

1. Title

Difficulty of biometric images and calculation of intraocular lens in a patient with Sjogren's syndrome

2. Introduction

Surface diseases are becoming a more common cause of consultation today. A general prevalence of dry eye syndrome (DED) around the world is estimated at 8-30% according to the DEWS II study¹. Within these diseases there are multiple causes, one widely known is Sjögren's syndrome (SS), which is a chronic, progressive, and inflammatory autoimmune condition, characterized by the infiltration of lymphocytes of the exocrine glands, especially the lacrimal and salivary glands. Within its multiple manifestations are direct and indirect corneal damage that generates difficult-to-manage keratitis².

Precorneal tear film is known to be the first and most powerful refracting medium of the ocular surface. In this case, its integrity is of vital importance to carry out precision tests such as topography, tonometry, and other biometric measurements of the eye. In the case of DED, loss of tear film stability results in ocular surface damage secondary to hyperosmolarity and chronic inflammation. This alteration in surface dynamics can lead to various problems in intraocular surgeries at the preoperative, intraoperative, and postoperative time. One of the most affected procedures in these cases is cataract surgery, which requires high dependence on this type of measurement to perform a reliable intraocular lens calculation³.

3. Case presentation with illustrations and figures

A 74-year-old female with a history of Sjogren's Syndrome since 12 years ago which has been very difficult to treat in both eyes, especially in the left eye, despite having received multiple treatments that are presented in Table 1. For several years, she achieved control of her disease with minimal keratitis in the right eye (OD) and microulcerations and filamentous keratitis in the left eye (OS), during all her visits she has had a maximum Schirmer test of 1/1, and a maximum tear breakup time (BUT) of 1/1. She has had maximum periods of remission of 1 year where, in addition to Sjogren's syndrome evidenced in the physical eye exam, she has had a severe blepharospasm in both eyes.

In the 2017 follow-up, she began with incipient cataract changes in both eyes (AO) that progressed especially in the left eye with uncorrected visual acuity (UDVA) of 0.18 LogMAR in the right eye and 0.88 LogMAR in the left eye, so in 2018 it was mentioned the possibility of performing assisted phacoemulsification plus intraocular lens implantation, but given the relapse of the ocular involvement with severe filamentous keratitis in OS, it was decided first to optimize the ocular surface, so a lacrimal duct plasty was performed on both eyes and lower lacrimal plugs were implanted in AO with amniotic membrane graft in AO. In addition, the patient was promptly referred for evaluation by her rheumatologist with whom she had been receiving chronic treatment with prednisolone 10 mg daily and pilocarpine 5 mg daily,

but due to her ocular refractoriness, he decided to increase the dose of pilocarpine to 15 mg daily, add oral azathioprine 50 mg every 12 hours and oral chloroquine 150 mg daily. 5 months later, the patient continued with short periods of remission but again with a serious relapse of the disease with the presence of severe keratitis in both eyes, for which she was again assessed by a rheumatologist who increased the dose of oral prednisolone to 30 mg per day and started cyclophosphamide 750 mg IV pulses. By 2020, the patient persisted without achieving control of the ocular surface and continued with mild keratitis in AO despite multiple treatments, but at that time with mature cataracts in AO and UDVA of OD 0.44 LogMAR and OS 1.0 LogMAR. Ocular biometry of both eyes and endothelial cell count were ordered, which reported endothelial cell density (ECD) 2463 and 2519 with coefficient of variability of 30 and 40 and hexagonality of 53 and 39 in right and left eye, respectively. The biometries performed were unreliable despite taking different images by different methods and biometric calculators, in which none of them managed to have reproducibility of the keratometric measurements and for this reason it was not possible to predict the power of the lens to be implanted as shown in figures 1-4. The high risk of postoperative refractive surprises due to severe dry eye was clearly explained to the patient, which she accepted and signed the informed consent, and it was followed by surgical procedure in the left eye. During the surgical procedure, a refraction was performed in aphakia, which was calculated again with a conversion factor of multiplication by 2, justified by the scientific literature on the calculation of intraocular lenses in patients with previous refractive surgery, which, although it was not the case of our patient, was the closest literature support available for decision-making added to pre-surgical data.

One month after surgery, the patient had a refraction of -1.50 -1.50 x 168° with a vision of 0.3 LogMAR and close vision to J1 with a Jaeger chart. During follow-up, the patient continued to lose vision due to OD with a vision of 1.0 LogMAR, so it was decided to undergo phacoemulsification with intraocular lens implantation in the right eye 17 months after the first intervention. Two weeks after surgery, the patient presented refraction of -0.50 -0.25 x 145° with vision of 0.3 LogMAR and J2 in close vision with Jaeger chart.

Table 2 shows the different intraocular lens calculations to be implanted based on the different measurement methods used and the final refraction.

The refractive parameters remain stable with good near and far visual acuity, palpebral ptosis is being managed by oculoplasty and the ocular surface continues without control of the SS, persisting with mild filamentous keratitis with greater involvement of the right eye that achieves symptomatic control with bandage contact lenses, transition aerial lenses to control photophobia and sodium hyaluronate 0.4% eye drops preservative free and Carbomer 974P – 2.5 mg/g.

Table 1. Treatments received chronically.

Treatment and dosage	Observation
prednisolone 5 mg oral	10mg daily

Tear duct plugs	Upper and lower occlusion of both eyes
eyelash electrolysis	multiple times
Biotin capsules 900 mcg	Every 24 hours orally
Glucosamine & chondroitin capsules	Every 24 hours orally
Pilocarpine HCL 5mg	10mg daily
cyclosporine ophthalmic emulsion 0.05%	Every 24 hours (intolerance with dose increase)
Sodium hyaluronate ophthalmic solution 0.4%, preservative free	Application every hour in both eyes
Carbomer 974P – 2.5 mg/g Dropper bottle	Application every 4 hours in both eyes
Carboxymethylcellulose ophthalmic solution 0.5%, preservative free	Application every 4 hours in both eyes
Loteprednol etobonate ophthalmic suspension 0.5%	Short cycles in crisis
Triamcinolone acetonide 10 mg/ 1 ml	Subconjunctival injection
Autologous 20% serum eye drops	Application every 3 hours in both eyes
N. Acetyl cysteine 5%	Application every 8 hours
Oral N. Acetyl cysteine 500 mg	2 gr every day
Topic regular insulin 1UI/ml	Application every 6 hours
Oxytetracycline hydrochloride Ophthalmic ointment	She did not tolerate due to repeated microulcers and filaments
Erythromycin ophthalmic Ointment 0.5%	Every night in both eyes
Retinol 5 mg + Methionine + Gentamicin ophthalmic ointment	Every 8 hours in both eyes
Contact lenses	Therapeutic bandage

Table 2. Calculation of intraocular lens power according to different measurement methods

Method	Preoperative refraction	IOL by biometry	IOL by Pentacam ERK Detail map report at 4.5 mm	IOL by intraoperative aphakic refraction (constant K of x2.0)	Implanted IOL	Final postoperative refraction
Right eye	Sph +1.50	it was not possible due to the impossibility of measuring keratometry	+23.00 (-0.04 expected refraction)	+12.00 D X 2.00 = IOL +24.00	IQ SN60WF +23.50 D	-0.50 -0.25 x 145° (0.3 LogMar)
Left eye	Sph +3.00	it was not possible due to the impossibility of measuring keratometry	+25.00 (-0.67D expected refraction)	+12.50 D x 2.00 = IOL +25.00	IQ SN60WF +25.00 D	1.50 -1.50 x 168° (0.3 LogMar)

4. Discussion

Sjogren's syndrome is a systemic pathology that, within its clinical presentation, generates great compromise in the ocular surface of different mechanisms and severity degrees⁴. This is the main etiology of water-deficient dry eye syndrome due to auto-inflammatory factors that attack the lacrimal gland; the lack of goblet cells, keratinization of the conjunctival tissue and direct damage to the corneal epithelial cells⁵. Another common presentation of the disease is keratoconjunctivitis sicca and filamentous keratitis, which occurs due to the great destruction of corneal epithelial cells, progressive thinning, and lack of tear production².

The treatment of SS is based on systemic and topical management, the first based on a parasympathomimetic agonist (pilocarpine) to stimulate the secretion of exocrine glands through M3 receptors⁶. On the other hand, there is a topical therapy based on the objective of proper ocular homeostasis and inflammatory control to avoid further damage to the ocular surface and thus symptomatic control of the entity⁵. In the case of our patient, she has had multimodal management of the disease with systemic secretagogues, bandage contact lenses, different schemes of ocular lubricants at maximum doses, steroidal anti-inflammatory drugs, immunomodulators, blood products, even surgical management with amniotic membrane graft and tear duct plugs, which demonstrates the severity of the condition and the difficult management over time with periods of relapses and partial remissions.

During follow-up, our patient presented visual loss secondary to lens sclerosis, which generated the great issue of when was the ideal time to operate, since control of her ocular surface was not achieved, and this represented a risk both preoperatively to perform biometric calculations and the imminent risk of postoperative refractive surprises and the worsening of her underlying disease that would translate into worsening symptoms. In this case, it was decided to undergo surgery when the patient had 3 months of mild but persistent keratitis in each eye that was going to be operated on.

The first fundamental step in this type of patient is to choose the right time to perform any type of intraocular intervention. This decision must be made once optimal control of the ocular surface is achieved to the extent that the disease of each patient allows it⁴. In our case, despite the multidisciplinary management with rheumatology who initiated immunomodulatory therapy due to the refractory presentation of the ocular disease, the multiple topical therapeutic schemes and even many of these not available in our country and imported by the patient, periods of recovery were not achieved, but a control of the disease with a decrease in the severity of the punctate keratopathy in both eyes was accomplished. Despite this, there was always persistence of blepharospasm and very short tear film breakup times, which made it very difficult to take and interpret the pre-surgical tests.

This is the greatest limitation of this type of disease at the preoperative level, in which an unstable tear film and punctate corneal staining can generate measurement variability in topographies, ocular biometry, keratometry, intraocular lens calculation (IOL) and the possible generation of higher order aberrations, which will be one of the main causes of suboptimal visual results after the intervention and symptomatic worsening^{7,8}. For this reason and due to the high level of dissatisfaction after phacorefractive surgeries in people with ocular surface diseases, in 2019, the Annual American Society of Cataract and Refractive Surgery (ASCRS) carried out an educational algorithm to deal with this type of cases and to detect those patients with pre-surgical dry eye syndrome who do not present symptoms and can also represent refractive surprises. Unfortunately, this is not useful for those cases of refractory dry eye in which pre-surgical control is not achieved despite the proposed measures⁹.

In scarred corneas, the average of keratometric value obtained in topography over the corneal center is used to calculate lens power. In those cases, with marked keratometric distortion, standard keratometry would help to calculate the IOL. In cases of unilateral surface disease, the contralateral eye could be used as reference⁸, which was a limitation in our patient due to having an immune cause that affects both eyes. In our case, an attempt was made to take optical biometry with the Zeiss IOLMaster[®] 700 and the LENSTAR LS900[®], which were not reliable due to the keratometry parameters, despite multiple lubrication attempts during the test. Because of this, the values were entered based on the best shot we could get after multiple tries of Scheimpflug corneal imaging (Oculus Wavelight Pentacam[®]) on the Holladay ERK Detail map report at 4.5 mm that for the left eye a K1

40.40 x 97° and a K2 40.71 x 7° were obtained, which combined with the other biometric values, calculated by different formulas. Similarly, given the difficulty of keratometric measurements by multiple methods and to reduce the risk of refractive surprises, an intraoperative refraction was performed in aphakia with frame box lenses, in which a 11.5 D refraction was obtained in the right eye and 12.5 D in the left eye. which, based on studies of patients undergoing phacoemulsification after refractive surgery, a multiplication constant x2 has been used, which was used in both eyes, again having values of lenses to be implanted of 23.00 in the right eye and 25.00 in the left eye⁹. it was decided to implant in left eye an Alcón IQ SN60WF +25.00 IOL achieving a refractive result of -1.50 -1.50 x 168° with UDVA of 0.3 LogMAR and close vision of J1. For the right eye, which was the second operated on, the Holladay ERK Detail map was also used with a report at 4.5 mm and keratometries K1 41.45 x 4° and a K2 42.37 x 94° for an IQ SN60WF +23.50 IOL with a refractive result of -0.50 -0.25 x 145° with UDVA of 0.3 LogMAR and close vision of J2.

In this type of patients, the use of premium or toric lenses is not recommended, since both have a reduced contrast sensitivity that would add to the visual deficit of the patient's surface, additionally, they are aberrated and multifocal corneas that will not be able to be compensated by the lens¹⁰. On the other hand, these diseases that compromise the ocular surface are dynamic over time, which makes reliable measurement more complex in this type of lens, which requires adequate optical performance in order to achieve adequate function¹¹. In this case, a monofocal lens was decided for the reasons mentioned above, achieving a very good near- and far-sighted vision.

Both intraoperative and postoperative moments of our patient required prior management with preservative-free medications, little irrigation of the surface in the intraoperative, and a greater care of the corneal tissue since it was not required to remove the epithelium to achieve better visualization. The postoperative was managed with preservative-free topical antibiotics and short-cycle corticosteroids, nonsteroidal anti-inflammatory drugs were avoided at this time, and monofocal lenses were used following the 2019 ASCRS recommendations¹⁰.

Among the postoperative problems that may exist, is well known the presence of epithelial defects or their worsening of them, corneal melting, surface infections or endophthalmitis, visual impairment or increased in severity of signs and symptoms of dry eye^{12,13} None of these was presented in our patient, what makes vitally important to continue optimal intra- and postoperative treatment.

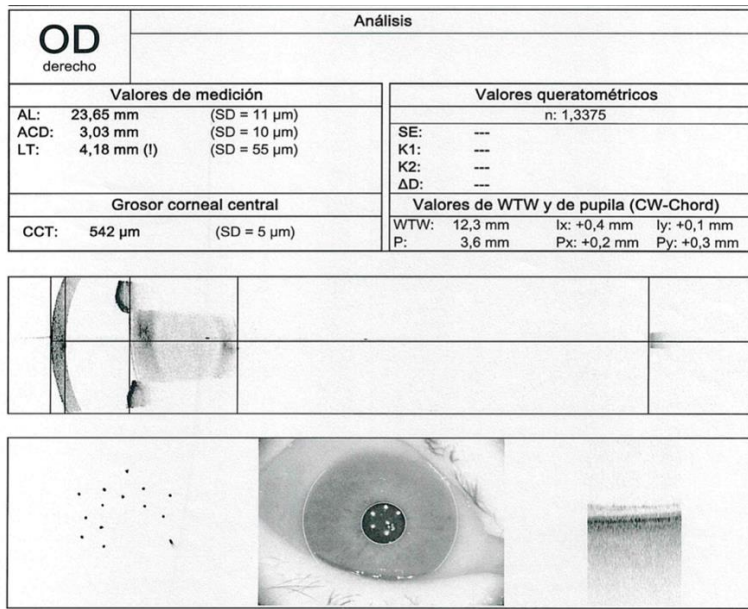


Figure 1. Biometry by IOL master with biometric measures of the right eye, but without corneal power data due to inability to be taken secondary to corneal surface compromise

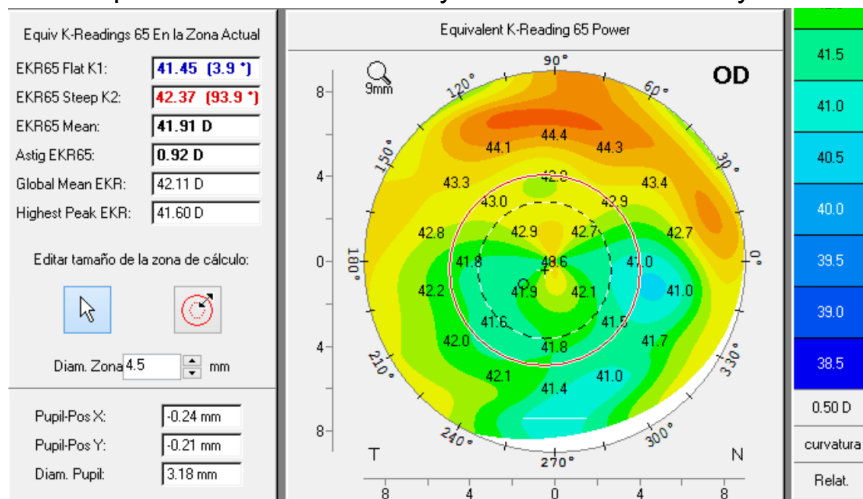


Figure 2. Holladay ERK Detail Report map of the right eye at 4.5 mm by Scheimpflug image (Oculus Wavelight Pentacam®)

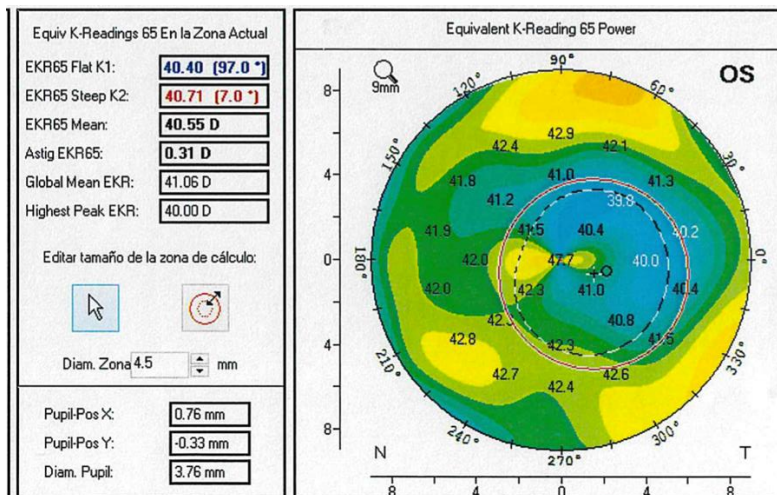


Figure 3. Holladay ERK Detail Report map of the left eye at 4.5 mm by Scheimpflug image (Oculus Wavelight Pentacam®)

Para este cálculo de IOL se han editado valores manualmente. OS: Cilindro del ojo izquierdo -2.55 D. - Nota: Fuerte astigmatismo. Atención: Se ha seleccionado LVC "No tratado". Los valores queratométricos han sido editados manualmente. El médico asume la responsabilidad.			
OD derecho		Cálculo de IOL (Multifórmula) (!) Marca un valor de medición inseguro. (*) Marca un valor editable manualmente. --- Marca un error de medición.	OS izquierdo
AL: --- ACD: --- LT: --- SE: --- K1: --- Ref: --- Refr. dest.: --- LS: Fáquico; VS: Humor vítreo; LVC: No tratado; Modo LVC: ---	WTW: --- ΔD: --- K2: --- AV: --- SIA: ---	AL: 23.59 mm (SD = 13 μm) ACD: 3.05 mm (SD = 4 μm) LT: 4.18 mm (SD = 32 μm) SE: 40.55 D (*) K1: 40.40 D @ 97° Ref: --- Refr. dest.: Plano LS: Fáquico; VS: Humor vítreo; LVC: No tratado; Modo LVC: -	WTW: 12.4 mm ΔD: -0.31 D @ 97° K2: 40.71 D @ 7° AV: --- SIA: +0.00 D @ 0°
		Haigis A0: -0.769 A1: +0.234 A2: +0.217 IOL (D) Ref (D) +25.00 -0.59 +25.50 -0.23 +25.00 +0.13 +24.50 +0.49 +24.00 +0.84 +25.18 Emet.	Hoffer® Q pACD: +5.64 IOL (D) Ref (D) +25.00 -0.66 +25.50 -0.31 +25.00 +0.04 +24.50 +0.39 +24.00 +0.73 +25.06 Emet.
		Holladay 1 SF: +1.85 IOL (D) Ref (D) +25.50 -0.66 +25.00 -0.30 +24.50 +0.06 +24.00 +0.41 +23.50 +0.75 +24.58 Emet.	SRK®/T Const. A: 119.00 IOL (D) Ref (D) +25.00 -0.66 +24.50 -0.29 +24.00 +0.07 +23.50 +0.43 +23.00 +0.78 +24.10 Emet.

Figure 4. Biometry with IOL calculation from corneal power entered manually with Pentacam® data.

5. Conclusion

Refractive surprises are a feared complication of cataract surgery that can occur due to pre-surgical measurement errors in concomitant surface diseases or intra-/post-surgical complications. All the diseases that affect the ocular surface are possible causes of these unexpected refractive measures, among the most common is Sjogren's syndrome due to its great corneal damage. In the case of our patient, it is a clear example of the difficult measurement of ocular biometry and preoperative keratometry due to her great involvement of keratitis that could not be recovered despite multiple topical treatments at maximum doses and management with immunomodulators with the help of rheumatology.

Despite the fact that there are indications and algorithms in the literature for those patients with pre-surgical ocular surface compromise, all of them clearly state stabilizing the compromise before intervening, but none of them give information on what to do in case of not being able to improve the keratopathy due to dry eye syndrome and that is why in our case we were limited to scientific recommendations for intraocular lens calculation and we chose to resort to pentacam keratometry measurements with very good postoperative results to date without having presented refractive surprises or major complications of her ocular surface.

6. References

1. Stapleton F, Alves M, Bunya V, Jalbert I, Lekhanont K, Malet F et al. TFOS DEWS II Epidemiology Report. *The Ocular Surface*. 2017;15(3):334-365.
2. Roszkowska AM, Oliverio GW, Aragona E, Inferrera L, Severo AA, Alessandrello F, et al. Ophthalmology manifestations of primary sjogren's syndrome. *Genes (Basel)* [Internet]. 2021 [cited 2022 Oct 10];12(3):365. Available at: <https://www.mdpi.com/2073-4425/12/3/365>
3. Ananya Sudhir Nibandhe & Pragnya Rao Donthineni (2022): Understanding and Optimizing Ocular Biometry for Cataract Surgery in Dry Eye Disease: A Review, *Seminars in Ophthalmology*, DOI: 10.1080/08820538.2022.2112699
4. Bron, AJ; de Paiva, CS; Chauhan, S.K.; Bonini, S.; Gabison, E.; Jain, S.; Knop, E.; Markoulli, M.; Ogawa, Y.; Perez, V.; et al. TFOS DEWS II pathophysiology report. *Eye Surfing*. 2017, 15, 438–510.
5. Mathews, PM; Robinson, SA; Turn, A.; Baer, AN; Akpek, EK Extraglandular ocular involvement and morbidity and mortality in primary Sjögren's syndrome. *PLoS ONE* 2020, 15, e0239769
6. Both, T.; Dalm, VA; van Hagen, PM; van Daele, PL Reviewing primary Sjögren's syndrome: Beyond the dryness—From pathophysiology to diagnosis and treatment. *Int. J. Med. _ Sci*. 2017, 14, 191–200.
7. Koh S. Irregular astigmatism and higher-order aberrations in eyes with dry eye disease. *invest Ophthalmol Vis Sci*. 2018;59 (14):DES36–DES40. doi:10.1167/iovs.17-23500.

8. Agarwal S, Srinivasan B, Harwani AA, Fogla R, Iyer G. Perioperative nuances of cataract surgery in ocular surface disorders. *Indian J Ophthalmol* 2022;70:3455-64.
9. Centuri3n V. *Cristalino de las Am3ricas*. 2nd ed. Panam3: Jaypee - Highlights Medical Publishers; 2016.
10. Starr CE, Gupta PK, Farid M, Beckman KA, Chan CC, Yeu E, et al. An algorithm for the preoperative diagnosis and treatment of ocular surface disorders. *J Cataract Refract Surg* [Internet]. 2019;45(5):669–84. Available from: <http://dx.doi.org/10.1016/j.jcrs.2019.03.023>
11. Sangwan VS, Gupta S, Das S. Cataract surgery in ocular surface diseases: Clinical challenges and outcomes. *curr opinion Ophthalmol* 2018;29: 81-7 .
12. Gupta P, Drinkwater O, VanDusen KW, et al. Prevalence of ocular surface dysfunction in patients presenting for cataract surgery evaluation. *J Cataract refract Surge* 2018; 44: 1090–1096
13. Kato K, Miyake K, Hirano K, et al. Management of postoperative inflammation and dry eye after cataract surgery. *Cornea* 2019; 38(1): S25–S33.