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Clinical and Biometric Factors Associated with Prediction Errors Related to Lens Position in Vitrectomized Patients

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Keywords

Cataract surgery · Pars plana vitrectomy · Intraocular lens · Biometry · Refractive outcome

Abstract

Introduction: The aim of the study was to evaluate clinical and biometric factors leading to a prediction error related to lens position in pars plana vitrectomy. **Methods:** This study was conducted as a consecutive retrospective case series at the Department of Ophthalmology, Montpellier University Hospital. All medical files and PCI biometrical reports from a single surgeon were reviewed from 2017 to 2019. Patients who had phacoemulsification with the ASPHINA 509 MP[®] intraocular lens were selected and stratified into 3 groups: phacoemulsification alone (group 1), phacoemulsification and vitrectomy with gas tamponade (group 2), and phacoemulsification and vitrectomy without tamponade (group 3). Clinical factors and biometry factors from initial and final biometry were collected. Refractive error, actual lens position, C constant, axial length delta, and pre-operative

and post-operative anterior and posterior segment variation parameters were calculated. **Results:** A total of 140 eyes were analyzed, 90 in group 1, and 25 in group 2 and 3. The mean prediction error was 0.10 ± 0.55 D (group 1); -0.36 ± 0.74 D (group 2); and -0.12 ± 0.54 D (group 3) with $p < 0.05$ for group 1 vs. group 2. The mean actual lens position was 5.25 ± 0.29 mm; 5.66 ± 0.60 mm; and 5.50 ± 0.43 mm for the 3 groups, respectively ($p < 0.001$). Axial length delta was -0.10 ± 0.13 mm in group 1, -0.062 ± 0.20 mm in group 2, and -0.022 ± 0.17 mm in group 3 ($p = 0.015$). Multilinear regression analysis found a significant and independent influence of vitrectomy and gas tamponade on prediction error. **Conclusion:** Myopic shift in the case of vitrectomy is multifactorial, effective lens position is modified by vitrectomy and vitreous refractive index is changing. The integration of these data in formulas may improve refractive outcome after cataract and vitrectomy surgery.

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Introduction

With optical biometry improvements and technical evolution, cataract surgery is now considered a true refractive surgery procedure. Postoperative results are not as good with phacovitrectomy. We commonly observe a myopic shift after a combined procedure [1–3] or after vitrectomy in a patient previously operated on for cataract [1]. This myopic shift could get worse in the case of gas tamponade [2–4].

Some authors recommend choosing an intraocular lens (IOL) with a lower power of 0.50 diopters during combined surgery to anticipate the vitrectomy-related anterior IOL displacement in the presence of tamponade [4–6]. Some studies have showed a backward movement of the IOL based on biometric parameters after phacovitrectomy compared to a phacoemulsification alone group [7]. Other studies reported no shift [8], while yet other studies showed a hypermetropic shift in the case of phacoemulsification in a previously vitrectomized eye [9, 10]. Literature data are divergent on this subject, and the elements responsible for this prediction error are under debate.

IOL power calculation is the main pre-operative step to reduce prediction error. The latest generation of optical biometers can reduce measurement errors of anatomical parameters with better accuracy for axial length (AL) and keratometry. According to Olsen [11], 42% of refractive errors are the cause of effective lens position (ELP) prediction error. There is no specific IOL formula for vitrectomy, and the IOL power calculation in the case of phacovitrectomy remains challenging. The aim of this study was to determine which clinical or biometric factors were responsible for a prediction error associated with the IOL position in vitrectomized patients.

Material and Methods

Study Population

We retrospectively and consecutively included all patients who underwent cataract surgery with ASPHINA 509 MP (Zeiss®) IOL implantation in the bag, either prior to, after, or in combination with vitrectomy to compare them to a control group of patients who underwent phacoemulsification alone by the same single surgeon with the same IOL in the same surgery conditions between May 2017 and May 2019 in the ophthalmology department of Gui de Chauliac Hospital of Montpellier.

The studied patients were stratified into 3 groups:

- Phacoemulsification alone (group 1).

- Phacoemulsification and vitrectomy with gas tamponade for retinal detachment and macular hole (group 2).
- Phacoemulsification and vitrectomy without gas tamponade for epiretinal membrane, vitreous hemorrhage, and complicated proliferative diabetic retinopathy (group 3).

Vitrectomy was performed using a 25-gauge three-port technique. Scleral plugs were put at 3.5 mm from the limbus at 2, 10, and 8 o'clock for left eyes and 2, 10, and 4 o'clock for right eyes. Systematic sclerotomy suture with resorbable wire was performed at the end of surgery. Gases used in our study were consistently isoexpansive, following the recommendations of the gas manufacturer.

For cataract removal, the technique included a 2.2-mm post-limbal incision, a 5.5-mm centered curvilinear capsulorhexis, and standard phacoemulsification with implantation of the ASPHINA 509 MP (Zeiss®) in the bag. All patients included in the study had uneventful phacoemulsification or vitrectomy surgery.

Exclusion criteria were keratoconus and pre-operative or postoperative astigmatism greater than 2D (diopters), pre-operative, or post-operative inability to achieve biometry with optical low-coherence reflectometry, capsular rupture during surgery, and implantation outside the capsular bag. Patients with retinal detachment recurrence, tractional retinal detachment, and detached macula were not included. The research was approved by the University Hospital of Montpellier and followed the tenets of the 1995 Declaration of Helsinki (revised in Edinburgh 2000).

Study Design

An Informatics file was created to report age, sex, ophthalmologic history, type of surgical procedure, vitrectomy indication, post-operative refraction, pre-operative, and post-operative biometry made with the Lenstar LS900®. For patients with vitrectomy prior to phacoemulsification, we used intermediate biometry to evaluate prediction error.

Ethics

This retrospective study was approved by the Institutional Review Board of Montpellier University Hospital (IRB ID: 202000607). Written informed consent from participants was not required in accordance with local guidelines.

Biometry Assessment

We analyzed pre-operative and 4–12-week post-operative biometry for each patient. A comprehensive biometric assessment was made with the Lenstar

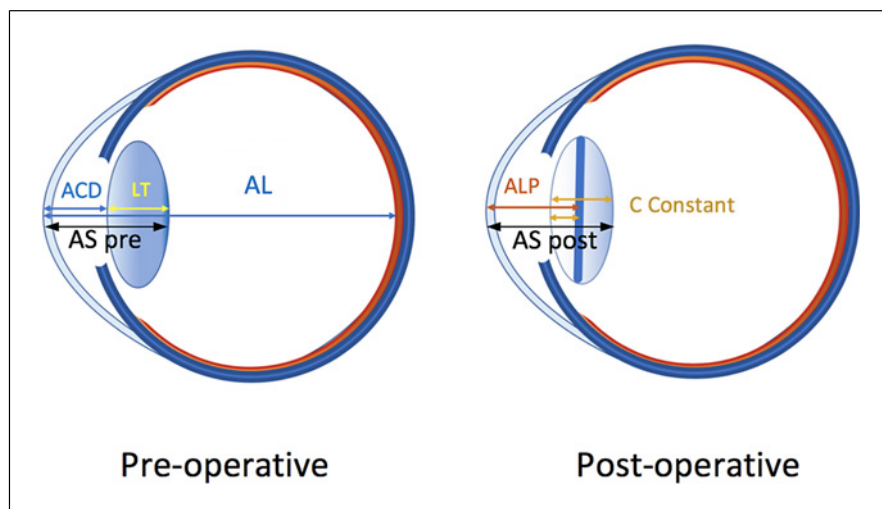


Fig. 1. Drawing of the different pre- and post-surgery measures AS pre was defined by ACD pre + LT pre and AS post by ACD post + LT post. AL, axial length; LT, lens thickness; AS, anterior segment (pre- and post-operative); ACD, anterior chamber depth; AL, actual lens position.

LS900[®] optical low-coherence reflectometry. The data were analyzed using EyeSuite[®] v3.1.1. provided with the biometer. The following parameters were measured: central corneal thickness, anterior chamber depth (ACD), lens thickness (LT), AL, retinal thickness, and mean K. The index of refraction was 1.3375 for the cornea. Calculating IOL power involved the Barrett Universal II formula for all patients [12].

Prediction Error

It was defined as the difference between the post-operative and the predicted spherical equivalent refraction error (i.e., post-operative refraction error – formula predicted refraction error) [13].

Actual Lens Position

The actual lens position (ALP) of the IOL was measured at the exact postoperative position of the center of the IOL from the corneal epithelium to the center of the IOL as follows [14]:

$$\text{ALP} = \text{ACD postoperatively} + 1/2 \text{ LT postoperatively}$$

C Constant

Defined by Olsen in 2014 [15], it is based on the observation that the IOL tends to locate itself in a defined position after standard cataract surgery, depending on the IOL type. The effective C constant has been calculated postoperatively as recommended in the literature after surgery as follows:

$$\text{C constant} = (\text{ACD post} + \text{LT post}/2 - \text{ACD pre}) / \text{LT pre}$$

where ACD post is the postoperative ACD and LT post is the postoperative LT. C constant of 0.5 means that the IOL is positioned at the equator of the pre-operative capsular lens bag.

Anterior Segment Parameters

In each group, we measured the anterior chamber deepening (ACD post-ACD pre) and the variation between the ratio anterior segment/AL in pre-operative (SA pre/LA pre) and post-operative (SA post/LA post). SA pre was defined by ACD pre + LT pre and SA post by ACD post + LT post (Fig. 1).

Statistical Analysis and Outcome

Descriptive statistics, such as means, standard deviations, and percentages, were used to summarize the demographic and clinical characteristics of the study population. We first performed linear univariate analysis to evaluate our outcomes in each group, then multivariate linear regression to detect independent relationships.

Multivariate linear regression was conducted, taking into account the significant confounding factors identified in the univariate analyses. This adjustment enabled us to better assess the independent effects of the variables of interest in controlling for potential influences from these confounders.

SAS 9 (SAS Inst., Cary, NC, USA) was used for data analysis. The significance level was set at $p < 0.05$.

Our main outcome was prediction error measure in the 3 groups. Our secondary aim was to study the ALP, the C constant, the AL delta, the ACD delta, SA pre/LA pre, and SA post/LA post delta in our 3 groups.

Table 1. Characteristics of the study population by procedure type

Patient's characteristics	Group 1	Group 2	Group 3	p value
	PCE only	PCE/ PPV/T+	PCE/ PPV/T-	
Clinical parameters				
Subject number = eye number, <i>n</i> (%)	90 (64.28)	25 (17.86)	25 (17.86)	
Side, right, <i>n</i> (%)	46 (51.1)	17 (68)	15 (60)	0.288
Age when PCE procedure was performed, years	75.1±10.4	66.7±8.0	68.4±8.3	<0.001 for G1 vs. G2 and G1 vs. G3
Gender, female, <i>n</i> (%)	46 (51.1)	13 (52)	8 (32)	0.161
Maculopathy history, <i>n</i> (%)	15 (16.6)	13 (52)	22 (88)	<0.000001 between each groups
Biometrical parameters				
IOL power, diopters	21.10±3.50	19.20±2.90	20.44±3.00	0.008 for G1 vs. G2
Pre-operative AL, mm	23.65±1.36	24.57±1.58	23.65±1.11	0.018 for G1 vs. G2
ACD pre, mm	3.12±0.41	3.37±0.34	3.16±0.41	0.020 for G1 vs. G2
LT, mm	4.51±0.44	4.34±0.38	4.48±0.47	0.211

Values are expressed as percentage, mean ± standard deviation. *N*, number of subjects; PCE, phacoemulsification; PPV, 3 ports pars plana vitrectomy; T+, gas tamponade; T-, no tamponade at all; D, diopters.

Results

Population Characteristics

The study population consisted of 140 eyes of 140 patients with a mean (SD) age of 72.41 ± 10.14 years. Patients were divided into 3 groups by type of procedure. Table 1 shows the patients' characteristics by group. Table 2 shows indications and temporality for the vitrectomy population. Group 1 and group 3 were comparable for biometric parameters. Group 2 had a higher myopic population than the other 2 groups due to the retinal detachment population.

Prediction Error

The mean prediction error was 0.107 ± 0.552 D, -0.362 ± 0.748 D, and -0.121 ± 0.545 D in group 1, group 2, and group 3, respectively, which was comparable to the literature's data (Table 3). Multiple pairwise comparisons (Bonferroni test) showed that groups 1 and 2 were significantly different.

Gas and Positioning

Table 3 describes the type of gas used for patients in group 2: SF6: 15 (60%), C2F6: 9 (36%), and C3F8: 1 (4%). The tamponade durations were approximately 3 weeks for SF6, 4 weeks for C2F6, and around 6 weeks for C3F8.

Regarding patient positioning post-surgery, those with retinal detachment were positioned on the operated side for the first 12 h. Following this, the positioning was determined based on the location of the retinal tears and maintained for 1 week. Patients operated on for macular holes were instructed to maintain a face-down position for 1 week.

Biometry Variables

The mean anterior lens position was 5.255 ± 0.290 mm, 5.664 ± 0.604 mm, and 5.664 ± 0.436 mm in group 1, group 2, and group 3, respectively (Table 4). Results were significant for group 1 versus group 3 ($p < 0.001$).

Mean C constant was 0.387 ± 0.040, 0.387 ± 0.040, and 0.417 ± 0.080 for the same groups ($p 0.136$). By comparing group 1 versus group 2 + group 3, we had a C constant at 0.420 ± 0.113 for the vitrectomy group ($p = 0.07$).

The AL variation was -0.108 ± 0.138 mm in the PKE group alone and 0.062 ± 0.205 mm and 0.022 ± 0.171 mm in groups 2 and 3 with a p at 0.015. The deepening of the anterior chamber was 1.397 ± 0.283 mm; 1.366 ± 0.585 mm; and 1.362 ± 0.304 mm, respectively, in the 3 groups ($p = 0.874$).

The ratio (SA pre/LA pre) was 32.4% ± 1.87, 31.5% ± 2.17, and 32.3% ± 1.78, respectively, in each group with $p = 0.074$. Postoperatively, these same ratios were 22.4% ± 1.39; 23.2% ± 3.07; and 23.3% ± 1.63 ($p < 0.015$) with a variation between the two at -30.8% ± 3.75 (group 1); -26.3% ± 8.57 (group 2); and -27.8% ± 6.52 (group 3) with $p < 0.01$. For the last two results, groups 2 and 3 were significantly different from group 1.

Multiple Linear Regression Analysis

To identify independent relation for prediction error, we performed multivariate regression analysis. The variables entered in the model were age, sex, gas tamponade, vitrectomy, pre-operative ACD, and pre-operative AL.

Table 2. Surgical parameters for vitrectomized patients

	Surgical indication, <i>n</i> (%)	Surgical procedure temporality, <i>n</i> (%)	Tamponade, <i>n</i> (%)
Group 2 PCE/PPV/T+	MH: 11 (22) RD: 14 (28)	Phacovitrectomy: 14 (28) PCE then PPV: 5 (10) PPV then PCE: 6 (12)	SF6: 15 (60) C2F6: 9 (36) C3F8: 1 (4)
Group 3 PCE/PPV/T-	ERM: 13 (26) IVH: 1 (2) PDR: 11 (22)	Phacovitrectomy: 23 (46) PCE then PPV: 1 (2) PPV then PCE: 1 (2)	None

Values are expressed as percentage, mean \pm standard deviation. PCE, phacoemulsification; PPV, 3 ports pars plana vitrectomy; T+, gas tamponade; T-, no tamponade; ERM, epiretinal membrane; MH, macular hole; RD, retinal detachment; IVH, intra-vitreous haemorrhage; PDR, proliferative diabetic retinopathy.

Table 3. Comparison of prediction error in diopters

	Absolute value (standard deviation)	Mean (standard deviation)	Median (Q25; Q75)	Number of patients in target refraction, <i>n</i> (%)			<i>N</i>	<i>p</i> value	Test
				± 1.00 D	± 0.50 D	± 0.25 D			
Group 1 PCE only (1 month)	0.420 \pm 0.336	0.107 \pm 0.552	0.140 (-0.140; 0.460)	82 (91)	61 (68)	38 (42)	90	0.005* (G1 vs. G2 and G1 vs. G3)	WMK Rk sum
Group 2 PCE/PPV/T+ (3 months)	0.653 \pm 0.503	-0.362 \pm 0.748	-0.275 (-0.770; 0.145)	19 (76)	10 (40)	6 (24)	25		
Group 3 PCE/PPV/T- (3 months)	0.426 \pm 0.351	-0.121 \pm 0.545	-0.035 (-0.510; 0.305)	23 (92)	16 (64)	10 (40)	25		

Values are expressed as percentage, mean \pm standard deviation. *N*, number of subjects; PCE, phacoemulsification; PPV, 3 ports pars plana vitrectomy; T+, gas tamponade; T-, no tamponade at all; D, diopters. *Significant.

In our different models, vitrectomy and gas tamponade significantly influenced the prediction error. We found the same relationship for C Constant and ALP (Table 5). In this analysis, the pre-operative AL and pre-operative ACD were not statistically significant predictors of prediction error.

Discussion

In the present retrospective consecutive case series, we observed, consistent with the literature, that vitrectomy was associated with a systematic myopic shift, particularly in cases with a history of gas tamponade. Previously, it was known that vitrectomy could cause refractive changes, but the exact mechanisms were unclear, with studies showing conflicting results. Our research adds new insights by demonstrating that, in phacovitrectomy

and vitrectomy without gas tamponade, the IOL tends to be positioned more posteriorly compared to the phacoemulsification alone group. This highlights the significant impact of ELP and changes in the vitreous refractive index on postoperative refractive outcomes.

With technical advancements in PCI biometry, the measurement errors for AL and keratometry have been reduced. In our study, the main contributing factor to the prediction error was an ELP as determined by our multiple linear regression analysis. Furthermore, by using a state-of-the-art biometer and small vitrectomy plugs, we minimized the risk of post-operative astigmatism and measurement errors.

Regarding the C constant for the implant used in our study, it aligned with the findings reported by Olsen and Hoffmann in 2014 [15] based on a sample of 2,043 patients, as well as the works of Plat and Hoa [14]

Table 4. Comparison of post-operative biometric characteristics

	Group 1	Group 2	Group 3	Test	p value
	PCE only (1 month)	PCE/PPV/T+ (3 months)	PCE/PPV/T- (3 months)		
ALP, mm	5.255±0.290	5.664±0.604	5.500±0.436	WMK Rk sum	<0.001* (G1 vs. G2 and G1 vs. G3)
C constant	0.387±0.040	0.422±0.141	0.417±0.080		0.136
AL delta, mm	-0.108±0.138	-0.062±0.205	-0.022±0.171		0.015* (G1 vs. G2 and G1 vs. G3)
ACD post – ACD pre, mm	1.397±0.283	1.366±0.585	1.62±0.304		0.874
AS pre/AL pre	32.4%±1.87	31.5%±2.17	32.3%±1.78		0.074
AS post/AL post	22.4%±1.39	23.2%±3.07	23.3%±1.63		0.015* (G1 vs. G2 and G1 vs. G3)
AS delta	-30.8%±3.75	-26.3%±8.57	-27.8%±6.52		<0.01* (G1 vs. G2 and G1 vs. G3)

Values are expressed as percentage, mean ± standard deviation. ALP, actual lens position; AL delta, post-operative axial length – pre-operative axial length; ACD, anterior chamber depth; AS, anterior segment; AS delta, (AS pre/AL pre) and (AS post/AL post) delta; PCE, phacoemulsification; PPV, 3 ports pars plana vitrectomy; T+, gas tamponade; T-, no tamponade. *Significant.

Table 5. Multivariate analysis with linear regression for prediction error

Variable	Beta coefficient	95% confidence interval		p value
		lower bound	upper bound	
Age	-0.0084	-0.0189	0.0022	0.1196
Gender M vs. F	0.108	-0.0926	0.3094	0.2880
Group 1 vs. group 3	-0.315	-0.5891	-0.0407	0.0247*
Group 1 vs. group 2	-0.545	-0.8278	-0.2620	0.0002*
ACD pre	0.196	-0.1069	0.4989	0.2029
AL pre	-0.049	-0.1366	0.0386	0.2703
Age	-0.009	-0.019	0.00089	0.0741
Gender M vs. F	0.119	-0.0706	0.3095	0.2161
Group 1 vs. group 3	-0.385	-0.6501	-0.1204	0.0047*
Group 1 vs. group 2	-0.629	-0.8968	-0.3615	<0.0001*
C constant	2.342	1.0797	3.6048	0.0004*
Age	-0.007	-0.0169	0.0024	0.1423
Gender M vs. F	0.0335	-0.153	0.22	0.7229
Group 1 vs. group 3	-0.3615	-0.6159	-0.107	0.0057*
Group 1 vs. group 2	-0.7157	-0.9806	-0.4509	<0.0001*
ALP	0.5669	0.3343	0.7995	<0.0001*

ACD pre, pre-operative anterior chamber depth; AL pre, pre-operative axial length; F, female; M, male. *Significant.

constant was modified, indicating a potentially more posterior position of the intraocular lens in this group. Furthermore, an analysis of the variation in

ratios (anterior segment/AL) before and after surgery also suggests that the implant is positioned more posteriorly than expected during vitrectomy.

Some authors have suggested that gas tamponade could induce zonular elasticity, causing the IOL to shift anteriorly once the gas has dissipated, resulting in a myopic shift [6, 16]. However, our biometric studies did not reveal any anterior movement of the IOL. Conversely, other authors have proposed that the presence of gas tamponade and zonular elasticity may lead to a more posterior positioning of the IOL. In our study, we observed a higher anterior lens position in group 3 compared to group 1, despite similar baseline biometric data.

The Wieger ligament can affect the capsular plane position [17] and may be altered during vitrectomy, especially with anterior vitreous and hyaloid removal. While hyaloid support and zonular damage influence IOL position, these factors are not yet fully integrated into IOL formulas, but their inclusion could improve refractive outcomes.

Origins of the Myopic Shift

In our study, there were 5 indications of vitrectomy, 3 of which involved a clear modification of the macular architecture (ERM, MH, and complicated PDR). Frings [18] showed on 47 consecutive phacovitrectomy that subjects with macular edema had less post-operative prediction error with a smaller myopic shift than subjects with normal macular profile. This result shows us the underestimation of the photoreceptors-cornea distance measure for subjects with macular edema. In our study, the retinal detachment population had a normal foveolar profile and the biggest myopic shift. Group 3 patients, with a modified macular architecture (ERM, PDR, MH), did not have such a high prediction error.

Comparative data from the initial and final biometry in our study suggest that vitrectomy induces a change in implant position, and it is likely based on our results that vitrectomy leads to poor prediction of ELP [11]. Group 3 patients, despite a more posterior position of the intraocular implant on post-operative biometric data, have rather good refractive results and are even very close to group 1. Between these 2 groups, the difference in prediction error was not significant. There seems to be an element responsible for myopia in this group that would “cancel” the hyperopia following the retreat of the implant (online Supplement 1; for all online suppl. material, see <https://doi.org/10.1159/000542358>).

Vitreous refractive index is a bit superior to the aqueous refractive index [19] and could explain myopic shift [16]. Replacement of vitreous by balanced salt solution is changing the refraction index of the eye optic

system. It is the only common parameter of all our patients.

Some studies have highlighted this element as potentially myopic but without fully integrating it as the source of a systematic prediction error. To provide context and contrast to our findings, a summary of past studies compared to our current study is presented in online Supplement 2.

Strengths and Weaknesses of Our Study

The strength of our study lies in its inclusion of a wide range of retinal surgical indications commonly encountered in everyday clinical practice, involving an unselected population of patients at a hospital setting. All patients were operated consecutively by the same surgeon under the same operating conditions and with the same techniques, both for the posterior and anterior segments. It was the same ASPHINA® IOL for all patients, ensuring standardized conditions across the study population.

The use of 25 G plugs ensures that significant topographic corneal changes or induced astigmatism are not caused [20, 21]. The use of absorbable sutures only results in refractive changes in the first few weeks, thus limiting the impact of sclerotomies on post-operative refraction [22]. Similarly, our results did not show any variation in AL for the vitrectomized patient groups.

The main limitation of this study is its small sample and its retrospective nature: a larger sample study should be conducted to confirm or not our assumptions. Second, our study focused solely on the Barrett 2 formula for refractive error calculations, which may limit the generalizability of our findings to other formulas. Conducting comparisons with different formulas could provide a more comprehensive understanding of the topic. However, considering the potential risk of increasing type I error and the widespread use of the Barrett 2 formula in clinical practice, we made a deliberate choice to maintain consistency and reliability.

Necessary Further Investigation

Plat et al. [14], in accordance with Olsen Hoffmann [15], demonstrated in their study that various IOLs are not positioned in the capsular bag in the same manner as each IOL possesses its specific C Constant. IOL design is a key factor for its position in the bag, as shown by Hwang and Jee [23] with a prediction error depending on the number of haptics, for example, 2 or 4. In our study we utilized a single IOL to limit design bias, although it

would be intriguing to compare our findings with another IOL design in a similar population. Most of our patients had a standard AL between 22 and 26 mm. Eyes with an AL <22 mm or >26 mm may be subject to other factors influencing IOL position.

Data from studies of phacoemulsification in patients already vitrectomized tend to show an absence of “shift” or even a slight hyperopia [9, 10]. In our study we compared the initial biometry (prior to vitrectomy and phacoemulsification) with the final biometry, without examining the intermediate biometry when it was available. However, the number of patients in our study was insufficient to establish a precise hypothesis for this particular scenario. For now, aiming for +0.50 diopters more than the true refractive target in the case of phacovitrectomy with gas tamponade for retinal detachment and macular hole to anticipate the myopic shift seems a good alternative.

Conclusions

This study determined that phacovitrectomy procedures are associated with a consistent prediction error leading to a myopic shift. This error is most pronounced when intraocular tamponade is present during retinal detachment or macular hole surgery. The advancement of formulas incorporating deep-learning techniques may contribute to improvements in this regard. Similarly, the inclusion in IOL power calculation formulas of the vitrectomy-related modification of the ELP and the change in the refractive index of the vitreous body could provide additional precision in the case of combined phacovitrectomy surgery.

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Statement of Ethics

This retrospective study was approved by the Institutional Review Board of Montpellier University Hospital (IRB ID: 202000607). Written informed consent from participants was not required in accordance with local guidelines.

Conflict of Interest Statement

The authors declare no conflicts of interest.

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Author Contributions

Eloi Debourdeau conducted the final manuscript preparation. Pierre Pineau was responsible for data collection and the initial manuscript drafting. Chloé Chamard, Julien Plat, Didier Hoa, Frederico Manna, Sandrine Akouete, Max Villain, and Sandrine Akouete provided critical reviews and comments. Thibaut Mural and Nicolas Molinari contributed to both the statistical analysis and the study methodology. Vincent Daien was involved in the initial study design and provided critical reviews and comments.

Data Availability Statement

The data supporting the findings of this study are not publicly available due to their containing sensitive information that could compromise the privacy of research participants. However, the data are available from the corresponding author upon reasonable request (email: e-debourdeau@chu-montpellier.fr).

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