ORIGINAL RESEARCH

Senile Cataract Formation Does Not Affect Crystalline Lens Thickness

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ABSTRACT

Introduction: Characterizing lens thickness (LT) in patients with cataracts is important for better understanding the lens aging process and for designing new intraocular lens power formulas. This study aimed to analyze the influence of common senile cataract formation on the LT, anterior (ACS) and posterior (PCS) cortex space, and nuclear thickness (NT), controlling for sex, age, and axial length.

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Methods: A cross-sectional study was performed. A consecutive sample of 603 volunteers (403 women, 200 men) aged 59.1 ± 18.8 years was recruited. The standardized Lens Opacification Classification System (LOCS)-III was used to classify eyes (randomly selected) into cataractous and non-cataractous groups. Also, they were classified according to the cataract location (presence or absence of cortical, nuclear, or posterior subcapsular cataract). Optical biometry was performed to measure LT, ACS, NT, and PCS. Propensity score was used to match participants one-to-one for sex, age, and axial length. Groups were compared using the Student's *t* test or Yuen's test.

Results: The four classifications divided unmatched eyes into: 361 cataractous lenses

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and 242 non-cataractous, 226 cortical and 377 non-cortical cataractous, 313 nuclear and 290 non-nuclear cataractous and 242 subcapsular and 361 non-subcapsular cataractous. Before matching, cataractous eyes showed significantly higher LT (4.52 ± 0.39 vs. 3.94 ± 0.46 mm, $p < 0.001$), ACS (0.75 ± 0.20 vs. 0.58 ± 0.23 mm, $p < 0.001$), NT (3.34 ± 0.23 vs. 3.18 ± 0.25 mm, $p < 0.001$) and PCS (0.42 ± 0.19 vs. 0.37 ± 0.19 mm, $p = 0.003$). Matched lens, cortical, nuclear, and subcapsular cataract samples comprised 146, 258, 182, and 226 eyes, respectively. After matching, no significant differences were observed in LT (4.34 ± 0.37 vs. 4.33 ± 0.36 mm, $p = 0.94$), ACS (0.72 ± 0.20 vs. 0.76 ± 0.19 mm, $p = 0.08$), NT (3.31 ± 0.22 vs. 3.30 ± 0.23 mm, $p = 0.24$) and PCS (0.42 ± 0.19 vs. 0.43 ± 0.16 mm, $p = 0.79$).

Conclusions: The presence of senile cortical, nuclear, and posterior subcapsular cataract have no effect on LT, ACS, NT, and PCS. Confounding factors should be controlled for when measuring LT and its main components.

Keywords: Cataract; Cortical; Lens; Nuclear; Subcapsular; Thickness

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Key Summary Points

Why carry out this study?

Crystalline lens thickness has been incorporated into formulas for intraocular lens (IOL) calculation.

The effect of cataract formation on lens thickness and the space of its main components is unclear since contradictory results had been reported.

What was learned from the study:

The presence of senile cortical, nuclear, and posterior subcapsular cataract have no clinical effect either on the full crystalline lens thickness nor on the anterior and posterior cortex space or the nuclear thickness.

Studies analyzing lens thickness and the space of its main components should control for confounding factors, mainly age and axial length, to avoid biased results.

Future IOL power formulas should consider the lack of effect of senile cataract formation on lens thickness.

INTRODUCTION

Cataract surgery is the most frequent ophthalmological surgery procedure worldwide. During cataract surgery, the implantation of an intraocular lens (IOL) replaces the crystalline lens power [1]. Currently, accurate IOL power calculations can provide successful postoperative refractive outcomes in most patients with cataracts. IOL power formulas have been continuously improving, resulting in lower mean absolute refractive errors after surgery. The last generation formulas incorporate multiple parameters, including lens thickness (LT) among others [2], allowing higher postoperative refractive accuracy. Therefore, the importance of the proper characterization of LT in patients with cataracts has increased. In fact, previous authors have provided normative LT data for patients with cataracts in different ethnic groups to help to improve the IOL designs and power calculations [3–6].

The interest in analyzing the effect of cataract formation on LT is not recent. Previous authors have assessed LT in different degrees of cataractous eyes using ultrasonography [7], or even with a less reliable technique, such as slit-lamp biomicroscopy [8, 9]. In recent years, precise LT measurements have been performed with optical biometers, which allow the space of its main components (i.e., the anterior and posterior cortex space and nuclear thickness) to be measured [10]. However, contradictory results have been reported on the influence of cataract formation on LT. While various authors have reported an association between the

presence of cataract and LT [9–11], other authors have not found any relationship [12, 13]. Thus, the effect of cataract formation on LT is still unclear.

LT and the space of its main components have been associated with demographic characteristics and some ocular parameters. Age has been the factor with the strongest association [8], with an estimated increase of about 0.12–0.15 mm per decade [4, 11, 14]. An increase in the anterior and posterior cortex space appears to be the main reason [10]. Another contributing factor that is also associated with wider LT is male gender [4, 15, 16]. Besides, axial length and the anterior chamber depth have been inversely related to LT [14, 17] and also to the space of its main components [10, 18]. Therefore, previous results analyzing the effect of cataract formation on LT are very likely to be affected by the above-mentioned confounding factors. In addition, these confounding factors might be the main reason to find contradictory outcomes in the literature. Finally, the literature is scarce regarding the effect of senile cataract formation on the space of the three main components of the crystalline lens [10].

Therefore, the aim of the present study was to analyze the influence of senile cataract formation on the LT and the space of its three main components (i.e., the anterior capsule, the nucleus, and the posterior capsule), controlling for the confounding effects of sex, age, and axial length.

METHODS

This prospective cross-sectional study was approved by the ethics committee of Hospital Universitario Rio Hortega (Valladolid, Spain; Reference number: 156/17) and was conducted in accordance with the Declaration of Helsinki guidelines. The study protocol was explained before written consent to participate in the study was obtained from all participants.

Participants

Volunteers were invited to participate if they were over 18 years of age. A consecutive sample of patients seeking eye care for examination at the same ophthalmology outpatient clinic was collected. Exclusion criteria for all participants were a history of previous eye surgery (including refractive surgery) or ocular trauma and any active anterior and/or posterior segment anomaly. All participants were initially classified into cataract and non-cataract groups. The cataract group was composed of patients diagnosed with age-related cataract in both eyes. Patients diagnosed with a cataract other than senile type (i.e., cataract with a congenital or traumatic origin, or associated with exposure to radiation or toxic agents) were excluded. Participants were classified into the cataract group if both eyes showed at least a grade 1 or higher cortical or posterior subcapsular cataract and/or a grade 2 or higher nuclear opacities (color and/or opalescence), according to the Lens Opacification Classification System (LOCS)-III system [19, 20]. The non-cataract group was composed of volunteers in whom no ocular anomalies were detected during the routine examination and complied with the inclusion and exclusion criteria.

In addition, all participants were also classified based on the presence or absence of cataract in any of the three main components of the crystalline lens. Thus, the presence or absence of cortical, nuclear, or posterior subcapsular cataracts was also considered. Consequently, all participants were grouped based on four different classifications: the lens cataract (cataract vs. non-cataract groups), cortical cataract (cortical cataract vs. non-cortical cataract groups), nuclear cataract (nuclear cataract vs. non-nuclear cataract groups) and posterior subcapsular cataract (subcapsular cataract vs. non-subcapsular cataract groups) classifications. Only one eye per participant was randomly selected for statistical purposes.

Optical Biometry

Five consecutive high-quality optical biometry measurements were performed per participant using the Lenstar LS900 biometer (Haag-Streit AG, Köeniz, Switzerland) by a single examiner (Cecilia Díez-Montero). For each measurement, the device software provides a graph representing the axial length, which shows several spikes corresponding to different ocular tissue surfaces. The spikes of the corneal, lens, and retinal surfaces are automatically detected by the software. In addition, the spikes corresponding to the anterior and posterior nuclear surfaces are easily detected, hence their locations were manually determined using the software cursors [10, 20]. The same examiner (Cecilia Díez-Montero) performed the measurements in all eyes to avoid inter-observer variability. Four spaces were calculated: LT (distance between the anterior and posterior lens surfaces), anterior cortex space (distance between the anterior lens and anterior nuclear surfaces), nuclear thickness (distance between the anterior and posterior nuclear surfaces) and posterior cortex space (distance between the posterior nuclear and posterior lens surfaces). For each distance, the mean of the five biometric measurements performed for each participant was computed for analysis.

Statistical Analysis

Statistical analysis was performed using the R statistical package version 4.2.2. Participants within each of the four cataract type classifications (lens, cortical, nuclear, and subcapsular cataract) were matched one-to-one for sex, age, and axial length using the propensity score matching provided by the "MatchIt" R package [21]. The nearest-neighbor method was used. The caliper width was progressively decreased, in 0.01 steps, from 0.20 until the standardized mean difference of the three parameters (sex, age, and axial length) was equal to or lower than 0.10 [22]. It should be noted that patients with opacities in a particular main lens component (anterior or posterior cortex and nucleus) may or may not have opacities in other

main lens components (e.g., a patient with a nuclear cataract may or may not have a cortical and/or subcapsular cataract). Therefore, each of the samples based on the cataract location was only used to analyze the space of the main lens component affected by the senile cataract formation (e.g., the nuclear cataract sample was only used to analyze the nuclear thickness).

Data were compared between cataract and non-cataract groups using independent tests for unmatched and matched samples, as recommended [23]. Categorical data were compared using the chi-squared test. Numerical data that accomplished with the normality assumption (Kolmogorov–Smirnov test) were compared using the independent Student's t test, applying the Welch approximation if data showed unequal variances (Levene test). When the normality assumption could not be confirmed, the robust Yuen's test was used. The significance level was established at two-tailed p values ≤ 0.05. Finally, the unstandardized effect sizes and 95% confidence intervals were calculated to report the magnitude and uncertainty of the observed effects [24].

RESULTS

A total sample of 603 participants (403 women and 200 men) with a mean age of 59.1 ± 18.8 years were included. The lens cataract group was composed of 361 eyes and the non-cataract group of 242 eyes. The classifications based on cataract location (cortical, nuclear, and posterior subcapsular) resulted in 226 cortical and 377 non-cortical cataractous eyes, 313 nuclear and 290 non-nuclear cataractous eyes and 242 subcapsular and 361 non-subcapsular cataractous eyes. The cataractous eyes included in the cortical, nuclear, and posterior subcapsular cataract groups showed a mean LOCS-III value and standard deviation of 1.8 ± 1.1 (range, 1–5), 2.6 ± 0.8 (range, 2–5) and 1.8 ± 1.0 (range, 1–5) units, respectively.

After propensity score matching, the lens cataract matched sample was composed of 73 cataract and 73 non-cataractous eyes, the cortical cataract sample of 129 cortical and 129 non-cortical cataractous eyes, the nuclear

Table 1 Descriptive data of sex, age, and axial length before and after matching

	Cataract location	Sample type	Cataract group	Non-cataract group	SMD	Variance ratio	*p* value
Sex (women/men) (*n*)	Lens cataract	Unmatched	230/131	173/69	– 0.16	NA	0.06
		Matched	48/25	47/26	0.02	NA	1.00
	Cortical cataract	Unmatched	144/82	259/118	– 0.10	NA	0.24
		Matched	81/48	80/49	0.02	NA	1.00
	Nuclear cataract	Unmatched	197/116	206/84	– 0.17	NA	***0.04***
		Matched	62/29	64/27	– 0.05	NA	0.87
	Subcapsular cataract	Unmatched	72/52	331/148	– 0.22	NA	***0.03***
		Matched	56/48	69/44	– 0.07	NA	0.69
Age (years)	Lens cataract	Unmatched	70.77 ± 9.34	41.67 ± 15.62	3.12	0.36	***< 0.001***
		Matched	60.56 ± 9.02	59.80 ± 7.12	0.08	1.61	0.96
	Cortical cataract	Unmatched	72.54 ± 8.50	51.02 ± 18.68	2.53	0.21	***< 0.001***
		Matched	69.57 ± 8.50	69.41 ± 8.60	0.02	0.98	0.88
	Nuclear cataract	Unmatched	72.01 ± 8.75	45.14 ± 16.66	3.07	0.28	***< 0.001***
		Matched	63.74 ± 7.61	63.29 ± 6.87	0.05	1.23	0.68
	Subcapsular cataract	Unmatched	69.38 ± 9.89	56.42 ± 19.64	1.31	0.25	***< 0.001***
		Matched	68.50 ± 9.47	69.29 ± 9.04	– 0.08	1.10	0.44
Axial length (mm)	Lens cataract	Unmatched	23.88 ± 2.00	24.12 ± 2.11	– 0.12	0.90	0.11
		Matched	24.08 ± 2.12	23.98 ± 2.47	0.05	0.74	0.40
	Cortical cataract	Unmatched	23.62 ± 1.86	24.19 ± 2.12	– 0.31	0.77	***0.001***
		Matched	23.78 ± 1.94	23.75 ± 2.06	0.02	0.89	0.77
	Nuclear cataract	Unmatched	23.71 ± 1.84	24.27 ± 2.21	– 0.31	0.70	***0.001***
		Matched	24.01 ± 1.88	23.92 ± 2.45	0.05	0.59	0.21
	Subcapsular cataract	Unmatched	24.26 ± 2.03	23.90 ± 2.04	0.17	0.99	0.12
		Matched	24.09 ± 1.80	23.89 ± 2.18	0.10	0.68	0.22

p values in bold and italic font indicate significant differences

Data of categorical parameters are presented as frequencies and data of numerical parameters are presented as mean ± standard deviation

NA not applicable, *SMD* standardized mean difference

cataract sample of 91 nuclear and 91 non-nuclear cataractous eyes and the subcapsular cataract sample of 113 subcapsular and 113 non-subcapsular cataractous eyes. The descriptive characteristics of unmatched and matched samples are shown in Table 1.

The comparisons of the unmatched participants revealed that patients with senile cataracts had significantly ($p \leq 0.003$) higher LT, anterior and posterior cortex space, and nuclear thickness (Table 2). However, no significant ($p \geq 0.08$) differences were observed for any

Table 2 Comparison of lens thickness (LT), anterior cortex space (ACS), nuclear thickness (NT), and posterior cortex space (PCS) between participants with and without senile cataracts before and after matching

Classification	Lens space	Sample type	Cataract group		Non-cataract group		p value
			n	Mean ± SD (mm)	n	Mean ± SD (mm)	
Lens cataract	LT	Unmatched	361	4.52 ± 0.39	242	3.94 ± 0.46	***< 0.001***
		Matched	73	4.34 ± 0.37	73	4.33 ± 0.36	0.94
	ACS	Unmatched	361	0.75 ± 0.21	242	0.49 ± 0.19	***< 0.001***
		Matched	73	0.65 ± 0.21	73	0.63 ± 0.18	0.59
	NT	Unmatched	361	3.33 ± 0.24	242	3.16 ± 0.25	***< 0.001***
		Matched	73	3.29 ± 0.21	73	3.33 ± 0.20	0.32
	PCS	Unmatched	361	0.44 ± 0.18	242	0.28 ± 0.15	***< 0.001***
		Matched	73	0.40 ± 0.16	73	0.38 ± 0.14	0.87
Cortical cataract	ACS	Unmatched	226	0.75 ± 0.20	337	0.58 ± 0.23	***< 0.001***
		Matched	129	0.72 ± 0.20	129	0.76 ± 0.19	0.08
Nuclear cataract	NT	Unmatched	313	3.34 ± 0.23	290	3.18 ± 0.25	***< 0.001***
		Matched	91	3.31 ± 0.22	91	3.30 ± 0.23	0.24
Subcapsular cataract	PCS	Unmatched	242	0.42 ± 0.19	361	0.37 ± 0.19	***0.003***
		Matched	113	0.42 ± 0.19	113	0.43 ± 0.16	0.79

p values in bold and italic font indicate significant differences
SD standard deviation

parameter in any of the matched samples (Table 2). The distributions of unmatched and matched samples are shown in Fig. 1. The observed effect size in the LT was 0.01 mm with a 95% confidence interval ranging from − 0.12 to 0.13 mm, while the observed effect size in the main components was between − 0.04 and 0.04 mm with the 95% confidence interval being equal to or below ± 0.10 mm. The observed effect size and 95% confidence intervals for the matched samples are shown in Fig. 2.

DISCUSSION

The effect of cataract formation on LT has previously been studied; however, contradictory results have been reported [9–13]. Since LT has been associated with demographic characteristics and some ocular parameters [4, 8, 10, 14–17], controlling for confounding factors is the most appropriate approach with which to provide reliable evidence. The present study aimed to analyze not only the influence of senile cataract formation on the LT but also its influence on the space of its three main components, controlling for relevant confounding factors: sex, age, and axial length.

Study participants were matched one-to-one for sex, age, and axial length using propensity score matching, a statistical approach that is widely used to control the bias associated with confounding factors [25, 26]. The quality of the matches can be easily assessed by evaluating the standardized mean difference (0.1 or below indicates a good balance) and the variance ratio (between 0.5 and 2.0 indicates a good balance) [22]. Prior to matching, no classification complied with such criteria, with age being the most
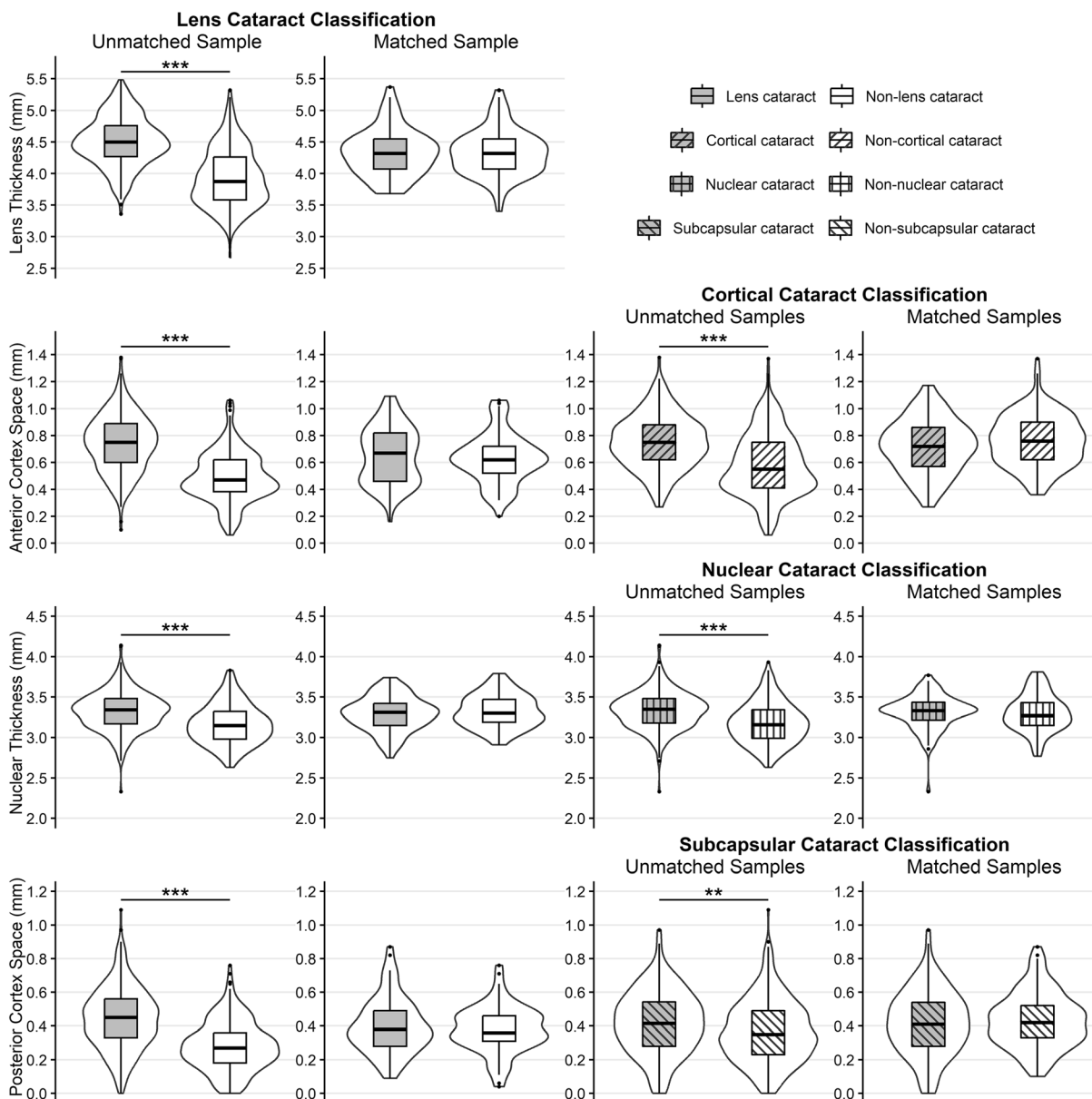
Fig. 1 Distribution of lens thickness, anterior cortex space, nuclear thickness, and posterior cortex space, using violin plots of density and boxplots. Data for the lens cataract classification (*left*) and the cortical, nuclear, and posterior subcapsular cataract classifications (*right*) are provided before and after matching. ***$p < 0.001$; **$p = 0.003$

unbalanced confounding factor; however, all matched samples complied after propensity score matching (Table 1). The sample sizes achieved after matching varied depending on the classification based on cataract location (Table 2). The cataract and non-cataract groups included in the four unmatched classifications were composed of all participants ($n = 603$),

while the matched samples were composed of 146, 258, 182, and 226 participants for the lens, cortical, nuclear, and posterior subcapsular samples, respectively. The most likely reason for the different sizes in the four matched samples might be the difference in age between the unmatched participants with and without senile cataracts. The initial differences for the
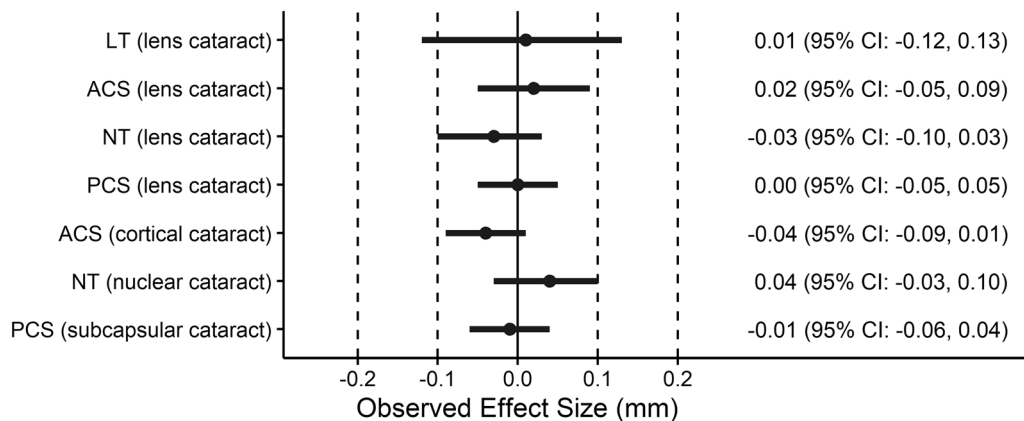
Fig. 2 Observed effect size (*dots*) and 95% confidence intervals ([CI] *horizontal lines*) for the lens thickness (LT), anterior cortex space (ACS), nuclear thickness (NT), and posterior cortex space (PCS) between participants with and without senile cataracts in the matched lens, cortical, nuclear, and subcapsular cataract samples. *Positive values* indicate higher values for participants with cataracts

other confounding factors (gender proportion and axial length) were much lower. Therefore, the high improvement in balance after matching suggests that controlling for the confounding factors was highly necessary.

The results of the study completely changed from unmatching to matching participants. All comparisons performed in the unmatched classifications showed statistically higher LT, anterior and posterior cortical space, and nuclear thickness in cataract groups. In contrast, no significant differences were found for any parameter after matching participants with and without senile cataracts in the four matched samples (Table 2, Fig. 1). The covariable most unbalanced prior matching was the age, which has indeed been reported to be the factor with the strongest association with LT [8]. Thus, the statistical results prior to matching were very likely to be biased, at least, by the age difference between groups.

Considering the results obtained from the matched samples, neither the LT nor the space of its main components were significantly different between the cataract and non-cataract groups. The lack of significant results is sometimes attributed to a low statistical power. Once the study has been conducted, the use of post hoc power is not advisable [24, 27]. Instead, it is recommended to report confidence intervals to understand how accurately the estimated value

for the entire population was determined [24, 27]. The mean difference between groups in the LT was 0.01 mm, while the difference in any of the main components was solely 0.04 mm at most. Even in the hypothetical case of having found statistical significance, such small differences could even be considered clinically negligible. In addition, the 95% confidence interval of the observed effect sizes was reported, ranging from − 0.12 to 0.13 mm for the LT and being equal to or below ± 0.10 mm for its main components (Fig. 2). Differences between such ranges cannot be completely discarded for the population; however, the data showed no relevant tendencies in either way. In fact, small differences in the anterior cortex space and nuclear thickness have opposite directions when analyzing the lens cataract sample or the samples for each main lens component. Therefore, as soon as the confounding factors were controlled, the presence of any cataract type (i.e., cortical, nuclear, or subcapsular) had a null effect on the LT and the space of its three main components.

Lens transparency has been previously related to crystalline proteins [28, 29]. Under some oxidative stress scenarios, such as aging or ultraviolet light exposure, crystalline proteins may experience folding, denaturing and aggregation, leading to high-molecular-weight structures [29]. Also, the presence of these

modified molecular structures might be responsible for light scattering and opacification [29]. However, the possible modifications in proteins associated with age-related cataract do not seem to have an effect on LT or the space of its main components, as observed in the present study.

The results of the present study differ from some previous works. Shammas et al. [10] found a higher LT, anterior cortex space, nuclear thickness, and posterior cortex space in patients with cataracts. However, their control subjects without cataracts were around 30 years younger than the recruited patients with senile cataracts. Therefore, the age difference is very likely to have influenced their results. Praveen et al. [11] found that, after adjusting for age groups, LT was thinner in subjects with cortical and posterior subcapsular cataract. However, the age groups had a wide range (25–40, 41–50, 51–60, 61–70, > 70), thus, it was very likely that the effect of age was still present within the groups. Besides, Klein et al. [9] found that thick crystalline lenses were more likely to develop nuclear cataracts and thin lenses to develop cortical cataract in a 5-year follow-up. Nonetheless, this approach does not demonstrate an effect of senile cataract formation on LT, but the opposite, the likelihood of developing cataract as a function of LT.

On the other hand, the lack of effect of senile cataract formation on LT agrees with previous reports. Henriquez et al. [13] found that, after controlling for sex, age, axial length, and anterior chamber depth, LT was independent of lens density in patients with mild-to-moderate cataracts. Likewise, Aly et al. [12] reported no differences in the nuclear density between similarly aged patients with cataracts with different LT (greater vs. lower than 4.8 mm). In addition, Jonas et al. [15] reported that the amount of nuclear cataract was associated with LT in univariate analysis; however, the significance disappeared when considering the effect of other parameters in a multivariable analysis. Therefore, previous studies that somehow avoided the effect of some confounding factors found no relationship between cataract degree and LT. In addition, the present study demonstrates that the presence of common senile cataract has no effect on LT or the space of its main components after assessing cataract and non-cataract eyes.

The present study may have some limitations. First, the LT and the space of each lens component were measured along the visual axis, which corresponds to a central location of the crystalline lens. Thus, LT measurements performed along other ocular axes (e.g., optical axis) might be slightly differently affected by the presence of cataract. However, first, this is a limitation inherent to the measurement procedure used by optical biometry devices and second, central LT measurements obtained along diverse anterior–posterior axes of the eye may not change so much. Second, participants with opacities in other lens locations may have been included in the non-cortical, non-nuclear, and non-subcapsular groups. It was assumed that the space of the analyzed lens component was not affected by an opacity located in a different lens component (e.g., a nuclear opacity does not necessarily affect anterior and posterior cortex spaces). This approach was followed because, to the best of our knowledge, there is no evidence to prove the opposite. In fact, the results of the present study, not finding significant differences in any main lens component between participants with and without opacities, highly support this hypothesis. Finally, the outcomes of the present study cannot be applied to types of cataracts other than common senile ones, including advanced cataracts (e.g., hypermature or intumescent cataracts) where optical biometry measurements cannot be obtained [30]. Nonetheless, these types of cataracts are not commonly found in the ophthalmology outpatient clinics of the occidental countries. In fact, the cataract group sample of the present study can be representative of the patients seeking cataract surgery, who usually show higher LOCS-III gradings for anterior cortical and nuclear opacities, than posterior cortical ones [31].

CONCLUSIONS

After controlling for the confounding effects of sex, age, and axial length, the presence of

common senile cataracts has no clinical effect on LT and the space of its three main components, the anterior and posterior cortex space and nuclear thickness. The lack of effect of senile cataract formation on LT and its main components may be of great interest not only for clinical purposes but also for research ones when designing new IOL power formulas. Finally, future studies analyzing LT and its main components should always control for at least the confounding factors considered in the present study, especially age; otherwise, the results are very likely to be strongly biased.

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

Declarations

Conflict of Interest. Alberto López-de la Rosa, Cecilia Díez-Montero, Elena Martínez-Plaza, Alberto López-Miguel, and Miguel J. Maldonado have nothing to disclose.

Ethical Approval. This prospective cross-sectional study was approved by the ethics committee of Hospital Universitario Rio Hortega (Valladolid, Spain; Reference number: 156/17) and was conducted in accordance with the Declaration of Helsinki guidelines. The study protocol was explained before written consent to participate in the study was obtained from all participants.

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