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# The effect of ageing on the ocular surface parameters

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## 1. Introduction

Ageing is a biological process that lead to a decline of biological functions and remains as the major risk factor for most of the prevalent diseases of developed countries [1]. In fact, the global population of older people is projected to be more than double its current amount by 2050, reaching nearly 2.1 billion as reported by United Nations. Nowadays, advancing age already has a profound impact on the economic, political and social processes [2]. Most components of the ocular surface experience age-related changes that might impact on the ocular surface equilibrium. Several ocular surface age-related changes have been reported in the literature such as [3] reduction in lacrimal secretion and changes on its composition [4]; reduction in functional meibomian glands and changes in lipid secretions [5]; the composition and amount of the tear film changes [6] and the conjunctival development of conjunctivochalasis [7]. Furthermore, the corneal sensitivity is reduced, epithelial and endothelial basement membranes increase its thickness, the number of keratocytes decrease [8] and there is an increased loss of corneal endothelial cells [9]. The incidence and prevalence of ocular diseases as age-related maculopathy, liquefaction of the vitreous, glaucoma, vascular occlusive diseases, cataract and dry eye increase significantly with age [10,11].

Currently, between 5 and 50% of people suffer from dry eye disease (DED) around the world [12]. This condition was recently re-defined by the *Tear Film and Ocular Surface Society* (TFOS) as *"multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles"* [13]. According to recent epidemiological studies, the prevalence of DED increases significantly and shows a linear association with age [12]. Moreover, it has been observed that the escalating prevalence of DED signs shows a greater increase than for a diagnosis based on symptoms. Regarding prevalence by sex, women with increased age show a higher DED prevalence than males, though there is considerable variability [12]. In fact, Guillon et al. [14] found higher tear film evaporation in older patients suggesting that it may be a significant contributing factor to DED in that population. Additionally, they found higher evaporation in women than in men in the 45 and over age group. It could explain the higher prevalence of DED complaints in the older women population [14].

Decades of knowledge about DED has been collected within the new DEWS II report [15] that confirm the great impact of this multifactorial disease on the ocular surface and on the lifestyle of the people who suffer from it, mostly from aged 40 when the presbyopia arises [12,16]. From these epidemiological data and considering that the most prevalence condition related with ageing is presbyopia [16], there are many patients worldwide in which both presbyopia and DED co-exist. Currently, multifocal contact lenses (MCLs) [17,18] and multifocal intraocular lenses (IOLs) [19] are both well-established and an effective way to compensate the presbyopia, reducing spectacle dependency. The ocular surface changes related to ageing may adversely affect the optical quality of the eye and could have a detrimental effect on the success of these treatments. For example, in the case of IOL implantation, optimal pre-surgical ocular conditions are required in order to avoid risks such as severe DED, inaccurate IOL power estimation [20] and ocular discomfort after IOL [21]. Despite the fact that most of the research studies conducted until now have demonstrated that MCLs provide good visual quality results [17,22–27], the prescription rate

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[28,29]) is low. Although many factors could be behind this low adherence, it should be noted that the CLs materials are the same as monofocal CLs.

For this reason, the main aim of this study is to assess the effect of ageing on the ocular surface parameters that would affect the MCLs fitting and even the IOL implants in this population.

## 2. Material and methods

### 2.1. Patients

This study was reviewed and approved by the Ethics Committee of San Carlos University Hospital (Madrid) and all the procedures followed the tenets of the Declaration of Helsinki. Written informed consent was obtained from all included participants after explanation of the purpose and possible consequences of the study. Exclusion criteria was: age < 18 years, participant unable to complete the questionnaire or understand the procedures or contact lens wore in the past 24 h before the study. A total of 110 participants were included, and were divided into three age groups: group A (61 participants; < 42 years), group B (24 participants; 42–65 years) and group C (24 participants; > 65years). This classification by age was done according the effect of the ocular surface changes may have on several optical corrections for presbyopia. The first group is composed by young adults (< 42 years) who do not experience presbyopia yet or begin to experience early symptoms. The second group is composed by presbyopes (42–65) who are eligible for MCLs wear and the third group are advanced presbyopes (> 65 years) presenting smaller pupils size, lens alterations and who could be benefited by IOL implantation instead of MCLs.

### 2.2. Clinical signs and symptoms assessment

#### 2.2.1. Symptomatology assessment

During the clinical examination, patients were required to complete five of the most common Dry Eye Questionnaires used in the clinical setting: The Ocular-surface-disease-index (OSDI) [30], Mcmonnies (MQ) [31], the standard patient evaluation of eye dryness (SPEED) [32], the Symptom Assessment in Dry Eye (SANDE) [33] and the Dry Eye Questionnaire (DEQ-5; short version) [34].

#### 2.2.2. Tear film osmolarity

Tear film osmolarity (TFO) was measured using the TearLab Osmolarity System (TearLab Corp, San Diego, CA, USA) in both eyes of each participant according to the manufacturer's instructions. It was conducted before other measurements in order to avoid reflex tearing or the instillation of any dye that could affect the results. One measurement per eye was performed but only the right eye (OD) and the difference between both eyes (intereye variability) of each patient were included in the analysis.

#### 2.2.3. Keratograph 5M

All the participants underwent imaging with the Keratograph 5M (K5M; Oculus GmbH, Wetzlar, Germany) equipped with a modified tear film scanning function. Three measurements of the tear meniscus height (TMHk), first break-up of the tear film (NIKBUT first), the average time of all tear film breakup incidents (NIKBUTavg), bulbar redness (BR) and limbal redness (LR) were obtained automatically by Oculus K5M software according to the manufacturer's instructions. The average of the measurements from OD of each participant was used for the statistical analysis. The meibography was performed using the K5M infrared camera system. Meibomian gland (MG) dropout of the upper and lower eyelid was graded subjectively by the examiner using the meiboscore (grade 0, no gland loss; grade 1, area of gland loss < 33% of the total gland area; grade 2, area of gland loss 33%–67%; and grade 3, area of gland loss > 67%) [35]. The meiboscore for each eyelid was summed to give a total score of 0–6.

#### 2.2.4. Ocular surface examination and lid margin Assessment/MG grading

Slit-lamp examination of the cornea, conjunctiva and eyelids (from the OD of each participant) was performed under diffuse illumination using ×10–×16 magnification. Before the fluorescein instillation, lid abnormalities and meibomian gland grading were observed and scored according to Foulks/Bron scoring [36] as recommended by the Diagnosis Subcommittee from International Workshop on Meibomian Gland Dysfunction [37]. The lid margin and MGs features used for the statistical analysis were as follows: the eyelid margin thickness was assessed on a scale from 1 to 5: 1–2 = thin; 3 = normal; 4–5 = thick. The meibum quality from the central 8 MGs of the lower eyelid was assessed on a scale from 0 to 3: 0 = clear meibum readily expressed; 1 = cloudy meibum expressed with mild pressure; 2 = cloudy meibum expressed with more than moderate pressure; 3 = meibum could not be expressed even with strong pressure. The number of functional MGs was assessed on a scale from 0 to 3: 0= > 5 glands expressible; 1 = 3–4 glands expressible; 2 = 1–2 glands expressible; 3 = no glands expressible. Lid wiper epitheliopathy (LWE) of the upper and lower lid was assessed using a combination of fluorescein and lissamine green (Korb Protocol B). The higher of the final fluorescein or lissamine green staining were used as LWE severity grade (0 = absent, 1 = mild, 2 = moderate and 3 = severe) [38].

Corneal integrity was assessed by instilling fluorescein dye and after that corneal staining was graded using the Oxford scoring scheme [39]. The tear film breakup time (BUT) was measured three times with a stopwatch and averaged for analysis. Furthermore, bulbar conjunctival integrity was assessed using lissamine green and graded using the Oxford scoring scheme.

#### 2.2.5. Tear film volume

Schirmer's test was performed with topical anaesthesia (Colirio Anestésico Doble®, Alcon Laboratories, Spain) as the final test performed in the examination. Before starting, one drop of topical anaesthesia was instilled on the conjunctival lower fornix of the OD, 5 min prior to the test. Afterwards, the Schirmer strip (35-mm Whatman filter paper; Tiedra Laboratories, Spain) was placed in the lower conjunctival sac at the junction of the lateral and middle thirds (avoiding touching the cornea) and the length of wetting was recorded after 5 min. The participants were seated at rest and their eyes closed during the test.

#### 2.2.6. Study protocol

As shown in Fig. 1, automated measurements and clinical examination were performed in the following order to minimize the effect of the previous measurement: TFO by the TearLab System; TMHk, BR, LR, NIKBUT-first, NIKBUTavg, by K5 M; ocular surface examination and MGD grading, ocular surface staining using fluorescein, TBUT, conjunctival staining using lissamine green dye by slit lamp; meibography by the K5M and Schirmer test with topical anaesthesia. A 5-min interval between each test was established, and all tests were performed in the same order. All the measurements were performed by the same examiner.

### 2.3. Data analysis

Statistical analysis was performed using SAS software, version 9.4 (SAS Institute, Inc., Cary, NC, USA). Normality of the data distribution was tested using the Kolmogorov–Smirnov test. ANOVA test and Kruskal–Wallis test were used for comparisons between age groups. When statistically significant differences were found, post hoc tests were performed for multiple comparisons (Duncan's Test for ANOVA and Bonferroni for Kruskal- Wallis). T-student and Wilcoxon Two-Samples test were used for comparisons between gender groups. Correlations among variables were assessed through Pearson and Spearman coefficients. The correlations were considered strong

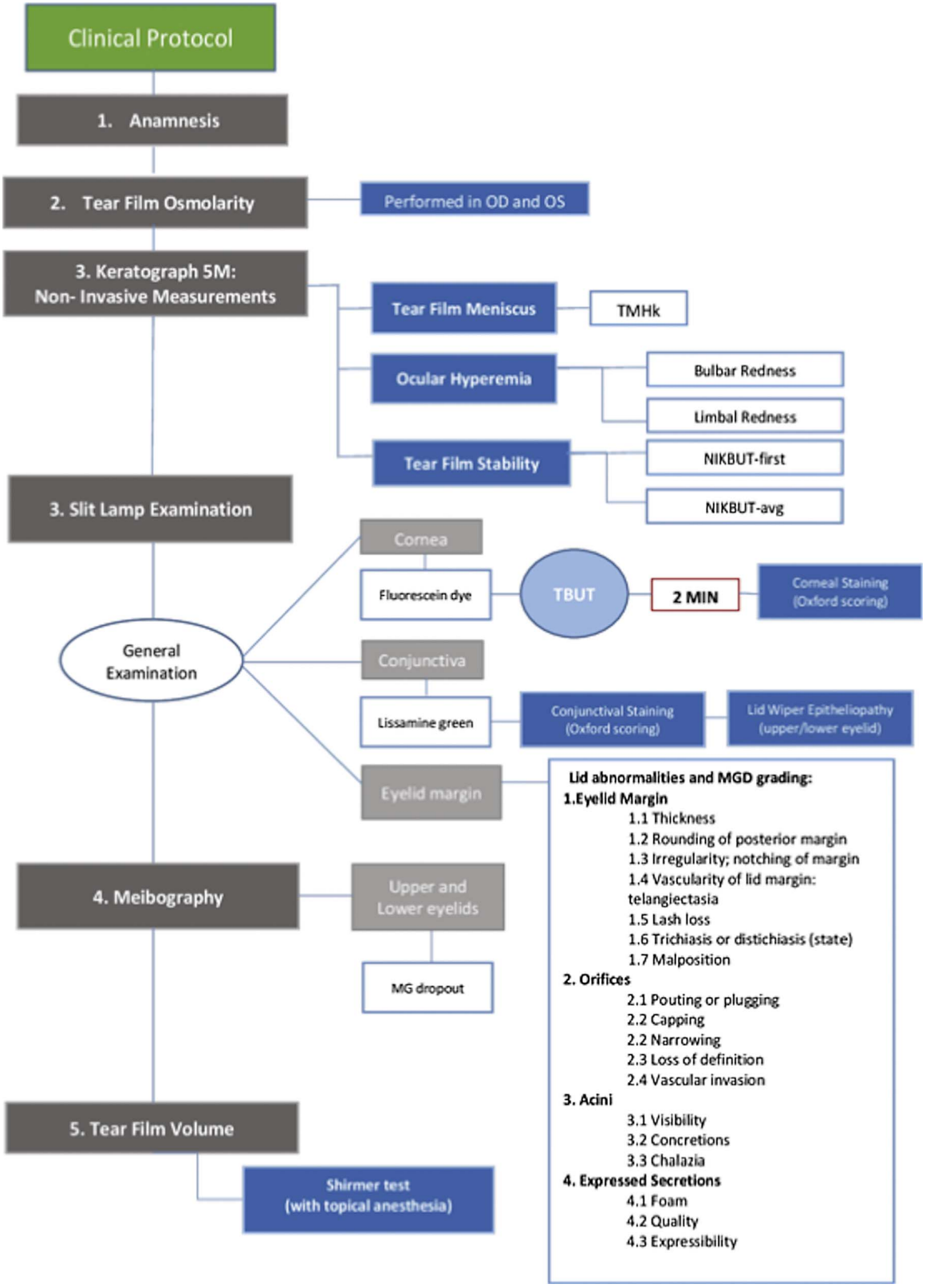


**Fig. 1.** Flow diagram of study protocol.

if > 0.80, moderately strong if between 0.5 and 0.8, fair within the range of 0.3 and 0.5 and poor if < 0.30 [40]. The values are expressed as mean ± SD and the significance level was set $p < 0.05$ with > 95% of confidence level.

## 3. Results

A total of 110 participants were enrolled in the study (70 women and 40 men). The mean age of the participants was 43.8 ± 19.4 years (ranging from 19 to 88 years).

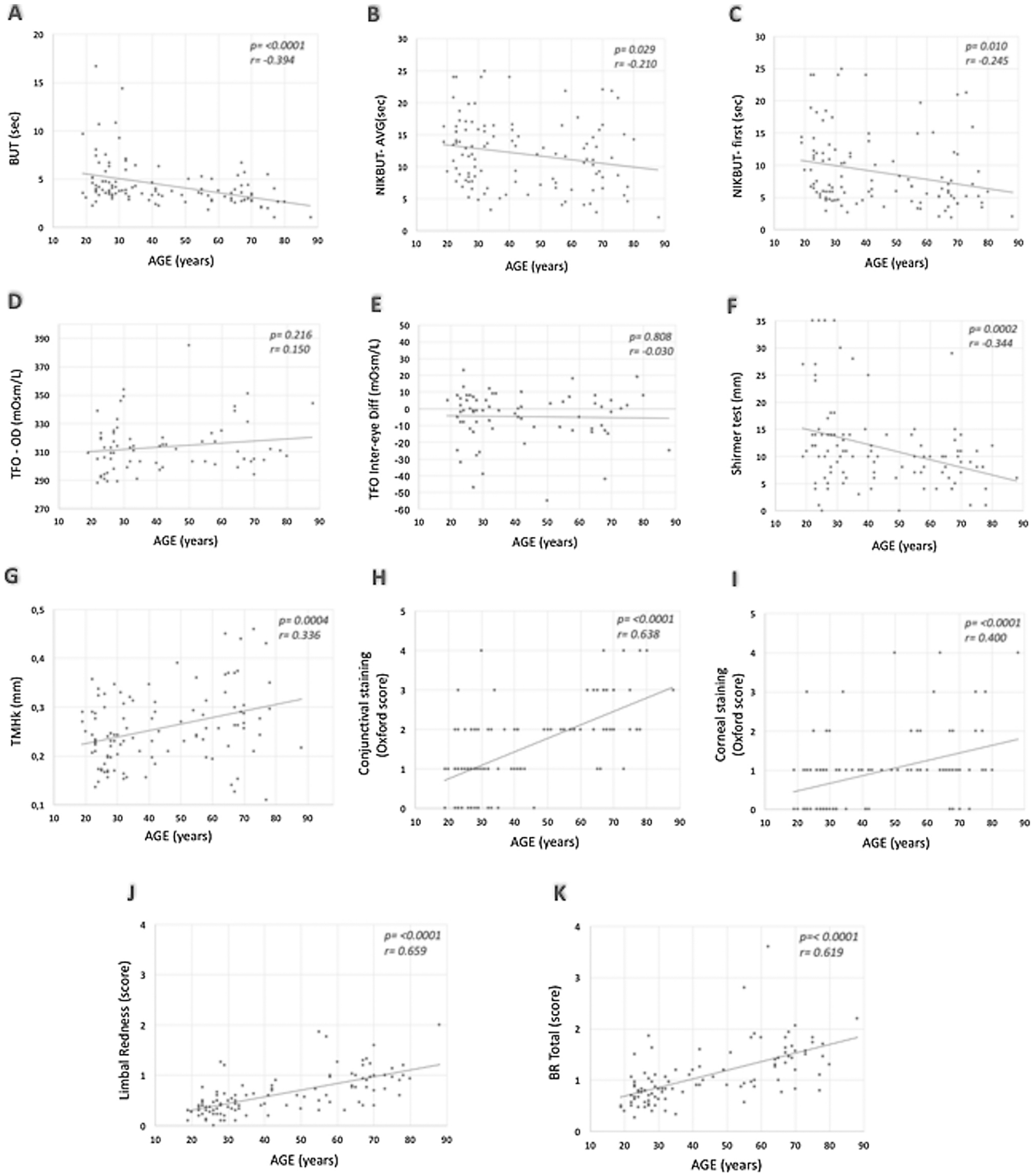


**Fig. 2.** Correlations between the Keratograph K5M parameters/several clinical parameters and Age: (A) BUT measured using fluorescein dye; (B) NIKBUTavg measured with the K5M; (C) NIKBUT first measured with the K5M; (D, E) TFO from OD measured with TearLab Osmolarity System; (F) Shirmer test performed with topical anaesthesia; (G) TMHk measured with the K5M; (H) Conjunctival staining graded the Oxford scoring scheme; (I) Corneal staining graded the Oxford scoring scheme; (J) Limbal Redness measured with the K5M and (K) BR Total measured with the K5M (r, Pearson correlation coefficient).

A negative correlation was observed between BUT and NIKBUT (first and average) with age (fair; $r = -0.394$, $p < 0.0001$; poor; $r = -0.210$, $p = 0.029$; poor; $r = -0.245$, $p = 0.010$, respectively) (see Fig. 2A, B, 2C).

As it is shown in Figs. 2D and E, TFO from OD and TFO inter-eye difference showed no significant correlation with age (poor; $r = 0.150$, $p = 0.216$ and poor; $r = -0.030$, $p = 0.808$, respectively).

Schirmer test (see Fig. 2F) showed a negative correlation with age (fair; $r = -0.344$, $p < 0.0001$). While TMHk showed a positive correlation with age (fair; $r = 0.336$, $p = 0.0004$) (see Fig. 2G).

Regarding staining and redness, significant positive correlations were observed between corneal and conjunctival staining score with age (fair; $r = 0.400$, $p < 0.0001$ and moderately strong; $r = 0.638$, $p < 0.0001$, respectively) (see Figs. 2H and I) and also between BR and LR with age (moderately strong; $r = 0.619$, $p < 0.0001$ and $r = 0.659$, $p < 0.0001$, respectively) (see Fig. 2J and K).

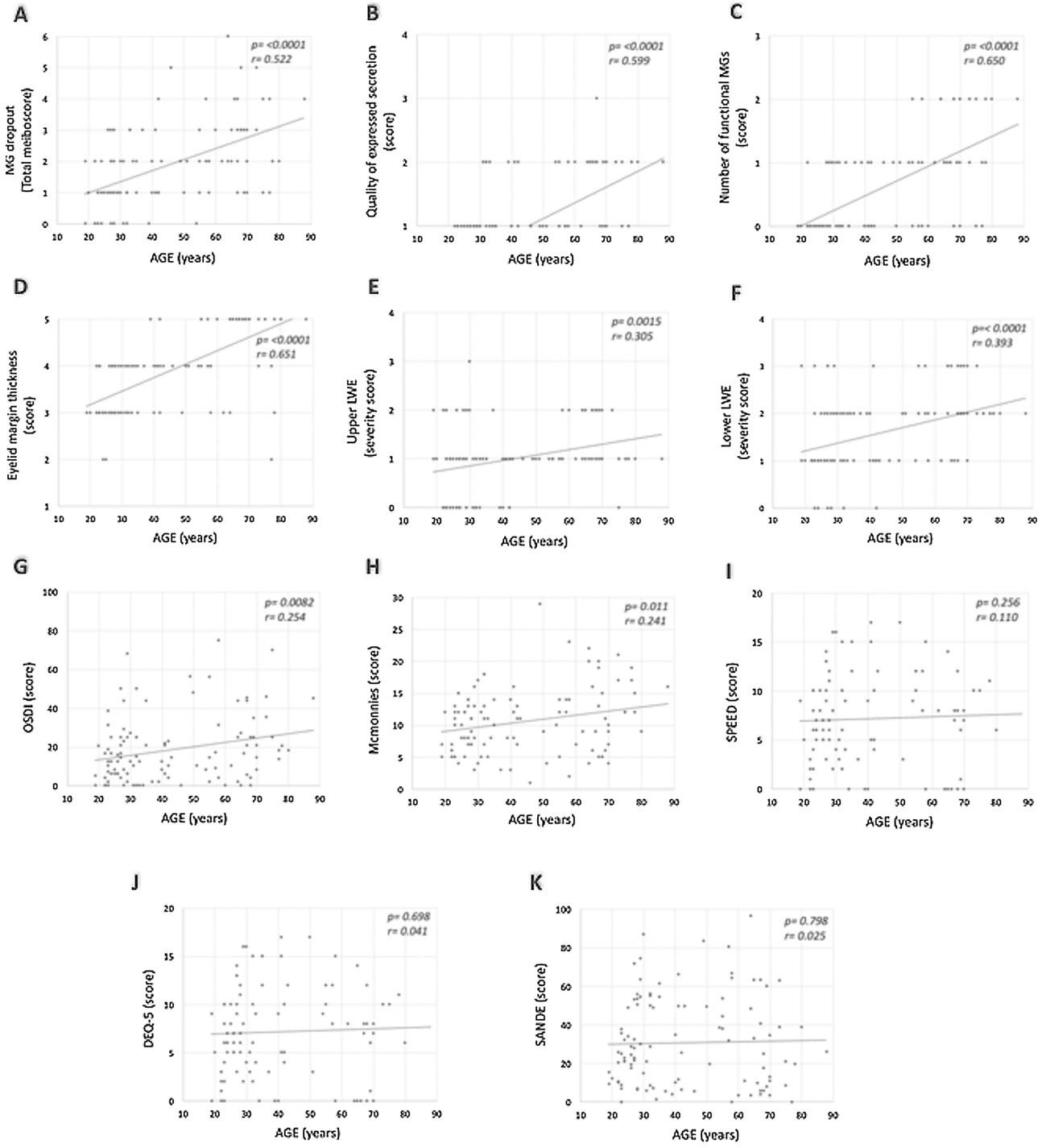


**Fig. 3.** Correlations between the ocular surface and lid margin/MG grade parameters and Age. (A) MG dropout observed by infrared meibography; (B) Quality of expressed MG secretion; (C) Number of functional MGs;(D) Eyelid margin thickness assessed by slit lamp;(E, F) LWE (upper, lower) assessed by slit lamp; (G) OSDI questionnaire;(H) Mcmonnies questionnaire; (I) SPEED questionnaire; (J) DEQ-5 questionnaire and (K) SANDE questionnaire (r, Pearson correlation coefficient).

Fig. 3 (from 3A to F) shows the lid margin and MGs features assessed. Significant correlations were observed between age and every lid margin/MGs features (MG dropout, quality of the secretion expressed, number of functional MGs, eyelid margin thickness and LWE from the upper and lower eyelid (moderately strong $r = 0.522$, $p < 0.0001$; $r = 0.599$, $p < 0.0001$; $r = 0.650$, $p < 0.0001$; $r = 0.651$, $p < 0.0001$; fair; $r = 0.305$ $p = 0.0015$; and $r = 0.393$ $p < 0.0001$; respectively).

Concerning symptomatology, both OSDI and Mcmonnies questionnaires showed a weak correlation with age (fair; $r = 0.254$, $p = 0.01$ and $r = 0.241$, $p = 0.01$, respectively). On the other hand, no significant correlations were observed between SPEED, DEQ-5 and SANDE with age (poor; $r = 0.110$, $p = 0.26$; $r = 0.041$, $p = 0.70$ and $r = 0.025$, $p = 0.80$, respectively) (see Fig. 3G–K).

Participants' demographics, clinical parameters and symptomatology scores classified by age groups are shown in Table 1. The ocular surface differences between women and men was also analysed (see Table 2).

**Table 1**
Demographic information and comparison of the clinical parameters among age groups. Data are expressed as the (mean ± SD).

| | | Classified by age (years) | | |
|---|---|---|---|---|
| | | **A.** < 42 | **B.** 42 to 65 | **C.** > 65 |
| Participants (n) | | 61 | 24 | 24 |
| Age | | 28 ± 6 | 54 ± 8 | 72 ± 5 |
| Female (%) | | 59 | 75 | 54 |
| TFO | OD | 311.05 ± 16.71 | 319.12 ± 21.13 | 314.33 ± 17.79 |
| | OS | 307.10 ± 14.59 | 313.59 ± 12.94 | 308.33 ± 11.62 |
| | Intereye Diff | −3.95 ± 14.47 | −5.52 ± 16.45 | −6.00 ± 16.27 |
| Keratograph K5M | TMHk | 0.24 ± 0.05*† | 0.28 ± 0.06 | 0.29 ± 0.10 |
| | BR Total | 0.80 ± 0.31*† | 1.37 ± 0.67 | 1.50 ± 0.37 |
| | Limbal Redness | 0.40 ± 0.23*† | 0.80 ± 0.40§ | 0.99 ± 0.37 |
| | NIKBUT first | 10.22 ± 5.99 | 7.31 ± 4.20 | 7.34 ± 5.36 |
| | NIKBUT avg | 13.14 ± 5.42 | 10.47 ± 4.55 | 10.86 ± 5.80 |
| | MG dropout | 1.26 ± 0.87*† | 2.45 ± 1.56 | 2.71 ± 1.27 |
| Slit Lamp Assessment | Corneal Staining (Oxford score) | 0.61 ± 0.76*† | 1.46 ± 0.97 | 1.25 ± 1.03 |
| | Conjunctival Staining (Oxford score) | 1.07 ± 0.89*† | 1.83 ± 0.70 | 2.54 ± 0.88 |
| | BUT | 5.11 ± 2.71*† | 3.52 ± 1.03 | 3.30 ± 1.43 |
| Lid Margin Assessment and MG grading | Lid margin thickness | 3.41 ± 0.58 | 4.17 ± 0.76 | 4.71 ± 0.75 |
| | Quality of the secretion expressed | 0.61 ± 0.67*† | 1.26 ± 0.69 | 1.58 ± 0.71 |
| | Number of functional MGs | 0.21 ± 0.41*† | 0.82 ± 0.71 | 1.21 ± 0.72 |
| | LWE (upper) | 0.83 ± 0.74† | 1.13 ± 0.54 | 1.33 ± 0.58 |
| | LWE (lower) | 1.38 ± 0.78† | 1.71 ± 0.86 | 2.04 ± 0.88 |
| Shirmer test | | 14.15 ± 9.08*† | 8.58 ± 3.40 | 8.75 ± 5.77 |
| Symptomatology | OSDI | 15.34 ± 14.50† | 20.53 ± 21.00 | 25.31 ± 16.91 |
| | Mcmonnies | 9.67 ± 3.96 | 11.46 ± 6.93 | 12.00 ± 5.24 |
| | DEQ-5 | 7.01 ± 4.68 | 8.38 ± 5.30 | 6.26 ± 4.13 |
| | SPEED | 7.03 ± 4.76 | 8.25 ± 5.66 | 7.83 ± 4.35 |
| | SANDE | 29.93 ± 21.72 | 39.87 ± 27.96 | 23.55 ± 19.88 |

*Indicates a statistically significant difference between groups A and B with $p < 0.05$.
† Indicates a statistically significant difference between groups A and C with $p < 0.05$.
§ Indicates a statistically significant difference between groups B and C with $p < 0.05$.
(**Units:** TFO (mOsms/L); TMHk (mm); NIKBUT first/avg (seconds); MG dropout (meiboscore); Corneal and Conjunctival Staining (Oxford score); BUT (seconds); LWE (score))

**Table 2**
Comparison of the clinical parameters between women and men groups. Data are expressed as the (mean ± SD).

| | Classified by GENDER | | | |
|---|---|---|---|---|
| Participants (n) | | Male 40 | Female 70 | **p** |
| Age | | 41 ± 19 | 45 ± 19 | |
| TFO | OD | 312.52 ± 16.09 | 314.23 ± 19.39 | 0.702 |
| | OS | 307.03 ± 13.09 | 310.04 ± 14.08 | 0.374 |
| | Intereye Diff | −5.48 ± 15.88 | −4.19 ± 14.71 | 0.729 |
| Keratograph K5M | TMHk | 0.26 ± 0.08 | 0.25 ± 0.08 | 0.219 |
| | BR Total | 1.17 ± 0.51 | 1.03 ± 0.54 | 0.160 |
| | Limbal Redness | 0.74 ± 0.42 | 0.70 ± 0.40 | 0.604 |
| | NIKBUT first | 11.93 ± 6.64 | 7.21 ± 4.07 | 0.0001* |
| | NIKBUT avg | 14.99 ± 5.66 | 10.29 ± 4.45 | < 0.0001* |
| | MG dropout | 1.75 ± 1.17 | 1.92 ± 1.41 | 0.734 |
| Slit Lamp Assessment | Corneal Staining (Oxford score) | 0.58 ± 0.64 | 1.17 ± 1.05 | 0.002* |
| | Conjunctival Staining (Oxford score) | 1.28 ± 1.04 | 1.73 ± 1.00 | 0.018* |
| | BUT | 5.30 ± 3.34 | 3.81 ± 1.30 | 0.010* |
| Lid Margin Assessment and MG grading | Lid margin thickness | 3.93 ± 0.86 | 3.81 ± 0.86 | 0.504 |
| | Quality of the secretion expressed | 1.08 ± 0.83 | 0.93 ± 0.81 | 0.310 |
| | Number of functional MGs | 0.57 ± 0.71 | 0.58 ± 0.72 | 0.986 |
| | LWE (upper) | 0.92 ± 0.79 | 1.04 ± 0.63 | 0.397 |
| | LWE (lower) | 1.43 ± 0.81 | 1.71 ± 0.78 | 0.085 |
| Shirmer test | | 13.25 ± 9.19 | 10.87 ± 6.96 | 0.160 |
| Symptomatology | OSDI | 12.44 ± 12.52 | 22.34 ± 18.15 | 0.001* |
| | Mcmonnies | 9.10 ± 4.03 | 11.61 ± 5.58 | 0.007* |
| | DEQ-5 | 5.17 ± 4.17 | 8.44 ± 4.64 | 0.0007* |
| | SPEED | 6.13 ± 4.66 | 8.27 ± 4.83 | 0.025* |
| | SANDE | 22.27 ± 19.25 | 35.91 ± 24.08 | 0.007* |

*statistically significant differences between groups; $p < 0.05$.
(**Units:** TFO (mOsms/L); TMHk (mm); NIKBUT first/avg (seconds); MG dropout (meiboscore); Corneal and Conjunctival Staining (Oxford score); BUT (seconds); LWE (score))

## 4. Discussion

Our study findings suggest that elderly population present more ocular surface changes when compare to young population. Although the majority of the ocular surface parameters studied presented a fair correlation with age, these results give us relevant information of the ageing of the ocular surface and how it could affect the optical aids or surgical therapies, especially in elderly patients. Additionally, women from this study showed more changes due to ageing than men who presented better ocular surface condition than their matched group.

In the current research study, moderate and positive correlations (BR Total, Limbal redness, Corneal and conjunctival staining and TMHk, respectively) and negative correlations (BUT and Schirmer test, respectively) were found with age. These results are in agreement with others research studies reported in the literature. Woods [41] found an increase in tear retention in patients older than 40 years that could be explained by the problems in lacrimal drainage and changes in the lid margin. Additionally, a reduction in tear secretion and BUT have been reported in elderly patients [42,43]. In fact, Andres et al. stablished the BUT as predictive factor of DED problems [44]. As well, Guillon et al. [14] found higher tear film evaporation in older patients (more in women than men) suggesting that it may be a significant contributing factor to DED in that population. Similarly, Maissa et al. [45]found that the tear film characteristics worsening with age. Another study conducted by Yeotikar et al. [46] where 185 participants (aged 25–66 years) were evaluated found statistically significant associations between age and TMHk, BUT, palpebral redness and roughness, and conjunctival staining. Conversely, they found a significant negative association between TFO and age that is not in agreement with our results. In addition, they did not found significant effect of age on NIBUT, tear volume (measured with phenol red) and LWE. These differences in the results might be due to the different measurements techniques, clinical devices used and the characteristics of the sample.

Likewise, MG dropout and MG function showed a moderate and positive correlation with age. The great amount of MG dropout in elderly patients and the reduction in the quality of the MG secretion are well-known and documented by several studies [35,47,48]. Moreover, an increase in lower eyelid margin thickness and in the LWE severity was observed with age. The eyelid laxity, more common in older individuals, has been reported to be associated with dry eye symptoms and abnormal tear parameters. It has impacts on tear function that lead to a greater exposure and increased irritation [49,50], which could explain our findings regarding the increased ocular redness with age.

Regarding the subjective questionnaires, our findings showed a weak correlation (OSDI and Mcmonnies questionnaires) or no correlation (SPEED, DEQ-5 and SANDE questionnaires) with ageing. Previous studies have already shown the lack of association between DED symptoms and ocular surface signs [51] and age [52]. Reduction of the tear secretion in dry eye patients induce inflammation and peripheral nerve damage [53]. This leads to sensitization of polymodal and mechanonociceptor nerve endings and an abnormal increase in cold thermoreceptor activity, evoking dryness sensations and pain. Prolongation of disturbances in ocular sensory pathways (molecular, structural or functional) eventually leads to dysestesias and neuropathic pain referred to the eye surface [54]. For example, Acosta et al. [55] conducted a study in rats and they found that the cold trigeminal neurons gradually die with ageing. In the case of the human eye, a possible cause of absence or reduced dryness sensations could be explained by the aforementioned changes, justifying the lack of the association between these variables [46]. Our study findings showed that higher scores were obtained by elderly patients but it is not consistent between questionnaires. These differences could be explained by different symptoms evaluated in each questionnaire and also by the nature of each instrument. The complexity of both central and peripheral neural mechanisms associated with ocular surface sensations and tissue homeostasis in relation to DED is still not entirely understood [54].

When the age groups were compared, statistically significant differences were found in the most of the parameters assessed. These major differences were between group A (< 42 years) with B (42–65 years) and C (< 65years), whereas the upper age groups (B and C) showed similar DED signs and symptoms. These findings highlight the differences between both age populations.

All these changes could have impact on the success of several optical correction alternatives for presbyopia, such as IOLs implantation and MCLs. MCLs demonstrated to be a good choice as they provide good visual quality [18,21,22] the desired independency from spectacles and, no less important, the aesthetic benefit (desirable mostly by women). Despite all the reported benefits, the prescription rate is still quite low. Studies as conducted by Sivardeen et al. [56] tried to determine the utility of clinical and non-clinical indicators to aid the initial selection of the optimum presbyopic CL. However, the features studies been demonstrated to be poor indicators of the preferred MCLs type. Most of the research studies conducted about MCLs focus on visual performance and only a few of them focus on the CL interaction with the ocular surface [52]. Concerning this issue, contact lens discomfort (CLD) is one of the major issues related to CL dropout in CL wearers of all ages [57]. It is important to mention that the materials of the MCLs are the same as those that fit in young CL wearers. We believe our results about ocular surface ageing changes will provide relevant information in order to understand better the CL interaction with the eye in each population and even how these changes could impact on surgical therapies as IOLs implants or MCLs fitting. In addition, all these changes on the ocular surface would have an effect on the optical quality of the eye determined by the stability of the tear film. Consequently, it could impact on visual quality outcomes after IOL implantation or MCLs. It has also been reported that the variability in the keratometry readings is higher in patients with a tear osmolarity value higher than 316 mOsm/L that could have relevant influence on the IOL power calculation [20].

Ocular surface differences between women and men were also assessed. Women had a worse ocular surface condition than men (NIBUT (first and average), corneal and conjunctival staining, BUT and all questionnaires performed). A study conducted by Maissa et al. [45] found that the changes in tear film stability and lipid layer characteristics are more marked in women than men. Such a finding and the higher evaporation rate in older women aforementioned could lead to a higher corneal and conjunctival damage by environmental exposure and therefore partly explain the higher symptomatology reported by women. The present study presents some limitations such as a lack of homogeneous distribution between groups and no limit of the maximum age. However, it confirms the decline in tear film with ageing by the early 40′s and that the ocular surface of women is more affected by men. In the light of these findings, a better knowledge of the ocular surface characteristics of each population will aid us to understand and seek improved optical solutions (MCLs and surgical therapies) that meet the patients' needs, especially in the elderly population.

## References

[1] L.P. Teresa Niccoli, Ageing as a risk factor for disease, Curr. Biol. 22 (2012) pR741–R752.
[2] Department of Economic and Social Affairs Population Division (World Health Organization), World Population Ageing, (2015).
[3] I.K. Gipson, Age-related changes and diseases of the ocular surface and cornea, Investig. Ophthalmol. Vis. Sci. 54 (2013) 13–12840, http://dx.doi.org/10.1167/iovs.
[4] H. Obata, Anatomy and histopathology of the human lacrimal gland, Cornea 25 (2006) S82–S89, http://dx.doi.org/10.1097/01.ico.0000247220.18295.d3.
[5] S.D.E. Knop, N. Knop, T. Millar, H. Obata, The international workshop on meibomian gland dysfunction: report of the subcommittee on anatomy, physiology, and pathophysiology of the meibomian gland, Invest. Ophthalmol. Vis. Sci. 52 (4) (2011) 1938–1978, http://dx.doi.org/10.1167/iovs.10-6997c.
[6] Research in dry eye: report of the research subcommittee of the international dry eye WorkShop (2007), Ocul. Surf. (2007) 179–193.
[7] L.Y. ZhangX, Q. Li, H. Zou, J. Peng, C. Shi, H. Zhou, G. Zhang, M. Xiang, Assessing

the severity of conjunctivochalasis in a senile population: a community-based epidemiology study in Shanghai, China, BMC Public Health 11 (11) (2011) 198, http://dx.doi.org/10.1186/1471-2458-11-198.

[8] J. Berlau, H.H. Becker, J. Stave, C. Oriwol, R.F. Guthoff, Depth and age-dependent distribution of keratocytes in healthy human corneas: a study using scanning-slit confocal microscopy in vivo, J. Cataract Refract. Surg. 28 (2002) 611–616, http://dx.doi.org/10.1016/S0886-3350(01)01227-5.

[9] C.J. Ko MK, W.K. Park, J.H. Lee, A histomorphometric study of corneal endothelial cells in normal human fetuses, Exp. Eye Res. 72 (4) (2001) 403–409.

[10] H.A.R. Ehrlich, N.S. Kheradiya, D.M. Winston, D.B. Moore, B. Wirostko, Age-related ocular vascular changes, Graefes Arch. Clin. Exp. Ophthalmol. 247 (5) (2009) 583–591, http://dx.doi.org/10.1007/s00417-008-1018-x.

[11] O.S.F. Orucoglu, M. Akman, Analysis of age, refractive error and gender relatedchanges of the cornea and the anterior segment of the eye with Scheimpflug imaging, Cont. Lens Anterior Eye 38 (5) (2017) 345–350, http://dx.doi.org/10.1016/j.clae.2015.03.009 (n.d.).

[12] F. Stapleton, M. Alves, V.Y. Bunya, I. Jalbert, K. Lekhanont, F. Malet, K. Na, D. Schaumberg, M. Uchino, J. Vehof, E. Viso, S. Vitale, The ocular surface TFOS DEWS II epidemiology report, Ocul. Surf. 15 (2017) 334–365, http://dx.doi.org/10.1016/j.jtos.2017.05.003.

[13] J.P. Craig, K.K. Nichols, J.J. Nichols, B. Caffery, H.S. Dua, E.K. Akpek, K. Tsubota, C.K. Joo, Z. Liu, J.D. Nelson, F. Stapleton, TFOS DEWS II definition and classification report, Ocul. Surf. 15 (2017) 276–283, http://dx.doi.org/10.1016/j.jtos.2017.05.008.

[14] M. Guillon, C. Maïssa, Tear film evaporation-Effect of age and gender, Contact Lens Anterior Eye 33 (2010) 171–175, http://dx.doi.org/10.1016/j.clae.2010.03.002.

[15] J.D. Nelson, J.P. Craig, E. Akpek, D.T. Azar, C. Belmonte, A.J. Bron, J.A. Clayton, M. Dogru, H.S. Dua, G.N. Foulks, J.A.P. Gomes, K.M. Hammitt, J. Holopainen, L. Jones, C.K. Joo, Z. Liu, J.J. Nichols, K.K. Nichols, G.D. Novack, V. Sangwan, F.J. Stapleton, A. Tomlinson, K. Tsubota, M.D.P. Willcox, J.S. Wolffsohn, D.A. Sullivan, TFOS DEWS II introduction, Ocul. Surf. 15 (2017) 269–275, http://dx.doi.org/10.1016/j.jtos.2017.05.005.

[16] A.D. Goertz, W.C. Stewart, W.R. Burns, J.A. Stewart, L.A. Nelson, Review of the impact of presbyopia on quality of life in the developing and developed world, Acta Ophthalmol. 92 (2014) 497–500, http://dx.doi.org/10.1111/aos.12308.

[17] R. Pérez-Prados, D.P. Piñero, R.J. Pérez-Cambrodí, D. Madrid-Costa, Soft multifocal simultaneous image contact lenses: a review, Clin. Exp. Optom. 100 (2017) 107–127, http://dx.doi.org/10.1111/cxo.12488.

[18] W.N. Charman, Developments in the correction of presbyopia I: spectacle andcontact lenses, Ophthalmic Physiol. Opt. 34 (1) (2014) 8–29, http://dx.doi.org/10.1111/opo.12091.

[19] W.N. Charman, Developments in the correction of presbyopia II: surgical approaches, Ophthalmic Physiol. Opt. 34 (4) (2014) 397–426, http://dx.doi.org/10.1111/opo.12129.

[20] A.T. Epitropoulos, C. Matossian, G.J. Berdy, R.P. Malhotra, R. Potvin, Effect of tear osmolarity on repeatability of keratometry for cataract surgery planning, J. Cataract Refract. Surg. 41 (2015) 1672–1677, http://dx.doi.org/10.1016/j.jcrs.2015.01.016.

[21] A. González-Mesa, J.P. Moreno-Arrones, D. Ferrari, M.A. Teus, Role of tear osmolarity in dry eye symptoms after cataract surgery, Am. J. Ophthalmol. 170 (2016) 128–132, http://dx.doi.org/10.1016/j.ajo.2016.08.002.

[22] D. Madrid-Costa, S. García-Lázaro, C. Albarrán-Diego, T. Ferrer-Blasco, R. Montés-Micó, Visual performance of two simultaneous vision multifocal contact lenses, Ophtalmic Physiol Opt. 33 (2013) 51–56, http://dx.doi.org/10.1111/opo.12008.

[23] E. Papadatou, A.J. Del Aguila-Carrasco, J.J. Esteve-Taboada, D. Madrid-Costa, A. Cervino-Exposito, Objective assessment of the effect of pupil size upon the power distribution of multifocal contact lenses, Int. J. Ophthalmol. 10 (2017) 103–108, http://dx.doi.org/10.18240/ijo.2017.01.17.

[24] W.N. Charman, Correcting presbyopia: the problem of pupil size, Ophthalmic Physiol. Opt. 37 (2017) 1–6, http://dx.doi.org/10.1111/opo.12346.

[25] S. Garcia-Lazaro, T. Ferrer-Blasco, D. Madrid-Costa, C. Albarran-Diego, R. Montes-Mico, Visual performance of four simultaneous-Image multifocal contact lenses under dim and glare conditions, eye contact lens-Science clin, Eye Contact Lens-Sci. Clin. Pract. (2015), http://dx.doi.org/10.1097/ICL.0000000000000060.

[26] T. Ferrer-Blasco, D. Madrid-Costa, Stereoacuity with balanced presbyopic contact lenses, Clin. Exp. Optom. 94 (2011) 76–81, http://dx.doi.org/10.1111/j.1444-0938.2010.00530.x.

[27] T. Ferrer-Blasco, D. Madrid-Costa, Stereoacuity with simultaneous vision multifocal contact lenses, Optom. Vis. Sci. 87 (2010) 663–668, http://dx.doi.org/10.1097/OPX.0b013e31820504b7.

[28] P.B. Morgan, N. Efron, C.A. Woods, An international survey of contact lens prescribing for presbyopia, Clin. Exp. Optom. 94 (2011) 87–92, http://dx.doi.org/10.1111/j.1444-0938.2010.00524.x.

[29] N. Efron, J.J. Nichols, C.A. Woods, P.B. Morgan, Trends in US contact lens prescribing 2002 to 2014, Optom. Vis. Sci. 92 (2015) 758–767, http://dx.doi.org/10.1097/OPX.0000000000000623.

[30] R.B. Schiffman RM, M.D. Christianson, G. Jacobsen, J.D. Hirsch, Reliability and validity of the ocular surface disease index, Arch. Ophthalmol. 118 (2000) 615–621.

[31] C.W. McMonnies, A. Ho, Patient history in screening for dry eye conditions, J. Am. Optom. Assoc. 58 (4) (1987) 296–301.

[32] S.T. Ngo W, P. Situ, N. Keir, D. Korb, C. Blackie, Psychometric properties and validation of the Standard Patient Evaluation of Eye Dryness questionnaire, Cornea 32 (9) (2013) 1204–1210, http://dx.doi.org/10.1097/ICO.0b013e318294b0c0.

[33] D.A. Schaumberg, A. Gulati, W.D. Mathers, T. Clinch, M. a Lemp, J.D. Nelson, G.N. Foulks, R. Dana, Development and validation of a short global dry eye symptom index, Ocul. Surf. 5 (2007) 50–57, http://dx.doi.org/10.1016/S1542-0124(12)70053-8.

[34] R.L. Chalmers, C.G. Begley, B. Caffery, Validation of the 5-Item Dry Eye Questionnaire (DEQ-5): Discrimination across self-assessed severity and aqueous tear deficient dry eye diagnoses, Cont. Lens Anterior Eye 33 (2010) 55–60.

[35] A.S. Arita R, K. Itoh, K. Inoue, Noncontact infrared meibography to document age-related changes of the meibomian glands in a normal population, Ophtalmology 15 (5) (2008) 911–915, http://dx.doi.org/10.1016/j.ophtha.2007.06.031.

[36] B.A. Foulks G.N, Meibomian gland dysfunction: a clinical scheme for description, diagnosis, classification and grading, Ocul. Surf. 1 (3) (2003) 107–126.

[37] D.M. Tomlinson A, A.J. Bron, D.R. Korb, S. Amano, J.R. Paugh, E.I. Pearce, R. Yee, N. Yokoi, R. Arita, The international workshop on meibomian gland dysfunction: report of the diagnosis subcommittee, Invest. Ophthalmol. Vis. Sci. 52 (4) (2011) 2006–2049, http://dx.doi.org/10.1167/iovs.10-6997f.

[38] F.V. Korb D.R, J.P. Herman, C.A. Blackie, R.C. Scaffidi, J.V. Greiner, J.M. Exford, Prevalence of lid wiper epitheliopathy in subjects with dry eye signs and symptoms, Cornea 29 (4) (2010) 377–383.

[39] S.J. Bro A.J, V.E. Evans, Grading of corneal and conjunctival staining in the context of other dry eye tests, Cornea 22 (7) (2003) 40–50.

[40] Y.H. Chang, Biostatistics 104: correlational analysis, Singapore Med. J. 44 (2003) 614–619.

[41] R.L. Woods, The aging eye and contact lenses – a review of ocular characteristics, J. Br. Contact Lens Assoc. 14 (1991) 115–127, http://dx.doi.org/10.1016/0141-7037(91)80004-6.

[42] W.D. Mathers, J.A. Lane, M.B. Zimmerman, Tear film changes associated with normal aging, Cornea 15 (1996) 229–234 http://www.ncbi.nlm.nih.gov/pubmed/8713923.

[43] S. Patel, J.C. Farrell, Age-related changes in precorneal tear film stability, Optom. Vis. Sci. 66 (1989) 175.

[44] O. Andres, S. Henriquez, A. Garcia, M.L. Valero, J. Valls, Factors of the precorneal tear film break-up time (BUT) and tolerance of contact lenses, Int. Contact Lens Clin. 14 (1987) 103–107.

[45] C. Maïssa, M. Guillon, Tear film dynamics and lipid layer characteristics-Effect of age and gender, Contact Lens Anterior Eye 33 (2010) 176–182, http://dx.doi.org/10.1016/j.clae.2010.02.003.

[46] N.S. Yeotikar, H. Zhu, M. Markoulli, K.K. Nichols, T. Naduvilath, E.B. Papas, Functional and morphologic changes of meibomian glands in an asymptomatic adult population, Investig. Ophthalmol. Vis. Sci. 57 (2016) 3996–4007, http://dx.doi.org/10.1167/iovs.15-18467.

[47] S. Den, K. Shimizu, K. Ikeda, S. Shimmura, J. Shimazaki, Association between meibomian gland changes and aging, sex, or tear function, Cornea 25 (2006) 651–655, http://dx.doi.org/10.1097/01.ico.0000227889.11500.6f.

[48] Y. Ban, S. Shimazaki-Den, K. Tsubota, J. Shimazaki, Morphological evaluation of meibomian glands using noncontact infrared meibography, Ocul. Surf. 11 (2013) 47–53, http://dx.doi.org/10.1016/j.jtos.2012.09.005.

[49] G.A. Ansari Z, R. Singh, C. Alabiad, Prevalence, risk factors, and morbidity of eye lid laxity in a veteran population, Cornea 34 (1) (2015) 32–36.

[50] X.J. Le Q, X. Cui, J. Xiang, L. Ge, L. Gong, Impact of conjunctivochalasis on visual quality of life: a community population survey, PLoS One 9 (10) (2014) (20).

[51] M. Cuevas, M.J. González-García, E. Castellanos, R. Quispaya, P. de la Parra, I. Fernández, M. Calonge, Correlations among symptoms, signs, and clinical tests in evaporative-type dry eye disease caused by meibomian gland dysfunction (MGD), Curr. Eye Res. 37 (2012) 855–863, http://dx.doi.org/10.3109/02713683.2012.683508.

[52] F.D. du Toit R, P. Situ, T. Simpson, The effects of six months of contact lens wear on the tear film, ocular surfaces, and symptoms of presbyopes, Optom. Vis. Sci. 78 (6) (2001) 455–462.

[53] I. Kovács, C. Luna, S. Quirce, K. Mizerska, G. Callejo, A. Riestra, L. Fernández-Sánchez, V.M. Meseguer, N. Cuenca, J. Merayo-Lloves, M.C. Acosta, X. Gasull, C. Belmonte, J. Gallar, Abnormal activity of corneal cold thermoreceptors underlies the unpleasant sensations in dry eye disease, Pain 157 (2016) 399–417, http://dx.doi.org/10.1097/j.pain.0000000000000455.

[54] C. Belmonte, J.J. Nichols, S.M. Cox, J.A. Brock, C.G. Begley, D.A. Bereiter, D.A. Dartt, A. Galor, P. Hamrah, J.J. Ivanusic, D.S. Jacobs, N.A. McNamara, M.I. Rosenblatt, F. Stapleton, J.S. Wolffsohn, TFOS DEWS II pain and sensation report, Ocul. Surf. 15 (2017) 404–437, http://dx.doi.org/10.1016/j.jtos.2017.05.002.

[55] M.C. Acosta, A. Peral, C. Luna, J. Pintor, C. Belmonte, J. Gallar, Tear secretion induced by selective stimulation of corneal and conjunctival sensory nerve fibers, Investig. Ophthalmol. Vis. Sci. 45 (2004) 2333–2336, http://dx.doi.org/10.1167/iovs.03-1366.

[56] A. Sivardeen, D. Laughton, J.S. Wolffsohn, Investigating the utility of clinical assessments to predict success with presbyopic contact lens correction, Contact Lens Anterior Eye 39 (2016) 322–330, http://dx.doi.org/10.1016/j.clae.2016.05.002.

[57] N.J. members of the T.I.W. on C.L.D. KK, Nichols, R.L. Redfern, J.T. Jacob, J.D. Nelson, D. Fonn, S.L. Forstot, J.F. Huang, B.A. Holden, The TFOS International Workshop on Contact Lens Discomfort: report of the definition and classification subcommittee, Invest. Ophthalmol. Vis. Sci. 54 (11) (2013), http://dx.doi.org/10.1167/iovs.13-13074.