteristics of the included studies.

Reference	Study design	Patients and eyes, N	Country	Age at uveitis diagnosis, years	Age at cataract surgery, years	Females, (%)	Follow-up after cataract surgery, years
Artigas et al. [30]	Retrospective chart review	7 patients, 11 eyes	USA	N/A	7.5 ± 2.5	57%	5.8 ± 4.0
Beal and Wang [31]	Retrospective chart review	25 patients, 32 eyes	USA	N/A	N/A	N/A	4.0
BenEzra and Cohen [31]	Retrospective chart review	17 patients, 20 eyes	Israel	5.7 ± 3.8	9.1 ± 4.6	71%	5.0
Guindolet et al. [32]	Retrospective chart review	16 patients, 20 eyes	France	N/A	7.9 ± 2.8	N/A	3.0
Kemp et al. [33]	Retrospective chart review	7 patients, 9 eyes	USA	4.4 ± 1.8	5.4 ± 2.1	57%	1.6 ± 0.8
Kotaniemi and Penttilä [20]	Retrospective chart review	25 patients, 39 eyes	Finland	6.8 ± 5.8	11.3	84%	3.3
O'Rourke et al. [34]	Retrospective chart review	7 patients, 10 eyes	Ireland	7.7 ± 2.2	N/A	57%	7.4 ± 2.7
Quinones et al. [35]	Retrospective chart review	34 patients, 41 eyes	USA	6.7 ± 3.0	9.8 ± 3.3	71%	4.1 ± 3.9
Sijssens et al. [36]	Retrospective chart review	29 patients, 48 eyes	The Netherlands	4.2 ± 1.6	7.1 ± 2.5	62%	7
Yangzes et al. [21]	Retrospective chart review	37 patients, 58 eyes	India	N/A	10.5 ± 5.4	68%	3.7 ± 7.2

Data are presented in mean ± standard deviation where possible. IOL = intraocular lens; N/A = not available; USA = United States of America.

Table 2: Distribution of uveitis subtypes among eligible patients for this review.

Reference	Uveitis subtypes
Artigas et al. [30]	JIA-associated uveitis (11 eyes)
Beal and Wang [31]	Any uveitis (32 eyes)
BenEzra and Cohen [31]	JIA-associated (9 eyes) and non-JIA-associated uveitis (11 eyes)
Guindolet et al. [32]	JIA-associated (9 eyes) and non-JIA-associated uveitis (11 eyes)
Kemp et al. [33]	JIA-associated (7 eyes) uveitis, juvenile xanthogranulomatosis (1 eye), and idiopathic uveitis (1 eye)
Kotaniemi and Penttilä [20]	JIA-associated uveitis (39 eyes)
O'Rourke et al. [34]	Idiopathic uveitis (5 eyes), JIA-associated uveitis (2 eyes), ocular tuberculosis (2 eyes), and HLA-B27 associated uveitis (1 eye)
Quinones et al. [35]	JIA-associated uveitis (21 eyes), pars planitis (7 eyes), other uveitis (6 eyes; idiopathic, HZV-associated, sarcoid panuveitis)
Sijssens et al. [36]	JIA-associated uveitis (48 eyes)
Yangzes et al. [21]	JIA-associated uveitis (19 eyes), ocular tuberculosis (8 eyes), idiopathic uveitis (4 eyes), Behçet's disease (2 eyes), VKH disease (2 eyes), HLA-B27 associated uveitis (1 eye), and toxocariasis (1 eye)

HLA = human leukocyte antigen; HZV = herpes zoster virus; JIA = juvenile idiopathic arthritis; VKH = Vogt-Koyanagi-Harada.

4.2. Secondary Outcomes: Risk of Ocular Hypertension and Glaucoma. Ocular hypertension as a separate diagnosis was reported in two studies with slightly different definitions not sufficiently homogenous for inclusion in a meaningful meta-analysis [16, 32]. BenEzra and Cohen [16] reported that four of 10 aphakic eyes needed treatment to control intraocular pressure, whereas the pseudophakic group with 10 eyes had one case with uncontrollable intraocular pressure and development of intractable glaucoma [16]. Guindolet et al. [32] reported that four of 14 pseudophakic eyes had secondary ocular hypertension and none among the six aphakic eyes [32].

Six studies reported on presence of glaucoma [16, 20, 21, 30, 34, 36]. Some of these studies also counted cases of glaucoma prior to cataract surgery. The random-effects risk estimate for glaucoma between IOL implantation and aphakia was OR 1.52 (95% CI: 0.73 to 3.17, $P = 0.26$) (Supplementary file 6), i.e., no significant difference in risk of glaucoma between IOL implantation and aphakia. The Funnel plot appeared

Table 3: Demographic and clinical comparison of study groups.

	IOL						No IOL					
Reference	Eyes, N	Age at surgery, years	Females, (%)	Uveitis subtypes	Pre-op BCVA, logMAR	Type of IOL	Eyes, N	Age at surgery, years	Females, (%)	Uveitis subtypes	Pre-op BCVA, logMAR	Significant differences
Artigas et al. [30]	9	N/A	N/A	9 JIA	N/A	Alcon Acrysof	2	N/A	N/A	2 JIA	N/A	N/A
Beal and Wang [31]	13	N/A	N/A	N/A	N/A	N/A	19	N/A	N/A	N/A	N/A	N/A
BenEzra and Cohen [16]	10	9.2 ± 4.5	70%	5 JIA, 5 idiopathic	2.8 ± 0.1	3M style 925 (3 eyes) and Allergan PC26 TB (7 eyes)	10	10.3 ± 5.1	71%	3 JIA, 3 idiopathic, 1 *Toxocara*	2.3 ± 0.6	Better pre-op BCVA in the aphakia group
Guindolet et al. [32]	14	8.6 ± 7.9	N/A	N/A	1.1 ± 0.5	Hydrophobic acrylic lens	6	6.1 ± 4.5	N/A	N/A	1.8 ± 0.4	No
Kemp et al. [33]	6	6.8 ± 1.7	50%	5 JIA, 1 idiopathic	1.8 ± 1.0	Alcon MA50BM (8 eyes) or SA60AT (1 eye)	3	8.7 ± 6.4	67%	2 JIA, 1 xanthogranulomatosis	1.9 ± 0.8	No
Kotaniemi and Penttilä [20]	36	N/A	86%	36 JIA	1.0 ± 0.6	Hydrophobic acrylic (25 eyes) or PMMA (11 eyes) lens	3	N/A	33%	3 JIA	1.6 ± 1.1	No
O'Rourke et al. [34]	9	N/A	56%	5 idiopathic, 2 ocular tuberculosis, 1 JIA, 1 HLA-B27	0.7 ± 0.3	N/A	1	N/A	100%	1 JIA	1.0	No
Quinones et al. [35]	13	11.4 ± 4.4	N/A	7 idiopathic, 4 JIA, 2 other	0.9 ± 0.5	PMMA lens	28	9.4 ± 3.9	N/A	23 JIA, 5 idiopathic	1.1 ± 0.5	More JIA in the aphakia group
Sijssens et al. [36]	29	6.3 ± 2.0	72%	29 JIA	1.0 ± 0.5	Hydrophobic acrylic or PMMA lens	19	7.6 ± 2.7	72%	19 JIA	1.2 ± 0.5	No
Yangzes et al. [21]	27	10.9 ± 4.1	N/A	18 anterior, 6 intermediate, 3 panuveitis, 0 posterior	0.8 ± 0.7	Hydrophobic acrylic or PMMA lens	31	7.8 ± 5.1	N/A	12 anterior, 7 intermediate, 11 panuveitis, 1 posterior	1.3 ± 0.6	More panuveitis and worse pre-op BCVA in the aphakia group

Data are presented in mean ± standard deviation. Demographic data here are presented per eye where possible. Data were transformed to mean ± standard deviation where possible. For BCVA, we converted reported values to logMAR for better comparability within study and across studies. For logMAR conversion, we used the following for extreme low vision values: counting fingers = +2.3, hand motion = +2.6, light perception = +2.9, no light perception = +3.2. IOL = intraocular lens; N/A = not available; PMMA = polymethyl methacrylate; USA = United States of America.

Table 4: Risk of bias assessment for each study using the Risk of Bias in Nonrandomized Studies of Interventions (ROBINS-I) tool.

Reference	Bias due to confounding	Bias due to selection of participants	Bias due to classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported results	Overall bias
Artigas et al. [30]	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear	Unclear
Beal and Wang [31]	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear	Unclear
BenEzra and Cohen [16]	Serious	Low	Low	Low	Low	Low	Moderate	Serious
Guindolet et al. [32]	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear	Unclear
Kemp et al. [33]	Unclear	Low	Low	Low	Low	Low	Moderate	Moderate
Kotaniemi and Penttilä [20]	Serious	Low	Low	Low	Low	Low	Moderate	Serious
O'Rourke et al. [34]	Serious	Low	Low	Low	Low	Low	Moderate	Serious
Quinones et al. [35]	Serious	Moderate	Moderate	Moderate	Low	Low	Moderate	Serious
Sijssens et al. [36]	Serious	Low	Low	Moderate	Low	Low	Low	Serious
Yangzes et al. [21]	Serious	Moderate	Moderate	Moderate	Low	Low	Moderate	Serious

Three studies [30–32] were conference abstracts, and risk of bias assessment of these studies was challenged by the limited insight obtainable from these abstracts.

symmetrical and the sensitivity analysis demonstrated robustness of the findings (Supplementary file 6).

4.3. Secondary Outcome: Visual Axis Opacification. Seven studies reported on the incidence of postoperative visual axis opacification, e.g., PCO or pupillary membrane formation [16, 20, 21, 30, 32–34]. Across all studies, any visual axis opacification was much more prevalent in the pseudophakic group [16, 20, 21, 30, 32–34]. The random-effects risk estimate for visual axis opacification between IOL implantation and aphakia was OR 6.76 (95% CI: 2.73 to 16.8, $P = 0.000037$ (Supplementary file 7); i.e., IOL implantation leads to significantly higher risk of visual axis opacification. The Funnel plot appeared symmetrical and the sensitivity analysis demonstrated robustness of the findings (Supplementary file 7).

Secondary outcomes: risk of hypotony, synechiae, retinal detachment, and phthisis bulbi.

Four studies reported on the incidence of postoperative hypotony [16, 21, 34, 36]. The random-effects risk estimate for hypotony between IOL implantation and aphakia was OR 0.19 (95% CI: 0.04 to 0.95, $P = 0.044$) (Supplementary file 8); i.e., IOL implantation leads to significantly lower risk of hypotony. We refrained from interpreting the Funnel plot or the sensitivity analysis due to the low number of studies in analysis (<5) (Supplementary file 8).

Postoperative posterior synechia was reported in three studies [16, 32, 33]. The random-effects risk estimate for posterior synechia between IOL implantation and aphakia was OR 3.70 (95% CI: 0.44 to 31.11, $P = 0.023$) (Supplementary file 9), i.e., no significant difference in risk of posterior synechia between IOL implantation and aphakia. We refrained from interpreting the Funnel plot or the sensitivity analysis due to the low number of studies in analysis (<5) (Supplementary file 9).

Postoperative retinal detachment was reported in five studies [16, 20, 21, 32, 34]. The random-effects risk estimate for retinal detachment between IOL implantation and aphakia was OR 0.79 (95% CI: 0.18 to 3.57, $P = 0.76$) (Supplementary file 10), i.e., no significant difference in risk of retinal detachment between IOL implantation and aphakia. The Funnel plot appeared symmetrical and the sensitivity analysis demonstrated robustness of the findings (Supplementary file 10).

Postoperative development of phthisis bulbi was only reported by Sijssens et al. [36]. Here, the authors reported one case among 19 aphakic eyes and no cases among the 29 pseudophakic eyes, which did not differ significantly (OR 0.21, 95% CI: 0.0081 to 5.41, $P = 0.35$).

Secondary outcomes: risk of intraocular lens explantation or resurgery for any reason.

None of the 10 studies with 166 pseudophakic eyes reported need for lens explantation [16, 20, 21, 30–36]. A substantial number of both pseudophakic and aphakic eyes had resurgery, primarily because of glaucoma, but also due to visual axis opacification, band keratopathy, retinal detachment, and vitrectomy to manage chronic inflammation

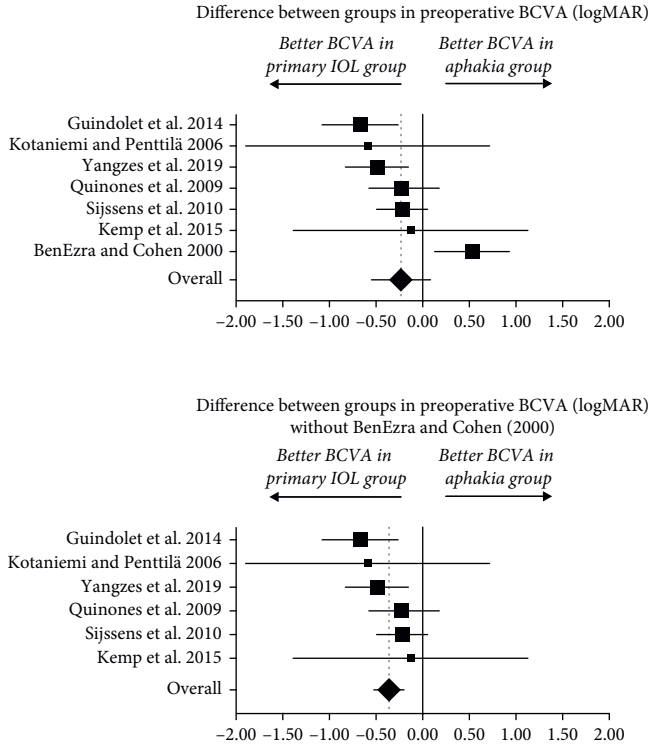

Figure 2: Forest plot of the differences between groups in the preoperative best-corrected visual acuity (BCVA). Top: Primary analysis with all eligible studies. In this analysis, BenEzra and Cohen [16] introduced a significant heterogeneity relative to the other studies. Bottom: Analyses were repeated after excluding BenEzra and Cohen [16], which significantly reduced heterogeneity. Summary estimates are weighted mean difference (WMD) in logMAR.

[16, 20, 21, 30–36]. It was not possible to extract data on number of eyes that had any resurgery (or eyes that did not have any resurgery) as data were not reported.

5. Discussion

This systematic review summarizes the evidence on modern cataract surgery in eyes with pediatric uveitis with either primary IOL implantation or aphakia. All ten studies eligible for review were retrospective chart reviews without randomization of eyes or patients, and further, several studies provided qualitative or quantitative evidence of selection bias. These limitations and the strong presence of selection bias must be kept in mind when interpreting the results of individual studies and our summary estimates. However, it is also important to realize that the evidence and estimates in this review are the best evidence the literature can present at this point.

Our meta-analyses revealed that the visual acuity was better in the IOL group one and five years after cataract surgery. Complications after cataract surgery in pediatric uveitis were included as secondary outcomes for the meta-analyses and a summary of these is presented in Figure 4. Compared to aphakia, statistically significant differences were only obtained in pseudophakia for higher rate of visual axis opacification and fewer cases of hypotony.

Included studies reported on different subtypes of pediatric uveitis. The various types of pediatric uveitis do not react to cataract surgery equally. JIA-associated uveitis is known to have a more severe manifestation of uveitis and a more complicated postoperative disease course than other types of uveitis [15, 16, 38]. Therefore, many surgeons may choose to leave eyes with JIA-associated uveitis aphakic. Quinones et al. [35] reported significantly more cases of JIA-associated uveitis in the aphakia group [35]. Similar considerations may underlie the decisions made in the study by Yangzes et al. [21], where the aphakia group had significantly more cases of panuveitis [21]. These studies highlight the selection bias that may influence our results. However, our review also includes data from a significant number of eyes with JIA-associated uveitis that underwent primary IOL implantation. In fact, more than half of the eyes (165 eyes out of 288) in this review had JIA-associated uveitis, and therefore it can be argued that primary IOL implantation can be an option for eyes with JIA-association uveitis but that randomized studies are warranted to determine the comparative efficacy and the primary choice of treatment.

Preoperative control of inflammation is generally recommended, and many prefer a practice of ≥3 months of quiescence before surgery to prevent complications and achieve the best possible visual acuity [37, 39, 40]. Five studies reported adequate preoperative immunosuppressive treatment [21, 33–36], three studies did not report if the eyes had been quiescent prior to surgery [30, 31, 41], and two studies reported that surgery was performed despite of in-

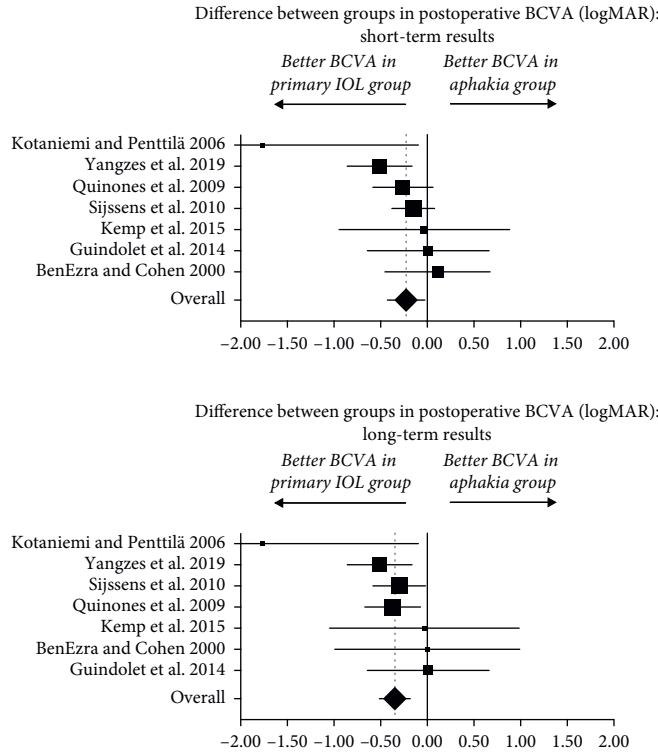

Figure 3: Forest plot of the differences between groups in postoperative short-term (1 year, top) and long-term (5 years, bottom) outcomes in the best-corrected visual acuity (BCVA). Summary estimates are weighted mean difference (WMD) in logMAR. To allow for easier interpretation of the overall study results, we refrained from adjusting figure to the study outcomes from Kotaniemi and Penttilä [20] which were subject to very large confidence intervals (−3.44 to −0.09 and −3.44 to −0.09, respectively, for short-term and long-term results).

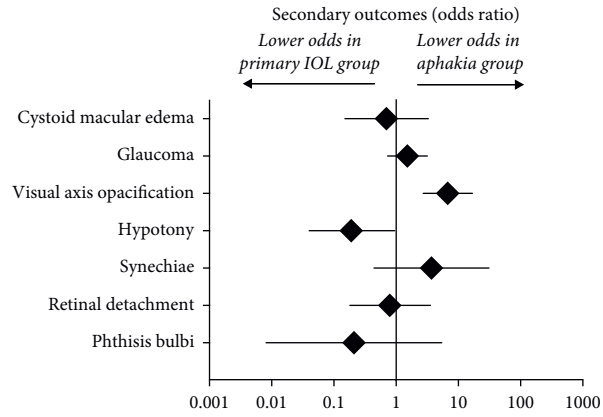

Figure 4: Overview of the secondary outcome meta-analyses. Summary estimates are odds ratio (OR). Significant differences between groups were visual axis opacification (OR 6.76, 95% CI: 2.73 to 16.8, $P = 0.000037$, i.e., more likely in those with primary IOL implantation group/less likely in aphakia) and hypotony (OR 0.19, 95% CI: 0.04 to 0.95, $P = 0.044$, i.e., less likely in those with primary IOL implantation group/more likely in aphakia).

flammation [16, 20]. Considering that preoperative inflammation control impacts postoperative outcomes and that preoperative inflammation control was subject to a certain heterogeneity, the results of this review should be interpreted with caution. It has been feared that implanting a foreign body, an IOL, during surgery may trigger an immune response and influence the postoperative need for anti-inflammatory treatment. Most studies did not describe the pre- or postoperative immunosuppressive treatment in detail. Guindolet et al. [32] reported a higher postoperative corticosteroid use after IOL implantation [32], while Kemp et al. [33] did not find any difference in medication between IOL implantation and aphakia [33].

A multicenter study from Alió et al. [30] with 140 eyes compared implantation of different types of intraocular lens material in adult patients with uveitis [42]. They found that

eyes with acrylic lenses had the lowest levels of postoperative inflammation in the first month and that heparin-coated PMMA lenses had the lowest incidence of uveitis relapses [42]. Silicone lenses had the highest rate of posterior capsular opacification and the highest rate of uveitis relapses [42]. Papaliodis et al. [43] found that implantation of acrylic lenses leads to less inflammation, fewer cases of PCO and CME, and better visual acuity when compared to heparin-coated PMMA, PMMA, or silicone lenses in a study with 36 eyes [43]. Studies in our review employed mainly acrylic or PMMA lenses, which may contribute to an explanation of the satisfactory clinical outcomes.

Not all children may be able to tolerate contact lenses after surgery and contact lens use concomitant with topical steroids to control inflammation may be problematic [16]. Aphakia spectacles can be impractical due to narrowing of the visual field and in case of unilateral cataract result in aniseikonia that affects stereopsis [44]. Therefore, a strong argument for choosing IOL implantation over aphakia is the easier optical rehabilitation.

6. Conclusion

Taken together, we conclude that in modern era cataract surgery of eyes with pediatric uveitis with IOL implantation leads to satisfactory and superior visual outcomes and no differences in complication rates apart from an increased prevalence of visual axis opacification and a decreased prevalence of hypotony when compared to aphakia. However, these results are subject to a certain degree of selection bias. Based on the current evidence and under careful patient selection and adequate pre- and postoperative inflammatory control, we consider IOL implantation to be a reasonable alternative to aphakia in pediatric uveitis. It must be stressed that randomized studies are needed to fully conclude which option should be considered superior or first line of therapy.

Data Availability

All data are included in this paper and its supplementary files.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Supplementary Materials

Supplementary file 1. Details of the literature search across different databases. *Supplementary file 2*. Details of the meta-analysis on the preoperative best-corrected visual acuity, including Funnel plot and sensitivity an1alysis. Supplementary file 3. Details of the meta-analysis on the postoperative short-term best-corrected visual acuity, including Funnel plot and sensitivity analysis. *Supplementary file 4*. Details of the meta-analysis on the postoperative long-term best-corrected visual acuity, including Funnel plot and sensitivity analysis. *Supplementary file 5*. Details of the meta-analysis on the postoperative cystoid macular edema, including Funnel plot and sensitivity analysis. *Supplementary file 6*. Details of the meta-analysis on the postoperative glaucoma, including Funnel plot and sensitivity analysis. *Supplementary file 7*. Details of the meta-analysis on the postoperative visual axis opacification, including Funnel plot and sensitivity analysis. *Supplementary file 8*. Details of the meta-analysis on the postoperative hypotony, including Funnel plot and sensitivity analysis. *Supplementary file 9*. Details of the meta-analysis on the postoperative posterior synechia, including Funnel plot and sensitivity analysis. *Supplementary file 10*. Details of the meta-analysis on the postoperative retinal detachment, including Funnel plot and sensitivity analysis. (*Supplementary Materials*)

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Research Article

Refractive Status in Eyes Implanted with Toric and Nontoric Intraocular Lenses during Combined Cataract Surgery and Microhook Ab Interno Trabeculotomy

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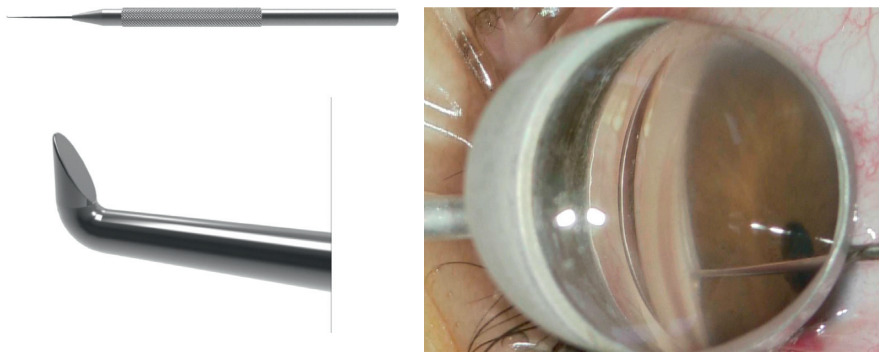
Purpose. To compare the refractive status between eyes implanted with toric and nontoric intraocular lenses (IOLs) during combined cataract surgery and microhook ab interno trabeculotomy (μLOT), a minimally invasive glaucoma surgery (MIGS). *Methods*. Twenty eyes of 20 patients who had open-angle glaucoma, cataract, and preexisting regular corneal astigmatism exceeding 1.5 diopters (D) and underwent combined μLOT and phacoemulsification were recruited retrospectively. Ten eyes were implanted with a toric IOL and 10 eyes with a nontoric IOL. The primary outcomes were the uncorrected visual acuity (UCVA) and refractive cylinder at 3 months postoperatively. *Results*. The mean UCVA of the toric IOL group (logarithm of the minimum angle of resolution (logMAR), 0.23 ± 0.25) was significantly better than that of the nontoric IOL group (logMAR, 0.45 ± 0.26) at 3 months postoperatively ($p < 0.05$). The mean absolute residual refractive cylinder of the nontoric IOL group (2.25 ± 0.62 D) was significantly greater than that of the toric IOL group (1.30 ± 0.68 D) ($p < 0.05$). Postoperatively, 60% of eyes in the toric IOL group and 10% in the nontoric IOL group had an absolute refractive astigmatism level of 1.5 D or less. Surgically induced astigmatism (0.77 ± 0.43 D for toric group and 0.60 ± 0.32 D for nontoric group) and IOP reduction ($33.9 \pm 15.6\%$ for toric group and $29.4 \pm 11.7\%$ for nontoric group) were not different between groups. *Conclusions*. Use of toric IOL during combined cataract surgery and μLOT is possible and better than not, but physician should prevent their patient of persisting residual astigmatism. The study was registered at https://www.umin.ac.jp/, and the clinical trial accession number is https://clinicaltrials.gov/ct2/show/UMIN000043141.

1. Introduction

Glaucoma is the leading cause of irreversible blindness globally. Glaucoma surgery is necessary when maximally tolerated medical therapy or laser treatments cannot control disease progression. Trabeculectomy (LEC) remains the standard surgical procedure for glaucoma to reduce the intraocular pressure (IOP). The astigmatic changes after LEC can lead to decreased visual acuity (VA) and might be problematic for patients [1]. As a result, a number of investigators have studied corneal refractive changes or surgically induced astigmatism (SIA) resulting from LEC [2, 3]. Minimally invasive glaucoma surgeries (MIGS) have been developed as safer and less invasive procedures with moderate IOP reduction and earlier treatment options compared with traditional surgery; these procedures often are performed in combination with cataract surgery. Despite the popularity of MIGS procedures on IOP reduction and safety, the impact of glaucoma surgical techniques on refraction, particularly astigmatism, is incompletely understood. While visual changes can result from decreased IOP [4], the direct effect of glaucoma surgery on the corneal topography is not fully known [2]. Microhook ab interno trabeculotomy (μLOT) is a novel procedure that uses microhooks and is a Schlemm's canal MIGS procedure reported by Tanito et al. (Figures 1(a) and 1(b)) [5]. The degrees of SIA were



(a) (b)

Figure 1: Microhook and intraoperative findings of microhook ab interno trabeculotomy. (a) The image shows the spatula-shaped microhook designed for use during ab interno microhook trabeculotomy (M-2215, Inami, Tokyo, Japan) and a photomacrograph of the tip of the microhook. (b) The tip of the microhook is inserted directly into Schlemm's canal temporally and moved circumferentially to incise the inner wall of Schlemm's canal and trabecular meshwork.

calculated to be 1.01, 0.62, 0.23, and 0.12 for LEC, EXPRESS® shunt (Alcon Vision LLC, Fort Worth, TX, USA), ab externo trabeculotomy, and μLOT groups, respectively [6]. Accordingly, minimal induction of astigmatism and less astigmatism-related decreases in the BCVA would be expected with the μLOT procedure. Recently, toric IOLs have been implanted increasingly in patients with corneal astigmatism during both cataract surgery alone and combined microincision vitrectomy surgery and cataract surgery to achieve postoperative spectacle-free distance vision [7, 8]; however, the use of toric IOL during MIGS is limited and far between in the literature [9], and the correcting astigmatism effect of toric IOL during combined MIGS is unclear.

AcrySof® IQ Toric IOL (Alcon Vision LLC, Fort Worth, TX, USA) had good rotational stability and favorable efficacy in patients with cataracts and corneal astigmatism [10]. To our knowledge, AcrySof® IQ Toric IOL implantation combined μLOT in patients who had cataract and preexisting astigmatism, and glaucoma has never been reported previously. The purpose of this study was to investigate the refractive changes in eyes implanted with AcrySof toric IOLs compared with nontoric IOLs combined with μLOT to treat glaucoma with preexisting corneal astigmatism.

2. Methods

The Ethics Committee of Shimane University Hospital approved the current study, which adhered to the tenets of the Declaration of Helsinki. The ethics committee waived the requirement for patients' informed consent regarding the use of their medical record data in accordance with the regulations of the Ethical Guidelines for Medical and Health Research Involving Human Subjects issued by the Japanese Government, and, instead, the protocol was posted on the department homepage to notify the potential participants about the study. We reviewed retrospectively the medical records of Japanese eyes, i.e., 10 consecutive eyes with open-angle glaucoma (OAG) implanted with a toric IOL and 10 eyes implanted with a nontoric IOL of patients who had preoperative regular corneal astigmatism exceeding 1.5 diopter (D) and underwent combined phacoemulsification and μLOT at Shimane University Hospital from February 2016 to December 2018. In our department, we began to use toric IOLs during combined μLOT procedure after 2018; therefore, most eyes in the nontoric group underwent surgery earlier in the study period, and those in the toric groups underwent surgery later in the study period. All patients underwent thorough ophthalmologic examinations that included measurements of the uncorrected VA (UCVA) and best-corrected VA (BCVA) values using a Landolt decimal acuity chart, refraction, and axial length measured by OA2000 (Tomey, Nagoya, Japan), number of glaucoma medications, and indirect ophthalmoscopy; the VA measurements were converted into the logarithm of the minimal angle of resolution (logMAR) VA. The inclusion criteria included OAG with cataract without any other ocular disease. Eyes were included that had no history of a previous intraocular surgery, no central visual field defect due to glaucoma, no complications during combined μLOT and cataract surgery, and no postoperative interventions. Patients who met those criteria and were implanted with an AcrySof ® IQ Toric IOL (Alcon Vision LLC, Fort Worth, TX, USA) were assigned to the toric IOL group; patients implanted with a nontoric IOL (XY-1, HOYA Corp., Tokyo, Japan) were assigned to the nontoric IOL group. The IOL spherical power was calculated for each case using the Barrett formula and the targeted refraction was emmetropia. In the toric IOL group, the IOL cylinder power and alignment axis were calculated using a web-based toric IOL calculator (available at http://www.acrysoftoriccalculator.com/) considering the keratometry readings and mandatory data input on the position of the incision and SIA by a superior incision (0.10 D). The manufacturer's information indicated that the SN6AT3, SN6AT4, SN6AT5, SN6AT6, SN6AT7, SN6AT8, and SN6AT9 toric IOLs (Alcon Vision LLC, Fort Worth, TX, USA) are intended for use when preexisting corneal astigmatism levels are about 1.03, 1.55, 2.06, 2.50, 3.00, 3.50, and 4.00 D, respectively.

2.1. Sample Size. A previous study that compared the absolute residual refractive astigmatism after cataract surgery between patients with cataracts and preexisting corneal astigmatism implanted with the AcrySof® IQ Toric IOL and AcrySof® spherical control IOL reported that the mean absolute residual refractive cylinder was 0.59 D after toric IOL implantation versus 1.22 D after nontoric IOL implantation [11]. If the difference in the residual refractive cylinder between the two groups was 0.33 D [12] with a significance level of 0.05 and a power of 0.8, an estimated sample size of at least six eyes in each group was calculated as essential for detecting a significant difference between the two groups. Considering the possibility of increasing the standard deviation, 10 eyes were enrolled in each group (a total of 20 eyes).

2.2. Surgical Method. Two surgeons (YT and MT) performed all surgeries. In the toric IOL group, a preoperative toric reference corneal marker (#17251 Moria S.A., Antony, France) was used to place two limbal reference marks at the 9 and 3 o'clock positions with the patient sitting upright. Cataract extraction was performed similarly in both groups through 2.4 mm superior limbal incisions. In the toric IOL group, the actual implantation axis was marked using an intraoperative toric axis marker (#17250, Moria S.A), and the toric IOL was implanted using a Monarch III injector (Alcon Vision LLC, Fort Worth, TX, USA). μLOT was performed through two corneal side ports as reported previously [13]. Briefly, a spatula-shaped microhook designed specifically for use during μLOT was used (M-2215, Inami, Tokyo, Japan) (Figure 1(a)). An ophthalmic viscosurgical device (PROVISC, Alcon Vision LLC, Fort Worth, TX, USA) was injected into the anterior chamber through two corneal side ports. A microhook was inserted into the anterior chamber through the corneal port using a Swan-Jacob gonioprism lens (Ocular Instruments, Bellevue, WA, USA) to observe the angle opposite to the corneal port. The tip of the microhook then was inserted into Schlemm's canal and moved circumferentially to incise the inner wall of Schlemm's canal and trabecular meshwork over 3 clock hours (Figure 1(b)). Using the same procedure, μLOT was performed in the opposite angle. After removal of the viscoelastic material, the IOL was rotated to align the cylinder axis to the marked axis. At the end of surgery, 2 mg of betamethasone sodium phosphate (Rinderon, Shionogi Inc., Osaka, Japan) was injected subconjunctivally and 0.3% ofloxacin ointment (Tarivid, Santen Pharmaceutical, Osaka, Japan) was applied. Postoperatively, 1.5% levofloxacin (Pfizer Japan Inc., Tokyo, Japan) and 0.1% betamethasone (Sanbetason, Santen Pharmaceutical) were applied topically four times daily for 4 weeks in all cases.

2.3. Primary Outcomes. The primary outcomes were the UCVA and absolute residual refractive cylinder at 3 months postoperatively. The astigmatic outcomes were calculated and visualized using the American Society of Cataract and Refractive Surgery Astigmatism Double Angle Plot Tool version 1.1.0 based on the vector analysis algorithm. With this tool, the preoperative corneal astigmatism was compared to the postoperative refractive astigmatism. The SIA was evaluated using SIA Calculator Tool (available at https://www.doctor-hill.com/iol-main/toric_sia_calculator.htm).

2.4. Statistical Analysis. Statistical analyses were performed using JMP version 11 (JMP Statistical Discovery, Cary, NC, USA). The differences between the preoperative and postoperative UCVA, BCVA, and refractive astigmatism were compared using the Wilcoxon signed-rank test. The differences between two groups were compared using the Mann-Whitney U test. For all statistical tests, $p < 0.05$ was considered significant.

3. Results

The demographic and clinical data from the toric and nontoric groups are summarized in Table 1. No significant differences were seen between the two groups in age, preoperative BCVA, absolute refractive cylinder, IOP, and number of glaucoma medications. The mean calculated target postoperative residual astigmatism was 0.57 ± 0.20 D. One eye (10%) each was implanted with SN6AT3, SN6AT4, and SN6AT7 IOLs, three eyes (30%) were implanted with SN6AT5 IOL, and four eyes (40%) were implanted with SN6AT6 IOL. No intergroup differences were seen in the BCVA and IOP preoperatively.

The status of the VA, astigmatism, and IOP at 3 months postoperatively is shown in Table 2. No intergroup difference was seen in the BCVA, while the UCVA in the toric IOL group was significantly better than that in the nontoric IOL group. The mean absolute residual refractive cylinder in the toric IOL group (1.30 ± 0.68 D) was significantly smaller than that in the nontoric IOL group (2.25 ± 0.62 D). No significant differences were seen in the corneal SIA, IOP, number of glaucoma medications, and reduction of IOP between the two groups.

Preoperative and postoperative astigmatic vectors and their means and distributions are shown in the double-angle plots in Figure 2(a) and 2(b) for the toric and nontoric IOL groups, respectively. Preoperatively, the centroids of corneal astigmatism in the toric (1.16 ± 1.90 D at 4 degrees) and nontoric (1.61 D ± 0.79 D at 4 degrees) groups were similar, while the centroids of postoperative residual astigmatism in the toric group (0.17 D ± 1.53 D at 18 degrees) were much smaller than those in the nontoric group (2.05 D ± 1.16 D at 5 degrees). The percentage of eyes with an absolute refractive astigmatism of 1.5 D or less was 60% in the toric IOL group and 10% in the nontoric IOL group (Figure 3).

4. Discussion

In the current study, postoperative UCVA was significantly better in toric IOL group than in nontoric IOL group due to the less refractive astigmatism, clearly presenting the efficacy of toric IOL use during combined cataract surgery and μLOT for correction of preexisting regular corneal astigmatism. This observation is unique in the literature.

Table 1: Demographic and preoperative clinical data.

	Toric IOL group	Nontoric IOL group	p value
No. of eyes (patients)	10 (10)	10 (10)	
Mean age (years)	74.6 ± 7.20	76.9 ± 6.82	0.5943[a]
Gender (male/female)	3/7	6/4	0.1775[b]
Mean preoperative BCVA (logMAR)	0.19 ± 0.23	0.26 ± 0.4	0.8194[a]
Mean absolute preoperative corneal cylinder (D)	2.09 ± 0.50	1.75 ± 0.30	0.0495[a]
Median absolute preoperative corneal cylinder (D)	2.05	1.63	
(Minimum—maximum)	1.52–3.25	1.50–2.25	
Mean absolute preoperative refractive cylinder (D)	2.70 ± 0.90	2.08 ± 0.58	0.1147[a]
Median absolute preoperative refractive cylinder (D)	2.75	2.13	
(Minimum—maximum)	1.25–4.00	1.51–3.00	
IOP (mmHg)	19.5 ± 6.17	18.8 ± 3.55	0.8197[a]
Medication	2.70 ± 1.06	2.70 ± 0.80	0.4453[a]
Toric IOL, no. (%)			
SN6AT3	1 (10)		
SN6AT4	1 (10)		
SN6AT5	3 (30)		
SN6AT6	4 (40)		
SN6AT7	1 (10)		

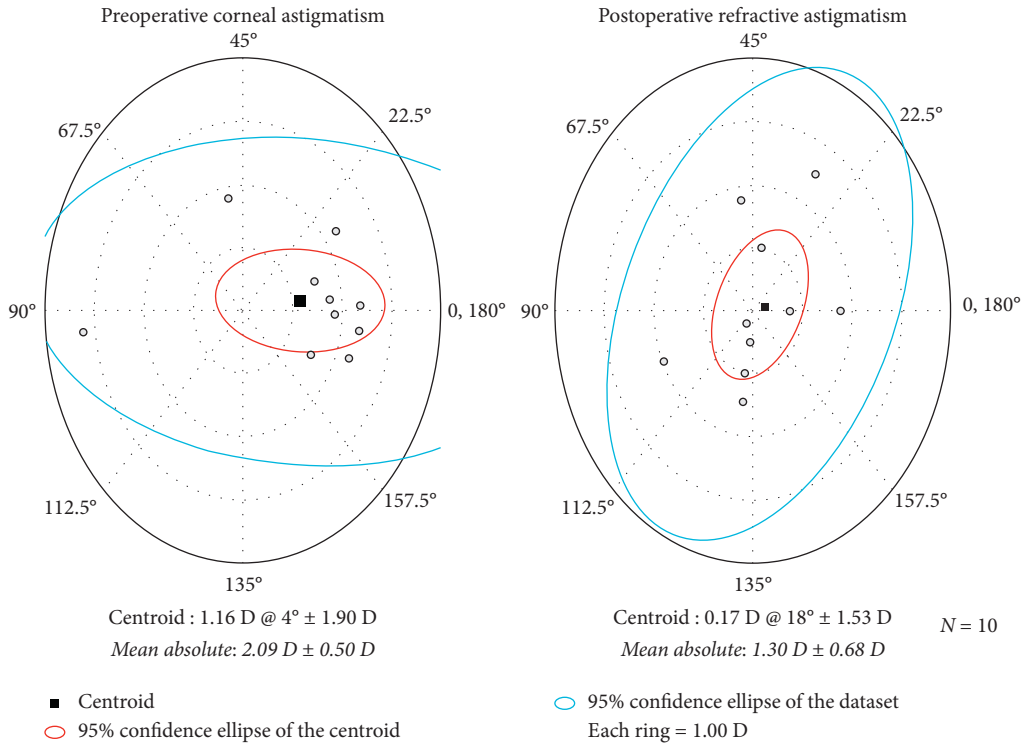
BCVA: best-corrected visual acuity; log MAR: logarithm of the minimum angle of resolution; IOP: intraocular pressure; IOL: intraocular lens. [a]Wilcoxon signed-rank test. [b]Mann–Whitney U test.

Table 2: Postoperative visual acuity, astigmatism, and IOP at 3 months in the toric IOL and the nontoric IOL groups.

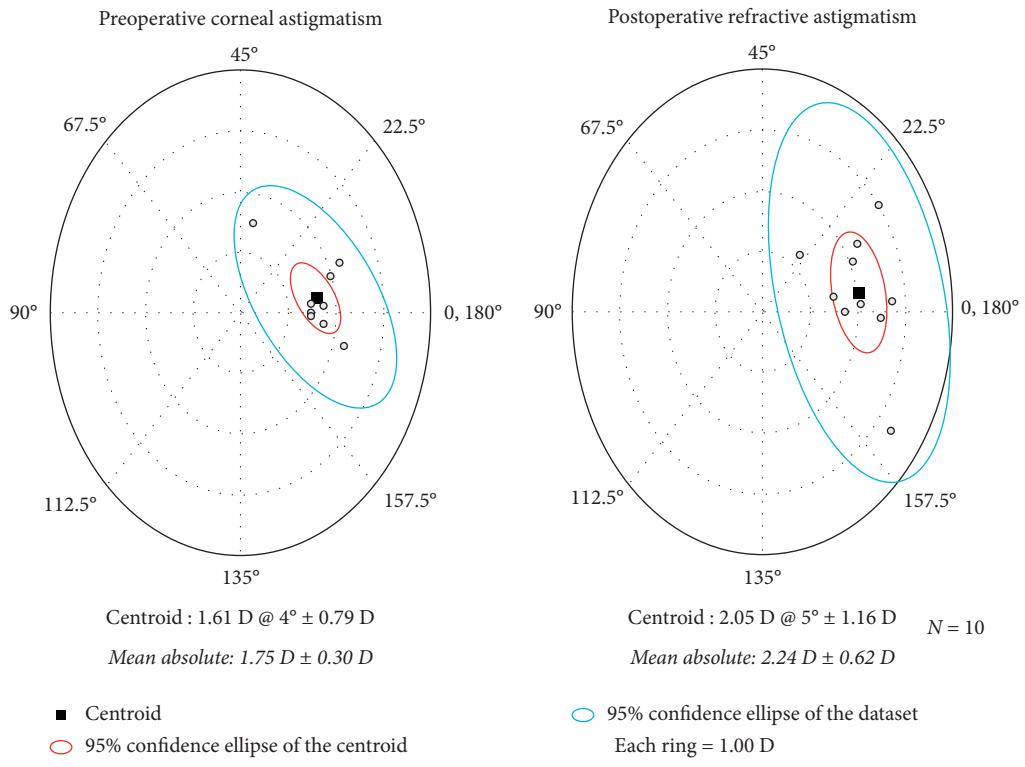
	Toric IOL group	Nontoric IOL group	p value
UCVA (logMAR)	0.23 ± 0.25	0.45 ± 0.26	0.0430*
BCVA (logMAR)	−0.11 ± 0.08	0.05 ± 0.12	0.2528
Mean absolute postoperative refractive cylinder (D)	1.30 ± 0.68	2.25 ± 0.62	0.0111*
Median absolute postoperative refractive cylinder (D)	1.25	2.25	
(Minimum—maximum)	0.25–2.50	1.25–3.25	
SIA (D)	0.77 ± 0.43	0.60 ± 0.32	0.3445
IOP (mmHg)	12.4 ± 3.41	13.0 ± 1.70	0.5421
Medication	1.70 ± 0.95	2.10 ± 0.88	0.3069
IOP reduction (%)	33.9 ± 15.6	29.4 ± 11.7	0.5706

UCVA: uncorrected visual acuity. The p values are calculated by Wilcoxon signed-rank test. *Significance levels of 5%.

LEC is the most commonly performed glaucoma surgery. Substantial evidence indicates that LEC is associated with significant astigmatic changes and increased refractive surprises, suggesting that more invasive glaucoma surgeries are not refractively neutral [2]. The possible mechanism of SIA after LEC may be tissue contraction around the LEC site secondary to extensive scleral cautery and suture, removal of the second scleral flap, the wound-healing process of the subconjunctiva [3, 14], and corneal steepening provoked by the pressure of a large drainage bleb under the eyelid [15]. In addition, Delbeke et al. reported that the lower IOPs achieved after filtration surgeries were associated with higher SIA and worse VA [4]. As the unpredictable astigmatic changes after LEC, toric IOL had been hardly used to correct preexisting regular corneal astigmatism so far. MIGS were developed to achieve safer and less invasive interventional treatments earlier in the disease process and are useful for moderately reducing IOP and/or medication dependence in combination with already planned cataract surgery to address visual disturbances associated with glaucoma. Therefore, patients treated with MIGS may place more importance on good visual quality than on IOP reduction because of their anosognosia with visual field loss. In the current study, combined μLOT and phacoemulsification with toric IOL implantation is an effective method to achieve better UCVA by correcting preexisting corneal astigmatism. In μLOT, conjunctival and scleral sparing with the ab interno technique, short surgical time, moderate IOP reduction, and no bleb-related complications [13] may contribute to the minimal induction of astigmatism and less astigmatism-related decreases in the BCVA. The SIA after combined μLOT and cataract surgery in the current study (0.77 ± 0.43 D in the toric IOL group and 0.60 ± 0.32 D in the nontoric IOL group) did not differ greatly from that after microincisional cataract surgery (mean SIA magnitude, 0.42 D after a 1.8 mm incision coaxial phacoemulsification and 0.5 D after 1.7 mm incision bimanual phacoemulsification) [16]. Manoharan et al. reported that refractive surprises occurred more often in patients with glaucoma, particularly those with angle-closure and pseudoexfoliation glaucoma treated with cataract surgery alone [17]. In two patients of the toric IOL group with high myopia and pseudoexfoliation (PXF), slight deterioration of postoperative absolute



(a)



(b)

Figure 2: The double-angle plots show the preoperative and postoperative astigmatic vectors and their means and spread in the toric IOL (a) and nontoric IOL groups (b). The black squares indicate the centroids, the red circles indicate the 95% confidence ellipses of the centroids, and the blue circles indicate the 95% confidence ellipses of the dataset.

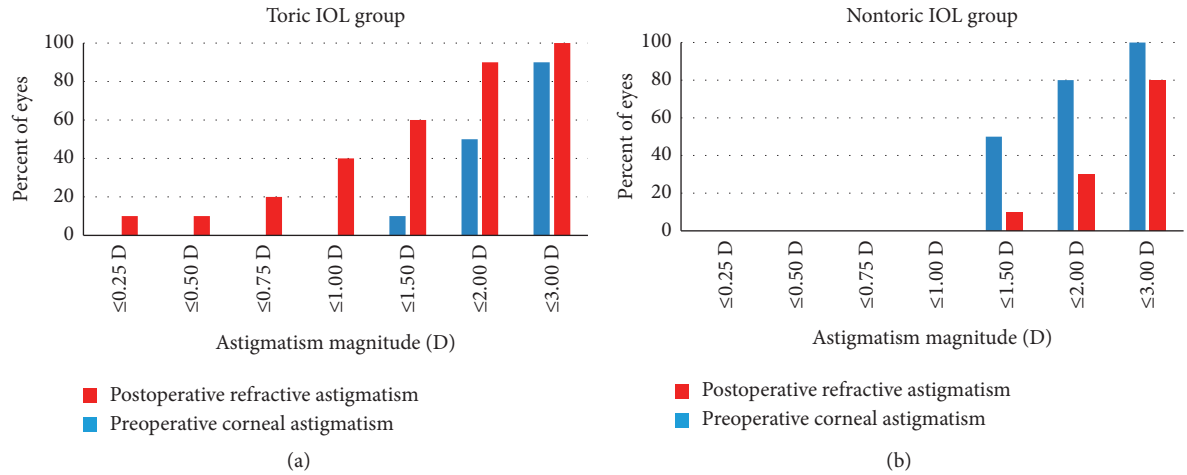


Figure 3: The magnitude of the preoperative corneal astigmatism and postoperative refractive astigmatism in the toric IOL and nontoric IOL groups.

refractive astigmatism compared to the preoperative values was observed. Postoperative refractive astigmatism is thought to include toric IOL rotation, lens capsule (and/or IOL) tilt, decentration, and unknown ocular components in addition to corneal astigmatism [18]. In the high myopic patients with lax capsule and PXF patients with zonular weakness, IOL and capsule tend to rotate and tilt [18, 19]. In the current study, postoperative toric IOL rotation was not examined, and IOL rotation and/or lens capsule IOL tilt after surgery may have occurred in our two cases; thus, we should take notice of the possibility to not correct the preoperative astigmatism in the patients with high myopia and PXF. Saheb and Ahmed reported that, compared to patients with OAG who underwent phacoemulsification alone, combined cataract and endoscopic cyclophotocoagulation (ECP) surgery had more myopic outcomes than predicted refractive outcomes [20]. Those authors hypothesized that because ECP targets the ciliary body, which is connected to the lens zonules, ciliary body changes resulting from ECP had the potential for unpredictable refractive outcomes. However, previous studies have reported that the combined trabecular microbypass, trabectome, and phacoemulsification procedures had similar refractive outcome to cataract surgery alone [21, 22]. They suggested that permanent removal of a portion of the trabecular meshwork and increased aqueous outflow did not result in significantly different refractive outcomes compared to cataract surgery alone. Thus, the subtypes of glaucoma and/or kinds of MIGS may affect the refractive outcomes, but this remains unclear. In the current study, less refractive surprises occurred; therefore, μLOT is not a factor that affects the final SIA when treating preexisting corneal astigmatism with glaucoma as previously described [6]. The strength of current results also suggested that AcrySof® IQ Toric IOL implantation in patients treated with combined μLOT and phacoemulsification is a favorable option for correcting preexisting corneal astigmatism and achieving better UCVA. In addition, 79% of patients treated with μLOT achieved successful IOP control of 18 mmHg or less and a 15% reduction or greater [13]; while the surgical indication for μLOT is for mild-to-moderate glaucoma, most patients treated with combined μLOT and phacoemulsification with toric IOL implantation more likely will achieve good visual quality, that is, good UCVA for years until the next surgical intervention such as LEC or tube-shunt surgery. With the unpredictable astigmatic changes after LEC, toric IOL had been hardly used to correct preexisting regular corneal astigmatism so far, then the weakness of toric IOL use in μLOT may have a negative influence on VA as an increase in aberration when the patients undergo LEC in the future. Thus, the further long-time observational studies are necessary to confirm the efficacy and safety. The IOP reduction ($33.9 \pm 15.6\%$ for toric group and $29.4 \pm 11.7\%$ for nontoric group) was not different between groups and the same as previous reports in combined μLOT and phacoemulsification [5]; this suggested that use of toric IOL did not affect the treatment effect.

5. Conclusions

Combined μLOT and phacoemulsification with AcrySof® IQ Toric IOL implantation is possible and better than not but physician should prevent their patient of persisting residual astigmatism. The current study was limited by its retrospective nature and short follow-up period. Further randomized and prospective studies may confirm the efficacy and safety of the combined μLOT and phacoemulsification with toric IOL implantation, and our study can be a useful reference for future trials.

Data Availability

The data that support the findings of this study are available from the corresponding author.

Conflicts of Interest

The microhooks used were codeveloped by Masaki Tanito, M.D., Ph.D., and Inami & Co., Ltd. (Tokyo, Japan). Dr. Tanito receives royalties from Inami & Co., Ltd. Other authors report no other conflicts of interest associated with this work.

Acknowledgments

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Review Article

Surgical and Perioperative Considerations for the Treatment of Cataract in Eyes with Glaucoma: A Literature Review

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Cataract surgery in the presence of glaucoma poses certain challenges that need to be addressed to offer the maximum benefit without complications. In this paper, we are reviewing the preoperative assessment, surgical options, the planning, and postoperative care. Cataract surgery can help reduce the intraocular pressure alone or combined with MIGS. When performed in patients with glaucoma, it can transiently increase the intraocular pressure and later on decrease the IOP to levels lower than the postoperative. The preoperative IOP and biometric characteristics are the main predictors of the postoperative course of IOP. The combination of cataract surgery with trabeculectomy remains controversial, in terms of best timing of each operation.

1. Introduction

Glaucoma has been ranked as one of the most common causes of visual impairment in the adult population worldwide. In people aged 50 years and older, the leading causes of blindness were cataract followed by uncorrected refractive error and glaucoma in 2015, with increasing prevalence since 1990. It has been calculated that 3.54% of the global population suffers from glaucoma. The vast majority of those cases account for open angle glaucoma (3.5%) and the rest accounts for primary angle closure glaucoma (0.5%). The number of people with glaucoma worldwide aged 40 to 80 years is expected to increase from 64.3 million in 2013 to 111.8 million in 2040 [1, 2].

With glaucoma being a widespread eye disease in the aged population, treatment of cataract needs to be planned while facing glaucoma as a comorbidity and vice versa. Our steps in the management of both eye conditions when coincident often need to be modified to achieve the best outcome for the patient. The cataract operation in such patients is done with special measures depending on the type and stage of glaucoma. Additionally, the IOP lowering medications prescribed to the patient often need to be adapted postoperatively. Combined techniques that manage both conditions simultaneously are also available in the surgical armamentarium and techniques have been developed, but the selection of the most suitable for each case demands careful consideration and is often controversial. It is known that the cataract operation has an IOP lowering effect and that in specific cases of glaucoma might be even the desired one to achieve a therapeutic effect [3].

2. Cataract Operation and Intraocular Pressure

Numerous studies have assessed the effect of cataract extraction on the IOP of the operated patients. The effect of the operation in IOP can be divided into 3 categories, the intraoperative effect, the short term postoperative effect, and the long-term effect. Each one needs to be taken into consideration in glaucoma patients.

During phaco surgery, it can be calculated that for every 15 cm of bottle height above the patient's eye level, there is a raise of 11 mm Hg in intraocular pressure (IOP) [4], when there is irrigation without aspiration. Consequently, when

the bottle height is adjusted at 1 meter, the IOP can reach as high as 70 mmHg which is around the closing pressure of the central retinal artery. Particularly in eyes with end-stage glaucoma, this could lead to severe vision loss, a phenomenon termed as wipe-out syndrome, that has been described, albeit rarely, after phacoemulsification surgery [5]. In eyes with end-stage glaucoma, it is safer to decrease bottle height and avoid keeping the phaco tip in the anterior chamber without active aspiration during surgery, so that IOP does not reach very high levels.

One of the most frequent complications after phacoemulsification surgery is the spikes of IOP in the immediate postoperative period [6]. The IOP after surgery can raise for several reasons, with the most common being the retained viscoelastic. Residue viscoelastic may cause obstruction of aqueous outflow and increase of IOP postoperatively as reported as early as 1983 [7]. For a given concentration of the viscoelastic in the AC, the lower the viscosity, the higher and more prolonged the IOP spike. The different viscoelastics demonstrate slightly different behaviours regarding the postoperative effect on IOP depending on their properties, such as molecular charge, chain length, and rigidity [8, 9]. The cohesive viscoelastics have larger molecular chains and are aspirated more easily, but may cause higher IOP spikes than the dispersive if not removed, although differences are not great [10]. On the other hand, the use of dispersive viscoelastic is responsible of this effect more often, since it cannot be easily removed from the eye without meticulous aspiration.

Other sources of IOP spikes after cataract include surgical trauma, prolonged surgery, retained lens debris, iris pigment scattering, inflammation, and hyphema [11]. Posterior capsule rupture, vitreous prolapse, and IOL placement in sulcus are considered risk factors for high IOP [12]. Other significant preexisting risk factors are glaucoma, pseudoexfoliation, tamsulosin intake, and myopia [13–18]. The longer axial length and the shallow AC are associated risk factors [19].

The immediate postoperative spikes usually happen 4 to 12 hours postoperatively. Very few patients developed IOP >30 mmg at 24 hours postoperatively, although hypertension can last up to a week [8, 11, 20]. In a study of eyes without glaucoma, IOP spikes of up to 68 mmHg were observed and 7.8% of eyes developed spikes of more than 40 mmHg 4 to 6 hours postoperatively [21], although most of the eyes that develop IOP spikes after cataract surgery will decrease to normal up to 24 hours postoperatively [20, 22].

Glaucoma is considered a risk factor for the development of an IOP spike after cataract surgery, and this has been demonstrated by studies that show increased incidence of early postoperative increase in IOP in eyes with glaucoma in comparison to normal eyes. IOP spikes over 30 mmHg were found in approximately 13% of eyes 1 day postoperatively in a study of eyes with POAG, and that was higher than the percentage found in nonglaucomatous eyes [17]. In a study that sets the threshold at 28 mmHg, the percentage in glaucomatous eyes was 46.4% versus 18.4% in nonglaucomatous [23]. A retrospective study of 271 eyes has shown that 17% of the operated eyes developed an IOP increase of at least 50% in comparison to the preoperative. Among glaucomatous eyes, those with increased risk are the cases with higher axial length and deeper anterior chamber, those that had required an increased number of antiglaucoma medications preoperatively, and those that had required preoperative laser trabeculoplasty. The protective effect of oral acetazolamide as adjunctive treatment in cataract surgery has been recognised in this study [13].

Prevention of IOP spikes is achieved with topical IOP lowering medication or more frequently with administration of oral acetazolamide [24]. This can be done preoperatively or postoperatively. According to a recent study, oral acetazolamide administration 1 hour preoperatively significantly reduced the IOP elevation from 1 to 24 hours postoperatively, while administration 3 hours postoperatively reduced the IOP elevation at 5 hours or more after surgery [25]. In eyes with glaucoma, the AC paracentesis has been shown to be successful as well, although in otherwise healthy eyes it has been demonstrated as having a nonlasting effect [21]. If left untreated, the IOP spikes in otherwise normal eyes might not be harmful for the visual fields according to clinical data [26], but for already compromised glaucomatous eyes, a significant albeit transient postoperative raise in IOP can be detrimental [27].

Apart from these reasons that lead to IOP raising up to 2 days postoperatively, there is a late postoperative risk of IOP rise due to steroid use after cataract surgery [28, 29]. Mostly myopic eyes but also others can be steroid responders, meaning that their IOP might raise most commonly 10 days to 2 weeks after starting topical steroid use. However, steroid induced IOP rise might appear as early as 5 days before surgery and up to several weeks later [28]. This effect is temporary but might be devastating if not timely detected and controlled in case of patients with glaucoma.

Albeit rising the IOP in the early postoperative period, it has been demonstrated by numerous studies that in the long term phacoemulsification has an IOP lowering effect to a variable extent. This result has been observed in both normal and glaucomatous eyes.

The most prominent lowering effect has been observed in eyes with narrow angle glaucoma. The angle configuration is the initial source of hypertension in such eyes, and the removal of the lens offers sufficient space for the iris to retract and increase the angle width. Progression of lens thickness with age is disproportional to the progression of total eye volume which seizes to increase usually in a young age. Consequently, the lens over time takes over more space in the anterior segment and contributes to IOP rise [30]. Removal of the crystalline lens and placement of a much thinner intraocular lens in all operated eyes lead to deepening of the anterior chamber and increase in angle width, an effect with increased clinical significance in eye with narrow preoperative angles. In addition, cataract surgery results in less IOP fluctuations in such eyes [31]. The amount of the effect is correlated with the preoperative IOP and the depth of the AC in such eyes. Other parameters associated to the effect are the lens thickness and the gonioscopy score [32, 33]. The implementation of cataract surgery as a treatment of choice instead of peripheral iridotomy for

primary angle closure glaucoma has been highlighted in the literature [34, 35].

The effect of cataract surgery on the IOP is also detectable in eye with open angles. A proposed mechanism for that is the increased posterior traction of the zonules to the ciliary body and the scleral spur due to the posterior displacement of the anterior capsule postoperatively [36]. According to this theory, this traction expands the trabecular meshwork and improves the aqueous outflow. An IOP raising effect of the aging crystalline lens also contributes to this effect [30]. The lowering effect is more prominent on eyes with an increased preoperative IOP and it depends on the biometric characteristics of the eye.

Several studies have looked into the predictive factors for the IOP lowering effect of cataract surgery. Issa et al. developed an index of the pressure to depth ratio in order to predict the lowering effect according to which the IOP reduction was positively correlated to the preoperative IOP and inversely related to the anterior chamber depth [37]. Liu et al. also suggested a formula that was based on IOP and ACD for eyes with ACG [38]. Most studies agree that if preoperative IOP is more than 20 mmHg, the IOP reduction after cataract surgery would be likely significant. Perez et al. in their formulas include as predictors the preoperative IOP in combination with other parameters such as anterior chamber depth, lens thickness, gonioscopy score, and glaucoma status [39].

3. Phacoemulsification Surgery in Eyes with Glaucoma: Surgical Technique Considerations

In eyes with primary open angle glaucoma, no special technique modifications are needed usually. In case of terminal stage glaucoma patients care should be taken to avoid significant increasing of the intraoperative IOP. In all patients with glaucoma, especially those that are in view of a possible surgery, the incisions should be placed in clear cornea to avoid damage to the conjunctiva, in order not to compromise future glaucoma surgery.

In patients with PXF, surgery might be demanding due to the zonular instability that many of these patients have. The weakened zonules might lead to zonular dehiscence intraoperatively and need for special measures in order to avoid complications. Additionally, pupil dilation in patients with PXF is often compromised. In patients with PXF glaucoma aspiration of the exfoliation material from the angle at the end of surgery might be beneficial for the postoperative IOP.

In eyes with angle closure, glaucoma surgery is always challenging due to the anatomical characteristics of those eyes and the effect of glaucoma and previous attacks of acute angle closure. Those eyes have shallow anterior chambers that incommode surgical maneuvers and also are often prone to intraoperative choroidal effusion. Posterior synechiae, poor dilation, weak zonules, and low endothelial cell count might complicate surgery furthermore. Surgery needs to be undertaken with caution. Preoperative administration of mannitol to reduce hyaloid volume might be helpful, as well as preoperative administration of acetazolamide to reduce IOP. Care must be taken in the construction of the wounds in order to avoid intraoperative iris prolapse. Maintaining a stable chamber by viscoelastic infusion prior to removal of irrigation handpiece from the eye during surgery is considered to protect from anterior chamber collapse and choroidal effusion in very short eyes. In eyes with extensive anterior synechiae, cataract surgery would be best combined with goniosynechiolysis, in order to separate the anterior synechiae from the trabecular meshwork and achieve more sufficient IOP control. In general, cataract surgery has been proven to be a sufficient first-line treatment for angle closure glaucoma, more effective than laser iridotomy and could be considered as an alternative to this.

4. Surgical Considerations in Patients with past Trabeculectomy

It has been well described that cataract surgery in patients with glaucoma is more complex than the routine phacoemulsification. Moreover it is still widely thought that cataract surgery following trabeculectomy will increase the risk of bleb failure [40] in spite of studies claiming otherwise [40, 41]. In fact some surgeons went as far as using cataract surgery in an attempt to treat postoperative hypotony and its complications with good success [42].

It is true that phakic patients with a functioning trabeculectomy will eventually need cataract surgery, especially considering that filtrating surgery is a risk factor for lens opacification. Eventually 50% of patients that underwent this kind of procedures will present with visually significant cataract over the next five years [43].

Taking into consideration this fact, we need to adjust our strategy to the specifics of trabeculectomised patients. Husein et al. showed that early cataract operation has higher incidence of trabeculectomy failure, considering a period of two years gap between the two operations being the safest option of those studied. Additionally, preoperative high intraocular pressure was deemed as a bad prognostic factor, presumably owing to an already malfunctioning bleb [44]. Some authors in fact have proposed the use of anterior segment optical coherence tomography (AS- OCT) [45] and ultrasound biomicroscopy (UBM) [46] to distinguish between well and not-so-well functioning blebs.

It seems clear that the postoperative inflammation induced by phacoemulsification is considered the main factor leading to bleb failure. Action therefore must be taken to perform the surgery in an atraumatic way, including minimal manipulation and a temporal main port incision all whilst maintaining anterior chamber stability. In the case of a malfunctioning bleb, a combined bleb revision approach could be considered [47]. Aggressive anti-inflammatory treatment intra- and postoperatively is adequate, with intraoperative injection of dexamethasone, 5 fluorouracil along with intensive steroid drops postoperatively being some examples [48].

Another risk that needs to be considered is the complete wipe out. Considerable variation exists between the

glaucoma specialists as far as the estimated risk is concerned. It has been reported to be higher than 1/100 to even lower than 1/1000. A current UK-based study by the NHS Health Research Authority is hoping to shed more light on this subject [5].

5. Minimally Invasive Glaucoma Surgery and Phacoemulsification

Over the past years we have witnessed the emergence of a number of techniques and devices that try to tackle the main problem of trabeculectomy surgery, which is none other than its safety profile and invasive nature. These techniques aim to either increase aqueous outflow either bypassing (e.g., Xen) or enhancing anatomical structures (e.g., gonioscopy assisted transluminal trabeculotomy (GATT), Hydrus, iStent©) or decrease aqueous production by cyclodestructive procedures such as endocyclophotocoagulation and micropulse cyclodiode laser.

MIGS are essentially a category of procedures that offer a higher safety profile but lower efficacy than trabeculectomy. The most usual clinical scenario is mild to moderate glaucoma which is either uncontrolled by drops or aims to reduce drops dependency, usually due to compliance issues pertaining to individual patient factors such as lifestyle, frailty, and drop side effects among others [49].

5.1. Phacoemulsification Alone. Phacoemulsification is a recognized modality for treating angle closure glaucoma and it can be even considered without the presence of visually significant cataract in clear lens extraction [50]. It has also been proven to lower the intraocular pressure in open angle patients even when performed as standalone. Its effects, albeit not permanent, should not be overlooked, since it is shown to decrease IOP by 5.1% in three years [51].

5.2. iStent and iStent Inject©. These two devices represent the two generations of a heparin-coated nonferromagnetic titanium stent which when inserted into the trabecular meshwork drain fluid directly to the canal of Schlemm, and their technical characteristics are beyond the scope of this article. Another advantage of iStent inject© is that it comes preloaded with two stents which further increases its efficacy. When combined with phacoemulsification, it has been proven to be more effective than phacoemulsification alone and it reduces the dependency to eye drops [1, 52–55]. Its major advantage however is the easier technique and excellent safety profile, as it was intended for the general ophthalmologist and not the glaucoma specialists alone.

5.3. Hydrus. This device, which is a crescent-shaped scaffold is made of nitinol (a nickel-titanium alloy) that is placed on the Schlemm's canal [56]. In a randomized control trial that compared phacoemulsification alone versus combined phaco/hydrus, it was found that 80% of patients that underwent the combined procedure had lower IOP and 73 % was free of drops in two-year follow-up period. The safety profile of the combined versus the standalone cataract operation was the same, besides 1-2 mm of focal peripheral anterior synechiae with no further implications [57].

5.4. Gonioscopy-Assisted Transluminal Trabeculotomy (GATT). It is not very frequent that a name is so descriptive that leaves so little to imagination. GATT is a development of the ab externo trabeculotomy thus salvaging the conjunctiva and sclera, using a Swan Jacob gonio lens and either an illuminated probe or a suture. When combined with phacoemulsification, it reduced the eye pressure from a mean of 23.9 mmHg to 15.5 mmHg and drop dependency from 2.9 to 1.0 during the first 12 months of follow-up. Hyphaema was the only side effect reported in 20% of patients that had the combined procedure. In patients that had standalone GATT choroidal folds, CMO and IOP spikes were seen [58].

5.5. Endocyclophotocoagulation (ECP). ECP is a recognized technique with a diode laser targeting directly on the ciliary processes, with minimal destruction of surrounding tissues and a greatly improved safety profile. When combined with cataract surgery, it can produce a modest yet significant drop in pressure. It was found to reduce the mean IOP from 18.7 mmHg to 14.0 mmHg in 106 eyes of 99 patients after three years of follow-up but with a failure rate of 60%. While this may look disheartening, the vast majority of patients were managed with drops and SLT and only seven ended up needing filtration surgery [59]. Similarly Francis et al. found a decrease of IOP by 13.6% in three years of follow-up [51]. On the downside, endoscopic surgery is a new skill for ophthalmologists that needs ad initio training, and the postoperative inflammation requires intensive anti-inflammatory drop regime.

A very similar but ab externo technique is micropulse cyclophotocoagulation laser. While no publications exist to date dealing with combined micropulse cyclophotocoagulation/phacoemulsification procedures, it has proven to be a safe and effective, minimally invasive treatment. It works by applying short bursts of energy (0.5 sec) followed by rest periods of 1.1 sec. Reported success rates range from 72.7 to 89.5% [59, 60].

5.6. Trabectome Combined with Cataract Surgery. Trabectome is a device known to be effective in lowering intraocular pressure with reported evidence since 2005. When combined with cataract surgery, it is found to cause an increased incidence of postoperative cystic macular oedema in comparison to the cataract alone group. However no effect was found in the postoperative refraction and it did not seem to affect the targets set by the surgeons. As such it is still considered to be a viable option [61].

In contrast to the aforementioned techniques and devices, Xen45 and InFocus are bleb forming procedures. When it comes to Xen, it has shown to be effective in reducing pressure and drop dependency quite significantly. Furthermore it has shown to have reduced effectiveness in

non-Caucasian patients and when combined with cataract surgery. On top of that it was found to have a high reoperation rate of 37.7% [62]. It has to be noted here that Xen implants are targeting mild to moderate glaucoma patients and cannot usually lower the pressure below mid-teens [63].

On the other side of the spectrum PRESERVFLO® MicroShunt (previously known as InnFocus MicroShunt) which is made of poly(styrene-block-isobutylene-block-styrene), or SIB—a biocompatible, bioinert material—is a bleb forming device which aims to replace trabeculectomy. It has, in fact, a good safety profile and a reduced operating time [64]. In contrast to what is known for trabeculectomy and Xen implants, in a study from the Dominican Republic, there was no significant difference in the drop of pressure between the patients having MicroShunt alone and those having combined Phacoemulsification with MicroShunt surgery [65].

Another device that is worth mentioning is Cypass. This device presented the novel approach of being inserted in the suprachoroidal space, giving a reduction of intraocular pressure of about 20% [66]. In fact it showed superiority over the iStent when combined with cataract surgery. It gained FDA approval following the 2-year long COMPASS study, but it was recalled from circulation following the reduction of endothelial cell count at the 5-year review of the initial study patient cohort [67].

6. Toric and Premium Intraocular Lenses in Patients with Glaucoma

Various studies have shown the advantage of the use of toric lenses in cataract patients. Indeed as IOL technology follows the demand of a sharper vision and spectacle free life, patients with glaucoma are no exception to that. It has been shown that toric lenses improve postoperative refractive outcomes in glaucomatous patients. Controversy still exists in patients with short axial length, however, because of biometry unpredictability and change of capsule, so there is a high risk of axis change [68].

Premium lenses on the other hand are less recommended. As a general rule, they decrease the quality of vision in patients with moderate disease. They have been successfully implanted in patients with very early glaucoma which is thought unlikely to progress and in patients with ocular hypertension or glaucoma suspects without disc damage or visual field loss [31]. In more detail aspheric lenses have shown conflicting evidence when it comes to contrast sensitivity. Blue filtering lenses show no difference in contrast sensitivity. Regarding the multifocal IOLs, they have been found to invariably decrease the contrast sensitivity to a greater extend, and even more for the near than the distance. Finally accommodative lenses seem to be affected by capsular thickening, which is worse in pseudoexfoliation patients, causing aberrant folding of the lens known as "Z-Syndrome" [69].

7. Conclusions

Cataract surgery in patients with glaucoma generates many considerations for the surgeon who seeks to prevent the possible additional complications and to take advantage of the favorable results. Avoidance of postoperative IOP spikes would protect many glaucomatous eyes from loss of visual fields, and timely use of cataract surgery could reduce the need for IOP lowering medication. Selection of type and time of operation must offer the highest amount of benefit without compromising the potential glaucoma surgery in the future.

Cataract surgery in a patient with a previous trabeculectomy certainly is more complicated in relation to the technique used, as it is widely thought to cause bleb failure. In order to avoid bleb scarring, it is advisable to wait for about two years after the trabeculectomy, if at all possible. Prior to the operation the functionality of the bleb should be checked, either by simply measuring the pressure and assessing its morphology or by using AS-OCT and UBM [45, 46]. If it is found to be malfunctioning and a combined bleb revision/phacoemulsification procedure should be planned [44, 47]. At the time of surgery, extra care must be taken to perform an atraumatic procedure and avoid placing incisions over the bleb (both main and side ports) [47].

The management is relatively less complicated when the newer MIGS procedures are paired with cataract surgery. These devices have given a solution to those patients who have mild to moderate disease but are still uncontrolled using maximum drug treatment, are unable to tolerate it, or have other compliance issues.

It is understandable that glaucoma patients will want the best possible visual outcome following their cataract surgery and as such they will inquire or even research independently about toric and premium lenses. Toric lenses have indeed proven to improve refractive outcomes in glaucomatous patients [68], but it is more complex about premium lenses as they invariably either decrease contrast sensitivity or do not affect it at all. The only category that seems to benefit is glaucoma suspects or ocular hypertension patients without visual field defects and disc damage, or patients with very early damage which is unlikely to progress [69]. Overall cataract surgery in the glaucomatous patient is a challenging feat, but appropriate steps can be taken for the benefit of the patients to enjoy a fulfilling and beneficial outcome.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

None of the authors has financial conflicts of interest in the present manuscript.

Authors' Contributions

Kleonikos Tsakiris and George Kontadakis contributed equally to the manuscript.

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Review Article

Comparative Efficacy of Phacotrabeculectomy versus Trabeculectomy with or without Later Phacoemulsification: A Systematic Review with Meta-Analyses

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There is no consensus on the surgical management of coexisting cataract in patients who undergo glaucoma surgery. In this study, we systematically reviewed the literature to compare the efficacy and safety of phacotrabeculectomy and trabeculectomy either alone or followed by later phacoemulsification. We systematically searched the literature databases PubMed/MEDLINE, EMBASE, and the Cochrane Central. Eligible studies were comparative trials of eyes with glaucoma that underwent either phacotrabeculectomy or trabeculectomy with or without later phacoemulsification. Our primary outcome measure was intraocular pressure (IOP) control closest to 12 months. Secondary outcome measures were efficacy closest to 12 months in terms of visual acuity, visual field, prevalence of complications, needling or revision, number of antiglaucomatous medications, and surgical success. We identified 25 studies with a total of 4,749 eyes. The IOP did not differ significantly between those who underwent phacotrabeculectomy versus trabeculectomy with (MD: 0.63, CI95%: −0.32, 1.59, $p = 0.19$) or without later phacoemulsification (MD: −0.52, CI95%: −1.45, 0.40, $p = 0.27$). However, phacotrabeculectomy was associated with lower risk of complications (RR: 0.80, CI95%: 0.67, 0.95, $p = 0.01$) and better visual acuity corresponding to a 1.4-line difference (MD: −0.14, CI95%: −0.27, −0.95, $p = 0.03$) compared to trabeculectomy. Other secondary outcome measures did not differ significantly (visual field, needling or revision, number of antiglaucomatous medications, and surgical success). In conclusion, postoperative IOP is comparable, and the number of complications is lower when phacotrabeculectomy is compared to trabeculectomy with or without later phacoemulsification in patients with coexisting glaucoma and cataract. However, our study also reveals that the level of evidence is low, and randomized clinical trials are warranted.

1. Introduction

Cataract and glaucoma are globally the most common causes of blindness and they frequently coexist [1–3]. It is believed that up to 10% of the elderly with cataracts have ocular hypertension (OHT) or glaucoma [4, 5], and in 2040, glaucoma is estimated to affect 111.8 million individuals worldwide [6]. Elevated intraocular pressure (IOP) is the only modifiable risk factor for the progression of visual field loss in patients with glaucoma. Among those who cannot achieve satisfactory target IOP and preservation of visual function, the current best practice is to consider filtration surgery. The most widely performed IOP-lowering procedure worldwide is trabeculectomy whereby a channel between the anterior chamber of the eye and the subconjunctival space is created [7].

An important number of patients requiring surgical intervention for glaucoma present with coexisting cataract, and it remains debated how best to manage these patients. Prior to trabeculectomy, it may be tempting to remove the lens and replace it with a thinner intraocular lens to increase anterior chamber depth in order to reduce the risk of the postoperative shallow anterior chamber [8]. However, trabeculectomy is often

performed prior to cataract surgery since the optic nerve head in these patients is at high risk of damage from postoperative IOP spikes, which is a known phenomenon after cataract surgery [9], and also because postponing the trabeculectomy may increase the risk of visual field loss. On the other hand, performing a trabeculectomy in a phakic eye is challenging due to vitreous pressure that pushes the phakic lens forward during the operation. Further, trabeculectomy may advance cataract progression, and 6–58 % of the patients have been reported to convert from no cataract at the time of filtration surgery to cataract requiring surgery within the first year [10–12]. Trabeculectomy-induced cataract progression which necessitates cataract surgery may lead to a subsequent increase in IOP due to bleb failure [13, 14]. It is believed that bleb failure is related to postoperative inflammation and a change in the microenvironment, causing the closure of the filtration route of the aqueous humor, thereby making the filtering bleb dysfunctional [15, 16].

One solution to this problem is the combined procedure phacotrabeculectomy. Although in theory, it may possess many benefits, in reality, it obtained a poor reputation in its early years and is now a rarely used procedure in many glaucoma centers [17, 18]. However, the development of small incision phacoemulsification surgery has improved the success rates and reduced the complication rates after cataract surgery. This leads to the question—does modern cataract surgery allow a less hazardous profile of phacotrabeculectomy? The answer remains unclear and there is a lack of consensus on the best surgical management for these patients [19–22].

Here, we systematically reviewed the literature to compare the efficacy of phacotrabeculectomy with trabeculectomy (with or without later phacoemulsification surgery) on the management of glaucoma and coexisting cataract. We focused on small incision phacoemulsification surgery to present relevance to current clinical practice.

2. Materials and Methods

2.1. Study Design. This systematic review and meta-analysis was designed following the principles of the Grading of Recommendation, Assessment, Development, and Evaluation (GRADE) working group [23]. The topic was defined using the PICO approach which in short stands for the patient (P), intervention (I), comparison (C), and outcome (O) [24]. According to Danish law, no ethical committee or institutional review board approval was required for this study. We followed the items of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) for all aspects of the reporting [25].

2.2. Eligibility Criteria and Outcome Measures. Eligible studies were defined as those who fulfilled the following criteria:

(1) Population: patients with any type of glaucoma

(2) Intervention: phacotrabeculectomy

(3) Comparator: trabeculectomy with or without later phacoemulsification surgery

(4) Outcomes: the primary outcome was the postoperative IOP closest to 12 months. Secondary outcomes were evaluated closest to 12 months and included visual acuity, visual field, the prevalence of complications with an exception for worsening of cataract, needling or revision, number of antiglaucomatous medications, surgical success, and failure

(5) Study type: a comparative clinical study of humans. Studies were eligible regardless of study time (retrospective or prospective) or randomization

Intervention and/or comparator could be with or without the use of antimetabolites during surgery. We only considered studies disseminated in the English language. Unpublished registry trials were disregarded.

2.3. Information Sources, Search Strategy, and Study Selection. We searched the literature databases PubMed/MEDLINE, EMBASE, and the Cochrane Central. The search was performed on January 20, 2020. Considering the immense development in cataract surgery in the 20th century and the differences between earlier practices and modern cataract surgery, we enforced a restriction on date of publication; i.e., we did not consider studies published prior to 1997 to ensure that only studies with modern surgical methods were included. Our search phrases and database searches were conducted with the assistance of a trained information specialist. We included a combination of keywords using the following search phrases:

(1) (phaco-trabeculectomy OR phacotrabeculectomy) AND ("phacoemulsification"[Mesh] OR "Trabeculectomy"[Mesh] OR phacotrabeculectomy OR trabeculectomy OR phacoemulsification)

(2) Trabeculectomy OR trabeculectomy failure OR trabeculectomy survival OR trabeculectomy success rate AND phacoemulsification AND (primary open-angle glaucoma OR POAG)

Two authors (A. A. and L. K.) screened titles and abstracts for eligibility and removed duplicates and obviously irrelevant reports. Remaining records were retrieved in full text to examine eligibility. All these records were read by two authors (A. A. and L. K.) who then discussed eligibility. In addition, reference lists of all articles read in the full text were crosschecked to identify other potentially relevant studies. Disagreements between the authors would lead to the involvement of a third author (D. B–H.) for further discussions and final decision making.

2.4. Data Collection and Risk of Bias Assessment. Two authors (A. A. and L. K.) extracted the following data from each eligible study: study design, study characteristics, glaucoma type, surgical methods, and outcomes of interest. The GRADEpro Guideline Development Tool was used to assess

the quality of evidence for each outcome across studies [26]. The quality of evidence for each outcome started out as high level and could subsequently be downgraded because of limitations in study design (e.g., lack of randomization), risk of bias [27], inconsistency (heterogeneity) [28], indirectness [29], imprecision [30], and publication bias [31] to moderate, low, or even very low quality of evidence.

2.5. Data Synthesis and Analysis. All eligible studies were reviewed qualitatively in text and tables. The Review Manager 5.3 Software [32] was used to calculate estimates of overall treatment effects, and random-effect models were used to calculate pooled estimates of effects. Continuous outcome data were analyzed using the mean differences (MDs) approach with 95% confidence intervals (CIs), and dichotomous outcomes data were analyzed using risk ratios (RRs) with 95% CI.

3. Results

3.1. Study Selection. Our search strategy yielded a total of 1,393 records. We included one other study, which we knew of *a priori*. After removing the duplicates ($n = 406$), 988 records were screened using title and abstract, and 48 records were deemed to be of potential interest and retrieved in full text. Of these, 20 records were not eligible for our review (Supplementary file 1). We concluded that 25 studies were eligible for our qualitative and quantitative review (Figure 1).

3.2. Study and Population Characteristics. We identified studies comparing (a) phacotrabeculectomy ($n = 2{,}315$ eyes) with trabeculectomy ($n = 2{,}216$ eyes) and (b) phacotrabeculectomy ($n = 75$ eyes) with trabeculectomy followed by phacoemulsification performed 3–6 months after trabeculectomy ($n = 71$ eyes). We did not identify studies with other combinations of phacotrabeculectomy, trabeculectomy, and phacoemulsification.

We did not identify any randomized studies. We included 19 retrospective and six prospective studies. The majority of the studies included a mixed group of glaucoma subtypes, and six studies consisted of patients with POAG only. Studies were based on populations in North and South America (USA, $n = 3$; Canada, $n = 2$; Chile, $n = 1$), Australia, $n = 1$, Europe (UK, $n = 2$; Italy, $n = 2$; Switzerland, $n = 1$; Belgium, $n = 1$; Turkey, $n = 1$), and Asia (China, $n = 3$; Singapore, $n = 1$; Japan, $n = 1$; Hong-Kong, $n = 1$; South Korea, $n = 2$; Iran, $n = 1$; Israel, $n = 1$; Saudi Arabia, $n = 1$). A detailed description of the included studies is available in Table 1.

3.3. Primary Outcome: Postoperative IOP in Phacotrabeculectomy versus Trabeculectomy Only. Twenty-one studies reported IOP control in patients undergoing phacotrabeculectomy versus trabeculectomy only. In total 1,682 eyes underwent phacotrabeculectomy versus 1,983 that received trabeculectomy. Evaluation of long-term IOP ranged from 1 month to 2 years in included studies [33–53] with 13 studies reporting IOP at 12 months after surgery [33, 36, 37, 39, 41, 43–45, 48, 49, 51–53]. Four studies included patients with POAG [33–36], and 17 studies included a mixed group of glaucoma patients [37–53]. The use of antimetabolites during the glaucoma procedures varied from the use of mitomycin C (MMC) or 5-fluorouracil (5-FU) or no use of antimetabolites to a combination of antimetabolites and no use of antimetabolites in the same study. Overall, we did not find any significant differences in long-term IOP control between the two groups, but the heterogeneity among studies was considerable ($I^2 = 93\%$) (Figure 2).

3.4. Primary Outcome: Postoperative IOP in Phacotrabeculectomy versus Phacoemulsification 3–6 Months after Trabeculectomy. Two studies reported IOP in patients with POAG or mixed glaucoma undergoing phacotrabeculectomy ($n = 75$ eyes) or trabeculectomy followed by phacoemulsification ($n = 71$ eyes). All patients received perioperative antimetabolite (MMC or 5-FU). Postoperative IOP was measured at 12 months [57] or 2 years [56] after the last procedure. There was no difference in long-term IOP control between the two groups (Figure 3).

3.5. Secondary Outcome: Visual Acuity in Phacotrabeculectomy versus Trabeculectomy Only. Five studies reported logMAR visual acuity at any follow-up time in a manner that could be included in a meta-analysis. One study was based on patients with POAG [35], and the four other studies were based on a mixed glaucoma group [38, 40, 48, 55]. All studies used a combination of some patients receiving antimetabolites and others not receiving antimetabolites during glaucoma surgery. A total of 797 eyes had phacotrabeculectomy versus 1,183 who had trabeculectomy only. Long-term visual acuity was on average 0.14 logMAR better in the group receiving phacotrabeculectomy, corresponding to a 1.4-line difference on a visual acuity chart ($p = 0.03$) (Figure 4).

3.6. Secondary Outcome: Prevalence of Complications in Phacotrabeculectomy versus Trabeculectomy Only. Eighteen studies reported complications at the latest reported follow-up in eyes undergoing phacotrabeculectomy or eyes receiving trabeculectomy only. Four studies were based on patients with POAG [33, 35, 36, 54]; the remaining 14 studies were based on a mixed glaucoma group [37, 39–43, 46, 48–53, 55]. The use of antimetabolites during the glaucoma procedures varied from the use of mitomycin C (MMC) or 5-fluorouracil (5-FU) or no use of antimetabolites to a combination of antimetabolites and no use of antimetabolites in the same study. The studies reported a wide range of complications ranging from less severe to very severe: hyphema, conjunctival scars, corneal edema, keratitis, postoperative IOP spike, bleb leak, flat/shallow anterior chamber, hypotony, hypotonous maculopathy, severe postoperative inflammation, fibrin reaction, iris prolapsed, lens malposition, blebitis, endophthalmitis, bleeding problems, posterior vitreous detachment, epiretinal membrane,

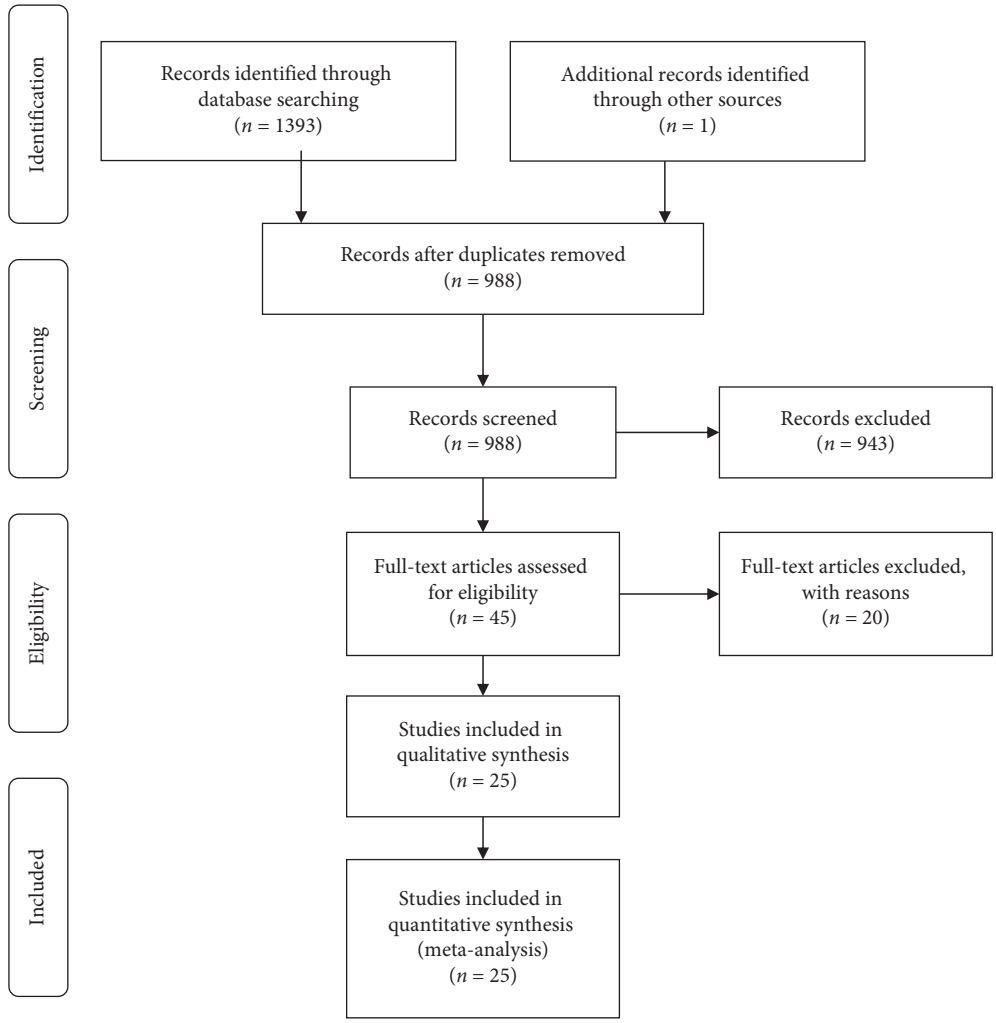

Figure 1: Flow diagram of the study selection process.

retinal detachment, serous choroidal detachment, neovascular glaucoma, hemispheric vein occlusion to aqueous misdirection syndrome. The included studies reported a total of 502 complications in the 2,203 eyes undergoing phacotrabeculectomy (22.8%) versus 540 complications in the 2,081 eyes (25.9%) undergoing trabeculectomy only. The difference was statistically significant (RR = 0.80, 95% confidence interval: 0.67 to 0.95, $p = 0.01$) (Figure 5).

3.7. Secondary Outcome: Prevalence of Complications in Phacotrabeculectomy versus Phacoemulsification 3–6 Months after Trabeculectomy. Prevalence of complications was evaluated in eyes undergoing phacotrabeculectomy ($n = 28/75$) or the consecutive procedure of trabeculectomy and phacoemulsification ($n = 37/71$) in patients with POAG or mixed glaucoma [56, 57]. All patients received perioperative antimetabolite (MMC or 5-FU). There was no significant difference in the risk of complications in eyes that had phacotrabeculectomy performed compared to the total number of complications in eyes that had a trabeculectomy followed by phacoemulsification (Supplementary Figure S1).

3.8. Secondary Outcome: Visual Field in Phacotrabeculectomy versus Trabeculectomy Only. Two studies [41, 48] reported the effects on visual fields in patients undergoing phacotrabeculectomy versus trabeculectomy only. The studies were based on a mixed group of glaucoma patients, some patients received antimetabolites, and some did not. In total, 669 eyes underwent phacotrabeculectomy versus 1,150 that received trabeculectomy. No significant difference was found between the two groups (Supplementary Figure S2).

3.9. Secondary Outcome: Needling or Revision in Phacotrabeculectomy versus Trabeculectomy Only. Nine studies reported the need for needling or revision. One study was based on patients with POAG [54], and the other studies were based on a mixed glaucoma group with a combination of some patients receiving antimetabolites and others not [37, 40, 41, 45, 46, 48, 50, 52]. 1,652 eyes received the combined procedure whereas 1,662 underwent trabeculectomy. No significant difference was found between the two groups (Supplementary Figure S3).

Table 1: Description of included studies.

Study	Methods	Glaucoma	Exclusion criteria	Surgical method (n)	Outcome measures	Notes
Phacotrabeculectomy versus trabeculectomy						
Li et al. 2019 [33]	Retrospective review	POAG	Other eye diseases, serious cardiovascular, cerebrovascular diseases, diabetes, cancer, mental defects, physical disabilities; patients with surgical tolerance; patients who transferred to other hospitals during treatment	Phacotrabeculectomy (49) mean age $37.40 \pm 10.90y$ Trabeculectomy (65) mean age $39.30 \pm 11.90\,y$ MMC	(1) IOP (12 months) (2) Visual acuity (12 months) (3) Complete success (IOP $\leq$ 21) (4) Qualified success (IOP > 21 mmHg, but decreased to $\leq$21 mmHg after taking IOP-lowering medication) (5) Failure (IOP > 21 mmHg	(2) Visual acuity not defined as LogMAR
Pakravan et al. 2014 [34]	Prospective comparative case series	POAG	History of contact lens wear, previous intraocular surgery, any corneal disease such as keratoconus, corneal dystrophies or corneal scars, CCT $\geq$ 580 or $\leq$ 500 microns, post-operative IOP $\geq$ 21 or $\leq$5 mmHg and occurrence of any surgical complications.	Phacotrabeculectomy (23) mean age $60.2 \pm 20.2y$ Trabeculectomy (23) mean age $54.7 \pm 24.2y$ MMC	(1) IOP (3 months)	—
Jung et al. 2014 [35]	Comparative retrospective consecutive case series review	POAG	Patients with glaucoma. Exclusion criteria prior filtering surgery, phacoemulsification in the previous 6 months, surgeries performed by residents in training.	Phacotrabeculectomy (51) mean age $73.7 \pm 7.5\,y$ Trabeculectomy (51) mean age $59.7 \pm 9.8\,y$ +/− anti-metabolite (1) Phacotrabeculectomy 0/51 received (2) Trabeculectomy 5/51 received	(1) IOP (6 months) (2) Log-MAR visual acuity (6 months) (3) Complications (4) Anti-glaucomatous medication (6 months) (5) Complete success (IOP < 21 mmHg /20% reduction on two consecutive follow-up visits after 3 months, without IOP-lowering medication) (6) Qualified success (IOP < 21 mmHg /20% reduction below baseline on two consecutive follow-up visits after 3 months with IOP-lowering medication) (7) Failure (IOP > 21 mmHg /<20% reduction below baseline on two consecutive follow-up visits after 3 months, IOP $\leq$ 5 mmHg on two consecutive visits after 3 months, reoperation for glaucoma, or loss of light perception vision)	—

Table 1: Continued.

Study	Methods	Glaucoma	Exclusion criteria	Surgical method (n)	Outcome measures	Notes
Lochhead et al. 2003 [36]	Retrospective study	POAG	—	Phacotrabeculectomy (44) Trabeculectomy (44) No anti-metabolite No significant differences between groups with respect to age $p = 0.75$	(1) IOP (12 months) (2) Complications (3) Anti-glaucomatous medication (4) Surgical success	(3) Anti-glaucomatous medication is only described as p value (0.4) (4) Graphs show results of surgical success but numbers could not be extracted
Chang et al. 2006 [37]	Retrospective, non-randomized study	POAG ACG CACG PXF PDG	Prior filtering surgery, excessive risk for conjunctival scarring	Phacotrabeculectomy (45) mean age 76.2 (58.0–94.0)y Trabeculectomy (47) mean age 70.0 (44.3–88.1)y 5-FU	(1) IOP (minimum 12 months) (2) Complications (3) Anti-glaucomatous medication (minimum 12 months) (4) Surgical success (5) Needling (6) Visual acuity	(6) Visual acuity means ± SDs could not be obtained from article.
Demir 2018 [38]	Prospective, non-randomized study	Mixed glaucoma	Optic disk anomaly except for glaucomatous changes, hereditary retinal diseases, retinal vascular diseases, fundus pathologies, those with low test reliability values, astigmatism higher than 3.00 D, cataract density higher than grade 2 according LOCS III, epinephrine corneal toxicity corneal disease and surgical history. Corneal endothelial density below 1300 cells/mm^2 and those who failed to continue their postop checkups for at least 1 month.	Phacotrabeculectomy (20) mean age $66.2 \pm 10.9y$ Trabeculectomy (20) mean age $61.6 \pm 12.1y$ 5-FU	(1) IOP (1 month) (2) Log-MAR visual acuity (1 month)	—
Derick et al. 1998 [39]	Retrospective review	POAG PXF ACG Other	Observation <12 months	Phacotrabeculectomy (42) mean age $75.9 \pm 8.0y$ Trabeculectomy (42) mean age $73.8 \pm 9.3y$ MMC	(1) IOP (minimum 12 months) (2) Anti-glaucomatous medication (minimum 12 months) (3) Complete success (IOP < 21 mmHg, no IOP-lowering medication) (4) Qualified success (IOP < 22 mmHg, with IOP-lowering medication) (5) Complications (6) Visual acuity	(6) Visual acuity described as snellen acuity

Table 1: Continued.

Study	Methods	Glaucoma	Exclusion criteria	Surgical method (n)	Outcome measures	Notes
Graf et al. 2019 [40]	Prospective study	POAG PEX NTG CAG SEC	—	Phacotrabeculectomy (161) mean age $74.7 \pm 8.1y$ Trabeculectomy (85) mean age $69.0 \pm 12.0y$ MMC	(1) IOP (24 months) (2) Log-MAR visual acuity (3 months) (3) Complete success (achieved target pressure according to visual field defects) (4) Failure (target pressure not achieved) (5) Anti-glaucomatous medication (3 months) (6) Complications (7) Needling	(1) No SD value for IOP at 3 months.
Jiang et al. 2018 [41]	Retrospective, cohort observational study	POAG PACG	Traumatic, neovascular, exfoliative, pigmentary, congenital and uveitic glaucoma	Phacotrabeculectomy (129) mean age $68.34 \pm 11.4y$ Trabeculectomy (148) mean age $63.5 \pm 11.1y$ MMC	(1) IOP (12 months) (2) Complete success (IOP < 20 mmHg and/or 20% reduction from baseline. (3) Qualified success (IOP < 20 mmHg, with single IOP-lowering medication) (4) Failure (requiring more than one topical agent and/or repeat surgery) (5) Complications (6) Needling (7) Visual acuity	(7) Visual acuity: SD value could not be obtained from article.
Kleinmann et al. 2002 [42]	Retrospective comparative study	POAG PXF ACG SEC	Surgery without use of MMC, prior ocular surgery	Phacotrabeculectomy (102) mean age $74.1 \pm 6.8y$ Trabeculectomy (33) mean age $69.0 \pm 14.6y$ MMC	(1) IOP (latest follow-up) (2) Anti-glaucomatous medication (latest follow-up) (3) Complications	—
Murthy et al. 2006 [43]	Retrospective, cohort study	POAG CACG PXF PDG NTG Neovascular uveitis-induced	Ocular conditions that could interfere with accurate assessment of IOP, including fuchs endothelial dystrophy and pseudophakic bullous keratopathy.	Phacotrabeculectomy (73) mean age $73.1 \pm 12.4y$ Trabeculectomy (49) mean age $66.1 \pm 16.7y$ MMC	(1) IOP (12 months) (2) Complications (3) Anti-glaucomatous medication (4) Surgical success	(3) Graphs show results of surgical success but numbers could not be extracted (4) Anti-glaucomatous medication no reported SD value
Polikoff et al. 2005 [44]	Retrospective review	POAG PXE Uveitis-induced LTG Congenital Neovascular PDG Traumatic	Eyes that required further surgical intervention within $1y$ from time of surgery, postoperative IOP > 21 mmHg.	Phacotrabeculectomy (53) mean age $70.3 \pm 14.8y$ Trabeculectomy (82) mean age $60.5 \pm 19.2y$ MMC/5-FU (1) IOP: Phacotrabeculectomy (49) Trabeculectomy (57) (2) Success: Phacotrabeculectomy (49) Trabeculectomy (72) (3) Failure: Phacotrabeculectomy (53) Trabeculectomy (82)	(1) IOP (12 months) (2) Complete success (IOP < 22 mmHg, no IOP-lowering medication, no further surgical interventions within 1 year) (3) Qualified success (IOP < 22 mmHg, with IOP-lowering medication, no further surgical interventions within 1 year) (4) Failure (IOP > 22 mmHg, further surgical interventions within 1 year	(1)–(4) All patients were not always included in the subsequent analyses.

Table 1: Continued.

Study	Methods	Glaucoma	Exclusion criteria	Surgical method (n)	Outcome measures	Notes
Seo et al. 2019 [45]	Retrospective review	POAG PACG Secondary glaucoma	Patients unwilling to perform bleb OCT-A, missed followup visits, or had poor OCT-A image quality.	Phacotrabeculectomy (28) mean age $66.75 \pm 7.77y$ Trabeculectomy (44) mean age $61.18 \pm 12.97y$ MMC	(1) IOP (12 months (2) Complete success (IOP ≤ Target mmHg) (3) Qualified success (IOP ≤ 21 mmHg) (4) Failure (reoperation due to an increase in IOP despite medication and needling) (5) Needling	—
Singh et al. 2001 [46]	Retrospective, unmatched, non-randomized study	POAG PXF PDS CACG Traumatic Congenital Possner-Schlossman syndrome	—	Phacotrabeculectomy (51) mean age $76.2 \pm 6.9y$ Trabeculectomy (56) mean age $63.3 \pm 12.1y$ 5-FU	(1) IOP (24 months) (2) Complications (3) Anti-glaucomatous medication (24 months) (4) Complete success (IOP < 16 mmHg and a 30% reduction in IOP, no medication after 24 months) (5) qualified success (IOP < 16 mmHg and a 30% reduction in IOP, with medication after 24 months) (6) failure (IOP > 15 mmHg /< 30% reduction in IOP even with medications, or required revision surgery within 24 months) (7) Needling (8) Visual acuity	(8) Visual acuity described as snellen acuity change
Zhong et al. 2019 [47]	Retrospective, case-control study	POAG PACG	Ocular surface diseases, dry eyes according to the Japanese dry eye diagnostic criteria, ocular injury, infection, surgery and using contact lens, using drugs including preservative benzalkonium.	Phacotrabeculectomy (24) mean age $53.25 \pm 3.40y$ Trabeculectomy (27) mean age $52.19 \pm 3.28y$ 5-FU	(1) IOP (3 months)	—
Hong et al. 2007 [48]	Retrospective review	POAG CPACG	Less than $3y$ follow-up, other ocular diseases or intraocular surgical histories, other diseases affecting their visual fields or diabetes.	Phacotrabeculectomy (540) mean age $66.2 \pm 11.0y$ Trabeculectomy (1002) mean age $51.4 \pm 16.3y$ +/−MMC (1) Phacotrabeculectomy 88,77% reccevied (2) Trabeculectomy 91,11% reccevied	(3) IOP (12 months) (4) LogMAR visual acuity (at last success follow-up) (5) Complications (at last success follow-up) (6) Antiglaucomatous medication (at last success follow-up) (7) Failure (at last success follow-up) (8) Success ((a) IOP was reduced by at least 30% from baseline; (b) IOP ≤ 21 mmHg; (c) IOP < 18 mmHg) (9) Visual field (at last success follow-up) (10) Needling	(8) We considered success criteria c) as complete, criteria b) as qualified, and criteria a) as failure (∗) Postoperative values were at last successful follow-up (1) Phacotrabeculectomy 9.21 ± 4.86y (2) Trabeculectomy 10.74 ± 4.43y

Table 1: Continued.

Study	Methods	Glaucoma	Exclusion criteria	Surgical method (n)	Outcome measures	Notes
Bellucci et al. 1997 [49]	Retrospective study	Mixed glaucoma	—	Phacotrabeculectomy (118) mean age $72 \pm 10y$ Trabeculectomy (75) mean age $55 \pm 16y$ no anti-metabolite	(1) IOP (12 months) (2) Complications (3) Anti-glaucomatous medication	(3) Anti-glaucomatous medication ± SDs could not be obtained from article.
Choy 2017 [50]	Retrospective review	POAG CACG Uveitic-glaucoma	—	Phacotrabeculectomy (20) mean age $65.7 \pm 14.8y$ Trabeculectomy (18) mean age $62.4 \pm 12.0y$ no anti-metabolite	(1) IOP (3 months) (2) Complications (3) Complete success (IOP < 22 mmHg and, no glaucoma medication) (4) Qualified success (IOP < 22 mmHg with the use of glaucoma medication) (5) Failure (IOP > 21 despite the use of glaucoma medications) (6) Needling (7) Visual acuity	(7) Visual acuity postoperatively described as acuity change
Cillino et al. 2004 [51]	Prospetive randomized clinical trial	POAG PEX	—	Phacotrabeculectomy (15) mean age $74.6 \pm 1.1y$ Trabeculectomy (18) mean age $71.3 \pm 1.2y$ no anti-metabolite	(1) IOP (12 months) (2) Complications (3) Complete success (IOP ≤ 21 mmHg and, no glaucoma medication) (4) Qualified success (IOP ≤ 21 mmHg with or without the use of glaucoma medication) (5) Anti-glaucomatous medication (12 months)	—
Guggenbach et al. 1999 [52]	Prospective study	POAG PXG	Previous surgery or laser trabeculoplasty performed 6 months or less before surgery, high risk patients primarily treated with antifibrotic agents at the time of surgery.	Phacotrabeculectomy (70) mean age $80.0 \pm 7.0y$ Trabeculectomy (54) mean age $72.2 \pm 9.0y$ no anti-metabolite	(1) IOP (12 months) (2) Complications (3) Anti-glaucomatous medication (12 months) (4) Needling (5) Visual acuity	(5) Visual acuity: Graphs show results but means ± SDs could not be obtained from article.
Noben et al. 1998 [53]	Retrospective review	POAG PXG PDS	Only one eye per patient was used. Use of anti-metabolite per- or postoperatively, previous glaucoma or other intraocular surgery.	Phacotrabeculectomy (28) mean age 76.17 (55–87)y Trabeculectomy (25) mean age 68.80 (52–83)y no anti-metabolite	(1) IOP (12 months) (2) Complications (3) Anti-glaucomatous medication (12 months) (4) Failure (IOP ≥ 21 mmHg or a less than 20% reduction from the preoperative level regardless the use of anti-glaucoma medications.	—
Tan et al. 2011 [54]	Retrospective review	POAG	Only one eye per patient was used. Surgery for acute primary angle closure.	Phacotrabeculectomy (608) mean age $70.3y$ Trabeculectomy (208) mean age 56.9 MMC/5-FU	(1) Complications (12 months) (2) Needling	—
Ogata-Iwao et al. 2013 [55]	Prospective study	POAG PXG	≤40y, IOP < 21 mmHg and history of ocular surgery.	Phacotrabeculectomy (25) mean age $73.1 \pm 6.9y$ Trabeculectomy (25) mean age $72.1 \pm 7.3y$ MMC	(1) Complications (2) Anti-glaucomatous medication (12 months) (3) Failure (IOP ≥ 26 mmHg at ≥ 3 months, despite completion of laser suture lysis and bleb needling) (4) Log-MAR visual acuity (12 months)	—

Table 1: Continued.

Study	Methods	Glaucoma	Exclusion criteria	Surgical method (n)	Outcome measures	Notes
Post-operative IOP in patients undergoing phacotrabeculectomy versus phacoemulsification 3–6 months after trabeculectomy						
Donoso and Rodríguez2000 [56]	Retrospective review	POAG	Patients with glaucoma.	Phacotrabeculectomy (22) mean age $75.0 \pm 5.0y$ Trabeculectomy + Phacoemulsification (18) mean age $78.0 \pm 6.7y$ 5-FU	(1) IOP (phacotrabeculectomy 28.00 ± 16.14 months, trabeculectomy + phacoemulsification 21.35 ± 16.8 months) (2) Complications (3) Success (IOP < 20 mmHg at 12 months)	(3) Success, described as % and could not be converted to numerical proportions and not described by the other article.
El-Sayyad et al. 1999 [57]	Retrospective review	POAG CACG Combined-glaucoma PXG Steorid induced	Corneal opacities, subluxated cataractous lens, significant posterior segment disorders and/or previous eye surgery.	Phacotrabeculectomy (53) mean age $49.9 \pm 14.3y$ Trabeculectomy + Phacoemulsification (53) mean age $50.3 \pm 12.2y$ MMC/5-FU	(1) IOP (12 months) (2) Complications	(2) Complications are seen as total numbers according to the two groups.

POAG = primary open-angle glaucoma; PACG = primary angle-closure glaucoma; ACG = angle-closure glaucoma; CACG = chronic angle-closure glaucoma; CPACG = chronic primary angle-closure glaucoma; PGD = pigment dispersion glaucoma; PEX = pseudoexfoliation glaucoma; PXF = pseudoexfoliation glaucoma; NTG = normal-tension glaucoma; LTG = low tension glaucoma; SEC = secondary glaucoma.

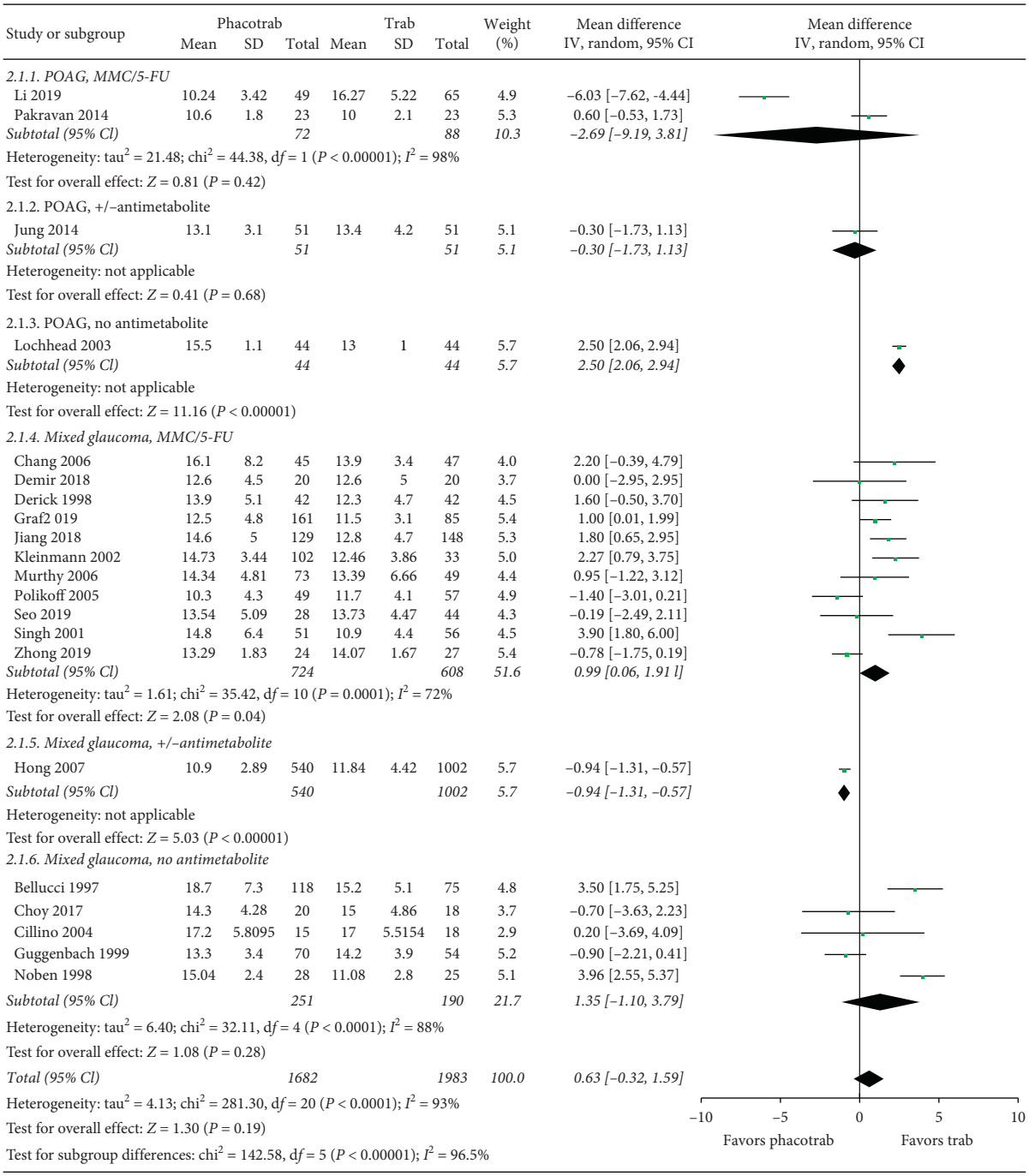

Figure 2: Forest plot of the IOP control at latest follow-up in eyes undergoing phacotrabeculectomy or trabeculectomy only. CI = confidence interval; d*f* = degrees of freedom; IV = inverse variance; SD = standard deviation. MMC = mitomycin c; 5-FU = 5-fluorouracil; +/− antimetabolite = not all eyes received antimetabolite during the procedure.

3.10. Secondary Outcome: Surgical Success in Phacotrabeculectomy versus Trabeculectomy Only

3.10.1. Complete Success. Twelve studies reported complete success, which was obtained in a total of 951 out of 1,184 (80.3%) eyes undergoing phacotrabeculectomy and 1,375 out of 1,658 (82.9%) eyes undergoing trabeculectomy only. Two studies were based on patients with POAG [33, 35] and ten studies based on the mixed glaucoma group [37, 39–41, 44–46, 48, 50, 51]. The use of antimetabolites during surgery varied between the included studies. There was no significant difference between groups

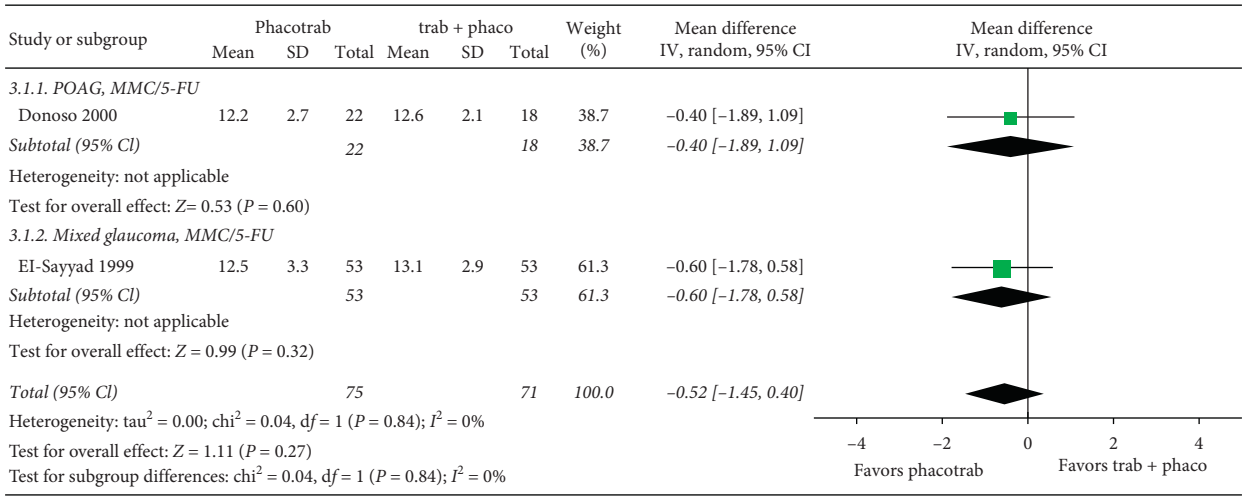

Figure 3: Forest plot of the IOP control postoperatively in eyes undergoing phacotrabeculectomy versus trabeculectomy with phacoemulsification 3–6 months later. CI = confidence interval; df = degrees of freedom; IV = inverse variance; SD = standard deviation. MMC = mitomycin c; 5-FU = 5-fluorouracil; ± antimetabolite = not all eyes received antimetabolite.

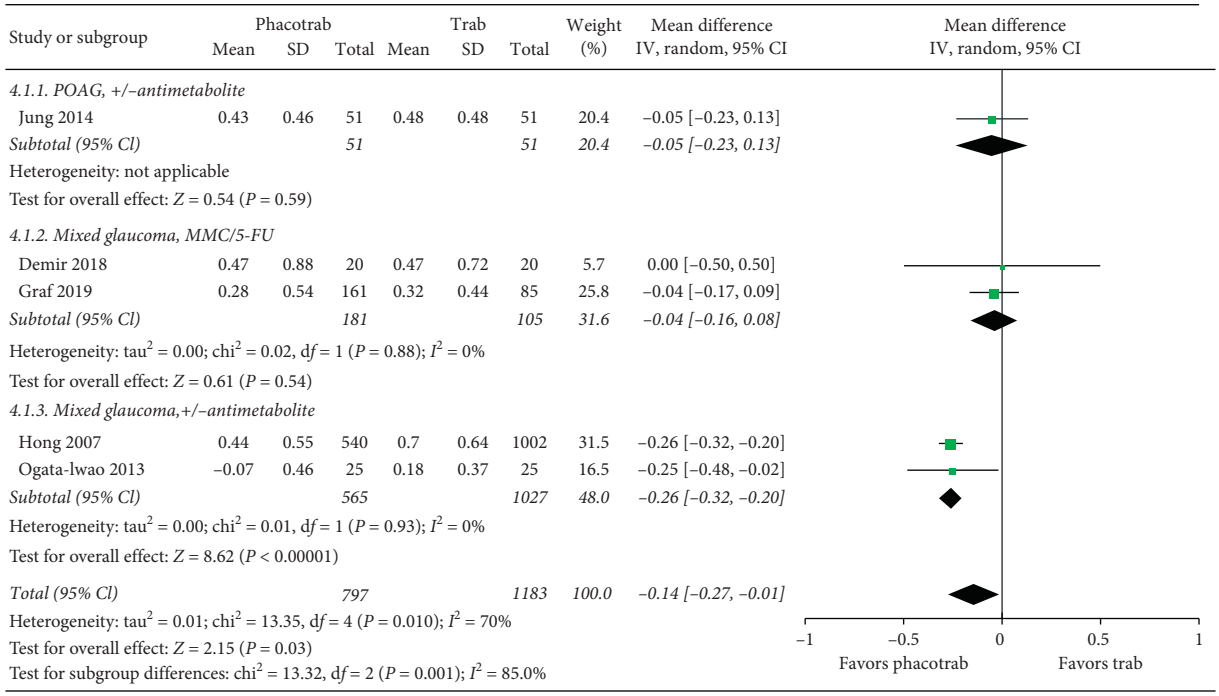

Figure 4: Forest plot of the visual acuity after phacotrabeculectomy versus trabeculectomy only. CI = confidence interval; df = degrees of freedom; IV = inverse variance; SD = standard deviation. MMC = mitomycin c; 5-FU = 5-fluorouracil; +/− antimetabolite = not all eyes received antimetabolite.

(Supplementary Figure S4). It should be noted that success criteria varied among included studies; a detailed description of success and failure criteria can be found in Table 1.

3.10.2. Qualified Success. Qualified success was reported in 12 studies, and its definition varied among the studies (Table 1). A total of 708 out of 1,041 (68.0%) eyes undergoing phacotrabeculectomy had qualified surgical success versus 1,191 out of 1,597 (74.6%) of patients undergoing trabeculectomy only. Two studies were based on patients with POAG [33, 35] and ten studies based on the mixed glaucoma group [37, 39, 41, 44–46, 48, 50, 51, 55]. The use of antimetabolites during surgery varied between the included studies. There was no difference in the likelihood of qualified success between groups (Supplementary Figure S5).

3.11. Secondary Outcome: Surgical Failure in Phacotrabeculectomy versus Trabeculectomy Only. Surgical failure

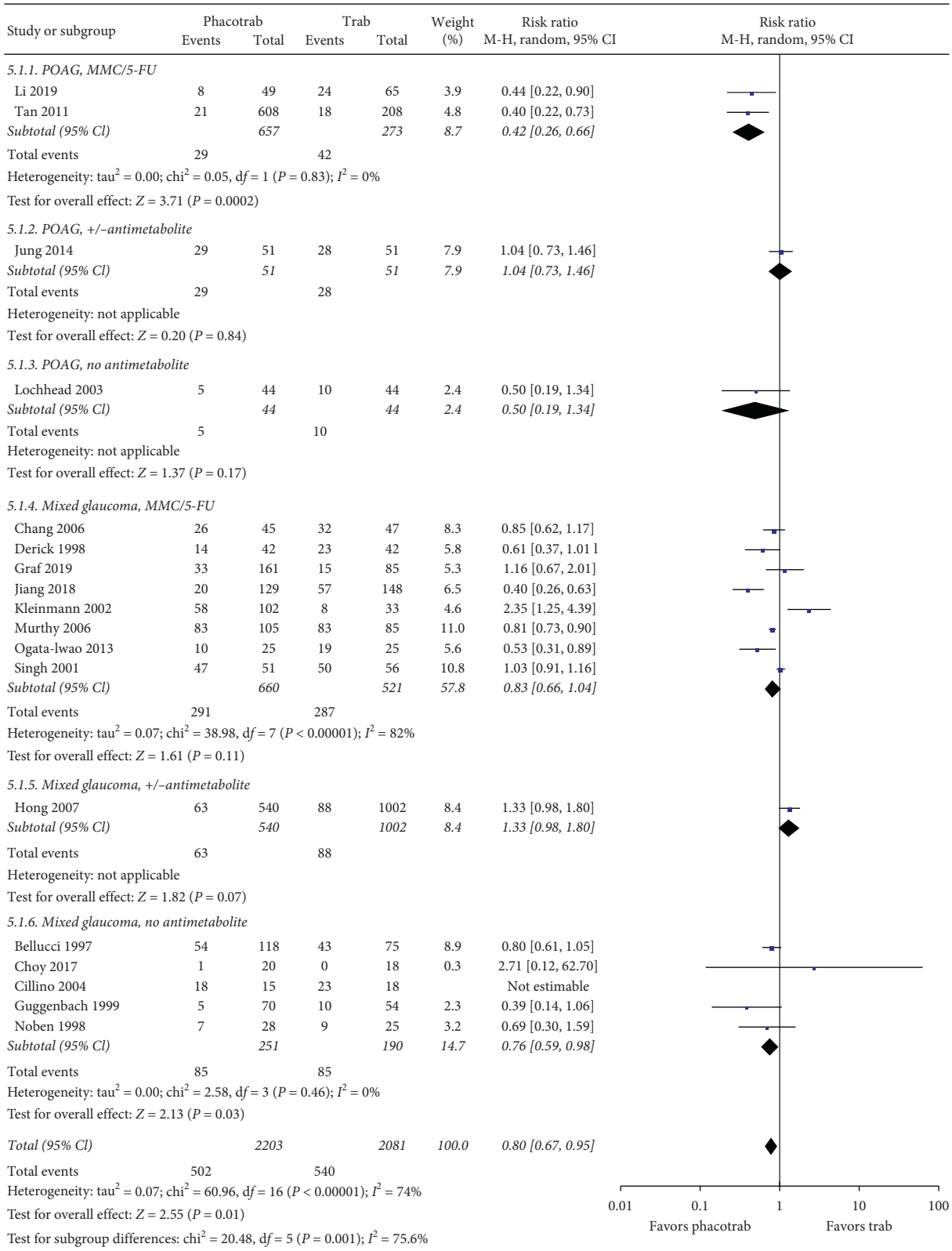

Figure 5: Forest plot of the risk of complications after phacotrabeculectomy versus trabeculectomy only. CI = confidence interval; df = degrees of freedom; IV = inverse variance; SD = standard deviation. MMC = mitomycin c; 5-FU = 5-fluorouracil; ± antimetabolite = not all eyes received antimetabolite.

was reported in 11 studies [33, 35, 40, 41, 44–46, 48, 50, 53, 55]. Two of these studies were based on patients with POAG [33, 35]. The use of antimetabolites during surgery varied between the included studies. Failure was reported in 117 out of 1,121 (10.4%) eyes undergoing phacotrabeculectomy versus 130 out of 1,596 (8.1%) eyes undergoing trabeculectomy only. There was no significant difference between groups (Supplementary Figure S6).

3.12. Secondary Outcome: Number of Antiglaucomatous Medications in Phacotrabeculectomy versus Trabeculectomy Only. Eleven studies reported the number of antiglaucomatous medications in 1,130 eyes receiving phacotrabeculectomy and 1,438 receiving trabeculectomy only. The latest available follow-up from where data were extracted ranged from 3 months [40] to 2 years [48]. However, the majority of studies reported the status at 12 months after surgery [37, 39, 42, 46, 51–53, 55]. One study was based on POAG patients [35], while the remaining 10 studies were based on a mixed group of glaucoma patients; some patients received antimetabolites and others not [37, 39, 40, 42, 46, 48, 51–53, 55]. There was no difference in the number of antiglaucomatous medications when comparing data from those undergoing phacotrabeculectomy versus trabeculectomy only (Supplementary Figure S7).

3.13. Risk of Bias within Studies. The quality of evidence was rated as very low for all outcomes (Supplementary File S2). The quality of evidence was downgraded due to the lack of randomized trials. In addition, the 25 included trials differed considerably in study design as well as included patients (e.g., glaucoma subtypes), details regarding the procedure (e.g., use of antimetabolites), and definition of outcomes (e.g., the definition of surgical success). The majority of the included studies except two reported the postoperative IOP [33–53, 56]. Postoperative complications were reported by 20 studies [33, 35–37, 39–43, 46, 48–57]. Use of antiglaucomatous medication after surgery was reported by 12 studies [33, 35, 37, 39, 40, 42, 46, 48, 51–53, 55]. Several studies reported success criteria subdivided as complete [33, 35,37, 39–41, 44–46, 48, 50, 51], qualified [33, 35, 37, 39, 41, 44–46, 48, 50, 51, 55], and failure [33, 35, 40, 41, 44–46, 48, 50, 53, 55], but the definition of complete and qualified success and failure varied among studies; see Table 1. The need for needling or revision in the intervention groups was reported by nine studies [37, 40, 41, 45, 46, 48, 50, 52, 54]. Visual acuity was reported by five studies [35, 38, 40, 48, 55]. Furthermore, the quality of evidence was downgraded because only half of the outcomes met the optimum information size, which is the number of participants needed for analysis to show a difference at a certain power [30] which means that for the other half of the outcomes, too few patients had been included collectively by the studies analyzed to reach any certainty as to which intervention provided a better or worse outcome.

4. Discussion

In this systematic review with meta-analyses, we found no difference in postoperative IOP control between phacotrabeculectomy and trabeculectomy with or without later phacoemulsification, whereas the complication rate was significantly lower with phacotrabeculectomy. The IOP-lowering effect is important, as low IOP is the primary goal of glaucoma surgery. The surgical complication rate is obviously another crucial factor to consider when choosing which surgical method to use. Additionally, we found a positive effect on visual acuity after phacotrabeculectomy compared to trabeculectomy. This difference is not surprising, and a comparison of the change in visual acuity after a phacotrabeculectomy compared to trabeculectomy followed by phacoemulsification would be ideal, but unfortunately, these results were not available in the included studies. Other outcome measures (needling or revision, number of antiglaucomatous medications, and surgical success) 12 months postoperatively did not differ significantly between the groups. When interpreting these results, it is important to remember that this evidence is based on nonrandomized comparative studies with a marked risk of biases. However, we summarize the best evidence available, which suggests that phacotrabeculectomy for glaucoma in eyes with coexisting cataract should be considered a reasonable option. Well-designed randomized clinical trials are warranted for more conclusive evidence.

There were significantly fewer postoperative complications among those undergoing phacotrabeculectomy when compared to trabeculectomy with or without later phacoemulsification (22.8% versus 25.9%). Postoperative endophthalmitis was reported in seven studies [37, 41–43, 48, 53, 54] at a rate of 0.4% versus 0.3% in phacotrabeculectomy and trabeculectomy, respectively. One of the most frequently reported complications was hypotony. Twelve studies [35, 37, 39–41, 43, 46, 48, 50, 51, 54, 55] reported hypotony in a total of 123 out of 2,203 (5.6%) eyes undergoing phacotrabeculectomy and 184 out of 2,081 (8.8%) eyes undergoing trabeculectomy only. One could hypothesize that the greater inflammation after phacotrabeculectomy decreased the risk of hypotony.

Remarkably, only two studies reported the effect of surgery on visual field preservation, which makes it difficult to draw any credible conclusion on this important topic. This problem—a plethora of IOP data and absence of visual field data—is a well-known issue in many glaucoma studies and limits the generalizability of the conclusions of this study in terms of what to expect regarding postoperative preservation of visual field.

The likelihood of surgical success was only reported by studies comparing phacotrabeculectomy with trabeculectomy. There was no overall significant difference in the likelihood of surgical success between the two procedures. The criteria used to define complete and qualified success and failure varied considerably among the included studies making a comparison between studies challenging. However, the criteria for surgical success were the same for all participants in the individual studies, making the study-

specific comparison usable. Differences in the definition of surgical success in glaucoma literature have been addressed previously. A systematic review with a search limit of 5 years found 92 IOP-related success definitions. When these criteria were applied to the same subset of eyes undergoing trabeculectomy, the success rate varied between 36 and 98% [58, 59].

Limitations of the present study should be taken into account when interpreting its results. First, our data is based on nonrandomized studies, which leads to a low evidence level for our conclusions. When patients are not randomized and data are obtained retrospectively, it should be remembered that the patient has been assigned to a certain intervention often based on what was considered to be the best option for the patient. This bias can only be addressed appropriately through prospectively designed randomized clinical trials. Second, the differences across studies in their design and definitions introduce a level of uncertainty when pooling data. This is unfortunately an issue in any systematic review, but within the field of glaucoma, there is an ambition of achieving stronger uniformity with the World Glaucoma Association Guidelines [60]. Hopefully, this limitation will be less of an issue in the future. Third, although we present analyses of different subtypes of glaucoma and use of metabolites separately, one limitation is that we look at different glaucoma subtypes collectively and not only on a specific subtype of glaucoma. This may introduce some uncertainty in the interpretation of the results. Fourth, although meta-analyses provide summary estimates of reported data and are high in the evidence pyramid, it should be remembered that the summary estimates in this study are a sum of nonrandomized comparative studies with important limitations. Therefore, our results should be interpreted with caution. Finally, to some extent, it is our perception that phacotrabeculectomy is a topic with different opinions. It can be speculated that such opinions influence publication decisions and therefore publication bias may be present.

5. Conclusions

We find similar postoperative IOP control, fewer complications, and better visual acuity with phacotrabeculectomy compared to trabeculectomy only. Phacotrabeculectomy addresses the patients´ two eye diseases simultaneously, possibly shortening the patients' contact to the health care system, and is a surgical option to consider when choosing the best surgical option for a patient with coexisting glaucoma and cataract and a need for an IOP-lowering procedure. Although this is the best evidence available, it should be noted that the level of evidence is low, based primarily on nonrandomized or retrospective studies, and better-designed studies are needed.

Data Availability

The original report data were obtained from the literature databases PubMed/MEDLINE, EMBASE, and the Cochrane Central.

Disclosure

The funding bodies had no influence on conception, design, data analysis, or the decision to publish the study.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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Supplementary Materials

Supplementary File 1: list of excluded studies. Supplementary File 2: a review of evidence quality. Supplementary Figure S1: forest plot of the risk of complications after phacotrabeculectomy versus phacoemulsification 3–6 months after trabeculectomy. Supplementary Figure S2: forest plot of the visual field after phacotrabeculectomy versus trabeculectomy only. Supplementary Figure S3: forest plot of the risk of needling or revision after phacotrabeculectomy versus trabeculectomy only. Supplementary Figure S4: forest plot of the complete success after phacotrabeculectomy versus trabeculectomy only. Supplementary Figure S5: forest plot of the qualified success after phacotrabeculectomy versus trabeculectomy only. Supplementary Figure S6: forest plot of the surgical failure after phacotrabeculectomy versus trabeculectomy only. Supplementary Figure S7: forest plot of the difference in a number of antiglaucomatous medications after phacotrabeculectomy versus trabeculectomy only. (*Supplementary Materials*)

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Research Article

Intraocular Suture Looping Technique for Flapless Four-Point Refixation of Dislocated Intraocular Lenses

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Purpose. To describe a flapless/grooveless technique for four-point refixation of a dislocated intraocular lens (IOL) with four fenestrated haptics. *Methods*. An intraocular suture looping technique was performed with the assistance of two 27-gauge needles. A looping needle was passed into the eye through paracentesis and was used to loop both fenestrated haptics on the same side with an 8–0 polypropylene thread. A guiding needle was used to guide the looping needle out of the eye at the scleral fixation sites. After looping each pair of fenestrated haptics on nasal/temporal sides with 8–0 polypropylene sutures, the IOL was refixated by definitive knotting. The exterior suture ends were buried into the sclera without the creation of scleral flaps/grooves. *Results*. The technique was employed in four eyes (three patients). The mean postoperative follow-up period was 13.8 ± 2.2 months. Postoperatively, the IOLs of all the eyes remained well positioned and stable. The postoperative visual acuities of all the eyes were improved. No suture erosion, hypotony, scleral atrophy, chronic inflammation, retinal tears, and/or detachments were observed within the follow-up period. *Conclusion*. The present technique provides minimal surgical invasion for the transscleral refixation of a dislocated IOL with four fenestrated haptics.

1. Background

There are various options for managing a dislocated intraocular lens (IOL) according to the status of dislocation and the type of IOL implanted [1–5]. A dislocated IOL-capsular bag complex or IOLs with closed-loop haptics can be managed by looping the encapsulated haptic or eyelet of the haptic with a suture for fixation [6–9]. Cases of completely dislocated IOLs with four fenestrated haptics present a unique challenge. To the best of our knowledge, no reports have been published on the performance of four-point intraocular refixation of IOLs with four fenestrated haptics. Transscleral four-point suture fixation for secondary IOL implantation without sufficient capsular support, performed by looping each pair of fenestrated haptics, provides several advantages, including avoidance of IOL tilt and postoperative pupil capture, enhanced IOL stability and centration, and a low risk of pigmentary dispersion glaucoma and cystoid macular edema [10–15]. Suture looping manipulation through two pairs of fenestrated haptics performed outside the eye for a secondary implantation is relatively straightforward. However, for a dislocated IOL with four fenestrated haptics, a four-point refixation requiring looping the pairs of fenestrated haptics inside the eye is technically difficult. Recently, we have presented a method of refixating an IOL with closed-loop haptics, namely, the "intraocular looping technique," to pass a suture through the closed-loop of the IOL haptic in the eye [16]. The technique can be further modified for four-point refixation of a special type of IOL. It provides minimal surgical invasion without the creation of scleral flaps, pockets, or grooves. It can also be performed transconjunctivally without conjunctival dissections.

2. Methods

A retrospective analysis of patients who underwent flapless four-point refixation of dislocated IOLs (Akreos AO60, Bausch and Lomb, North Clearwater, FL) with four

fenestrated haptics enrolled between January 2019 and July 2020 was performed. The present study adhered to the tenets of the Declaration of Helsinki and was approved by Institutional Ethics Board of Tenth People's Hospital affiliated to Shanghai Tongji University School of Medicine. Written informed consent was obtained from all patients. All patients provided informed consent after description of the nature and consequences of the study. Data collection included demographic details, indication for surgery, intraoperative and postoperative complications, follow-up duration, preoperative and postoperative intraocular pressure, visual acuity, IOL position evaluated by anterior segmental photograph and the Scheimpflug imaging system (Pentacam, Oculus Optikgeräte GmbH, Wetzlar, Germany), posterior segment photograph, and optical coherence tomography (RTVue-100, Optovue Inc., Fremont, CA, US) for macular evaluation.

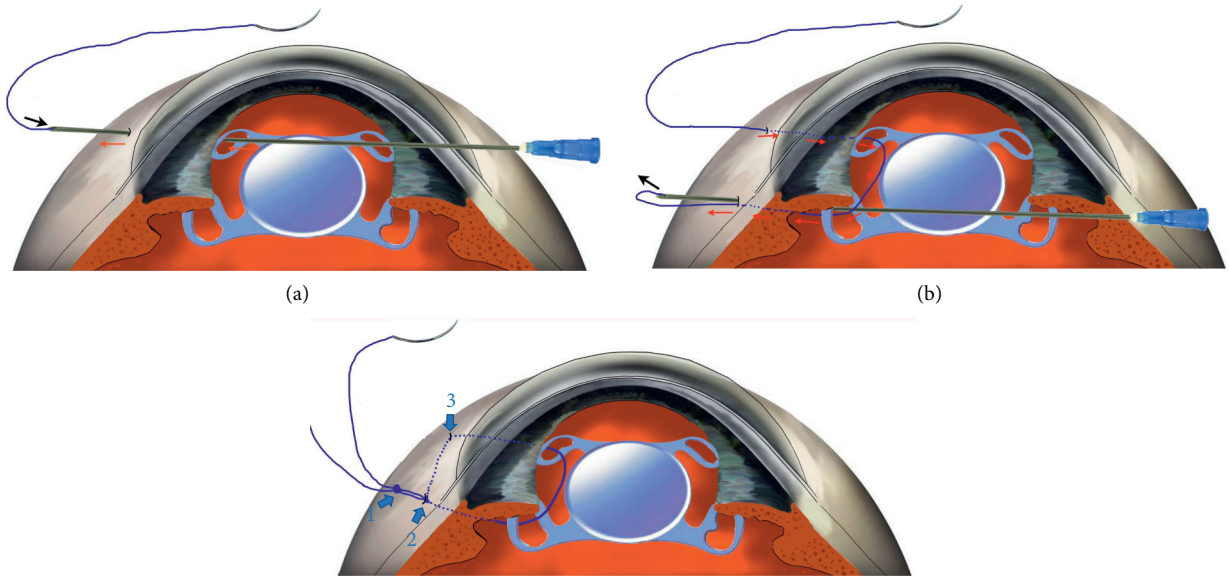
2.1. Surgical Technique. All the surgeries were performed under retrobulbar anesthesia by one of the authors (H.J.). The supplemental video (Video, Supplement Digital Content 1) and Figure 1 demonstrate the procedures. For cases with a completely dislocated IOL-capsular bag complex dropping into the vitreous cavity, complete 25-gauge pars plana vitrectomies were performed. The two pars plana sclerotomies were placed 2 mm from the limbus and were designed as the two superior sites for IOL fixation. The IOL was gripped with end-griping forceps and placed above the iris plane. The IOL was orientated horizontally. The four-point fixation sites were placed superiorly and inferiorly to 3 and 9 o'clock, 2 mm posterior to the limbus, and 5 mm apart. Two corneal paracenteses were separately performed, approximately 180 degrees apart on the nasal and temporal sides. Two 27-gauge needles (or 27-gauge/30-gauge needles) were bent at the hubs. An ab externo penetration was performed with one needle (the guiding needle) at the inferior fixation site 2 mm from the limbus on the temporal side. The other needle (the looping needle) was passed into the eye through the previous created corneal paracentesis located on the opposite side. The intraocular suture looping technique modified from our previously published method was performed in a bimanual manner. [15]. Either of the two needles was passed through the eyelet of the inferior haptic. The tip of the looping needle was then docked into the guiding needle in a needle-needle manner and was guided out of the eye. An 8–0 polypropylene thread (Prolene, Polypropylene Suture; Ethicon, Johnson-Johnson, New Brunswick, NJ) was bisected. The end of one half of the suture was inserted into the lumen of the looping needle for approximately 4-5 mm. The other side of the thread connected to a curved needle was left outside the eye. The looping needle with the thread was then recoiled into the globe. An ab externo passage of the guiding needle was then performed through the superior fixation site. The same method was performed to pass the looping needle through the eyelet of the superior haptic. The looping needle in the anterior chamber was guided out of the superior fixation site in a similar manner. The end of the suture in the looping needle was pulled out from the needle lumen with forceps. A suture loop was thus created passing through the pair of fenestrated haptics on the temporal side. The same set of manipulations was performed to loop the pairs of fenestrated haptics on the nasal side. Thus, two pairs of suture loops for a four-point IOL fixation were created. The curved needle attached to the external suture was started with an intrascleral pass from the inferior fixation site to the adjacent transscleral penetration site parallel to the limbus. A second intrascleral pass of the needle from the exiting site of the sclera to the superior fixation site was performed. The same set of manipulations was performed for the nasal side. After adjusting the suture tension on both sides to center the IOL, the two ends of the suture were tied for definitive knotting fixation (the fixation knot) into the sclerotomy for both sides. Another overhand knot (anchor knot) was then created approximately 3 mm from the first knot. The technique of burying the anchor knot and the ends of the sutures into the scleral tunnel was identical to our previous publication [15, 16]. A 27-gauge needle was used to create an intrascleral tunnel from the sclerotomy approximately 3-4 mm in length parallel to the limbus aiming either superiorly or inferiorly. The curved needle, connected to the anchor knot, was introduced with an intrascleral pass from the sclerotomy to the adjacent transscleral penetration site through the scleral tunnel. After pulling out the needle transconjunctivally, the attached suture was further pulled to bury the second knot and the suture ends in the sclera. The externalized ends of the sutures were cut flush to the scleral surface. The conjunctival openings were left sutureless or closed with a one-stitch 10–0 nylon suture.

3. Results

The technique was adopted in four eyes of three patients (2 male and 1 female) with a mean age of 56 ± 8 years. The mean follow-up period was 13.8 ± 2.2 months (range 11–16 months). Uncorrected visual acuities improved from a mean of 1.10 ± 0.08 logMAR (Snellen 20/250) preoperatively to 0.22 ± 0.05 logMAR (Snellen 20/32) at the final follow-up. No intraoperative surgical complications were observed. The IOLs remained well centered throughout the follow-up period. No erosion or exposure of the trimmed ends of the sutures was observed (Figure 2). No postoperative complications of hypotony, elevated intraocular pressure, hyphemia, vitreous hemorrhage, abnormal inflammation, cystoid macular edema, or retinal detachment were observed during the postoperative follow-up period.

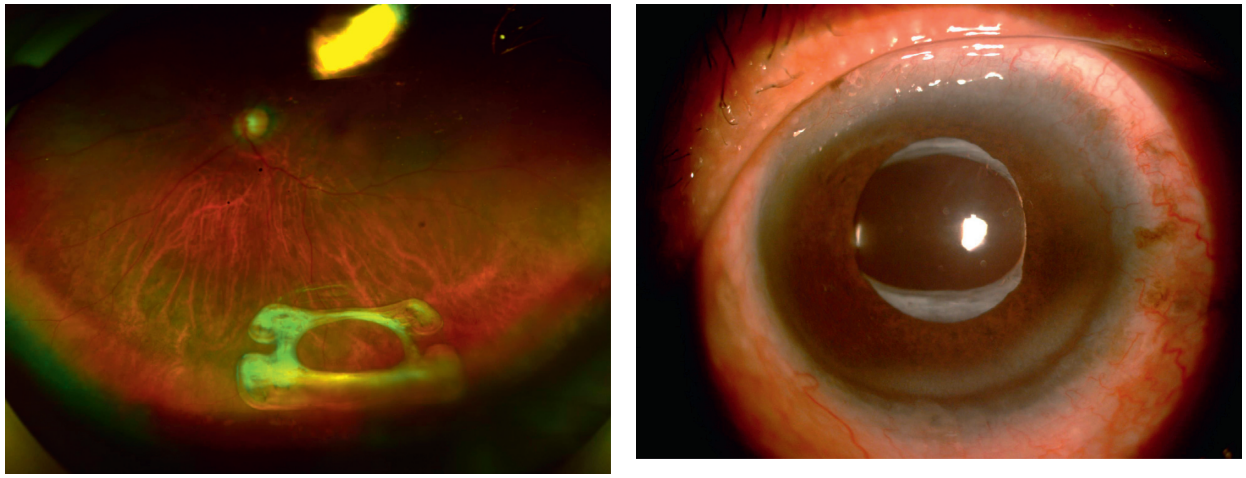
4. Discussion

Several strategies have been published for the management of dislocated IOLs or an IOL-capsular bag complex, including IOL exchange and refixation of the dislocated IOL using various methods [1–5]. Refixation techniques are less surgically traumatic due to the avoidance of creating a large corneal/scleral incision for the IOL exchange. To the best of our knowledge, no publications have been reported on a four-point refixation of a dislocated IOL typed with four fenestrated haptics. We have previously presented an



(a) (b) (c)

Figure 1: Schematic figure of the intraocular looping technique for four-point fixation (drawn by Haiying Jin). This figure is authorized to be published by the present journal to demonstrate the surgical procedures. (a) The looping needle is externalized from the first fixation point and loaded with an 8–0 polypropylene thread in its lumen (arrow). Red arrows show the needle path from the eyelet of the IOL to the sclerotomy. (b) After loading the thread, the looping needle is recoiled into the anterior chamber and passed through the following paths: the first eyelet of the IOL, the second eyelet of the IOL, and ab externo pass through the second sclerotomy (red arrows). The thread in the lumen of the needle is finally pulled out (black arrow). A suture loop is created passing through both eyelets on the same side. (c) After the intrascleral passing (arrow 3) of the thread from the first fixation site to the second fixation site, a double knot technique is performed for a flapless IOL fixation. The first overhand knot in the sclerotomy (arrow 2) is used for the IOL fixation. The second knot (1) is used to lead the ends of the threads for burying in the sclera.



(a) (b)

Figure 2: (a) Preoperative overview of a dislocated IOL-capsular bag complex (arrow) in the vitreous cavity. (b) Postoperative overview of the well-positioned four-point refixated IOL-capsular bag complex. No erosion or exposure of the trimmed ends of the sutures and no scaring of the conjunctiva were observed.

intraocular looping technique to loop the suture through the fenestrated haptics for two-point IOL refixation in our previous publication [16]. The technique involves manipulations with two needles, a guiding needle and a looping needle, and has multiple advantages, including simplified surgical procedure, satisfactory maneuverability, and avoidance of haptic-externalization or repeated passing of long needles through the globe. In this study, the intraocular looping manipulation was further modified to loop a pair of fenestrated haptics for four-point fixation other than a single haptic. After loading the suture into the looping needle, the needle was passed through the eyelet of the first haptic,

sequentially passed through the eyelet of the second haptic, and finally passed out from the second fixation site to deliver the suture end for its externalization.

Another approach adopted in this technique for minimizing surgical trauma is intrascleral manipulation, similar to our published techniques [15, 17, 18]. The suture was passed intrasclerally from the fist fixation site to the second one with the aid of an attached curved needle. Fixation of the IOL was accomplished by tying the two ends of the suture in the sclerotomy. As the tensions of the bilateral suture loops were adjusted before fastening the knots, well centration of the IOL can be achieved. The second knot, approximately 3 mm from the fixation knot, was used for intrascleral anchoring of the suture ends without creating scleral flaps, pockets, or grooves. The manipulations can be performed under sutureless small conjunctival incisions and, therefore, greatly reduce the surgical trauma that requires the creation of large conjunctival incisions and scleral flaps. As the suture cutting ends lie tangential to the sclera, the technique inherits the major advantage of the friction knot method for preventing suture erosion. [19]

A limitation of this study is its small sample size due to relatively rare occurrence of dislocation of the type of IOL with four fenestrated haptics. Studies evaluating more cases might be necessary to evaluate other potential complications.

In conclusion, this technique represents a safe, effective, minimally invasive procedure for the management of dislocated IOL/IOL-capsular bag complex with four fenestrated haptics.

Data Availability

The datasets analyzed during the current study are available from the corresponding author upon request.

Ethical Approval

The study was conducted under the tenets of the Declarations of Helsinki and was approved by the Ethics Board of Tenth People's Hospital affiliated to Shanghai Tongji University School of Medicine, Shanghai, China.

Consent

All patients provided informed consent after a thorough description of the nature and consequences of the study. The pictures detailing each step of the surgery and the postoperative photograph of the anterior segments were taken authorized for its publication on signed informed consent from the patient.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

Authors' Contributions

Hu Z and Zhao B contributed equally to this research.

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Supplementary Materials

Supplemental digital content: Video1. Intraocular suture looping technique for flapless four-point refixation of dislocated intraocular lenses. (*Supplementary Materials*)

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Research Article

Intrascleral Suture Anchoring: A Flapless/Grooveless Four-Point Intraocular Lens Fixation Technique

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Purpose. We describe a minimally invasive suture fixation technique for four-point fixation of intraocular lenses (IOLs) in the treatment of aphakic eyes, namely, the intrascleral suture anchoring technique. Neither scleral flaps nor large conjunctival dissections are required. *Methods*. This study included 11 eyes (11 patients). After looping the eyelets on the IOL haptics and externalizing the threads, the curved needle attached to the externalized thread was started with two sequential intrascleral passes from the first fixation point to reach the second fixation point. The same procedure was performed for the other side of the IOL. A fixation knot was created in the sclerotomy by the two ends of the thread to close the suture loop for IOL fixation. Another knot was created about 2 to 3 mm from the exiting point and was intrasclerally anchored by the aid of the attached curved needle. *Results*. The mean postoperative follow-up period was 9.7 ± 5.8 months (range 5–15 months). The IOLs of all eyes remained well positioned and stable postoperatively. The postoperative visual acuities were improved. No suture erosion, suture loosening, hypotony, scleral atrophy, chronic inflammation, retinal tear, and/or detachment were observed within the follow-up period. *Conclusion*. The present technique is an alternative, flapless method for the four-point suture fixation of IOLs. It provides both minimal surgical trauma and reliable stability.

1. Introduction

Intraocular lens (IOL) implantation in cases of insufficient capsular support after lens extraction is challenging. Various techniques are used to fixate the IOL within the eye, including transscleral suture fixation, [1–3] intrascleral fixation of IOL haptics, [4] flanged fixation, [5] glued IOL technique, [6] iris suture fixation of posterior chamber IOLs [7], and iris claw fixation [8]. Each method has its advantages and disadvantages. The four-point IOL fixation using two suture loops to fixate the four haptics has been reported to provide a variety of advantages, including enhanced IOL stability and centration, avoidance of IOL tilt and postoperative pupil capture, and low risk of cystoid macular edema and pigmentary dispersion glaucoma [9–13]. As there are four fixation points at the sclera, excessive conjunctival dissections and large scleral flaps are commonly performed to cover the exterior threads and knots of the fixating suture loops. These dissections and scleral manipulations are surgically traumatic. In cases with previously performed surgeries or ocular trauma, scarring of the conjunctiva-scleral tissue may add to the difficulty of performing conjunctival dissections and scleral flaps. An alternative approach to avoid creations of large scleral flaps is to leave the exterior threads on the surface of sclera and bury the knot by rotating it into the sclerotomy [11, 12]. The exterior threads are covered by conjunctiva; however, there are concerns of suture erosion and postoperative endophthalmitis. Moreover, for cases with excessive conjunctival scarring, the technique is impractical. We present a technique that anchors the sutures intrasclerally. The procedures are performed under the four transconjunctival puncture sites

created by using a 30-gauge needle. Using this technique, neither large conjunctival dissections nor manipulations (flaps, grooves, or pockets) on the sclera are required.

2. Methods

A retrospective analysis of patients who underwent flapless four-point fixation of dislocated IOLs (Akreos AO60, Bausch and Lomb, North Clearwater, FL) after lens extraction, enrolled between January 2019 and July 2020, was performed. The present study adhered to the tenets of the Declaration of Helsinki and was approved by institutional ethics board of Tenth People's Hospital affiliated to Shanghai Tongji University School of Medicine. Written informed consent was obtained from all patients. All patients provided informed consent after a description of the nature and consequences of the study. Data collection included demographic details, indication for surgery, intraoperative and postoperative complications, follow-up duration, preoperative and postoperative intraocular pressure, visual acuity, IOL position evaluated by anterior segmental photograph and Scheimpflug imaging system (Pentacam, Oculus Optikgeräte GmbH, Wetzlar, Germany), posterior segment photograph, and optical coherence tomography for macular evaluation.

2.1. Surgical Technique. Surgeries were performed under general anesthesia (2 cases) or retrobulbar anesthesia (9 cases) by one of us (J.H.). Figure 1 and the supplemental video demonstrate the procedures (see Supplementary Materials (Available here)). An 8–0 polypropylene thread (Prolene, Polypropylene Suture; Ethicon, Johnson-Johnson, New Brunswick, NJ) with a curved needle was bisected in its middle. The procedures of introducing the thread into the eye and looping the eyelets on the haptics of the Akreos AO60 (Bausch and Lomb, North Clearwater, FL) foldable posterior chamber IOL were similar to those of previously published methods [14, 15]. The suture-in-needle technique was performed to introduce the thread into the eye. The free end of the 8–0 polypropylene thread was threaded approximately 3-4 mm into the tip of a 30-gauge needle. A direct transconjunctival ab externo puncture of the 30-gauge needle was performed at the first fixation site to introduce the loop of the suture into the eye, leaving the other end of the thread connected to the curved needle exterior to the eye. The loop of the suture was then grasped by forceps introduced through the main incision. The end of the suture in the 30-gauge needle was taken out from the main incision using forceps. The 30-gauge needle was withdrawn from the eye. The suture was then looped though eyelets of both haptics of the IOL on the left side. Another 30-gauge needle was curved by using a needle holder. An ab externo transconjunctival puncture of the curved 30-gauge needle was performed at the second fixation point, and then its tip was guided out from the main incision by using forceps. The curved 30-gauge needle avoids the distortion of the globe during pass-through of the sclera and the main incision that occurs when using a straight needle. The end of the polypropylene thread (after looping the eyelets of the IOL) was inserted into the lumen of the curved 30-gauge needle from its tip. After withdrawing the needle, the end of the suture was externalized from the second fixation point. The same procedures were repeated to loop the haptics and externalize the ends of the thread on the other side of the eye. After folding and implanting the IOL into the posterior chamber, the intrascleral suture anchor technique was performed. The conjunctival incisions of the second and fourth fixation points were slightly enlarged by blunt dissection to expose the underlying sclera. The curved needle attached to the exterior suture was held by a needle holder and was then started with an intrascleral pass from the first fixation site of the sclerotomy to the adjacent transscleral penetration site parallel to the limbus. The tip of the needle was then pulled out transconjunctivally using a needle holder. A second intrascleral pass of the needle from the exiting point of the sclera to the second fixation point was performed in a relaying manner. The tip of the curved needle was then passed out from the sclerotomy of the second fixation point. The two ends of the same suture loop thus converged from the same coincident sclerotomy. The coincident may not be accomplished on the first manipulation of the relaying intrascleral pass; however, by withdrawing the needle tip back into the scleral tunnel and adjusting the length and direction of the needle track, it can be easily accomplished in a second maneuver. The same manipulations were performed for the other side of the eye. Thus, the two suture loops were formed to fixate the IOL for both sides. After adjusting the tensions of the suture loops to center the IOL, a 2-1-1 overhand fixation knot was created in the sclerotomy by the two ends of the thread to close the suture loop for each side. Another overhand knot (friction knot) was then created about 2 to 3 mm from the first fixation knot. The technique of anchoring the friction knot into the scleral tunnel to bury the ends of the thread was identical to our previous publication [16]. A 27-gauge needle with a sharp beveled tip was used to create a wage-shaped intrascleral tunnel from the sclerotomy approximately 3-4 mm in length parallel to the limbus. Avoid accidently cutting the sutures by staggering the 27-gauge scleral tunnel from the previous needle track of the buried sutures. The curved needle connected to the overhand knot was then held by a needle holder and was started with an intrascleral pass from the sclerotomy to the adjacent transscleral penetration site through the scleral tunnel. The needle was then pulled out transconjunctivally. The thread was then further pulled to lead the friction knot tucked into the scleral tunnel. The same manipulations were performed for the other side. After cutting the four externalized ends of the threads flush to the scleral surface, all the exterior threads and knots were anchored in the intrascleral needle tracks. The small conjunctival openings were left sutureless.

3. Results

A total of 11 eyes of 11 patients (6 men and 5 women) were included. The mean age was 36.0 years (±standard deviation, 21.7; range, 10–68 years). The mean follow-up

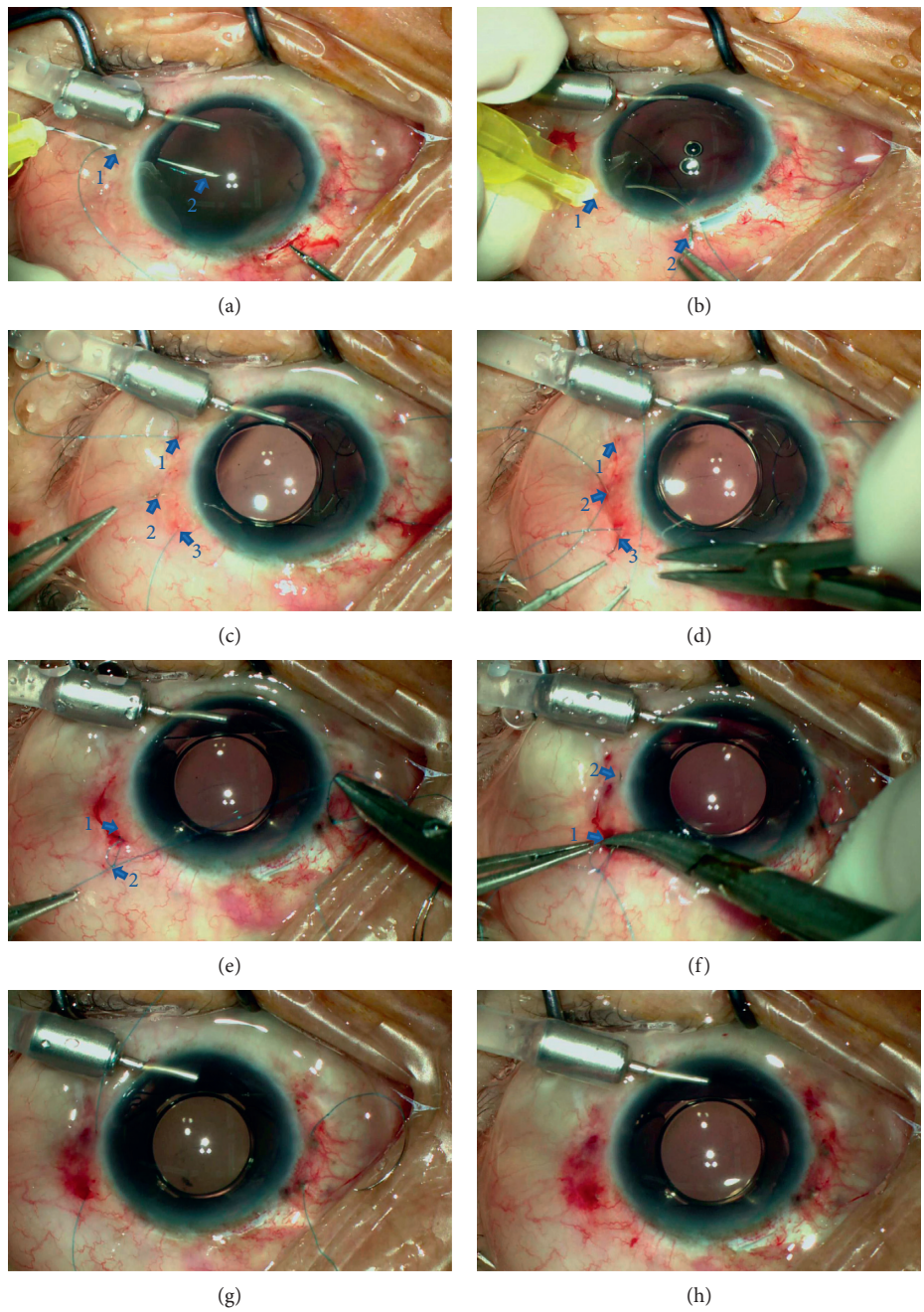

Figure 1: Intraoperative view of the surgical procedures. (a) Introduce the 8–0 polypropylene thread into the eye by the suture-in-needle technique using direct ab externo puncturing of a 30-gauge needle. Arrow 1: the first fixation point; arrow 2: the loop of the suture can be grasped by using forceps to retrieve it from the main incision. (b) After looping through the eyelets of the IOL, the thread is externalized by the curved-needle-retrieving technique. Arrow 1: the second fixation point; arrow 2: the tip of the curved 30-gauge needle. (c) After externalizing the four fixation sutures and implanting the IOL into the posterior chamber, the curved needle attached to the suture is held by a needle holder and intrascleral pass from the sclerotomy of the first fixation point (arrow 1) to the adjacent sclera (arrow 2) is performed. Arrow 3: the second fixation point. (d) Perform a relay intrascleral pass from the exit point (arrow 2) to exit the needle from the second sclerotomy (arrow 3). (e) Create the overhand fixation knot (arrow 1) by the two ends of the sutures to fixate the IOL. Create a second knot (arrow 2) 3 mm from the exit point and perform the intrascleral incarceration of the knot. (f) Perform the intrascleral pass of the curved needle attached to thread and knots from the second fixation point (arrow 1) to the adjacent sclera (arrow 2). (g) After pulling the thread to lead the threads and knots into the scleral tunnel, only four threads remain from the sclera. (h) After cutting all the externalized threads flush to the sclera, the IOL is well centered. Conjunctival incisions are left sutureless.

period was 9.7 ± 5.8 months (range 5–15 months). The indications for surgery included aphakia after pars plana vitrectomy (PPV) and retinal repair secondary to traumatic retinal detachment ($n = 3$), aphakia after PPV secondary to traumatic dislocated crystalline lens and vitreous hemorrhage ($n = 2$), dislocated crystalline lens

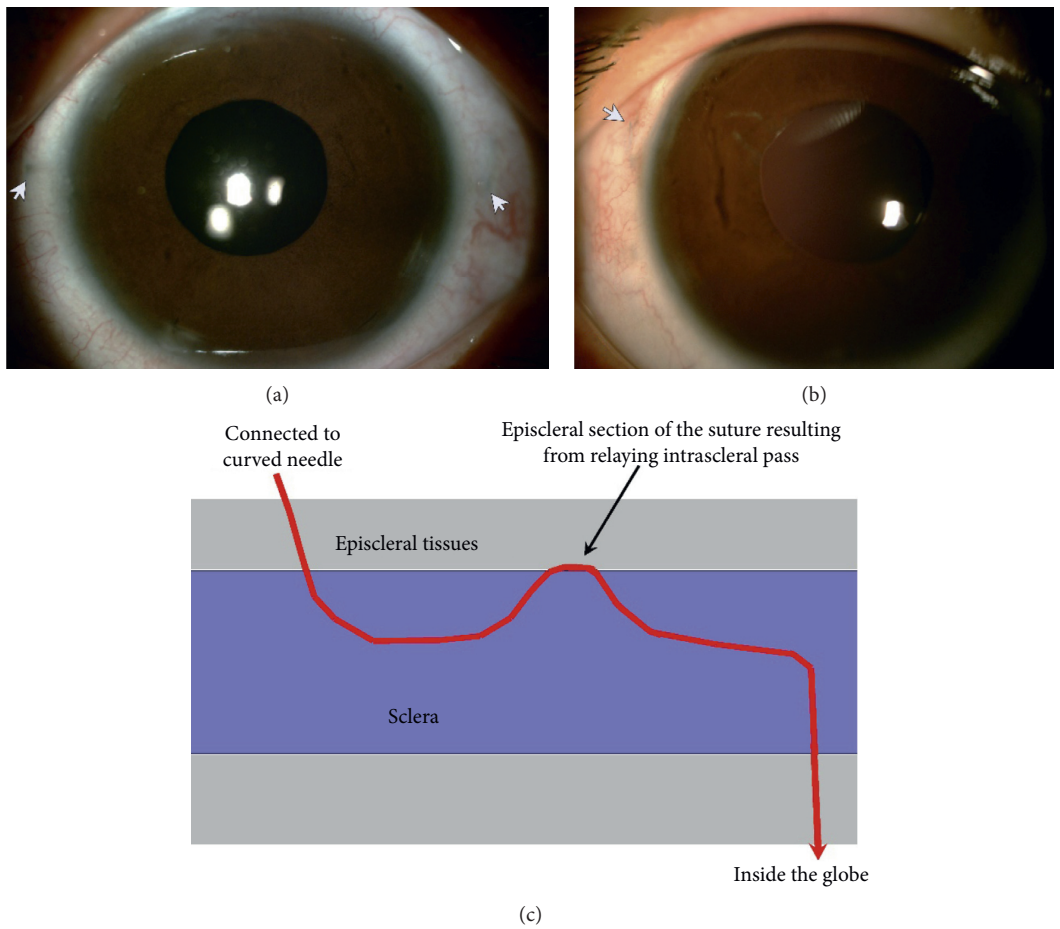

Figure 2: Postoperative overviews. There was barely conjunctival and scleral scarring after surgery. Only very short sections of the thread (arrows) resulting from the relaying intrascleral pass can be observed under the episcleral tissue in some of the cases. This phenomenon is identical to the turning point of the *Z*-suture technique.

due to Marfan syndrome ($n = 2$), aphakia after PPV secondary to traumatic dislocated crystalline lens ($n = 1$), and aphakia after PPV and repair of cyclodialysis secondary to traumatic dislocated crystalline lens, vitreous hemorrhage, and cyclodialysis ($n = 1$). The preoperative logarithm of the minimum angle of resolution visual acuity was 1.12 ± 0.47 (Snellen 20/264). The logarithm of the minimum angle of resolution visual acuity at the final follow-up was 0.48 ± 0.24 (Snellen 20/60). No intraoperative complications were observed except a transient mild ciliary hemorrhage during the needle puncture in one eye. No evidence of suture erosion, suture loosening, hypotony, scleral atrophy, chronic inflammation, or retinal tear and/or detachment was observed in any of the patients. The IOLs were well centered within the follow-up period. The sutures were invisible in most of the cases ($n = 8$) at the final examination. Very short sections (about 0.5 mm) of the sutures resulting from the relaying intrascleral pass were observed ($n = 3$) with careful examination under the episcleral tissues; however, these sections were barely visible (Figure 2).

4. Discussion

Various innovations in IOL suture fixation in patients with insufficient capsular support have reduced surgical trauma and improved long-term postoperative stabilization; however, the technique still has limitations and is technically challenging. The use of 8–0 or 9–0 polypropylene thread or polytetrafluoroethylene thread reduces the risk of postoperative IOL redislocation resulting from suture breakage of the 10–0 polypropylene thread. Surgical trauma of the scleral suture fixation is reduced by two flapless techniques: the *Z*-suture and the friction knot techniques [17, 18]. The four-point fixation of IOL with four-eyeleted haptics provides high stability and centration and avoids tilt and pupil capture of the IOL, thereby avoiding the limitations of the conventional two-point fixation. However, as there are four fixation points on the sclera, the technique commonly involves large conjunctival dissections and scleral flaps to cover the exterior threads and knots of the two suture loops, which results in excessive surgical trauma [9–13]. Although a less traumatic technique has been advocated, which involves

leaving the exterior threads on the surface of the sclera and rotating the knot into the sclerotomy, it has the risks of suture erosion and endophthalmitis due to the subconjunctival sutures externalizing directly from the sclerotomies [11, 12]. Moreover, for cases with conjunctival scarring or atrophic Tenon's capsule, the technique is impractical.

To inherit the advantages of four-point fixation and to reduce surgical trauma, we present an intrascleral suture anchoring technique. The advantages of this technique are multifold. First, the technique uses 8–0 polypropylene thread [13, 15, 16]. The thread is thicker and has a higher tensile strength than the 10–0 polypropylene thread and thus improves intraoperative manipulations and reduces late IOL dislocation due to suture breakage. Second, the exterior knots and sutures are anchored intrasclerally without exposure. The sutures were invisible in most of the cases at the final examination. Only very short sections of the thread resulting from the relaying intrascleral pass were observed that was covered by episcleral tissue in some of the cases (Figure 2), which is similar to the turning point of the *Z*-suture technique and does not relate to any side effect [17]. Third, the securing of the sutures is accomplished by overhand knots. By adjusting the tensions of the bilateral suture loops before fastening the knots, the centration of the IOL could be acquired. Fourth, unlike the conventional suture technique fixation methods that secure the suture by lamellar scleral tissue beneath the scleral flap, there is no risk of late IOL dislocation due to tissue dehiscence induced by the consistent cutting effect of the suture. The intrascleral incarceration of the cutting ends used in the present technique is a modified technique of the friction knot method first published by Oskala [18]. The technique was further modified by us into an overhand friction knot technique to fixate dislocated IOLs [16]. The modified technique was adopted in this research to lead the ends of the threads anchored into the scleral tunnel, which can be a satisfactory approach to bury the knots and cutting ends of the suture without creating scleral flaps, pockets, or grooves. The manipulations can be performed under the sutureless small conjunctival incisions; therefore, the present technique greatly reduced the surgical trauma noted in other techniques that require the creations of large conjunctival incisions and scleral flaps. As the cutting ends lie tangential to the sclera, the technique inherits the major advantage of the friction knot method of preventing suture erosion. Finally, the present technique presented a method of externalizing the thread using a curved 30-gauge needle, which inherits the advantages of the ab externo technique. The curving modification of the 30-gauge needle avoids distortion of the globe during passing through the scleral fixation point and the main incision (Figure 1(b)). As compared with the technique of retrieving the threads by using 27-gauge or 25-gauge (with or without assistance of trocars) microforceps, the 30-gauge sclerotomies are self-sealing and less traumatic [11, 12]. Therefore, the technique reduces the risk of wound leakage and postoperative hypotony.

In summary, the present technique is an alternative, flapless method for the transscleral four-point fixation of IOLs. It provides both minimal surgical trauma and reliable stability. A study with a longer follow-up time and more cases is required to confirm the long-term stability of this method and compare it with other fixation methods.

Data Availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical Approval

This study was conducted under the tenets of the Declarations of Helsinki and was approved by the ethics board of Tenth People's Hospital affiliated to Shanghai Tongji University School of Medicine, Shanghai, China. Written informed consent was obtained from all patients. All patients provided informed consent after a thorough description of the nature and consequences of the study.

Consent

The patient from whom pictures detailing each step of the surgery and the postoperative photograph of the anterior segments were taken authorized their publication and signed informed consent.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Xin Hu and Bo Zhao contributed equally to this research.

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Supplementary Materials

Video Clip 1: intrascleral suture anchoring: a flapless four-point intraocular lens fixation technique. (*Supplementary Materials*)

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Research Article

Modified Four-Point Scleral Suture Fixation Technique for Repositioning a Dislocated Intraocular Lens in the Absence of Capsule Support

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Purpose. To study the efficacy of a modified four-point fixation technique for the repositioning of a dislocated intraocular lens (IOL) with four eyelets in the absence of capsule support. *Methods*. Four patients with dislocated four-eyelet hydrophilic acrylic IOLs (Akreos AO60) were enrolled. The modified technique combined four-point fixation with intrascleral sutures and suture burying. The technique minimized the limbus incision to 1 mm with no externalization of the IOL or its haptics. Follow-ups included routine ophthalmic examinations, corneal endothelial cell counts, and measurement of IOL tilt and decentration (measured using Pentacam® HR images). *Results*. The IOLs were successfully repositioned in all cases. After a mean follow-up period of 19.75 ± 7.85 months (range: 8 to 24 months), the patients' best-corrected vision acuity (BCVA (LogMAR), before: 0.63 ± 0.36, after: 0.58 ± 0.43, $P = 0.604$) and intraocular pressure (pre 13.35 ± 0.85 mmHg, post 14.80 ± 2.03 mmHg, $P = 0.150$) remained unchanged. Corneal endothelium density decreased about 6.84 ± 2.97%. In all cases, the IOL was well positioned during the follow-up. At the final visit, the average IOL tilt was 1.36 ± 0.35° horizontally and 1.31 ± 0.14° vertically. The average IOL decentration was 0.23 ± 0.12 mm horizontally and 0.18 ± 0.13 mm vertically. *Conclusions*. With this modified technique, dislocated IOLs with four-eyelets could be treated safely with favorable outcomes.

1. Introduction

Intraocular lens (IOL) dislocation has become increasingly problematic; the incidence of IOL dislocation is reported to be 0.2 to 3.0% [1]. Techniques to manage dislocation include IOL exchange and IOL repositioning [2]. Exchange techniques usually require a larger incision to extract the IOL, subsequently increasing the risk of significant astigmatism, vitreous prolapse, and intraocular bleeding [3]. Repositioning is beneficial as there is reduced postoperative astigmatism and other complications. Among all techniques used for IOL repositioning, the sutured scleral-fixed technique continues to be widely used [4]. With the sutured scleral-fixed technique, the IOL is placed in the correct anatomic position, thereby reducing the number of optical aberrations and decreasing the rate of secondary glaucoma, pigment dispersion, and abnormal pupillary movement. But in geometry, two points only define a line, whereas three points are required to define a plane. And, two-point scleral fixation has been reported to have less favourable IOL positioning [5]. In contrast, the Akreos IOL has four eyelets in haptics [6], which allow for four-point fixation to minimize IOL tilt and decentration. Here, we describe a modified four-point scleral fixation technique, which also combined intrascleral suture and suture burying, for the repositioning of dislocated four-eyelet IOLs.

2. Materials and Methods

This study was approved by the Ethics Committee of the Eye and ENT Hospital of Fudan University and adhered to the Declaration of Helsinki. Informed consent was obtained from each patient.

Four patients diagnosed with Akreos AO60 IOL (Baush and Lomb, Inc.) dislocation were consecutively enrolled and treated by a single retina specialist (CH. J.) at the Eye and ENT Hospital, Fudan University, between May 2018 and November 2019.

The patients underwent a thorough ophthalmic examination before the operation, and the following measurements were collected: best-corrected visual acuity (BCVA); intraocular pressure (IOP) using a noncontact tonometer; spherical equivalent (SE), calculated as one-half of the cylindrical dioptric (C) plus the spherical diopter (D) power; corneal endothelium count using a noncontact specular microscope (Topcon America Corporation, Paramus, NJ, USA); and axial length (AL) using an IOLmaster (version 3.01; Carl Zeiss Meditec, Jena, Germany). Postoperatively, the patients were examined 1 day, 1 week, 1 month, 3 months, 6 months, 1 year, and 2 years later, and the following data were recorded: slit-lamp microscopy examination findings, BCVA, SE, IOP, and corneal endothelial cell density. IOL tilt and decentration were measured using anterior segment tomography with a Pentacam HR (Oculus Optikgeräte GmbH, Wetzlar, Germany) [7, 8].

2.1. Statistical Analysis. Statistical analyses were performed using SPSS Statistics (Version 20.0, IBM Corp., Armonk, NY, USA). Paired t tests were used to compare the differences in BCVA, SE, IOP, and ECD pre- and postoperation. One-way analysis of variance was used to compare IOL tilt and decentration at 1 month, 6 months, and 2 years after surgery, followed by a least significant difference test for multiple comparisons. A level of $P < 0.05$ was considered statistically significant.

2.2. Surgical Technique. After pupil dilation and retrobulbar block anesthesia, standard 23-G pars plana vitrectomy (PPV) was performed, except for one patient who had previously undergone vitrectomy. All dislocated IOLs were checked and were found to be hydrophilic acrylic IOLs (Akreos AO60, Bausch and Lomb Inc., Rochester, NY, USA) (Figure 1(a)). Two conjunctival snips were made at the nasal and temporal. Two limbus incisions were created at the nasal and temporal limbi with an angled (15 degree) blade. Using two 23-G vitreous forceps and the hand-shaking technique or by making it float to the posterior chamber using perfluorocarbon liquid (PFCL), the IOL was brought to the posterior chamber and incarcerated into the pupil, with one eyelet stretching into the anterior chamber. The anterior chamber was filled with viscoelastic material (DisCoVisc; Alcon Laboratories, Inc., Fort Worth, TX, USA). Two scleral incisions were made at 3 and 9 o'clock, 2 mm posterior to the limbus, with a 23-G MVR knife. Thereafter, a CIF-4 needle with a double 10-0 polypropylene (Prolene®) suture passed through a partial thickness of the sclera, entered at the incision at 9 o'clock, and exited at 7 o'clock (Figure 1(b)). A rather long suture tail was left at the 9 o'clock position. The needle was then inserted into the posterior chamber at the exit position; then, using 23-G vitreous forceps to hold the IOL, the needle was passed through the nasal inferior eyelet and exited the eye through the limbus at the 1 o'clock position (Figure 1(c)). The needle was then removed from the suture, and the suture was reintroduced into the anterior chamber, passed through the nasal superior eyelet, and exited the eye through the scleral incision at 9 o'clock, with the help of two 23-G vitreous forceps (Figures 1(d) and 1(e)).

On the temporal side, we adopted another maneuver. After the needle was passed through the sclera from 3 o'clock to 1 o'clock, it was introduced into the posterior chamber and passed through the temporal superior eyelet. Using the guidance of a 23-G vitreous forceps, the needle exited the eye through the nasal limbus incision that had previously been created (Figure 1(f)). Then, through the same incision, the needle was reintroduced into the anterior chamber, passed through the temporal inferior eyelet and exited the eye through the scleral incision at 3 o'clock with the help of 23-G vitreous forceps (Figure 1(g); the two different maneuvers are presented in Video 1). At this point, the two ends of the suture were tied on both sides, and care was taken to centralize the IOL. The suture with the CIF-4 needle was tied to the other tail or tails of the knot that were without a needle (Figure 1(h)) and was passed through the partial thickness of the sclera twice, using a technique similar to the Z-suture technique described by Szurman et al. [9]. Then, after a thorough check of the fundus, the PFCL was removed (if used) and the scleral and conjunctival incisions were closed with 8-0 sutures (Figure 1(i)). Video demonstrating the surgical procedure was available at https://drive.google.com/file/d/1ABxiA9scqA-DbO63JoIWdMYxAZfTlgx4/view.

3. Results

Four patients (mean age: 59.75 ± 13.72 years) were enrolled. The average axial length was 28.97 ± 4.53 mm (range: 24.84–33.33 mm), and IOL dislocation occurred an average of 8.5 ± 1.29 (range: 7–10) years from the time of cataract surgery. On average, the operations took 41.00 ± 9.42 minutes and were completed without severe complications, except for mild hemorrhage at the site of scleral incision in one case (Table 1).

IOP was elevated in case 1 at the 1-month follow-up. Antiglaucoma medication (brimonidine tartrate eye drops® 0.15%; Alphagan® P.0. 15%; Allergan, Inc., Irvine, CA, USA) was used and gradually withdrawn over 3 weeks. Case 2 suffered from transitory elevated IOP with hyphemia 3 days after surgery. With paracentesis and topical antiglaucoma agents, the IOP returned to normal; at the 1-month follow-up, the patient did not require any antiglaucoma medication. The IOP was then maintained and remained within a normal range in these two patients throughout the 2-year follow-up period without antiglaucoma medication. No other postoperative complications were noticed during the follow-up period.

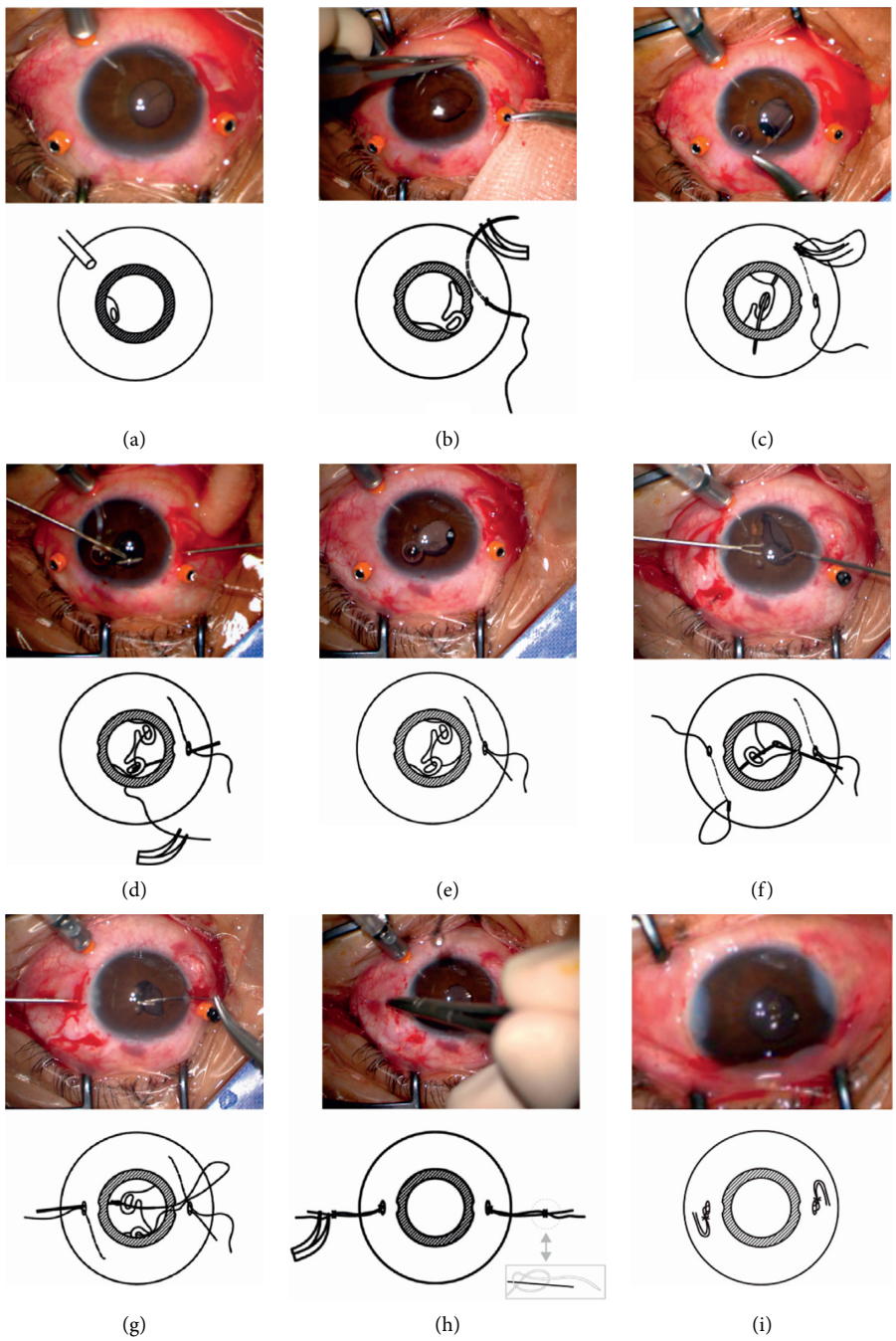

Figure 1: Surgical steps. (a) A dislocated intraocular lens (IOL). (b) After the IOL was brought to the posterior chamber, a CIF-4 needle with a double 10-0 polypropylene (Prolene®) suture was passed through the partial thickness of the sclera at the incision from the 9 o'clock to the 7 o'clock position. (c) The needle was inserted into the posterior chamber through the sclera at the 7 o'clock position and was passed through the nasal inferior eyelet and then externalized through the limbus at the 1 o'clock position. (d) The needle was then removed, and the suture was reintroduced into the anterior chamber and passed through the nasal superior eyelet using vitreous forceps. (e) Using these vitreous forceps, the suture was then externalized through the scleral incision at 9 o'clock. (f) On the temporal side, after passing through the sclera from 3 o'clock to 1 o'clock, the needle was introduced into the posterior chamber, passed through the temporal superior eyelet, and externalized through the nasal limbus incision with the help of vitreous forceps. (g) Through the same incision, the needle was reintroduced into the anterior chamber, passed through the temporal inferior eyelet, and externalized through the scleral incision at 3 o'clock using vitreous forceps. (h) The two ends of the suture, on both sides, were tied and care was taken to centralize the IOL. Then, the suture with a CIF-4 needle was tied to the other suture tail (or tails lacking a needle) using a sliding knot (shown in the small diagram). (i) The sutures were passed through the partial thickness of the sclera, twice, using a technique similar to the Z-suture technique described by Szurman et al.

Table 1: Individual patient characteristics.

Case	Sex (F/M)/age (years)/eye (R/L)	Axial length (mm)	Other ocular disease	IOL implantation to repositioning (years)	Risk factor(s) for zonular defect	Operation time (minutes)	Follow-up (months)
1	M/40/L	25.28	None	8	Unknown	48	24
2	F/68/L	32.41	High myopia	10	Unknown	35	24
3	M/70/R	24.84	Rhegmatogenous retinal detachment (2 years ago)	7	PPV + silicone oil tamponade	30	23
4	F/61/L	33.33	Uveitis optic atrophy	9	Unknown	50	8

F, female; M, male; R, right; L, left.

After the surgery, bare vision improved rapidly in all cases. The IOLs were found to be well-centered and remained stable throughout the follow-up period. After an average follow-up period of 19.75 ± 7.84 (range: 8–24) months, the BCVA (LogMAR, pre 0.63 ± 0.36, post 0.58 ± 0.43, $P = 0.604$) and IOP (pre 13.35 ± 0.85 mmHg, post 14.80 ± 2.03 mmHg, $P = 0.150$) remained unchanged. The average corneal endothelial cell density decreased from 2344.50 ± 441.24 cells/mm^2 to 2192 ± 465.95 cells/mm^2 ($P = 0.009$); average decrease was $6.84 \pm 2.97\%$ (Table 2).

At the last follow-up visit, the average IOL tilts were $1.36 \pm 0.35^\circ$ horizontally and $1.31 \pm 0.14^\circ$ vertically. The average IOL decentration was 0.23 ± 0.12 mm horizontally and 0.18 ± 0.13 mm in vertically. In three cases with more than 1 year follow-up (Table 3), the IOL position remained stable throughout the 1-month, 6-month, and 2-year follow-up periods (Table 4).

4. Discussion

Posterior chamber IOL (PCIOL) dislocation is one of the most serious complications following phacoemulsification. Management includes IOL exchange or IOL repositioning [4]. Repositioning is beneficial as it only requires a small incision, thus reducing the risk of additional endothelial cell trauma and postoperative astigmatism [2]. Here, we presented a technique that combined four-point scleral fixation, the intrascleral suture technique, and suture burying to reposition dislocated four-eyelet hydrophilic acrylic IOLs (Akreos AO60, Bausch and Lomb Inc., Rochester, NY, USA). The main purpose of this new technique is to minimize the incision as well as IOL tilt and decentration. Our primary results suggested that, with incisions <1 mm, the modified technique achieved good IOL positioning.

The modified technique ensures that the incision is minimized. Despite improved techniques which are currently used, extracting an IOL [10] or eternalizing the haptics [11, 12] would induce a larger wound. However, our technique minimized incisions to less than 1 mm, as only side ports and 23-G scleral incisions were made. Various studies have demonstrated that a smaller incision size is beneficial for (1) reducing surgical astigmatism [13–15], (2) rapid wound healing, (3) decreasing the risk of endophthalmitis, and (4) incurring fewer intraoperative complications. With a minimized incision, astigmatism remained unchanged in all four cases in this study (Table 2). Moreover, the endothelial cell density loss (ECL), an important indicator of surgical safety, was $6.84 \pm 2.97\%$ in our study, close to the ECL following an uneventful phacosurgery [16].

It has previously been reported that IOL tilt and decentration with two-point scleral fixation are much higher than that with in-the-bag IOL implantation (two-point scleral vs in-the-bag: tilt 6.0° vs 1.5°, decentration 0.6 mm vs 0.3 mm) [5, 17–20] (Supplemental Table 1). Further, an in vitro experiment demonstrated that it is very difficult to avoid tilt and decentration if two-point scleral fixation is used [21]. In 2009, Oren first reported four-point Akeros AO60 IOL scleral fixation for IOL implantation without sufficient capsular support, and their results were encouraging [22]. To the best of our knowledge, no previous study has directly compared IOL positioning between two- and four-point scleral fixation. In our study, the average H-IOL tilt was $1.36 \pm 0.35^\circ$ and V-IOL tilt was $1.31 \pm 0.14^\circ$, while the average H-IOL decentration was 0.23 ± 0.12 mm and H-IOL decentration was 0.18 ± 0.13 mm. These results were better than those obtained with two-point fixation [17] and were comparable to the results after uneventful phacoemulsification [18].

Another technique used in our approach was intrascleral sutures, which negated the need for a scleral flap or groove. Compared to the flap and groove technique, the intrascleral suture is easier to make, and if the needle does not exit at the ideal location (i.e., 2 mm from the limbus and 4-5 mm from the scleral incision), the needle can simply be withdrawn and another attempt can be made. Additionally, the position of the first set of sutures is directly visible, which makes it easier to place the second set of sutures exactly 180° opposite to the first set. In addition, at all four points, the suture was introduced through the sclera using an ab externo technique; thus, it was easy to ensure that all four points were at the same distance from the limbus and in the same plane [23]. Consequently, IOL tilt should be greatly reduced.

Moreover, we made use of the intrascleral burying technique to protect the suture knot. After making the suture knot, instead of cutting the suture and rotating it, we tied the double 10-0 polypropylene (Prolene®) with a CIF-4 needle to the tail or tails of the knot and buried the tails into the sclera. The main purpose of this step was to reduce the friction between the suture tails and the sclera or conjunctiva, which was the main reason for erosion and exposure. The rationale behind this was that, once the suture is cut, the short cut-ends are quite stiff and may erode the

Table 2: Comparison of clinical data before surgery and at the last visit after surgery.

Case	BCVA (LogMAR)		Refraction (D)		SE (D)		IOP (mmHg)		ECD (cells/mm^2)		
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Decreased (%)
	$P = 0.604$				$P = 0.157$		$P = 0.150$		$P = 0.009^*$		
1	0.1	0.0	+11.00DS − 0.50DC ∗ 170	+0.50DS − 1.00DC ∗ 170	+10.75	0.000	13.2	16.5	2433	2222	8.67
2	0.9	0.8	−0.00DS − 1.00DC ∗ 105	−1.50DS − 0.75DC ∗ 100	−0.5	−1.875	14	15	2708	2613	3.51
3	0.7	0.5	+9.25DS − 0.75DC ∗ 150	−2.00DS − 1.25DC ∗ 145	+8.875	−2.625	12.2	11.9	2532	2399	5.25
4	0.8	1.0	−3.75DS − 0.5DC ∗ 80	−3.00DS − 1.25DC ∗ 85	−4.000	−3.625	14	15.8	1705	1536	9.91
Mean ± SD	0.63 ± 0.36	0.58 ± 0.43			+3.78 ± 7.15	−2.03 ± 1.53	13.35 ± 0.85	14.80 ± 2.03	2344.50 ± 441.24	2192.50 ± 465.95	6.84 ± 2.97

A paired sample t test was used to compare the clinical data pre- and postoperatively. $^*P < 0.05$, statistically significant. †BCVA, best-corrected visual acuity; LogMAR, logarithm of the minimum angle of resolution; IOP, intraocular pressure; ECD, endothelial cell density; SE, spherical equivalent; SD, standard deviation; D, diopter; IOL, intraocular lens; Pre, preoperatively; Post, postoperatively.

Table 3: Postoperative intraocular lens position at the last follow-up.

Case	Horizontal decentration (mm)	Vertical decentration (mm)	Horizontal tilt (degree)	Vertical tilt (degree)
1	0.09	0.04	1.62	1.48
2	0.30	0.24	1.69	1.27
3	0.35	0.32	1.03	1.33
4	0.17	0.10	1.09	1.14
Mean ± SD	0.23 ± 0.12	0.18 ± 0.13	1.36 ± 0.35	1.31 ± 0.14

SD, standard deviation.

Table 4: IOL position at 1 month, 6 months, and 2 years postoperatively for 3 cases.

Case	Horizontal decentration (mm)			Vertical decentration (mm)			Horizontal tilt (°)			Vertical tilt (°)		
	1 month	6 months	2 years	1 month	6 months	2 years	1 month	6 months	2 years	1 month	6 months	2 years
		$P = 0.733$			$P = 0.796$			$P = 0.369$			$P = 0.334$	
1	0.09	0.10	0.09	0.14	0.15	0.04	1.04	1.01	1.62	1.29	1.59	1.39
2	0.26	0.38	0.3	0.13	0.16	0.24	1.11	1.68	1.69	1.14	1.19	1.27
3	0.24	0.38	0.35	0.18	0.22	0.32	1.06	1.07	1.03	1.14	1.29	1.33
Mean ± SD	0.20 ± 0.09	0.29 ± 0.16	0.25 ± 0.14	0.15 ± 0.03	0.18 ± 0.04	0.20 ± 0.14	1.07 ± 0.04	1.25 ± 0.37	1.45 ± 0.36	1.19 ± 0.09	1.36 ± 0.21	1.33 ± 0.06

One-way analysis of variance was used to compare IOL tilt and decentration 1-month, 6-months, and 2-years post-surgery. $P < 0.05$, statistically significant. SD, standard deviation; IOL, intraocular lens.

sclera [24]; however, as the tails used in our approach were much longer, they should have better pliability and lie tangential to the sclera and thus should stay within the sclera without creating much friction.

5. Conclusions

The number of cases and follow-up period were limited, but the primary data suggested that with this new technique, dislocated four-eyelet IOLs could be repositioned successfully with reduced surgical trauma, and good IOL positioning.

Data Availability

The data used to support the findings of this study are included within the article.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

Authors' Contributions

Kaicheng Wu and Wangyi Fang contributed equally to the work.

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Supplementary Materials

Supplemental Digital Content 1: video demonstrating the surgical procedure (MP4) ; Supplemental Table 1: comparison of the IOL tilt and decentration in four-point scleral suture fixation, two-point scleral suture fixation, and phacoemulsification. (*Supplementary Materials*)

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