

Prevalence of cataract complications in patients with pseudoexfoliation syndrome in Northwestern Spain

A prevalência de complicações de catarata em pacientes com síndrome pseudoesfoliativa no noroeste da Espanha

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ABSTRACT | Purpose: To assess the relationship between pseudoexfoliation syndrome and incidence of complications and related clinical factors in patients undergoing cataract surgery. **Methods:** We conducted a retrospective cohort study of 503 of 551 patients who underwent phacoemulsification surgery over 2 years in a health care district in Northwest Spain. In total, 120 of 681 eyes undergoing the procedure had pseudoexfoliation syndrome. Data on the surgical procedure and associated complications were extracted from the medical record. Complications included any combination of posterior capsular rupture, vitreous loss, zonular dialysis, and nuclear or lens luxation. **Results:** We found a significant association between pseudoexfoliation syndrome and zonular dialysis (odds ratio [OR], 6.89; 95% CI, 2.27-20.93), intraoperative miosis (OR, 2.15; 95% CI, 1.10-4.22), and lens luxation >1.5 mm (OR, 9.49; 95% CI, 0.85-105.54). However, when adjusting for the overall risk of complications in pseudoexfoliation syndrome patients in consideration of myopia, use of anticoagulants or α -agonists, previous mydriasis, and anterior chamber length, the OR decreased to 1.02 (95% CI, 0.47-2.21) and was therefore not significant. **Conclusion:** Zonular dialysis and intraoperative miosis were intraoperative complications in cataract surgery patients with pseudoexfoliation syndrome when compared to controls.

Keywords: Exfoliation syndrome; Phacoemulsification; Cataract extraction/adverse effects

RESUMO | Objetivo: Avaliar a relação entre a síndrome de pseudoexfoliação e a prevalência de complicações e fatores clínicos relacionados em pacientes submetidos à cirurgia de catarata. **Métodos:** Foi realizado um estudo retrospectivo de coorte de 503 de 551 pacientes que se submeteram à cirurgia de facoemulsificação durante 2 anos em um distrito de saúde no noroeste da Espanha. No total, 120 dos 681 olhos submetidos ao procedimento apresentavam síndrome de pseudoexfoliação. Dados sobre o procedimento cirúrgico e complicações associadas foram obtidos dos prontuários médicos. As complicações incluíram qualquer combinação de ruptura da cápsula posterior, perda de humor vítreo, diálise zonular e luxação do núcleo ou do cristalino. **Resultados:** Encontramos uma associação significativa entre síndrome de pseudoexfoliação e diálise zonular (razão de probabilidade [RP]: 6,89; IC 95%, 2,27-20,93), a miose perioperatória (RP: 2,15; IC 95%, 1,10-4,22) e luxação do cristalino >1,5 mm (RP: 9,49; IC 95%, 0,85-105,54). Porém, ao ajustar para o risco global de complicações em pacientes com síndrome de pseudoexfoliação em consideração à miopia, uso de anticoagulantes ou α -agonistas, midríase prévia e comprimento da câmara anterior, a RP diminuiu para 1,02 (IC 95%, 0,47-2,21) e não foi, portanto, significativo. **Conclusão:** A diálise zonular e a miose intraoperatória foram complicações intraoperatórias em pacientes submetidos à cirurgia de catarata com síndrome de pseudoexfoliação quando comparados aos controles.

Descritores: Síndrome de exfoliação; Facoemulsificação; Extração de catarata/efeitos adversos

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an essential enzyme in the synthesis of elastin components of connective tissue. Environmental factors are also thought to play a part in PES, and although these factors have not been fully elucidated, prevalence rates vary considerably according to geographic latitude⁽³⁾. For instance, PES is extremely common in Scandinavia⁽⁴⁾, with an incidence of approximately 22.4%, but it is rare in China, with a rate of approximately 0.4%⁽⁵⁾.

PES is a well-known risk factor for complications in cataract surgery and is associated with worse response to mydriatic agents, which, together with zonular weakness, increases the risk of intraoperative zonular dialysis and luxation of the nucleus and even the lens⁽⁶⁾, which can develop years after surgery⁽⁷⁾. One premise is that production of pseudoexfoliative material by the lens epithelium might disrupt the zonular fibers attached to the lens, affecting its position in the lens capsule. Fibrillar material accumulation in the ciliary epithelium could also disturb the attachment of zonular fibers, which, together with fiber destruction by lysosomal enzymes, could lead to capsular rupture⁽⁶⁾.

In recent years, the overall risk of complications during phacoemulsification surgery in PES patients has decreased due to improved surgical techniques and considering certain factors during surgery^(8,9).

The present study aims to examine the prevalence of complications during cataract surgery in patients with PES.

METHODS

This retrospective observational study was performed according to the principles of the Declaration of Helsinki and approved by the local ethics committee (2015/502). The study sample included 120 eyes of 106 patients with PES operated from 2009 to 2010 at the ophthalmology department of a regional hospital. In total, 561 eyes of 487 patients undergoing cataract surgery during the same period were considered as the non-PES control group.

We initially included all cases undergoing phacoemulsification surgery over a 2-year period at the ophthalmology department of a 74-bed regional hospital providing care for approximately 50,000 patients. The study period was from January 13, 2009, to December 31, 2010. Criteria for inclusion in the study were a) age ≥ 18 years; b) diagnosis of age-related cataract with an indication for surgery (severity ≥ 2 in the Lens Opacities Classification System (LOCS) III⁽¹⁰⁾ as per hospital protocol); and c) visual acuity of ≤ 0.3 on the Early Treatment

Diabetic Retinopathy Study chart. The exclusion criteria were a) traumatic cataracts, congenital cataracts, drug-induced cataracts (corticosteroids), uveitic cataracts, and a history of eye surgery (including refractive surgery) and b) age-related cataracts with complications due to concomitant eye conditions, such as anterior segment ischemia and glaucoma not controlled by medication, defined as glaucoma with visual field worsening and/or insufficient control of ocular tension according to the European Glaucoma Society.

Our hospital protocol for cataract surgery includes clinical examination before and after mydriasis with tropicamide using a slit lamp with a calibrated Goldmann tonometer. All cases used the same model of lamp and the same lighting conditions. The examination included best-corrected visual acuity (BCVA) measurement using a 5-m Snellen chart under standard conditions. PES was defined as the presence of a distinctive fibrillar material forming nearly a complete ring on the lens surface⁽¹¹⁾. Isolated flakes of exfoliative material were not considered to indicate PES. Cataracts were categorized by type and severity using the photographic LOCS III cataract grading system. Additional tests included intraocular pressure measurement before dilation using a Goldmann tonometer, anterior chamber depth, and pupil diameter. In addition, we performed keratometry (Huvitz HRK-7000A) and contact biometry (Alcon UltraScan) using the Sanders-Retzlaff-Kraff regression formula⁽¹²⁾.

Finally, all patients underwent funduscopy with a detailed optic nerve examination. Nerves that were not fully visible were assessed using B-mode sonography.

Mydriasis was obtained during surgery using a preoperative combination of topical tropicamide 1% (Alcon), phenylephrine 10% (Alcon), and cyclopentolate 1% (Alcon). Topical anesthesia (lidocaine 3%) was used in all cases. The surgical procedure included bimanual phacoemulsification with a temporal 2.75-mm limbal incision using the divide and conquer approach (WhiteStar Signature Phaco Machine, Advanced Medical Optics, Inc.). The primary intention was to insert a 1-piece hydrophobic acrylic foldable intraocular lens into the capsular bag or a rigid polymethyl methacrylate (PMMA) lens in cases of zonular insufficiency. In cases of zonular deficiency, we implanted an anterior chamber intraocular lens (primary or secondary intention). All procedures for the study were performed by 3 surgeons.

Postoperatively, the patients were administered tobramycin-dexamethasone (1 mg/mL + 3 mg/mL) drops

in a weekly regimen of decreasing doses (every 3, 4, 6, 8, and 12 hours). The patients were examined the day after surgery, at 7 and 30 days, and at 6 and 12 months. At each follow-up visit, patients underwent slit-lamp examination with biometry as well as intraocular pressure measurements and fundus examination using indirect ophthalmoscopy. Refraction and BCVA were assessed at 30 days.

On statistical analysis, categorical values were expressed as frequencies and continuous variables as means and standard deviations. Associations between variables were measured using parametric or nonparametric tests (χ^2 , *t*-test, paired *t*-test, Mann-Whitney *U* test, and Pearson test) according to the normality of distribution, which was evaluated using the Shapiro-Wilk test. Finally, we used logistic regression to calculate crude and adjusted odd ratios (ORs) for complications utilizing the Maldonado and Greenland criteria⁽¹³⁾ to control for confounders. In the regression model, we analyzed the presence of at least 1 of the following to adjust for the incidence of numerous complications in the same patient: posterior capsular rupture, vitreous loss, zonular dialysis, nuclear luxation, and lens luxation.

Of the variables included in the initial study-presence of PES; patient age and sex; presence of narrow chamber; use of corticosteroids; myopia; use of antiplatelets, anticoagulants, or α -agonists; anterior chamber length; cataract type and severity (LOCS III classification); and maximum mydriasis-we selected only those resulting in a change of >10% in the magnitude of the overall OR.

All statistical analyses were performed using STATA 15 (StataCorp LP, College Station, TX, USA).

RESULTS

Of 551 cataract patients (730 eyes) analyzed in the retrospective chart review, a total of 48 (59 eyes) were excluded. Of the remaining 503 patients (681 eyes) (Figure 1), 106 (120 eyes) had PES and 487 (561 eyes) did not. The PES group comprised more men (50.94% vs 39.6%) and had a higher mean age (77.9 ± 5.57 vs 75.8 ± 6.89 years), with both variables being significant ($p < 0.05$). Table 1 summarizes the distribution of the other variables, including surgical risk factors described in other series. Overall, maximum mydriasis (7.24 ± 0.88 mm in the PES group vs. 7.80 ± 0.88 mm in the non-PES group) and presence of glaucoma (36.79% in the PES group and 18.69% in the non-PES group) were the only variables for which significant differences were identified between the groups.

Table 2 illustrates the incidence of intraoperative and early postoperative complications, together with the corresponding crude ORs. Intraoperative complications consisted of posterior capsular rupture, vitreous loss, luxation of the nucleus, and lens luxation/subluxation.

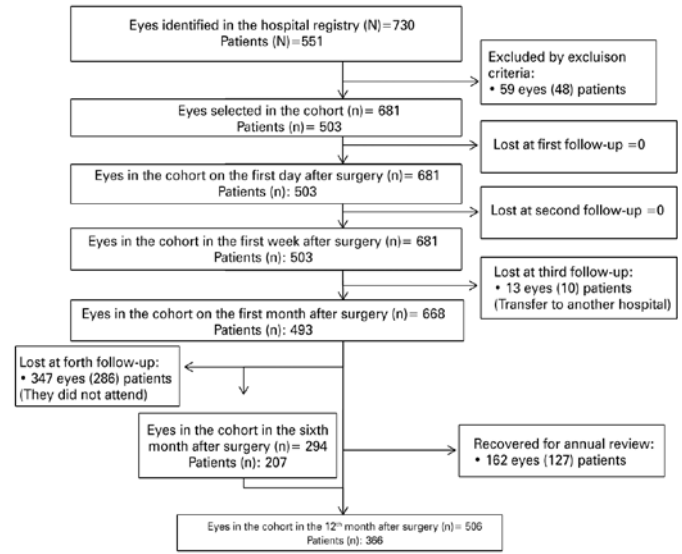


Figure 1. Flowchart.

Table 1. Demographic and clinical characteristics

Characteristics	PES group	Non-PES group	P value
Eyes/patients (n)	120 (106)	561 (487)	
Male, % (n)	50.94% (52)	39.96% (201)	0.0373**
Age (years, mean ± SD)	77.87 ± 5.57	75.75 ± 6.89	0.0031**
Follow-up (days, mean ± SD)			
Visit 1	1.01 ± 0.10	1.01 ± 0.08	0.6883
Visit 2	8.93 ± 1.98	9.26 ± 1.70	0.0855
Visit 3	40.14 ± 3.25	40.72 ± 5.56	0.3414
Visit 4	231.39 ± 22.85	236.58 ± 25.29	0.1387
Visit 5	394.21 ± 42.76	395.46 ± 42.65	0.8075
Maximum mydriasis (mean ± SD)	7.24 ± 0.88	7.80 ± 0.88	0.0000***
Nuclear hardness ≥3% (n)	30.36% (34)	32.08% (150)	0.7288
Anterior chamber depth <3% (n)*	15.09% (16)	14.31% (72)	0.8355
Glaucoma % (n)	36.79% (39)	18.69% (94)	0.0000***
α -agonists % (n)	20.75% (22)	20.68% (104)	0.9855
Use of antiplatelets % (n)	33.96% (36)	25.45% (128)	0.0725
Use of anticoagulants % (n)	25.47% (27)	19.28% (97)	0.1510
High myopia % (n)	15.09% (16)	14.71% (74)	0.9196
Corticosteroids % (n)	21.70% (23)	17.69% (89)	0.3335

PES= pseudoeffoliation syndrome* Van Herick technique.
** Significant at 0.05; *** Significant at 0.01.

Table 2. Main intraoperative and postoperative complications in patients with and without PES

		PES group			Non-PES group			OR	95% CI	P value
		n	Risk	95% CI	n	Risk	95% CI			
Intraoperative complications	PCR	6	0.05	0.02-0.10	28	0.05	0.03-0.07	1.00	0.42-2.41	0.9968
	VL	2	0.02	0.01-0.06	11	0.02	0.01-0.03	0.85	0-3.46	0.8308
	NL	0			0					
	ZD	7	0.06	0.03-0.12	5	0.01	0.01-0.02	6.89	2.27-20.93	0.0002**
	IM	13	0.11	0.06-0.18	30	0.05	0.04-0.08	2.15	1.10-4.22	0.0249*
Early postoperative complications	RD	0	0.01	0-0.04	8	0.02	0.01-0.03	0.27	0.02-4.71	0.1882
	NC	0	0.01	0-0.04	2	0.01	0-0.01	0.93	0.04-19.47	0.5124
	END	0	0.01	0-0.04	3	0.01	0-0.02	0.66	0.03-12.90	0.4221
	LL	0			0					

PCR= posterior capsular rupture; VL= vitreous loss; NL= nuclear luxation; ZD= zonular dialysis; IM= intraoperative miosis; RD= retinal detachment; SC= suprachoroidal hemorrhage; END= endophthalmitis; LL= lens luxation.

95% CI= confidence interval calculated using the Cornfield method; P value= calculated using the Pearson test; risk= risk proportion, A correction has been applied in studies with zero elements in either of the two branches (control or study group), eliminating the study if both branches were zero.

Significant ORs were detected for zonular dialysis (OR, 6.89; 95% CI, 2.27-20.93; $p=0.0002$) and intraoperative miosis (OR, 2.15; 95% CI, 1.10-4.22; $p=0.0249$). Retinal detachment, choroidal detachment, endophthalmitis, and lens luxation were detected within 1 year of surgery, with no significant differences in any of these complications. No cases of cystoid macular edema or shrinkage of the anterior capsule were seen in the present study.

When adjusting for confounders, the following variables were included in the logistic regression model: PES, myopia, use of anticoagulants and α -agonists, previous mydriasis, and anterior chamber length (Table 3). The adjusted OR for PES was 1.02 (95% CI, 0.47-2.21; $p=0.9642$). According to the LOCS III system, age and cataract severity were not significant risk factors for complications.

The results for pre- and postoperative BCVA and intraocular pressure are shown in table 4, which demonstrates significant changes in both the PES and non-PES groups (Figure 2). The mean reduction in intraocular pressure from baseline to day 30 was -1.62 (95% CI, -2.21 to -1.02) in the PES group and -0.81 (95% CI, -1.12 to -0.49) in the non-PES group ($p=0.0303$). Mean intraocular pressure was significantly different between the 2 groups (21.41 [95% CI, 20.08-22.74] in the PES group vs 19.92 [95% CI, 17.48-18.37] in the non-PES group) on the day after surgery ($p<0.001$). No significant differences were detected for mean improvement in BCVA (0.49 [95% CI, 0.44-0.53] in the PES group vs 0.46 [95% CI, 0.44-0.48] in the non-PES group; $p=0.3316$). Finally, no significant between-group differences in the clinical course were noted over the follow-up period (Figure 3).

DISCUSSION

We found that patients with PES undergoing phacemulsification surgery have an increased risk of intraoperative miosis and zonular dialysis, and these rates are consistent with those reported elsewhere, i.e., 0.3% and 3.4% for lens luxation and zonular dialysis⁽⁸⁾; 0%, 10%, and 6% for lens luxation, miosis, and zonular dialysis⁽¹⁴⁾; and approximately 25% for miosis⁽¹⁵⁾. In addition, the complication rates for capsular rupture (5%) and vitreous loss (2%) are comparable to those reported in other series, i.e., 2.9% for both complications⁽¹⁶⁾ and 4% for capsular rupture and 6% for vitreous loss in patients without PES⁽¹⁴⁾. PES is also associated with poor dilation and small capsulorhexis, both of which increase the risk of capsular rupture and zonular dialysis.

Moreover, it is notable that cataract severity was not a significant risk factor for complications. We believe that this is because of the small sample size, including few patients with low nuclear hardness and many uniformly distributed patients with high degrees of hardness. In addition, no differences were seen in the prevalence of PES according to type of cataract in contrast to other reports showing very high rates of PES in patients with nuclear cataracts^(17,18). Previous mydriasis (possibly linked to the presence of pseudoexfoliation), use of α -agonists, and anterior chamber depth were associated with an increased odds of complications, though age was not. In the adjusted analysis, the ORs for intraoperative and early complications were considerably lower, thus PES lost its significance as a risk factor for complications. Although this loss of significance can be explained in part by our small sample size, larger series have reported

Table 3. Logistic regression according to the Maldonado criteria

	Odds ratio	Standard error	Z value	p > z	95% CI
PES	1.02	0.4	0.045	0.9642	0.47-2.21
Myopia	2.19	2	0.858	0.3909	0.36-13.16
Anticoagulants	0.6	0.42	-0.734	0.4628	0.16-2.32
α-agonists	0.66	0.46	-0.589	0.5558	0.17-2.62
AC	0.57	0.19	-1.662	0.0966	0.3-1.1
Mydriasis	0.52	0.08	-4.339	0.0000	0.39-0.7
Constant	53.14	77.12	2.738	0.0062	3.09-913.58

PES= pseudoexfoliation; AC= length of anterior chamber (mm); Mydriasis= mean mydriasis (mm).

Table 4. Comparison of preoperative and postoperative values

Values (30 days after surgery)	PES group				P value	Non-PES group				P value
	Pre-surgery		Post-surgery			Pre-surgery		Post-surgery		
	Mean	SD	Mean	SD		Mean	SD	Mean	SD	
BCVA (total)	0.23	0.15	0.71	0.25	0.000	0.23	0.15	0.69	0.23	0.000
(0.5-1]	0.25	0.16	0.82	0.14	0.000	0.25	0.15	0.79	0.13	0.000
(0.1-0.5]	0.16	0.10	0.35	0.11	0.000	0.18	0.13	0.41	0.11	0.000
(<0.1]	0.02	0.02	0.03	0.01	0.000	0.02	0.02	0.05	0.03	0.000
IOP (mmHg)	17.13	2.80	15.51	3.28	0.000	16.01	3.37	15.20	1.74	0.000

PES= Pseudoexfoliation; BCVA= Best-corrected visual acuity; IOP= Intraocular pressure (mmHg).

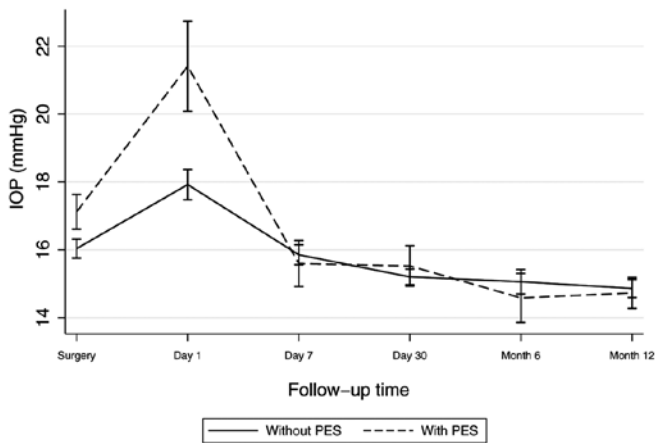


Figure 2. Intraocular pressure (IOP) over the follow-up period in patients with and without pseudoexfoliation syndrome (PES).

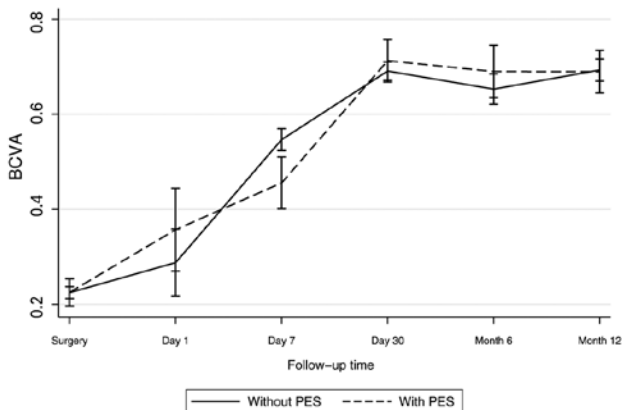


Figure 3. Best-corrected visual acuity (BCVA) over the follow-up period in patients with and without pseudoexfoliation syndrome (PES)

a similar loss^(8,9), and our results may reflect improvements in the phacoemulsification technique.

In our series, PES was particularly common, with a prevalence of 17.4%. Few data are reported for the prevalence of PES in Spain, and those studies that have been performed have reported variable rates, i.e., 13.19% in Tarragona⁽¹⁹⁾, 6.5% and 21.6% in 2 regions in Galicia (Salnés⁽²⁰⁾ and Orense⁽²¹⁾), and 18.9% in an older study conducted in Pontevedra, also in Galicia⁽²²⁾.

Our study has several strengths. As it was performed in a small health care district (with just over 50,000 inhabitants) that conducts the bulk of the phacoemulsification procedures in the region, we assume it is a relatively accurate representation of the true prevalence of PES in the area. Moreover, the low loss to follow-up rate and the homogeneous nature of the data further support our findings, as all operations and examinations were performed by ophthalmologists.

An obvious limitation is the lack of randomization due to the cohort nature of the study. Moreover, the surgeons could not be blinded to the PES status of patients. Thus, our data may have been affected by selection bias, as patients with more complicated conditions or those with PES could have been operated on using phacoemulsification techniques with fewer risks of complications. Finally, because this is a retrospective study, the quality of the data is strongly dependent on the quality of the information recorded in the patients' medical charts. In summary, the generalizability of these findings is limited due to the risk of bias.

Our findings show that zonular dialysis and intraoperative miosis are intraoperative complications in patients with PES compared to controls.

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