**Original Article** 

# Ocular Risk Factors Affecting Intraoperative Complications In Mature Cataract Surgery

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### ABSTRACT

**Purpose:** To identify the demographic and ocular risk factors associated with complications in phacoemulsification and planned extracapsular cataract extraction (PECCE) for mature cataracts.

#### Study Design: Retrospective chart analysis.

**Place and Duration of Study:** Haydarpaşa Numune Training and Research Hospitalfrom January 2018 and December 2021.

**Methods:** A total of 236 eyes of 236 patients who underwent surgery for mature cataracts between 2018 and 2021 were included in the study. Demographic characteristics, presence of pseudoexfoliation, cataract type, pupil dilation, anterior chamber depth, presence of phacodonesis, preoperative best-corrected visual acuity, intraocular pressure, intraoperative and postoperative surgical complications, and postoperative first month visual acuity were analyzed.

**Results:** A total of 194 eyes (82%) underwent phacoemulsification, while 42 eyes (18%) underwent PECCE. The mean age and mean preoperative BCVA LogMAR values were significantly higher in the PECCE group (p=0.001 and p=0.027, respectively). Among ocular risk factors, only pupillary mid-dilation was significantly higher in the PECCE group (p=0.04). Intraoperative complications were more frequent in brown cataracts within the PHACO group compared to eyes without brown cataracts (p=0.004). Additionally, intraoperative complications, postoperative complications, and the need for postoperative revision were significantly higher in the PECCE group (p<0.05 for all).

**Conclusion:** The preoperative rate of mid-dilated pupils was higher, and preoperative visual acuity was lower in eyes with mature cataracts undergoing PECCE surgery. The presence of brown cataracts was associated with an increased risk of complications in PHACO surgery.

**Keywords:** Phacoemulsification, Extracapsular Cataract Extraction, Mature Cataract, Visual Acuity, Intracapsular Cataract Extraction.

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#### **INTRODUCTION**

Cataract remains the leading cause of avoidable blindness worldwide.<sup>1</sup> Cataract surgery is the most performed intraocular procedure globally, with surgical techniques evolving from intracapsular cataract extraction (ICCE) to planned extracapsular cataract extraction (PECCE) and, more recently, to phacoemulsification (PHACO). Despite

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This work is licensed under a Creative Commons Attribution-Non-Commercial 4.0 International License. advancements, the prevalence of mature cataracts remains high in developing countries.<sup>2</sup> While PHACO is the preferred technique, including for mature cataracts, PECCE is still utilized in complex cases. Conventional PHACO for mature cataracts is associated with a higher risk of intraoperative and postoperative complications, such as failed continuous curvilinear capsulorhexis (CCC) leading to radial anterior capsule tears extending to the equator, posterior capsule rupture with vitreous loss and nucleus drops persistent corneal edema, intraocular lens (IOL) dislocation, corneal burns, elevated intraocular pressure (IOP), and anterior chamber inflammation.<sup>3,4</sup>

There are some studies comparing Planned ECCE and PHACO surgeries in terms of postoperative visual acuity, endothelial cell number and size, and corneal thickness.<sup>5,6</sup> However, further studies are needed on the relationship between ocular and systemic risk surgeries factors that complicate these and intraoperative or postoperative complications. Risk factors associated with mature cataracts such as poor pupil dilation, presence of pseudoexfoliation (PEX) material, shallow anterior chamber, glaucoma, and phacodenesis lead to surgical difficulties and complications. The objective of this study was to evaluate the intraoperative and postoperative complications in patients with mature cataracts and their relationship with ocular risk factors and visual outcomes.

## METHODS

The files of 236 eyes who underwent surgery for mature cataracts at Haydarpaşa Numune Training and Research Hospital between January 2018 and December 2021 were reviewed. This study was completed in accordance with all necessary national regulations, institutional policies and the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Haydarpaşa Numune Training and Research Hospital (22.12.2023/HNEAH-KAEK 2023/220/4335). The sample size was calculated using the free software PS Power and Sample Size Program (Version 3.1) based on a power of 80% and a significance level of less than 0.05. A sample size of 42 subjects per group was deemed necessary to achieve the desired level of statistical power.

Age, sex, laterality of mature cataract, anesthetic method, systemic disease hypertension (HT), chronic

renal failure (CRF), diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), benign prostatic hyperplasia, coronary artery disease (CAD) and malignancy were noted preoperatively. As ocular surgical risk factors, presence of sunken globe, presence of PEX, cataract type (intumescent or brown cataract), pupil dilation, anterior chamber depth, and were phacodonesis analyzed and noted. findings Ophthalmologic examination and measurements including preoperative best corrected visual acuity (BCVA), spherical and cylindrical refraction values, IOP using air puff tonometer (TX-F, Topcon), axial length (AL), and IOL power using optical biometry (IOL master 500; Carl Zeiss Meditec) were analyzed and noted. BCVA values recorded in decimals were converted to LogMAR.7 Additional ocular pathologies accompanying mature cataracts (glaucoma or phacomorphic glaucoma, corneal diabetic retinopathy non-proliferative scarring. (NPDRP), corneal guttata) were noted. Patients with cataract types other than mature cataracts, history of trauma, significant strabismus (exotropia or esotropia >10 prism diopters), history of vitrectomy, uveitis or intraocular inflammation were excluded. Forty-two eves undergoing PECCE surgery and 194 eves undergoing PHACO surgery that met these criteria were included in the study. The presence of shallow anterior chamber, PEX, glaucoma and middilated pupil, brown cataracts or phacodonesis were considered as ocular risk factors.

In addition to routine ophthalmologic examination (BCVA, biomicroscopic and fundus findings examination, IOP), intraoperative and postoperative complications, and postoperative first-month BCVA were evaluated in all cases. Vitreous loss, zonule iridodialysis, dialysis, descemet membrane detachment, and nucleus drop were recorded as intraoperative complications.Cases requiring revision, such as postoperative wound suturing, IOL repositioning, anterior chamber air injections, anterior chamber lavage, aspiration of retained cortical fragments, and cases with IOP elevation and complications were evaluated and compared between the two groups. In addition, the types of IOLs implanted or aphakic leaving rates were compared in eyes undergoing PHACO and PECCE surgery. Preoperative and postoperative visual acuity was compared within and between both groups.

PECCE procedures were performed using the canopener or envelope capsulotomy technique. Following subtenon anesthesia, a partial thickness 10-mm incision was made. From this incision area, a 3.2-mm blade was inserted into the anterior chamber at 12 O'clock and the anterior chamber was filled with viscoelastic material. After a horizontal or can-opener capsulotomy in the upper quadrant with a cystotome, the lens nucleus was mobilized through hydrodissection. The corneal incision was cut through the entire full-thickness incision using a 3.2-mm blade. With gentle pressure applied at 12 O'clock and a hydrodissection cannula manipulated inside the eye, the lens was mobilized and the nucleus was expressed out of the eye. The remaining cortical material was removed from the anterior chamber using a Simcoe irrigation aspiration cannula. A three-piece intraocular lens was implanted into the sulcus using viscoelastic material. After the viscoelastic material inside the eye was removed by irrigation aspiration, the main incision in the cornea was sutured using 10/0 nylon suture.

PHACO surgeries were performed under subtenon anesthesia with the Infiniti Vision System (Alcon Laboratories, Fort Worth TX, USA). Two lateral port incisions were made using an MVR blade. Trypan blue 0.1% (0.1 mL) and air was injected slowly into the anterior capsule. All mature cataracts without a red fundus reflex were treated with Trypan blue. After staining the anterior capsule, sodium hyaluronate was injected to deepen the anterior chamber and provide clarity. A 2.8-mm disposable metal blade was used to make a three-stage transparent corneal tunnel incision. After creating a smooth capsular flap in the center of the anterior capsule with the cystotome, a 5.0-mmdiameter capsulorhexis was performed using Uttrata forceps. After hydrodissection, the mature nucleus was rotated using a cannula. Vannas scissors were used to prevent unplanned tears in case the capsulorhexis was directed towards the periphery. Endocapsular PHACO was performed in all mature cataract eyes usingdivide and conquer technique. The cortex was cleaned using bimanual irrigation/aspiration handpieces. A foldable hydrophilic acrylic intraocular lens with a total size of 12.0 mm was implanted into the sac with viscoelastic material in appropriate cases and a three-piece intraocular lens was implanted into the sulcus in cases with nonintact posterior capsules. Antibiotics were administered to the anterior chamber and the wound sites were sealed by hydrating the stroma. All patients received 0.3% ofloxacin and 1% prednisolone acetate eve drops four times per day for 1 month postoperatively.

The SPSS software version 16 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Numerical data were expressed as mean and standard deviation (SD). Categorical variables were expressed as frequency (n) and percentage (%). Descriptive and univariate analysis was performed. Significance was tested using the Chi-Square test and the Mann-Whitney U test when appropriate. P<0.05 was considered statistically significant.

### RESULTS

The mean age of the patients who underwent surgery for mature cataracts was 70.06±12.8 (range, 23-98) years. Among the 236 patients, 135 (57.2%) were males and 101 (42.8%) were females. One hundred ninety-four (82.2%) eyes underwent PHACO and 42 (17.8%) eyes underwent PECCE surgery. No statistically significant differences were observed in the demographic data of patients who underwent PHACO and PECCE with respect to sex, side of mature cataract, preoperative IOP, type of anaesthesia, AL, and IOL measurement. However, there was a statistically significant difference between the surgical methods in terms of age, the presence of additional ocular pathology, and preoperative visual acuity (Mann-Whitney U test; p=0.001 and p<0.01, respectively), (Chi-square test; p=0.002 and p<0.01, respectively), (Mann-Whitney U test; p=0.027 and

Table 1:	Demograph	ic findings	of the	patients.
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	FACO	PECCE	
Variables	(n=194)	(n=42)	-
variables	n (%) or	n (%) or	р
	Mean± SD	Mean± SD	
Age	$68.79 \pm 12.6$	$75.88 \pm 12.2$	0.001*
Gender			
Female	78 (40.2)	23 (54.8)	0.091#
Male	116 (59.8)	19 (45.2)	0.084#
Operated eye			
Right	113 (58.2)	21 (50)	0.220#
Left	81 (41.8)	21 (50)	0.526#
Ocular comorbidity			
No	181 (93.3)	32 (76.2)	0.002#
Yes	13 (6.7)	10 (23.8)	0.002#
General Anesthesia			
No	184 (94.8)	40 (95.2)	0.016#
Yes	10 (5.2)	2 (4.8)	0.910#
Baseline IOP (mmHg)	$14.25 \pm 3.2$	$14.86 \pm 5.2$	0.981*
Baseline BCVA (LogMar)	$2.6 \pm 0.6$	$2.86 \pm 0.4$	0.027*
Axial Lenght (mm)	$23.23 \pm 2.2$	$23.19 \pm 1.1$	0.614*
IOL power (D)	$21.72 \pm 3.6$	$22.36 \pm 2.2$	0.341*

IOP: Intraocular pressure, BCVA: Best-corrected visual acuity, IOL: Intraocular lens

p\* : Mann Whitney U test, p#: Chi-square test

p<0.05, respectively). The mean age, frequency of additional ocular pathology, and preoperative logMAR values were higher in patients who underwent PECCE surgery. Demographic data are summarized in Table 1.

A statistically significant difference was observed between the PHACO and PECCE groups concerning the presence of DM (Chi-square test, p=0.038 and respectively), with DM p<0.05, detected in approximately 40.5% of eyes undergoing PECCE surgery. However, no significant difference was found between the surgical techniques regarding systemic risk factors, including HT, CAD, COPD, CRF, prostate disease, and malignancy. The proportion of female patients was higher in the PECCE group, while preoperative BCVA was significantly lower (p=0.029). Postoperative BCVA improved significantly in both surgical groups; however, the improvement was more pronounced in eyes that underwent PHACO (p=0.001).

**Table 2:** Comparison of surgical methods in terms of ocular riskfactors.

Ooulan Diak	РНАСО	PECCE	
Eactors	( <i>n=194</i> )	( <i>n=42</i> )	р
1 401013	n (%)	n (%)	
Sunken globe			
No	191 (98.5)	42 (100)	1
Yes	3 (1.5)	0 (0)	
Shallow AC			
No	191 (98.5)	40 (95.2)	0.217
Yes	3 (1.5)	2 (4.8)	
Gloucoma			
No	191 (98.5)	41 (97.6)	0.546
Yes	3 (1.5)	1 (2.4)	
Small pupil			
No	179 (92.3)	34 (81)	0.04*
Yes	15 (7.7)	8 (19)	
PEX			
No	171 (88.1)	40 (95.2)	0.268
Yes	23 (11.9)	2 (4.8)	
Brown Cataract			
No	187 (96.4)	39 (92.9)	0.389
Yes	7 (3.6)	3 (7.1)	
Morgagnian			
No	190 (97.9)	40 (95.2)	0.29
Yes	4 (2.1)	2 (4.8)	
Phacodonesis			
No	193 (99.5)	40 (95.2)	0.083
Yes	1 (0.5)	2 (4.8)	

AC: Anterior chamber, PEX: Pseudoexfoliation p: Chi-square test

Among ocular risk factors, a statistically significant difference was noted in the presence of pupillary mid-dilatation between the PHACO and PECCE groups (Chi-square test, p=0.04 and p<0.05, respectively), with a higher prevalence in the PECCE group. No significant difference was observed between the surgical techniques concerning other ocular risk factors (Table 2).

A statistically significant association was observed between the presence of brown cataracts and the incidence of intraoperative complications in eyes undergoing PHACO surgery (Chi-square test, p=0.004 intraoperative p<0.01, respectively). The and complications included posterior capsule rupture (PCR) with vitreous loss in 18 patients, zonular dialysis in seven patients, Descemet's membrane detachment in five patients, and both nucleus drop and iridodialysis in three patients. Brown cataracts were significantly more prevalent in patients who experienced intraoperative complications compared to those who did not (Table 3). The percentage of threepiece IOL implantations and postoperative aphakia were statistically higher in the PECCE group (p<0.001).

At the postoperative 1-month follow-up, BCVA improved in 233 out of 236 eyes, while no improvement was observed in three eyes. Among these three cases, intraoperative nucleus drops with vitreous loss occurred in two eyes, and intraoperative zonular dialysis was noted in the third eye, which had phacomorphic glaucoma. Corneal edema was the most common postoperative complication, occurring in 65% of cases. The incidence of corneal edema was 62% in patients who underwent PHACO surgery and 78% in those who underwent PECCE.

Postoperative revision was required in 5.2% of patients in the PHACO group, compared to 21% in the PECCE group, with a statistically significant difference between the two groups (p=0.002). In the PHACO group, 10 patients underwent revision procedures: corneal suturing (n=2), anterior chamber (AC) air injection (n=3), AC lavage with cortex aspiration (n=1), pars plana vitrectomy (PPV) with scleral fixation of an intraocular lens (SFIOL) (n=3), and SFIOL alone (n=1).In the PECCE group, nine patients required revision: corneal suturing (n=2), SFIOL (n=3), SFIOL with iridoplasty (n=2), AC lavage (n=1), and iris repositioning (n=1) (Table 4).

We also compared senior surgeons and experienced residents. The incidence of intraoperative

complications did not differ significantly based on the surgeon's level of experience (p=0.568 for PHACO and p=0.582 for PECCE) (Table 5).

Table 4:	Association	between	surgical	methods	and	intraocular
complicat	ion, postoper	ative con	nplication	, postope	rativ	e revision.

	Type of surgery					
	PHACO	PECCE	ъ			
	n=194	n=42	r			
	n (%)	n (%)				
Intraoperative	complication					
No	172 (88.7)	31 (73.8)	0.013*			
Yes	22 (11.3)	11 (26.2)	0.012*			
Postoperative c	complication					
No	71 (36.6)	7 (16.7)	0.012*			
Yes	123 (63.4)	35 (83.3)	0.015*			
PostoperativeR	evision					
No	184 (94.8)	33 (78.6)	0.007**			
Yes	10 (5.2)	9 (21.4)	0.002**			

p: Chi-square test

Although there was no significant difference in spherical refraction between the two surgical groups, the mean cylindrical refraction was  $-1.48\pm1.1$  in patients who underwent PHACO surgery, compared to  $-3.29\pm1.7$  in those who underwent PECCE, with a statistically significant difference (p=0.006).

#### DISCUSSION

It is possible to encounter some difficulties in the surgery of mature cataracts that present as both brown and white intumescent cataracts. Intraocular complications are more common in these cases and associated ocular risk factors are also important. There are some important considerations when performing both PECCE and PHACO surgery. For an uncomplicated surgery, ocular risk factors should be well known and precautions should be taken along surgical expertise with the and necessary modifications.8,9

Table 3:	Comparison	of the	effects o	f ocular	risk factors	on intraoperative	e complication	between surgi	cal method.
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	PHACO	) n=194		PECCI			
Ocular Dick Factors	Intraoperative	e Complication	-	Intraoperative	Complication		
Ocular Kisk Factors	No	Yes	Р	No	Yes	р	
	n=172 (%)	n=22 (%)		n=31 (%)	n=11 (%)		
Sunken globe							
No	169 (98.3)	22 (100)	1	31 (100)	11 (100)		
Yes	3 (1.7)	0 (100)	1	-	-	-	
Shallow AC							
No	169 (98.3)	22 (100)	1	31 (100)	9 (81.8)	0.064	
Yes	3 (1.7)	0 (100)	1	0 (0)	2 (18.2)	0.064	
Gloucoma							
No	170 (98.8)	21 (95.5)	0.304	31 (100)	10 (90.9)	0.262	
Yes	2 (1.2)	1 (4.5)	0.304	0 (0)	1 (9.1)		
Small pupil							
No	158 (91.9)	21 (95.5)	0.552	25 (80.6)	9 (81.8)	0.932	
Yes	14 (8.1)	1 (4.5)	0.552	6 (19.4)	2 (18.2)		
PEX							
No	152 (88.4)	19 (86.4)	0.794	30 (96.8)	10 (90.9)	0.46	
Yes	20 (11.6)	3 (13.6)	0.784	1 (3.2)	1 (9.1)	0.46	
<b>Brown Cataract</b>							
No	169 (98.3)	18 (81.8)	0.004**	29 (93.5)	10 (90.9)	1	
Yes	3 (1.7)	4 (18.2)	0.004	2 (6.5)	1 (9.1)	1	
Morgagnian							
No	169 (98.3)	21 (95.5)	0.205	29 (93.5)	11 (100)	1	
Yes	3 (1.7)	1 (4.5)	0.385	2 (6.5)	0 (0)	1	
Phacodonesis							
No	172 (100)	21 (95.5)	0.112	30 (96.8)	10 (90.9)	0.46	
Yes	0 (0)	1 (4.5)	0.115	1 (3.2)	1 (9.1)	0.40	

AC: Anterior chamber, PEX: Pseudoexfoliation

p: Chi-square test

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Surgeons	РНАСО	) n:194		PECCI	E n:42	
	Intraoperative	Complications	п	Intraoperative Complications		
	No n=172	Yes n=22	P	No n=31	Yes n=11	р
	n (%)	n (%)		n (%)	n(%)	
Seniors	140 (88.1)	19 (11.9)	0 568	25 (75.8)	8 (24.2)	0.582
Residentals	32 (91.4)	3 (8.6)	0,308	6 (66.7)	3 (33.3)	0.382

Table 5:	Comparison of	of the surgeons	according to the	presence of intra	operative com	plications and t	vpe of	surger
		J		p			JP J	~···

p: Chi-square test

Measures taken to better visualise anterior capsule in eyes with white mature cataracts include reduction of illumination in the operating theatre, high magnification microscope setting, use of oblique illumination, use of endoilluminators, capsular stains and two-step capsulorhexis.<sup>10,11</sup> Staining of the anterior capsule can be performed either under viscoelastic or with air. In all cases, we stained the capsule trying to create a single air bubble. In addition, these eyes have difficulties that prevent proper capsulorhexis, such as red fundus reflex, white fluid draining no intotheanterior chamber when the capsule is perforated, and a fragile anterior capsule. In addition, because of the high IOP, the capsular tear tends to extend peripherally and control of the capsulorhexis becomes difficult.<sup>12</sup> In most cases, we tried to achieve a single-stage, 5.5-mm CCC.

In addition, failed CCC, inadequate dilation, overly hard cataract, zonule weakness and subluxated lens, or PCR requires conversion of the PHACO surgery to PECCE surgery.<sup>10</sup> Although PECCE is not commonly performed nowadays, this method is used in our hospital in patients with mature cataracts for resident training.<sup>13</sup> There are many studies indicating that PCR can occur in PECCE as well as PHACO.<sup>14-17</sup> Interestingly, National Eye database (NED) data from 2002 to 2011 showed that the occurrence of PCR was similar in PHACO and PECCE.<sup>18</sup> In our study, thefrequency of PCR and vitreous loss was similar in both surgical methods.

The present study revealed a significant correlation between the surgical method and BCVA. Visual recovery was found to be higher in eyes that underwent PHACO (p=0.001). This result was consistent with earlier studies. In two randomized studies conducted at Moorfields and Oxford Eye Hospitals, the proportion of patients with BCVA of 6/9 or better was significantly higher in the PHACO group (69%) than in the PECCE group (57%).<sup>19</sup> In another study, good visual acuity was achieved in 80% of patients who underwent PHACO.<sup>5</sup> In addition, all

except three patients in our study had improved vision and these patients developed serious complications.

Katsimpris et al, performed a study on cataract surgery in eyes with PEX, small pupils, and phacodonesis.<sup>17</sup> In this study, the incidence of PCR was 17.0% in PECCE and 4.2% in PHACO. In our study, among the risk factors such as shallow anterior chamber, glaucoma, inadequate dilation, PEX, phacodonesis and brown cataracts, only brown cataracts were associated with intraoperative complications in PHACO surgery (p=0.004). This result showed that PECCE surgery may be preferred as a safer method in patients with brown cataracts instead of PHACOsurgery.

Perioperative complications developed in 22 (11.3%) of the PHACO surgeries, and 11 (22%) in PECCE surgery. When we look at the complications encountered in the postoperative period, the most common, corneal edema, was found to be around 63% in PHACO surgery, and this rate was 83% in PECCE surgery. In another study, 89.8% patients in the PECCE group showed mild corneal oedema and this rate was 76.2% in the PHACO group.<sup>20</sup> A notable discrepancy was observed between the two surgical procedures with regard to both perioperative and postoperative complications. However, revision was required in approximately 20% of cases after PECCE surgery. Intraoperative complications. postoperative complications, and the need for postoperative revision were significantly higher in PECCE surgery.

One of the most important differences between the surgical methods was the significant difference in postoperative cylindrical refraction in eyes with PECCE (p=0.006). We think that the greater astigmatism in eyes undergoing PECCE has an effect on the final visual acuity. As another complication, cystoid macular edema was detected only in one eye undergoing PHACO, but no serious complication such as retinal detachment was encountered.

In our study, we analyzed eyes with mature

cataracts treated with PHACO and PECCE surgeries, identifying key findings. Eyes undergoing PECCE were older, had lower preoperative BCVA, a higher prevalence of comorbid ocular conditions, and a greater incidence of mid-dilated pupils. Additionally, PHACO performed on eyes with brown cataracts was associated with a higher complication rate. Overall, both intraoperative and postoperative complication rates were significantly higher in the PECCE group.

However, our study has some limitations. First, the retrospective design and the inclusion of only the firstmonth postoperative data are significant constraints. The varying levels of surgeon experience may have influenced our results, as we included all mature cataract surgeries performed by different surgeons during the study period. Additionally, surgical selection bias may have contributed to the higher complication rate in the PECCE group, as PECCE was performed on patients with higher rates of mid-dilated pupils and lower BCVA, potentially reflecting a bias in surgical method selection. Nonetheless, our study provides valuable real-life insights into cataract surgery in mature cataracts.

## CONCLUSION

Ocular risk factors accompanying mature cataracts should be carefully identified and recorded during the examination. In light of this study, we found that there was a high risk of complications in eyes with brown cataracts. Patients with brown cataracts should be informed about possible complications before surgery. We found a higher rate of postoperative complications in PECCE surgery compared with PHACO surgery; however, we also found that eyes that underwent PECCE were older with middilated pupils and had lower BCVA. It is imperative that multicentre, prospective and randomised studies be conducted to ascertain the surgical complication rates associated with both surgical procedures in cases of mature cataracts.

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**Patient's Consent:** Researchers followed the guidelines set forth in the Declaration of Helsinki.

**Conflict of Interest:** Authors declared no conflict of interest.

**Ethical Approval:** The study was approved by the Institutional review board/Ethical review board (22.12.2023/HNEAH-KAEK 2023/220/4335).

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Okşan Alpoğan; Associate Professor: Design, Data acquisition, Data analysis, Statistical analysis, Manuscript review.

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