

## ORIGINAL ARTICLE

# Forward-scattered and backward-scattered light in moderate keratoconus

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## Abstract

**Introduction:** To evaluate the backscattered light, objective scatter index (OSI) and retinal straylight in patients with moderate keratoconus and healthy control subjects.

**Methods:** A prospective observational study was developed with 33 patients in the moderate-keratoconus group (KC) and 34 in the non-keratoconus group (NKC). Corneal densitometry was obtained using Scheimpflug corneal tomography and measurements were expressed in grayscale units (GSU) over four zones within a 12.00 mm diameter around the corneal apex. A straylight meter was used to determine the amount of intraocular straylight under scotopic conditions, and the straylight parameter (LOG(s)) and test duration were recorded. The Optical Quality Analysis System based on the double-pass technique determined the OSI value.

**Results:** Significant differences were observed between the KC and NKC groups for corneal densitometry (except in the 6–10 mm zone), OSI and retinal straylight. A moderate and significant correlation was found between OSI and retinal straylight LOG(s) ( $r = 0.52$ ,  $p = 0.002$ ). Weaker and non-significant correlations were found between corneal densitometry and the other parameters analysed (i.e., OSI, retinal straylight LOG(s) and retinal straylight times).

**Conclusions:** Backscattered light, retinal straylight and the OSI show clear differences between healthy eyes and those with moderate KC. The changes present in the stages of KC evaluated in the current study (stages II and III according to the Amsler–Krumeich classification) might alter the scattering of the light entering the eye.

## KEYWORDS

backward scattering, corneal densitometry, forward scattering, keratoconus, retinal straylight

## INTRODUCTION

Keratoconus (KC) is a progressive corneal stromal thinning disorder in which the cornea bulges outwards into a cone-like shape.<sup>1,2</sup> It is the most common primary corneal ectasia with a multifactorial aetiology, including genetic and environmental factors.<sup>3</sup> KC causes a myopic shift and irregular astigmatism, but its progression can also lead to

thinning and protrusion.<sup>4</sup> These changes are caused by a disturbance of the fragile balance of well-distributed corneal extracellular matrix and cells.<sup>5</sup> In advanced cases, this disarrangement may lead to corneal scarring and hydrops with evident opalescence.<sup>6</sup> In the first stages of the disease, the patient is typically asymptomatic, but as it progresses, the visual symptoms get worse. In the advanced stages, common symptoms of KC are blurry and distorted vision,

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sensitivity to light and glare, loss of contrast sensitivity and poorer vision under mesopic conditions.<sup>6</sup>

The anterior corneal surface is the first and largest determinant of optical power (around 70%), and as such, it is primarily responsible for the optical aberrations of the eye.<sup>7</sup> Therefore, any change that occurs in the cornea, such as decreased transparency, can affect the patient's vision significantly. This reduced transparency may be the reason for backscattered light in the different regions of the cornea, which can be detected by non-invasive Scheimpflug analysis with the corneal densitometry map.<sup>8</sup> Scattering of light at the cornea can lead to high values of straylight, which represents the light entering the eye but not reaching the retina in a focused manner, thereby forming a veil of light over the retina. The effect of glare sensitivity resulting in visual impairment is called disability glare, which is defined by the CIE (*Commission Internationale d'Eclairage*) as retinal straylight, a result of studies that showed that disability glare can be understood on the basis of light scattering in the eye.<sup>9</sup> This disability glare represents the loss of retinal image contrast as a result of intraocular light scatter, or straylight, and it is one of the most widely reported symptoms by patients with KC.<sup>10</sup>

For those reasons, as KC progresses, not only is the perceived vision altered but also the optical quality of the eye and the patient's quality of life are affected. It is important to highlight that in moderate and advanced KC, in many cases, the loss of visual function as perceived by the patient is disproportionate to that reflected by clinical measurements.<sup>11</sup> Retinal straylight plays a crucial role in everyday life because of its impact on driving, particularly at night.

The objective scatter index (OSI) is a single number quantification derived from a double-pass retina point imaging device determined by examining the ratio of peripheral (scattered) to central (unscattered) light. This index provides information on the relevant forward scatter that affects vision. It has been reported that the OSI is increased in keratoconic eyes, and it could be considered as a clinically significant parameter to stage KC.<sup>12</sup>

Because straylight represents an aspect of vision quality, both forward-scattered and backward-scattered light may be significant parameters in the evaluation of patients with KC. Therefore, the purpose of this study was to evaluate three scatter metrics in patients with moderate KC (i.e., stages II and III based on the Amsler–Krumeich classification)<sup>13</sup> and also to compare these parameters with those obtained in normal subjects to investigate whether they can help in screening for KC. Therefore, backscattered light, retinal straylight and the OSI were analysed.

## METHODS

A prospective observational study was developed. A total of 67 eyes in 67 patients were classified into two groups: a KC group of 33 patients and a non-keratoconus (NKC) group of 34 patients.

### Key points

- A reduction in corneal transparency due to keratoconus can cause an increase in scattered light across different regions of the cornea, resulting in visible backscatter and high values of straylight, thus forming a veil of light scattered over the retina.
- The amount of backscattered light, retinal straylight and the objective scatter index show clear differences when comparing healthy eyes with those having moderate keratoconus.
- Corneal densitometry, straylight measurement and the objective scatter index are parameters that can be used for the evaluation of keratoconus.

The sample size was calculated based on previous data from Pircher et al.,<sup>14</sup> who evaluated the change in backward-directed and forward-directed corneal straylight in eyes after corneal collagen crosslinking. The pre-operative corneal densitometry value was the reference selected for the calculation. Accepting an alpha and beta risk of 0.05 and 0.2, respectively, in a two-sided test, 33 subjects were necessary to recognise a statistically significant difference  $\geq 1$  unit. The assumed standard deviation was 2.01 GSU. A drop-out rate of 0% was assumed because all tests were performed at the same visit. For comparison, Krumeich et al.<sup>13</sup> included 31 patients.

General inclusion criteria included no contact lens wear within the last 6 months, at least 18 years of age and no previous ocular surgery. For the KC group, patients had previously been diagnosed with the condition (stages II and III according to Amsler–Krumeich classification)<sup>13</sup> but had not received any treatment. The clinical characteristics of stage II KC included myopia and/or astigmatism  $>5.00$  to  $\leq 8.00$  D, a keratometric reading  $\leq 53.00$  D and pachymetry  $\geq 400$   $\mu\text{m}$ . Stage III characteristics were induced myopia and/or astigmatism  $>8.00$  to  $\leq 10.00$  D, a keratometric reading  $>53.00$  D and pachymetry of 200–400  $\mu\text{m}$ .<sup>15</sup>

For the NKC group, non-pathological, that is, healthy subjects were included, with normal anterior and posterior corneal topography and regular corneal astigmatism  $\leq 1$  D.

Informed consent for participation was obtained from each patient. The protocol adhered to the tenets of the Declaration of Helsinki. The study was approved by the Ethics Committee of the Hospital Clínico San Carlos (C.I. 17/461-E), Madrid, Spain.

A comprehensive ophthalmological examination was performed. Corrected distance visual acuity (CDVA) was measured using an ETDRS chart<sup>16</sup> under photopic conditions. A Scheimpflug tomographer (Pentacam HR, [penta.com](http://penta.com)) was used to measure central corneal thickness (CCT), the thinnest corneal thickness (TCT), mean

keratometry (Km) and the anterior chamber depth measured from both the corneal endothelium (ACDen) and epithelium (ACDep).

## Corneal densitometry

Corneal densitometry was obtained with the Pentacam HR, taking a series of 25 images (1003 × 520 pixels) from different meridians with a uniform blue light source. The program locates the corneal apex and analyses a 12-mm-diameter area around it, expressing the output in grayscale units (GSU). The GSU defines a minimum light scatter of 0 (maximum transparency) and maximum light scatter of 100 (minimum transparency). Measurements included the 12-mm-diameter corneal area subdivided into four concentric radial zones pre-entered in the software: a central zone 2 mm in diameter, a first annulus extending from 2 to a 6-mm-diameter circle, a second annulus extending from 6 to 10 mm and the total cornea.<sup>6</sup>

## Straylight measurements

A straylight meter (C-Quant, [en.oculus.de](http://en.oculus.de)) was used to quantify the intraocular straylight. With this psychophysical method, intraocular straylight can be measured by compensating for the amount of straylight (induced by a peripheral light source) on a test field, with counterphase flickering of the test field of variable intensity. Thus, the intensity of the counterphase flickering required to offset the flicker induced by the straylight represents a measure of intraocular straylight. The test field was divided into two half fields, with and without counterphase compensation light. The patient stated which of the two fields had stronger flicker. This method is known as compensation comparison. A convenient way to express straylight measurements is in terms of the logarithm of the straylight parameter (s), denoted as LOG(s).<sup>17,18</sup> The straylight values measured with the

C-Quant were performed under scotopic conditions, and the time spent performing the test was also recorded.

## Optical quality analysis system – High-definition analyser

The Optical Quality Analysis System™ ([visiometrics.com](http://visiometrics.com)), based on the double-pass method, provides an objective clinical evaluation of the optical quality of the eye. A double-pass retinal point imaging device is based on imaging a point source onto the retina, whereupon the light is reflected and recorded after its second pass through the ocular media. From the double-pass image, the ocular point spread function (PSF) and the modulation transfer function can be obtained.<sup>19</sup> OSI is defined as the ratio of the amount of light within an annular area of 12–20 arcmin to that recorded within a circular area having a 1 arcmin radius, centred on the central peak of the acquired double-pass PSF image.<sup>19</sup> The higher the OSI value, the greater the level of intraocular scattering. This system is based on an unequal pupil configuration,<sup>20</sup> with a diameter of 2 mm in the entrance pupil and a variable diameter for the exit pupil. In this study, the diameter of the exit pupil was set to 4 mm for the entire procedure. All measurements were recorded by the same expert technician.

## Statistical analysis

Descriptive and inferential data analysis were carried out using IBM SPSS Statistics Base 22.0 for Windows. ([ibm.com](http://ibm.com)). Data are expressed as the mean ± standard deviation and range. The Shapiro–Wilk test was used to assess the normality of each parameter. Parametric (Student's *t*-test) and non-parametric (Wilcoxon–Mann–Whitney) tests were used for comparison between groups. Correlations among variables were evaluated using the Pearson and Spearman coefficients. Differences were considered statistically significant for  $p < 0.05$ .

**TABLE 1** Descriptive data for both groups.

	NKC		KC		p-Value
	Mean ± SD	Range	Mean ± SD	Range	
Age (years)	34.3 ± 11.1	18 to 55	37.3 ± 10.4	18 to 54	0.24
CDVA (logMAR)	−0.06 ± 0.08	−0.2 to 0.1	0.27 ± 0.23	−0.1 to 1.0	<0.001*
Km (D)	43.1 ± 1.4	40.3 to 46.1	46.6 ± 2.6	42.1 to 52.3	<0.001*
CCT (µm)	546 ± 29	493 to 611	485 ± 40	393 to 544	<0.001*
TCT (µm)	541 ± 30	485 to 609	459 ± 38	374 to 520	<0.001*
ACDen (mm)	3.08 ± 0.47	2.26 to 4.49	3.19 ± 0.37	2.28 to 4.04	0.23
ACDep (mm)	3.63 ± 0.47	2.81 to 4.90	3.68 ± 0.36	2.79 to 4.45	0.59

Abbreviations: ACDen, anterior chamber depth measured from the endothelium; ACDep, anterior chamber depth measured from the epithelium; CCT, central corneal thickness; CDVA, corrected distance visual acuity; KC, patients with keratoconus stage II and stage III; Km, mean keratometry; NKC, non-keratoconus; SD: standard deviation; TCT, thinnest corneal thickness.

\* $p < 0.05$ .

## RESULTS

A total of 67 eyes from 67 patients were evaluated: 33 patients in the KC group and 34 in the NKC group. The sex distribution was 55.9% (19) male and 44.1% (15) female in the NKC group, whereas it was 60.6% (20) male and 39.4% (13) female in the KC group. Table 1 shows the age,

**TABLE 2** Corneal densitometry values for the total corneal thickness over 0–2, 2–6, 6–10 mm and total zone for both groups.

Total corneal thickness region	NKC	KC	p-Value
0–2 mm zone	16.4 ± 0.9	19.3 ± 3.5	<0.001*
2–6 mm zone	15.2 ± 0.9	16.4 ± 3.2	<0.001*
6–10 mm zone	17.0 ± 5.0	17.7 ± 3.5	0.18
Total	17.6 ± 2.6	18.8 ± 2.7	0.02*

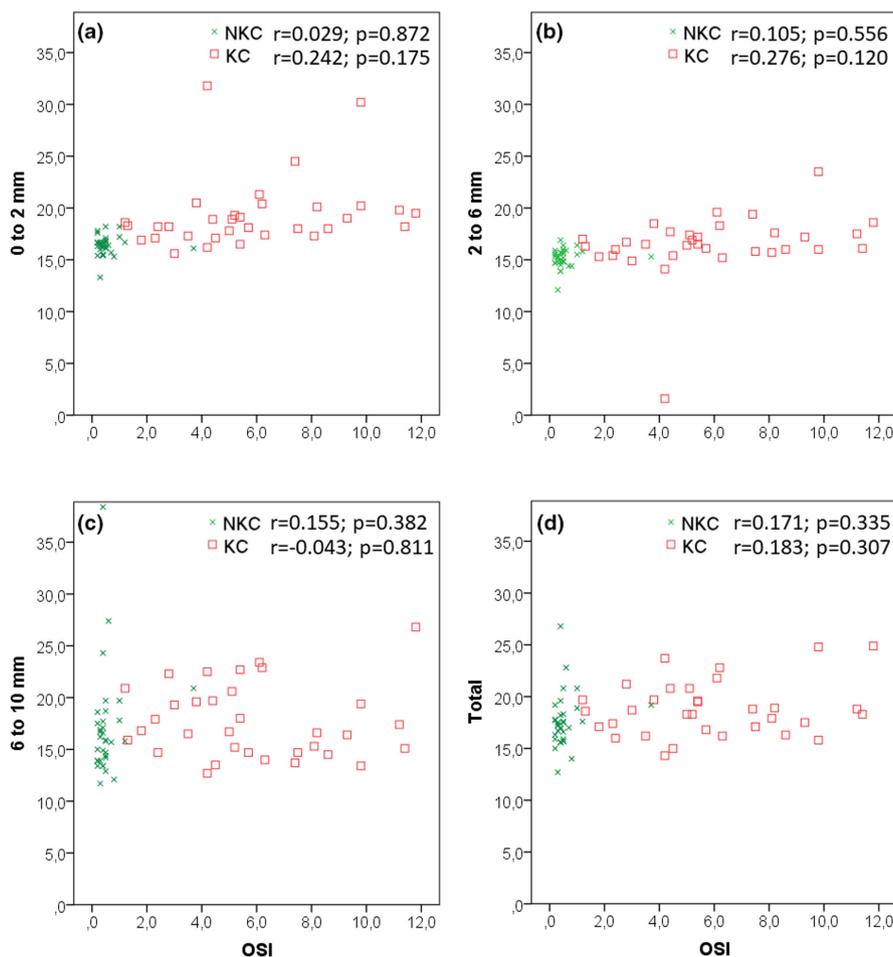
Abbreviations: NK, non-keratoconus; KC, patients with keratoconus stage II and stage III; 0–2 mm zone: circular area 2 mm in diameter at the centre of the cornea; 2–6 mm zone: 2–6 mm annular area; 6–10 mm zone: 6–10 mm annular area; total zone: circular area 12 mm in diameter at the centre of the cornea.

\* $p < 0.05$ .

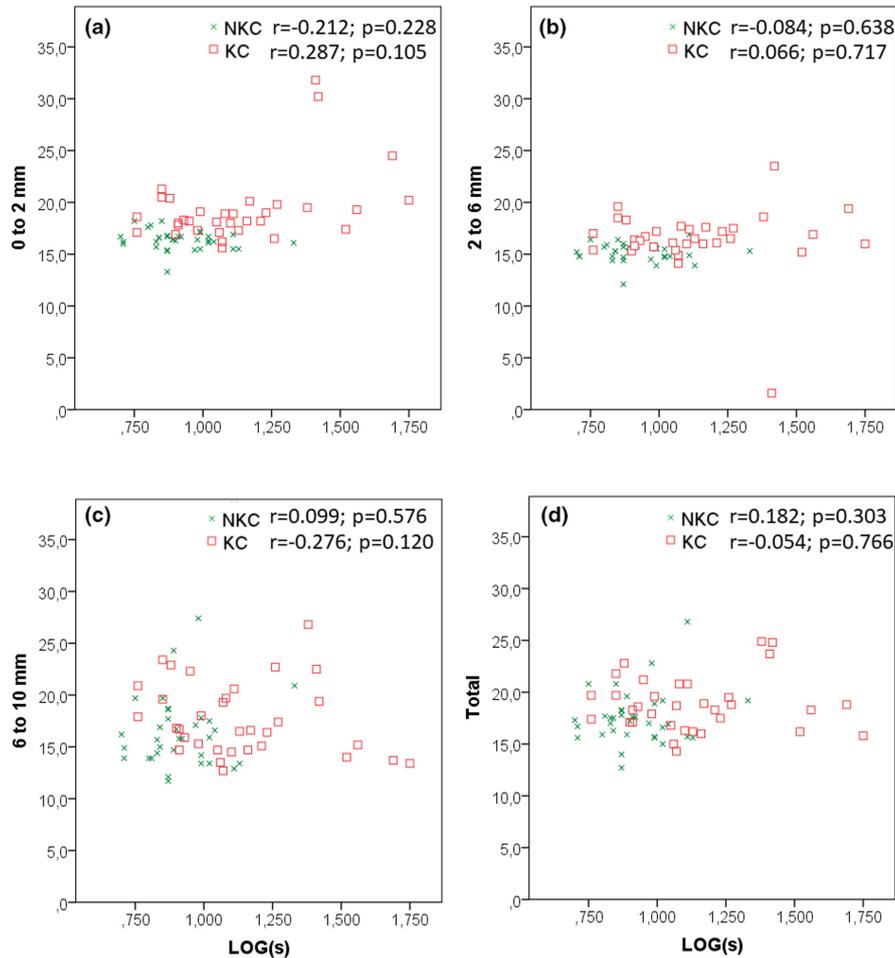
CDVA, Km, pachymetry and ACD values for each group. The mean age for the total sample was  $35.79 \pm 10.76$  years (range: 18–55 years) and no significant differences in age, ACDep or ACDe were observed between the two groups. However, significant differences between the KC and NKC groups were found for CDVA, Km, CCT and TCT (see Table 1). Furthermore, significant differences between the two groups were noted for all densitometric values except within the 6–10 mm zone (Table 2).

Analysis indicated significant differences in the OSI between the groups with values of  $0.56 \pm 0.61$  and  $5.85 \pm 2.97$  for the NKC and KC groups, respectively ( $p < 0.01$ ). In addition, significant differences in retinal straylight were observed; retinal straylight (LOG(s)) values were  $0.91 \pm 0.13$  (NKC) and  $1.13 \pm 0.25$  (KC) ( $p < 0.01$ ). Time of examination was  $91.62 \pm 18.99$  s and  $105.61 \pm 22.38$  s for the NKC and KC groups, respectively ( $p = 0.004$ ).

Correlations between densitometry values for each evaluated zone, as well as OSI values and retinal straylight items (LOGs and Time) are shown in Figures 1, 2 and 3, respectively, for each group. Figure 4 shows the correlation between the OSI values and retinal straylight items



**FIGURE 1** Correlations between densitometry values for each zone and objective scatter index (OSI) values for both groups. (a) Correlation between circular area 2 mm in diameter at the centre of the cornea (0–2 mm zone) and OSI. (b) Correlation between 2 and 6 mm annular area (2–6 mm zone) and OSI. (c) Correlations between 6 and 10 mm annular area (6–10 mm zone) and OSI. (d) Correlations between circular area 12 mm in diameter at the centre of the cornea (Total) and OSI. NK, non-keratoconus; KC, patients with keratoconus stage II and stage III.



**FIGURE 2** Correlations between densitometry values for each zone and retinal straylight (LOG(s)) values for both groups. (a) Correlation between circular area 2 mm in diameter at the centre of the cornea (0–2 mm zone) and LOG(s). (b) Correlation between 2 and 6 mm annular area (2–6 mm zone) and LOG(s). (c) Correlations between 6 and 10 mm annular area (6–10 mm zone) and LOG(s). (d) Correlations between circular area 12 mm in diameter at the centre of the cornea (Total) and LOG(s). NKC, non-keratoconus; KC, patients with keratoconus stage II and stage III.

(LOG(s) and Time) for both groups. A significant correlation between OSI and LOGs was observed in the KC group ( $r = 0.52$ ;  $p = 0.002$ ).

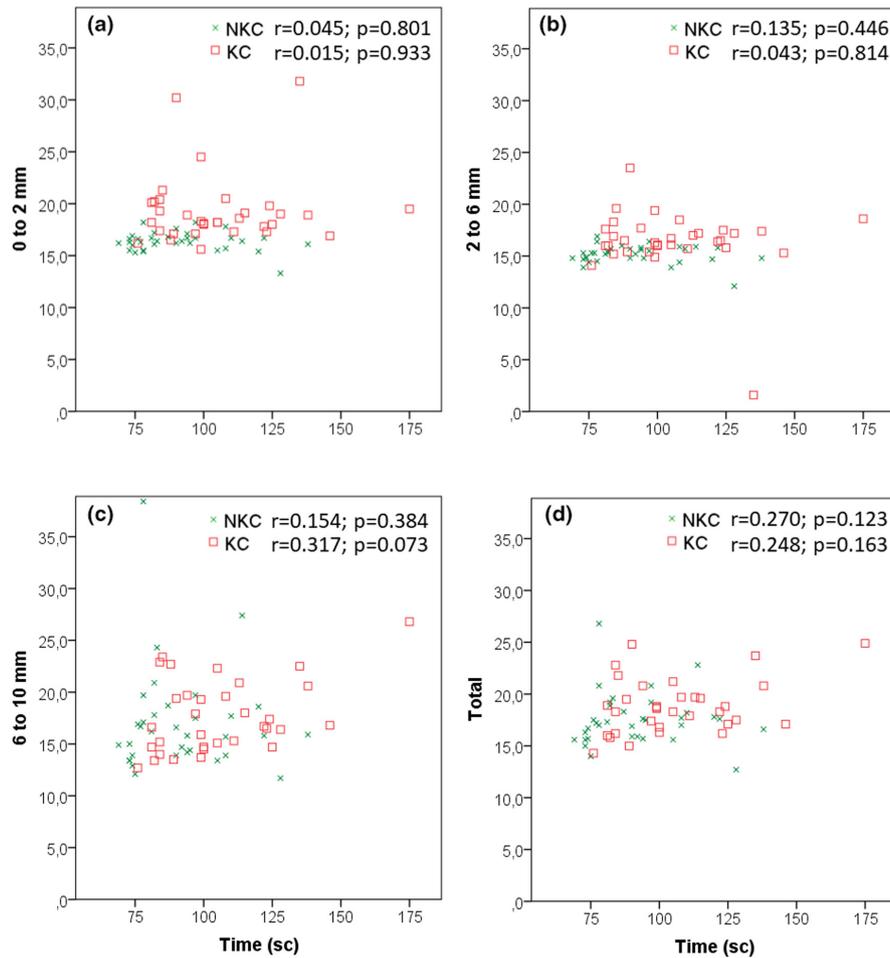
## DISCUSSION

Corneal backscatter per se does not impact vision because backscattered light does not affect retinal image quality, whereas forward light scatter degrades the retinal image and can affect contrast perception,<sup>21</sup> inducing light sensitivity and photophobia in patients with KC. While some authors have analysed the association between forward and backward scatter in eyes undergoing penetrating keratoplasty<sup>22</sup> as well as in patients with dry eye,<sup>23</sup> to the authors' knowledge this is the first study that evaluated these correlations in moderate keratoconic eyes that had not previously undergone surgical procedures.

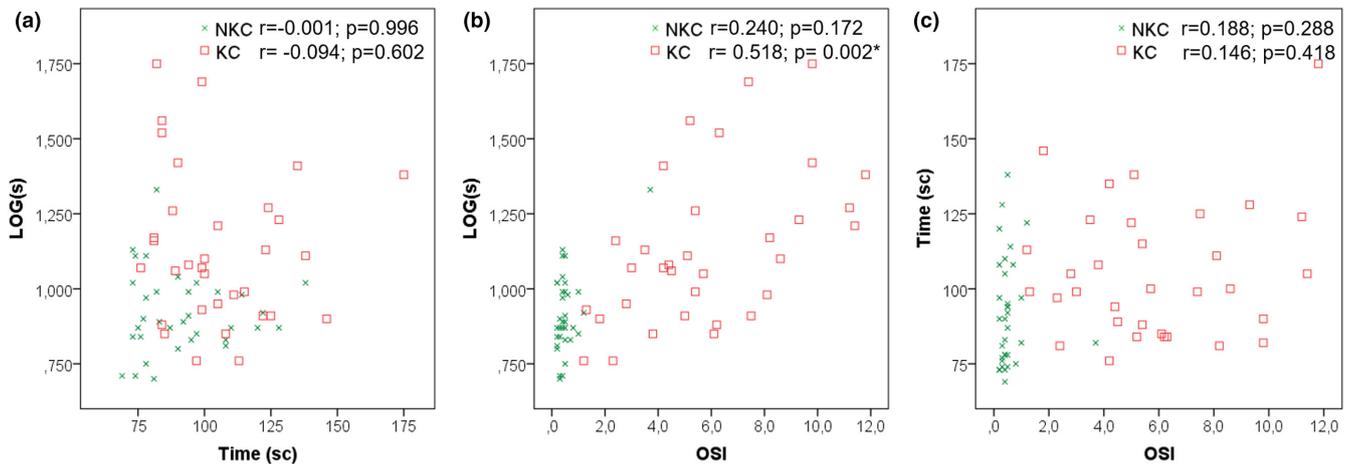
Corneal densitometry, measured to evaluate changes in corneal transparency, showed significant differences between the KC and NKC groups for all the annuli analysed except for the 6–10 mm zone. These densitometric results

are in agreement with previous studies.<sup>14,24,25</sup> Regarding the NKC results, Wu et al.<sup>24</sup> found slightly lower densitometric values for the control group compared with the current study, probably due to differences in age, which has been shown to correlate with corneal densitometry.<sup>25</sup> For the KC group, Pircher et al.<sup>14</sup> obtained similar preoperative densitometric values before a cross-linking procedure. Comparing KC and NKC eyes, Anayol et al.<sup>25</sup> found significant differences in the 0–2 and 2–6 mm annuli and total diameter. These findings are consistent with the results of the present study. Furthermore, a trend of increased densitometry as the KC stage evolved has also been noted.<sup>6</sup> Shen et al.<sup>26</sup> observed significantly higher densitometry in their KC group, while Koc et al.<sup>27</sup> reported significant differences between subclinical KC, clinical KC and NKC groups for the 0–2 and 2–6 mm zones.

Based on the previous literature and the findings of the current study, it seems that KC subjects exhibit significantly higher corneal densitometry compared with controls, mostly at the central cornea (0–2 and 2–6 mm annular zones). Both Tomlinson<sup>28</sup> and Edmund<sup>29</sup> reported an inferior displacement of the corneal apex with KC, noting



**FIGURE 3** Correlations between densitometry values for each zone and retinal straylight times values for both groups. (a) Correlation between circular area 2 mm in diameter at the centre of the cornea (0–2 mm zone) and time. (b) Correlation between 2 and 6 mm annular area (2–6 mm zone) and time. (c) Correlations between 6 and 10 mm annular area (6–10 mm zone) and time. (d) Correlations between circular area 12 mm in diameter at the centre of the cornea (Total) and time. NKC, non-keratoconus; KC, patients with keratoconus stage II and stage III.



**FIGURE 4** Correlations between objective scatter index (OSI) values and retinal straylight items (LOGs and time) for both groups. (a) Correlation between LOG(s) and time. (b) Correlation between LOG(s) and OSI. (c) Correlations between time and OSI. NKC, non-keratoconus; KC, patients with keratoconus stage II and stage III. \* $p < 0.05$ .

that the apex lay within 1 mm of the visual axis in the majority of keratoconic eyes. This may explain why statistically significant differences between the two groups were

not found in the area furthest away from the corneal centre, although in the current study, values were higher in the KC group.

In addition, displacement of the cone could account for the large standard deviation found in the 6–10 mm zone, both in KC and healthy eyes. Several studies have shown that corneal densitometry in eyes with KC displays a higher standard deviation in the areas away from the corneal centre. While this increase was also seen in healthy eyes, it was not significant.<sup>6,8,25</sup>

Regarding the current study, the patients included had been diagnosed with stages II and III KC according to the Amsler–Krumeich classification.<sup>13</sup> We selected this scale as it is one of the most widely used systems for the identification of KC and evaluation of progression. This scale classifies astigmatism based on four parameters (myopia and/or induced astigmatism, corneal radii, central scars and corneal thickness) without considering the cone location. Most studies agree that the cone is decentred. After reviewing the corneal topography, most subjects included here had an off-centre cone, extending its surface to the area >6 mm, which would explain the increased standard deviation in this zone.

As noted above, since straylight is an aspect of vision quality, forward and backward light scattering may be a valuable parameter to measure in KC patients. The present study evaluated LOG(s) and time of examination. Additionally, Cerviño et al.<sup>30</sup> found similar intraocular straylight values (LOG(s)) in NKC subjects to those recorded in our control group.

The findings of the present study showed a significant increase in intraocular straylight in the KC group. This result is in agreement with Jinabhai et al.,<sup>31</sup> although their sample size was smaller. Puell and Carballo-Álvarez<sup>32</sup> found correlated high straylight values measured with corneal disturbances. Both Pircher et al.<sup>14</sup> and Guber et al.<sup>33</sup> obtained similar intraocular straylight values to this study in subjects before they underwent crosslinking procedure. Also, these values are in agreement with Franssen et al.,<sup>17</sup> who associated values around 1 or more log units in patients with early cataracts or corneal disturbances compared with young normal population.

Moreover, the time of examination was significantly higher in the KC group. This result was expected due to the corneal disturbances present, but to our knowledge, there is no supporting evidence in the scientific literature showing this outcome. Additionally, Wu et al.<sup>24</sup> found a significant positive correlation between densitometry and straylight measurement for 0–2, 2–6 and 6–10 mm annuli in healthy eyes, although this correlation was weak in all cases ( $r = 0.13, 0.15, 0.16$ ;  $p = 0.04, 0.03, 0.02$ , respectively). In comparison with the findings of Wu et al.,<sup>24</sup> the results of the current study showed weak and non-significant correlations between straylight measurement (LOG(s)) and densitometry (GSU) for 0–2, 2–6 and 6–10-mm annuli ( $r = 0.21, -0.08$  and  $0.10$ , respectively), in the NKC group.

The current results indicate that the OSI may be useful to analyse intraocular scattering objectively in moderate keratoconic patients. Leonard et al.<sup>12</sup> also reported that the OSI was increased in keratoconic eyes, while Ren et al.<sup>34</sup>

reported differences in OSI between normal ( $0.44 \pm 0.18$ ) and KC eyes at stage II ( $9.88 \pm 3.86$ ). In addition, they showed good repeatability of the OSI in moderate KC. In the present study, no association was found between the OSI and retinal straylight in NKC eyes. However, in the KC group, the OSI index was significantly correlated with LOG(s) ( $r = 0.52$ ,  $p = 0.002$ ). In any case, although this correlation is significant, it had moderate weight. The size of the correlation could be influenced by our sample size, even though it was previously calculated.

One limitation of this study is that no subjective tests were included, such as questionnaires, to determine any association between the objective and psychophysical parameters and the patients' perception. Another limitation is that corneal and retinal backscatter were measured using different devices, since there is no single device that can measure both scattering parameters. Further research is needed to determine whether an association exists between corneal and retinal backscatter in higher stages of KC.

In conclusion, backscattered light, retinal straylight and the OSI values show clear and significant differences in eyes with moderate KC versus healthy eyes. These differences indicate that the clinical changes present in KC stages II and III affect the scatter of light entering the eye.

## AUTHOR CONTRIBUTIONS

**Celia Villanueva:** Conceptualization (equal); data curation (equal); formal analysis (equal); investigation (equal); methodology (equal); project administration (equal); resources (equal); supervision (equal); writing – original draft (equal); writing – review and editing (equal).

**Francesco Viviano:** Conceptualization (equal); data curation (equal); formal analysis (equal); investigation (equal); methodology (equal); project administration (equal); resources (equal); supervision (equal); writing – original draft (equal); writing – review and editing (equal).

**María García-Montero:** Conceptualization (equal); data curation (equal); formal analysis (equal); investigation (equal); methodology (equal); project administration (equal); resources (equal); supervision (equal); writing – original draft (equal); writing – review and editing (equal).

**Amalia Lorente-Velázquez:** Conceptualization (equal); data curation (equal); formal analysis (equal); investigation (equal); methodology (equal); project administration (equal); resources (equal); supervision (equal); writing – original draft (equal); writing – review and editing (equal).

**Irene Martínez-Alberquilla:** Conceptualization (equal); data curation (equal); formal analysis (equal); funding acquisition (equal); investigation (equal); methodology (equal); project administration (equal); resources (equal); supervision (equal); writing – original draft (equal); writing – review and editing (equal).

**Nuria Garzón:** Conceptualization (equal); data curation (equal); formal analysis (equal); investigation (equal); methodology (equal); project administration (equal); resources (equal); supervision (equal); writing – original draft (equal); writing – review and editing (equal).

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## CONFLICT OF INTEREST STATEMENT

None.

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