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ORIGINAL RESEARCH

Mesopic Disability Glare in Stage-Two Dysfunctional Lens Syndrome

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ABSTRACT

Introduction: There is a lack of evidence about the exact deterioration of visual function associated with the age-related natural changes in the lens, particularly in intermediate (stage-2) dysfunctional lens syndrome (DLS). Standard photopic visual acuity and contrast sensitivity tests may not show the visual worsening in daily life activities, such as oncoming vehicle headlights at night. The purpose of this study was to analyze visual function under different conditions and glare sources in stage-2 DLS.

Methods: Forty patients over 49 years of age with initial bilateral lens opacification (Lens Opacities Classification System III [LOCS-III] scores up to 3), best-corrected visual acuity of 20/25 or better, and no ocular disease were evaluated. Binocular photopic and mesopic contrast sensitivity (CS) with/without halogen and xenon increasing glare sources were analyzed. Mesopic disability glare (MDG) was calculated as the difference between mesopic CS with/without the glare source.

Results: The median logarithmic CS (logCS) values were lower under mesopic conditions (1.05) than under photopic illumination (1.65; $P < 0.001$). Halogen and xenon glare further decreased mesopic CS (both, median logCS 0.75, $P < 0.001$). The mean MDG was 0.31 ± 0.10 log units for halogen glare and 0.33 ± 0.09 log units for xenon glare. The mesopic CS and MDG were not associated with any photopic test. The mesopic CS with glare but not photopic CS or mesopic CS was correlated with the LOCS-III scores. The best association was provided by MDG, which showed a pooled correlation with LOCS-III nuclear opalescence ($r = 0.411$, $P < 0.001$) and cortical scores ($r = 0.226$, $P = 0.04$).

Conclusion: The mesopic CS under a glare source is an independent early indicator of visual impairment in stage-2 DLS patients, and appears to be substantial. Furthermore, the MDG is more sensitive than photopic and mesopic CS for evaluating patients with initial phacosclerosis. Surgeons should consider this in the decision-making process of the correct timing for lens surgery.

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Keywords: Contrast sensitivity; Dysfunctional lens syndrome; Glare

Key Summary Points

Why carry out this study?

Advanced (stage-3) dysfunctional lens syndrome (DLS) corresponds to a clearly developed cataract with overt morphological and functional alterations; thus, the indication for surgery is straightforward. However, more intermediate (stage-2) DLS poses a challenge in routine clinical practice because standard tests of visual function, such as photopic visual acuity and contrast sensitivity (CS), may not reflect the visual impairment associated with initial changes in the aging crystalline lens.

Evidence is lacking regarding the actual visual functional impairment that intermediate DLS patients may suffer.

What was learned from the study?

While stage-2 DLS patients may exhibit normal visual function under photopic conditions, under mesopic conditions, particularly with oncoming glare sources, vision may be profoundly impaired.

In intermediate DLS patients, mesopic CS adds new independent information about visual function over standard tests, which is augmented by including a glare source. Moderate nuclear and cortical phacosclerosis is associated with lower mesopic CS function under glare sources.

Mesopic disability glare measurement appears to be a more useful, sensitive tool for in-office evaluation of patients with intermediate DLS than standard visual function tests under photopic or mesopic conditions and should be regarded when considering the benefits of lens surgery for functional improvement in patients with initial phacosclerosis.

INTRODUCTION

The concept of dysfunctional lenses, introduced more than 15 years ago, defines the natural age-related changes in the crystalline lens [1]. Subsequently, the term dysfunctional lens syndrome (DLS) was coined [2] and staged as (1) near visual loss and development of higher-order aberrations (HOAs) between 40 and 50 years of age; (2) accommodative loss, further HOA increases and forward light scatter, decreased contrast sensitivity (CS) and night vision, and early lens opacities, typically at 50 years and older; and (3) full cataract, poor visual quality, lens nucleus opacification affecting color perception, typically at 65 years and older [2, 3]. DLS is thought to be linked closely with modern technological developments for assessing potential candidates who may benefit from lens surgery [2–11], and the need for further evidence-based information about measures of visual performance has been emphasized [7].

CS is more fundamental than other measures of visual function for daily activities, including driving [12–18]. A photopic Pelli-Robson CS score under the 1.25 logarithmic CS (logCS) level is associated with an eight-fold increase in vehicular accident risk [16]. Furthermore, real-world night-driving studies have shown that simulated visual impairment and glare significantly reduce the frequency with which drivers recognize pedestrians and the distance at which the drivers first see them [19, 20]. In this context, simulated lens opacification is significantly more disruptive by impairing CS and increasing disability glare (DG) than moderate levels of refractive blur even though photopic visual acuity (VA) levels are equal for both conditions [19].

While the visual impairment with minor stage-1 and major stage-3 DLS is clear [2, 3], in stage-2 DLS it remains unknown and may be challenging countless patients in daily activities, such as with oncoming vehicle headlights at night.

The current study for the first time analyzed in stage-2 DLS patients the CS function in standard photopic and mesopic conditions

with/without glare sources simulating halogen and xenon oncoming headlamps and evaluated the associated DG, discomfort glare, and the photostress recovery time. We also investigated the visual function measure that is best related to initial grades of cortical, nuclear, and posterior subcapsular phacosclerosis in stage-2 DLS patients, which should be useful for evaluating DLS patients.

METHODS

This cross-sectional study was performed at Instituto de Oftalmobiología Aplicada (IOBA-Eye Institute, University of Valladolid, Spain) after the University Clinic Hospital Ethics Committee (Valladolid, Spain) approved it (PI 15-220). The study complied with the tenets of the Helsinki Declaration of 1964; all subjects provided written informed consent.

Sample

The inclusion criteria were age 50 years and older with bilateral crystalline lens characteristics within the definition of stage-2 DLS [2, 3], which encompassed Lens Opacities Classification System III [LOCS-III] [21] scores up to 3, and corrected distance visual acuity (CDVA) of 20/25 or better. The exclusion criteria were amblyopia; abnormal binocular vision; previous ocular trauma or surgery; ocular diseases; and cortical, nuclear opalescence, or posterior subcapsular scores exceeding 3 with the LOCS-III in either eye based on previous criteria for classification of early versus late cataract [6].

All subjects underwent measurement of the CDVA, cover–uncover test, the Worth Four Dot Test, noncontact tonometry, slit-lamp biomicroscopy, perimetry, dilated fundus examination to ensure the absence of ocular disease, and measurement of photopic and mesopic pupil diameters (Wavelight Topolyzer Vario, Alcon Laboratories, Inc., Fort Worth, TX, USA) after dark adaptation.

The lens sclerosis grades were classified according to the LOCS-III. Nucleus color evaluation was not considered because lens density has a stronger correlation with nuclear opalescence [4, 22]. The same experienced examiner (MJM) evaluated all patients. The lens scores of the distance-dominant eye, measured three times using the hole-in-card test, were used for statistical analyses.

Visual Function Tests

The subjects wore optimal spherocylinder correction for distance during all tests. The VA was measured in logarithm of the minimum angle of resolution (logMAR) units using the Early Treatment Diabetic Retinopathy Study chart (Precision Vision, Woodstock, IL, USA) at 4 m.

Contrast Sensitivity Testing

The CS examination was performed using the Pelli-Robson test (Clement Clarke International Ltd., Harlow, Essex, UK) at 1 m under binocular viewing to characterize visual performance in daily activities [14, 19, 23, 24]. The value of the last triplet (logCS) at which the subject correctly identified two letters was recorded [15, 24].

For photopic and mesopic CS examinations, the test luminance levels were 100 cd/m^2 and 0.38 cd/m^2, respectively [12, 25]. Participants had a 10-min adaptation period to the mesopic light [25]. Photopic and mesopic CS measures were performed using a different randomly ordered chart for each measure to avoid familiarity with the letters. In accordance with previous studies, scores were classified as below or above 1.25 log units [15, 16].

Headlight Glare Simulator

We used the IOBA Halogen-Xenon Mesopic Contrast Sensitivity Test headlight glare simulation system (Fig. 1) [26, 27]. The setup included a focal light 0.2 m behind the patient and 2 m high aimed ahead to reproduce the ambient light from the driver's headlamps reflecting on the road. A headlamp beside the Pelli-Robson chart at an angle of 20° from the participants' line of sight produced increasing light intensity to simulate the dynamic nature of an oncoming car's headlight glare approaching from 100 to

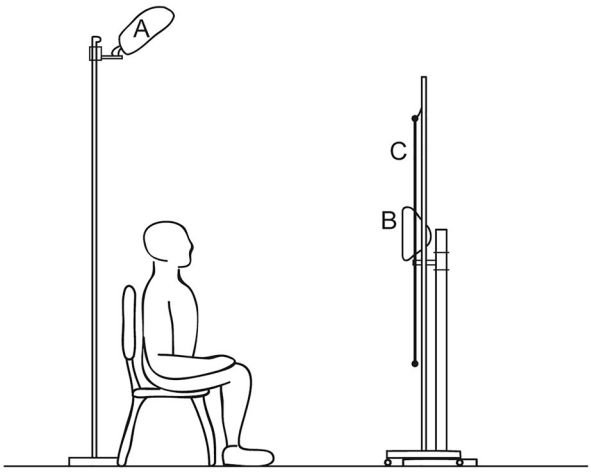

Fig. 1 Graphical representation of the IOBA Halogen-Xenon Mesopic Contrast Sensitivity Test (a progressive headlight glare simulation system) setup. The testing room is windowless, and the walls are covered by nonreflecting black paper to avoid unwanted light sources. Setup includes **a** focal light situated 2 m above the floor pointing ahead to reproduce the ambient light of the driver's car headlamps reflecting on the road, **b** headlamp positioned 1.11 m above the floor with increasing intensity to simulate the dynamic nature of an oncoming car's headlight glare, **c** Pelli-Robson contrast sensitivity chart located 1 m away from the seated patient

40 m over 5 s, as during nighttime driving. The produced glare illuminance ranged from 1.4 to 3.9 lx in the halogen setting and 4.6–15.8 lx in the xenon setting. The CS was measured during the progressively more intense halogen or xenon glare administered randomly with a 10-min break in between. The photostress recovery time necessary to achieve the previous mesopic CS level then was measured [26, 27].

DG was defined as the Pelli-Robson score without glare minus the CS score with glare [12, 16, 28], and it was classified as below or above 0.25 log units [16]. Finally, discomfort glare from halogen and xenon sources also was recorded with the de Boer rating scale ranging from 0 (unbearable) to 9 (unnoticeable) [26, 27, 29].

Statistical Analysis

Data were analyzed using SPSS 26.0 software (IBM Corp., Armonk, NY, USA). Descriptive statistics included the means and standard deviations and medians and interquartile range (IQR) 25th and 75th percentiles of the distribution to facilitate comparisons with published data. The normality of the variables was analyzed using the Shapiro–Wilk test. As CS values were not normally distributed, comparisons among various conditions were performed using the Friedman test, and subsequent paired analysis using the Wilcoxon test with the Bonferroni correction. Data from dependent samples following a normal distribution were analyzed with the paired *t*-test, and the 95% confidence intervals (CI) were provided. Significant correlations were evaluated using Pearson or Spearman correlation coefficients according to data normality. To assess the relationship between LOCS-III scores and visual function tests, standard correlation coefficients were calculated first, and the pooled correlation coefficients of the mesopic disability halogen and xenon glare tests were combined. Two-sided $P \leq 0.05$ was considered significant.

RESULTS

The mean age of the nine (22.5%) women and 31 (77.5%) men was 59.63 ± 5.18 years (range, 50–71 years). The mean binocular VA was −0.05 ± 0.09 logMAR (range, −0.24 to 0.12), mean spherical equivalent −0.49 ± 2.31 diopters (D) (range, −7.50 to +4.25), mean pupil diameter in the photopic range 2.34 ± 0.41 mm (range, 1.58–2.90) and in the mesopic range 4.56 ± 0.93 mm (range, 2.88–6.20), mean lens opacification 0.90 ± 0.90 (range, 0–3) in the cortical score, 1.89 ± 0.84 (range, 0–3) in the nuclear opalescence score, and 0.44 ± 0.36 (range 0–1.5) in the posterior subcapsular score. Figure 2 shows the distribution of the LOCS-III grading.

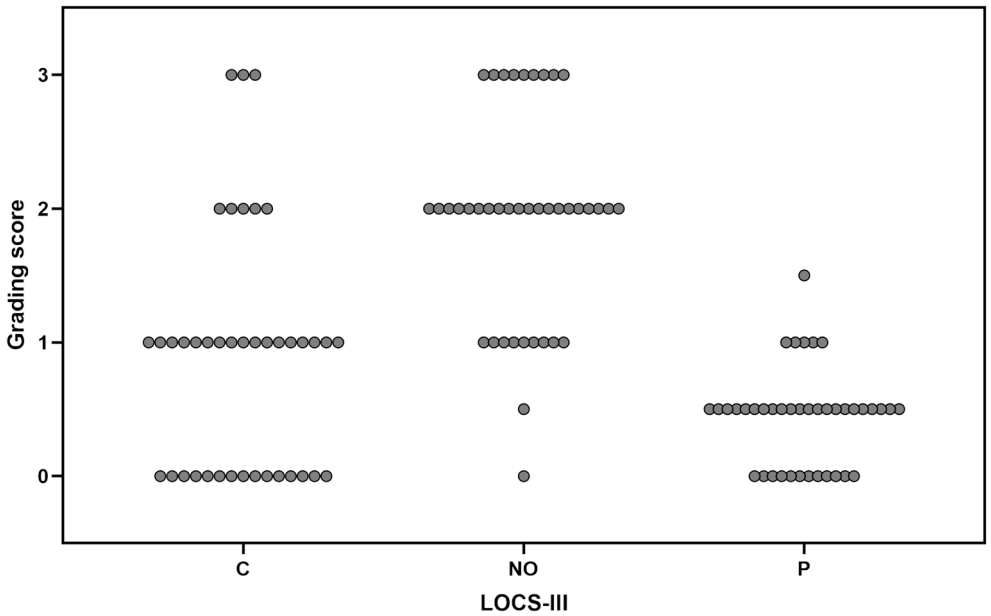

Fig. 2 The dot plot shows the distribution of the LOCS-III scores. The median values were 1.0 [interquartile range (IQR), 1.0–2.75] in the cortical score, 2.0 (IQR, 0–1.0) in the nuclear opalescence score, and 0.5 (IQR, 0–0.5) in the posterior subcapsular score. *C* cortical; *LOCS-III* Lens Opacities Classification System III; *NO* nuclear opalescence; *P* subcapsular posterior

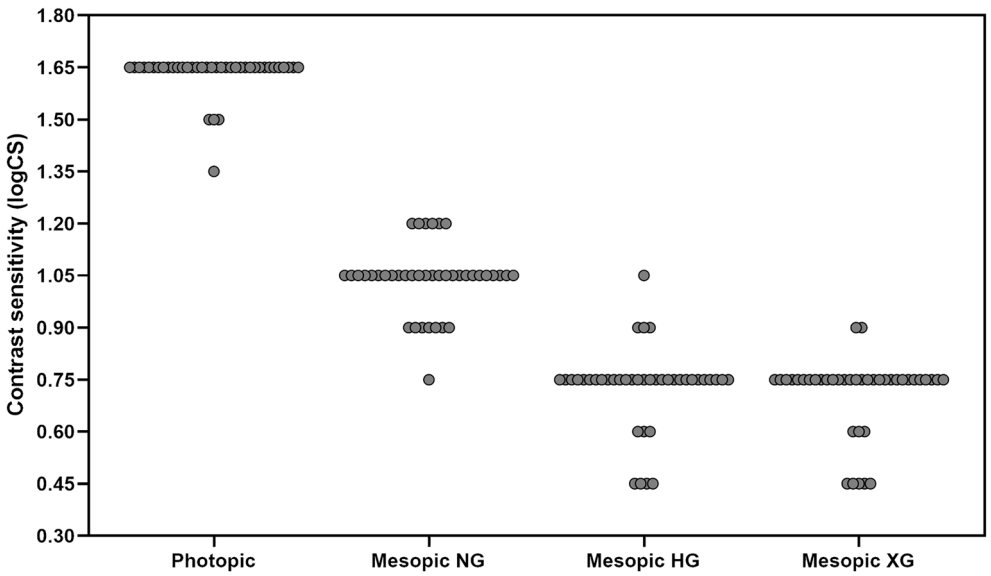

Fig. 3 The graph shows the binocular Pelli-Robson contrast sensitivity scores under various conditions: photopic, mesopic, mesopic with halogen glare, and mesopic with xenon glare. *HG* halogen glare; *NG* no glare; *XG* xenon glare

Contrast Sensitivity

Figure 3 shows that CS function differed significantly ($P < 0.001$) among the varying conditions. Under photopic conditions, no subjects attained logCS values under 1.25; under mesopic conditions with/without glare sources, all patients scored below 1.25.

The logCS values were lower under mesopic conditions (1.04 ± 0.10; median, 1.05; IQR, 1.05–1.05) than under photopic illumination (1.63 ± 0.06; median, 1.65; IQR, 1.65–1.65; $P < 0.001$). The mean difference in logCS was 0.59 ± 0.11 (median, 0.60; IQR, 0.60–0.60; range, 0.30–0.90).

The logCS values under halogen glare (0.73 ± 0.12; median, 0.75; IQR, 0.75–0.75) and xenon glare (0.71 ± 0.11; median, 0.75; IQR, 0.75–0.75) were lower than under mesopic conditions without glare ($P < 0.001$ for each comparison). The difference in logCS values between halogen and xenon glare conditions was not statistically significant ($P = 0.09$).

The photopic CS, binocular photopic VA, and mesopic CS were not significantly correlated. The values for mesopic CS with halogen and xenon glare were correlated with the mesopic CS without glare ($r = 0.612$, $P < 0.001$; $r = 0.634$, $P < 0.001$, respectively) but not with other visual function measures.

Mesopic Disability Glare

The mean difference between the mesopic CS score with/without the halogen glare source was 0.31 ± 0.10 log units (median 0.30; IQR, 0.30–0.30; range, 0.15–0.60). The MDG was 0.25 or greater in 34 (85%) subjects.

The average difference between the mesopic CS score with/without the xenon glare source was 0.33 ± 0.09 log units (median 0.30; IQR, 0.30–0.41; range, 0.15–0.60). MDG of 0.25 or greater was found in 37 (92%) subjects.

The MDG, either halogen or xenon glare, was not significantly correlated with other visual function measures, except for their respective mesopic CS with halogen and xenon glare ($r = -0.612$, $P < 0.001$; $r = -0.551$, $P < 0.001$).

Photostress Recovery Time

The mean mesopic CS photostress recovery times after halogen and xenon glare were 4.30 ± 2.15 s (95% CI 3.61, 4.99) and 4.85 ± 1.93 s (95% CI 4.23, 5.47), respectively ($P = 0.01$). No significant associations were found between photostress recovery times and their respective MDG measures of halogen or xenon glare.

Discomfort Glare

The mean de Boer rating scales for halogen glare (4.93 ± 1.82 units; 95% CI 4.34, 5.51) and for xenon glare (4.40 ± 1.78; 95% CI 3.83, 4.97) did not differ significantly ($P = 0.08$). No statistically significant associations were found between the de Boer scores and their respective MDG measures for halogen ($r = -0.31$, $P = 0.06$) or xenon glare ($r = 0.13$, $P = 0.41$).

Relationship between LOCS-III Scores and Visual Function Tests

No statistically significant correlation was found between the LOCS-III cortical, nuclear opalescence, and posterior subcapsular scores and photopic VA, CS, or mesopic CS.

The mesopic CS with a halogen glare source was significantly correlated with the LOCS-III nuclear opalescence score ($r = -0.349$, $P = 0.03$) but not with other component scores. The mesopic CS with a xenon glare source was correlated with the LOCS-III cortical score ($r = -0.330$, $P = 0.04$) but did not differ significantly from the nuclear opalescence score ($r = -0.287$, $P = 0.07$) and was not correlated with the subcapsular posterior component.

The halogen MDG was significantly correlated with the LOCS-III nuclear opalescence score ($r = 0.462$, $P = 0.003$) but not with other component scores. The xenon MDG was significantly correlated with the LOCS-III nuclear opalescence score ($r = 0.361$, $P = 0.02$) but not with other component scores. The MDG of the halogen and xenon glare sensitivity tests combined provided a significant pooled correlation with the LOCS-III nuclear opalescence

($r = 0.411$, $P < 0.001$) and cortical scores ($r = 0.226$, $P = 0.04$).

No statistically significant relationship was seen between LOCS-III scores and photostress recovery time after either halogen and xenon glare or the corresponding de Boer scale scores.

DISCUSSION

The concept of the DLS has gained acceptance for describing the aging spectrum of the crystalline lens [2–6]. However, only analyses of lens density, objective scatter index, and HOAs have been published [1–7]. No information has been published about the disrupted visual function that intermediate DLS patients experience, and only standard photopic VA and CS results have been published [1, 3, 4, 6, 7]. Consequently, we investigated for the first time the relationship between the initial sclerosis of the different lens parts and mesopic visual performance, including under diverse progressive oncoming glare sources, in subjects with intermediate stage-2 DLS. Our results indicated that the visual impairment under mesopic conditions is pronounced and even more aggravated by oncoming glare sources. Furthermore, MDG appears to be more sensitive than photopic and mesopic CS for evaluating initial phacosclerosis in DLS.

Visual impairment in lens opacification is caused predominantly by increased intraocular forward light scatter [7, 17, 18, 30–33]. VA measurements assess the impact of narrow-angle light scatter, which may make measurement of high-spatial-frequency CS unnecessary [31]. However, high-contrast VA measurements alone may be insufficient, and measurement of wide-angle light scatter is required [15, 31]. This can be evaluated directly using stray light measurements or indirectly using low-spatial-frequency CS or DG tests [31–34]; it is important to perform them binocularly [14, 19] to better reflect functional impairment in daily activities, such as the binocular task of driving [31].

In our stage-2 DLS 50- and 60-year-old study population, lens opacification did not exceed the LOCS-III score of 3 for any component in both eyes [6]. Additionally, all eyes had a CDVA of 20/25 or more, which met the driving requirements of many countries [13, 15]. Moreover, considering that standard binocular Pelli-Robson scores are typically 0.18 log units higher than monocular scores [24], 98% of our DLS patients scored well over the monocular threshold of 1.25 logCS under photopic conditions, suggested by some authors as an additional requirement for driving licensure [13, 15, 35]. However, we found that mesopic CS was significantly lower than photopic CS, on average by 0.59 logCS. This difference is broader than that observed between mesopic and photopic CS in healthy young subjects (mean, 0.40 log unit) at low spatial frequencies [36] and higher than that reported by Charalampidou et al. [37] (0.15 logCS) between mesopic and photopic conditions at medium spatial frequencies in patients with mild cataracts. Interestingly, the mesopic CS was not correlated with photopic CS or VA in our series, which, in addition to the absence of overlap between photopic and mesopic CS scores (Fig. 2), suggests that mesopic CS adds new information to the standard visual function tests in intermediate DLS patients.

DG refers to the reduced visual performance caused by a retinal veil of luminance caused by light sources [12, 17, 28, 31, 38]. The detrimental effects of increased glare sensitivity on visual function occur especially during reduced light levels (evening and nighttime) [12, 31, 38]. These effects are enhanced when the driver tries to identify low-contrast objects along the roadside [19], which has been related to traffic injuries [16]. We found that in stage-2 DLS patients, the mesopic CS with halogen and xenon glare sources further decreased visual performance (average, 0.31 and 0.33 log units, respectively). This DG is well above the 0.25 cutoff value proposed by Owsley et al. [16] in cataractous eyes using photopic Pelli-Robson CS. The difference between two increasing intensities, halogen and xenon, was not significant, suggesting that the presence/absence of a glare source is more influential than its intensity for the ranges tested. This finding agreed with previous studies reporting detrimental effects on visual performance even with low-intensity glare [20, 39].

We also found that the mesopic CS with glare sources and MDG were only moderately correlated with the mesopic CS without glare sources but not with any photopic visual function test, which indicates that adding a glare source to a mesopic CS test provides supplementary information in DLS patients. The data (Fig. 3) imply that with glare, the mesopic Pelli-Robson CS value of 0.75, and particularly below this threshold, may indicate meaningful visual impairment. These findings agreed with those of Puell et al. [38], who found that mesopic vision without glare starts to decrease around ages 51 to 60, whereas mesopic vision with glare starts to decrease around ages 41–50 [38].

Patients may be handicapped by DG and a prolonged photostress recovery time [40], which was on average 4 s and nearly 0.5 s longer after the higher-intensity xenon glare than with the relatively lower-intensity halogen glare in intermediate DLS patients. These results are well below the average 13.14 s reported after a higher-glare illumination of 320 lx and longer (10-s) exposure [13], indicating that photostress recovery time is related directly to glare intensity and duration. Ocular conditions that may affect glare recovery time are mostly age-related such as crystalline lens optical density, photopigment regeneration, and optical aberrations [41]; lens opacification playing a minor role [13]. This can explain the absence of a relationship between photostress recovery time and MDG.

While DG causes visual function impairment, discomfort glare is merely bothersome. The discomfort ratings have been correlated with illuminance [42, 43]. Discomfort with the higher-intensity xenon glare tended to be slightly greater (lower de Boer score) than the halogen counterpart in our series, although the difference was nonsignificant. Interestingly, the lack of association between the de Boer scores and halogen and xenon MDG suggested that DLS patients with more visual impairment may be unaware of the magnitude of their handicap.

We sought associations between visual function and the degree of initial phacosclerosis in DLS patients according to the LOCS-III. No components were correlated with photopic VA or CS or even mesopic CS. Conversely, measurements obtained under mesopic glare, and more significantly halogen and xenon MDG, were significantly associated with the nuclear opalescence degree and to a lesser extent the cortical component. This is explainable because the cortical component affects the optical quality more (Strehl ratio, modulation transfer function) than the scattering and CS [32]. In addition, opacity location affects ocular aberrations differently; i.e., nuclear and cortical cataracts are mostly associated with spherical and coma aberrations, respectively [7, 44]. The absence of correlations with the posterior subcapsular component may be explained by the narrow range of scores.

The current study had limitations. First, lens opacification was assessed with the LOCS-III, an accepted subjective, cost-effective grading method based on slit-lamp examination [4, 6], but interobserver and intraobserver variations can occur [4]. However, the same experienced examiner performed the assessment to assure data consistency. Second, CS was examined using the Pelli-Robson test, which only measures one spatial frequency, while grating tests define CS in various cycles/degrees [24]. However, the Pelli-Robson chart is a quick, reliable clinical test with good discriminative ability that makes CS analysis readily available in any clinic [24]. Moreover, it measures dependable CS at low spatial frequencies, which are more important for pedestrian or vehicle identification and overall road safety [13, 19]. Lastly, our sample was small but allowed identification of significant differences and associations that provided valuable insights. Larger studies are warranted to more thoroughly evaluate the visual implications of DLS and early phacosclerosis.

CONCLUSIONS

This is the first study to provide evidence-based data that support the serious visual impairment stage-2 DLS patient's experience under mesopic conditions when faced with oncoming halogen and xenon glare sources despite normal photopic VA and CS. Moreover, in intermediate DLS patients, the mesopic CS provides new

independent information over standard photopic tests, which can be further complemented by MDG testing. Actually, the latter is best correlated with the initial degrees of phacosclerosis in these patients, who may be unconscious of their visual handicap since disability and perceived discomfort glare are not closely interrelated. Therefore, mesopic CS and DG measurements are accessible tests [28] that may potentially become clinically useful to assess intermediate DLS patients, who despite having relatively good VA, may be suitable candidates for functional lens surgery [2, 3, 5]. Future studies should explore the impact of stage-2 DLS on driving performance and safety, particularly at night. In the meantime, in-office MDG testing should provide useful additional information regarding the decisions to perform lens surgery in intermediate DLS patients, and the most appropriate timing, according to the risks and benefits, which should be considered on a case-by-case basis.

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Disclosures. Alfredo Holgueras, Manuel Marcos, Elena Martínez-Plaza, Alberto López-Miguel, Alberto Mansilla and Miguel J. Maldonado confirm that no author has a financial or proprietary interest in any material or method mentioned.

Compliance with Ethics Guidelines. This study was performed after the University Clinic Hospital Ethics Committee (Valladolid, Spain) approved it (PI 15-220). The study complied with the tenets of the Helsinki Declaration of 1964; all subjects provided written informed consent.

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

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