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CORNEAL PROPERTIES IN PRIMARY OPEN ANGLE GLAUCOMA ASSESSED THROUGH SCHEIMPFLUG CORNEAL TOPOGRAPHY AND DENSITOMETRY

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DECLARATION OF INTEREST

The authors report no conflicts of interest.

ABSTRACT

Purpose: To compare corneal topography and densitometry measurements in patients with primary open angle glaucoma (POAG) and healthy subjects.

Patients and methods: 200 eyes of 75 patients with POAG and 125 healthy controls underwent corneal topography and densitometry (Oculus Pentacam HR). The data compared in the two groups were: anterior chamber angle (ACA), depth (ACD) and volume (ACV), keratometry (K minimum, K maximum and K mean), central corneal thickness (CCT), central anterior elevation (CAE), anterior elevation apex (AEA), maximum anterior elevation (MAE) and posterior elevation apex (PEA). Densitometry measurements were made at three depths on a 12 mm-diameter circle divided into 4 concentric rings (0-2 mm, 2-6 mm, 6-10 mm and 10-12 mm). The diagnostic capacity of the corneal variables was assessed through the areas under the receiver operator characteristics (ROC) curve (AUC).

Results: The corneal density of practically all depth layers and total corneal density were significantly higher in the POAG than control group ($p<0.05$). Total corneal density was positively correlated with age ($r=0.623$; $p<0.001$) and also showed a good diagnostic capacity for glaucoma (AUC=0.617; IC 95% [0.541-0.697]; $p<0.001$). In a multiple linear regression designed to assess its relationship with age, gender, CCT and Km, age emerged as a significant confounder both in controls (coef. 0.315; $p<0.001$; 95% CI [0.246-0.384]) and patients (coef. 0.370; $p<0.001$; 95% CI [0.255-0.486]).

Conclusion: Corneal densitometry measurements showed a good diagnostic capacity for POAG suggesting this type of examination could have clinical applications in the diagnosis and management of glaucoma.

KEYWORDS: CORNEAL DENSITOMETRY; PRIMARY OPEN ANGLE GLAUCOMA; CORNEAL TOPOGRAPHY; SCHEIMPFLUG.

INTRODUCTION

Primary open angle glaucoma (POAG) is a progressive optic neuropathy and the second leading cause of blindness worldwide. [1]

Intraocular pressure (IOP) is the only modifiable risk factor for POAG, so measurements must be reliable and reproducible. However, the current gold standard procedure for IOP measurement, Goldmann applanation tonometry (GAT), is considerably influenced by several well-defined variables such as central corneal thickness (CCT) and keratometry (K). [2,3]

With the new devices that we have today, several new variables can be determined that give a good idea of individual corneal boimechanics (hysteresis and resistance factor) and the state of the cornea (corneal densitometry). [4]

The Pentacam HR (Oculus, Wetzlar, Germany) is a non-invasive device that offers a good predictability and reproducibility of measures. It is based on a Scheimpflug imaging system and its new software allows for the rapid and objective assessment of corneal densitometry. This measurement correlates with corneal light scatter and transparency. Readings provide information on corneal clarity and are provided as a gray scale (GSU) that goes from 0 (full transparency) to 100 (full opacity or clouding), depending on luminance per unit volume. [4,5]

Corneal densitometry has been used in the study of both systemic diseases (eg, diabetes mellitus, mucopolysaccharidosis) and eye diseases (eg, keratoconus, pseudoexfoliation syndrome) and also for the follow up of refractive surgery or bacterial keratitis. [6-13]

Some studies have examined corneal densitometry in patients with glaucoma other than POAG such as pseudoexfoliative glaucoma (PEG) or primary congenital glaucoma (PCG). Sekeroglu et al. found no significant differences in corneal densitometry between patients with PEG and healthy control subjects. [9] In contrast, Morales et al. detected higher corneal densitometry measurements in patients with PCG compared to controls, and densitometry was found inversely correlated with best corrected visual acuity (BCVA). [14]

The purpose of this study was to examine corneal densitometry in patients with POAG and to determine the diagnostic capacity of differences in its measurements in relation to healthy control subjects.

PATIENTS AND METHODS

This was a descriptive cross-sectional study carried out at the Ophthalmology department of the Hospital Clinico San Carlos, Madrid, Spain. All patients gave their consent to participate and also for results to be published in accordance with the tenets of the Declaration of Helsinki. Over the period January to September 2019, we recruited 200 consecutive Caucasian subjects. Of these, 125 were healthy individuals and 75 were patients with POAG. In turn, patients were divided into 3 groups of 25 patients according to the Glaucoma Staging System (GSS2), which considers the state of the visual field measured as the mean defect (MD) as the most important reference: early POAG MD <6, moderate POAG MD 6-12 and advanced POAG MD> 12. [15,16] Subjects with other types of glaucoma were excluded.

For the control group, inclusion criteria were healthy volunteers older than 18 years, no eye disease, IOP <21 mmHg, normal optic disc, normal visual field, best corrected visual acuity (BCVA) greater than 0.8 (Snellen), spherical refractive defect < 5 diopters (D) and cylinder less than 3 D. Exclusion criteria were a history of corneal, macular or optic nerve disease as well as eye surgery or ocular trauma.

For the study group, inclusion criteria were patients diagnosed with POAG showing an open angle on gonioscopy, narrowing of the neuroretinal rim, visual defects through Octopus TOP perimetry (Haag-Streit, Koenig, Switzerland) and optic nerve damage in the retinal nerve fiber layer as determined by spectral domain optical coherence tomography (SD-OCT Heidelberg Engineering, Inc., Heidelberg, Germany). Exclusion criteria were a BCVA of less than 0.3 (Snellen), spherical refractive defect >5 D, cylinder greater than 3 D or incapacity to collaborate with the tests required.

For analysis, one eye per subject was randomly selected using a sequence generated at www.randomization.com. The data obtained in each patient were age, sex, eye examined, IOP (Perkins hand-held Goldmann tonometer, Clement-Clarke, Columbus, OH), and Pentacam HR topography and densitometry data.

The Pentacam exam was conducted by a single experienced investigator (MMS) who was masked to the study group of the subject tested. In each participant, the same device was used in the same room and under constant dim-light conditions. The test was performed in automatic mode to minimize human error. Measurements were taken once per patient, checking the "examination quality specification" OK index, given the good reproducibility and repeatability of this device. IOP was measured after the Pentacam exam to avoid altering the ocular surface, and thus corneal measurements.

The data compiled in each patient were: sex, age, IOP, keratometry (K minimum, K maximum and K mean), cylinder and CCT. In addition, corneal densitometry measurements were obtained over a 12 mm-diameter circle centered at the apex of the cornea divided into 4 concentric rings (0-2 mm, 2-6 mm, 6-10 mm and 10-12 mm) and also at three depths or layers: anterior (120 µm thickness from surface), mid-stroma (thickness 120-60 µm) and posterior (thickness 60 µm). Other variables recorded were central anterior elevation (CAE), anterior elevation apex (AEA), maximum anterior elevation (MAE) and posterior elevation apex (PEA) and the anterior segment measurements anterior chamber depth (ACD), anterior chamber volume (ACV) and anterior chamber angle (ACA). Finally, we also collected data on the treatment received and previous surgeries for POAG.

As the literature lacks information on correlations between total densitometry and age, gender, CCT and Km, we could not perform a sample size calculation. Hence, we consider this to be a pilot study whose findings will provide the grounds for sample size determinations in further studies.

Statistical analysis

All statistical tests were performed using the software package SPSS 25.0 for Windows (SPSS Inc., Chicago, IL). The Kolmogorov-Smirnov test was used to check the normality of the distribution of quantitative variables, which were expressed as mean and standard deviation. Corneal parameters were compared with the Student's t test for independent samples. The possible effects of age, CCT, keratometry and glaucoma stage on densitometry were assessed through Pearson's correlation. The level of significance for each contrast was set at $p < 0.05$.

Receiver operating characteristics curves (ROC) were constructed and areas under the curve (AUCs) used to assess the capacity of each variable to distinguish between glaucomatous and healthy eyes. AUCs were compared for the different variables using the DeLong Method to provide the sensitivity and specificity of each model (FIGURE 2).

RESULTS

Participants were 200 consecutive Caucasian subjects seen at our center, of whom 125 were healthy controls and 75 were POAG patients. Mean ages were 64.16 (± 1.34) years for the control group and 72.20 (± 1.38) years for the POAG group. Proportions of men were 35.2% in the control group was 42.66% in the POAG group. Both groups were comparable in terms of age (p = 0.063), sex (p = 0.290) and eye examined (p = 0.100). (TABLE 1) The mean defects in each group (mean±SD) used to grade glaucoma severity are displayed in Figure 1. In the early POAG group, MD was 2.85 (±1.23), in the moderate POAG group MD was 8.26 (± 1.90) and in the advanced POAG group MD was 15.66 (±3.46).

Treatment received by the POAG patients was monotherapy in 20% (15/75), combined therapy with two drugs in 8% (6/75) and three drugs in 5% (4/75). Remaining patients were not under any medical treatment (66%) (50/75). 20% (15/75) of the patients had had cataract surgery, 16% (12/75) trabeculectomy, 4% (3/75) microinvasive glaucoma surgery (MIGS) and 1% (1/75) had undergone selective laser trabeculoplasty (SLT).

Among the topographic factors compared in the two groups, the only significant differences detected were a higher CAE (p=0.004) and PEA (p=0.042) in the POAG group (TABLE 2). Among the anterior chamber parameters examined, only anterior chamber angle (ACA) emerged as significantly greater in the POAG group (p=0.006) (TABLE 3). Corneal density was also found to be higher in the POAG patients than healthy subjects in practically all layers: anterior, mid-stroma and full thickness. In the posterior layer, no significant differences in density were recorded with the exception of the 2 to 6 mm ring (p=0.034) (TABLE 4).

Significant correlation was noted between corneal density and age (r=0.623; p<0.001). Corneal density showed no correlation with keratometry (Kmax, Kmin or Km; p>0.01) or with the severity of glaucoma according to the mean defect. (TABLE 5)

The variable showing the best diagnostic capacity of all those examined was total corneal density referring to the full thickness of the total area examined (AUC=0.617; (p<0.001). Other factors also showing discriminatory capacity to detect POAG were: ACA (AUC = 0.607; p = 0.011), PEA (AUC = 0.613; p = 0.006), corneal density of rings 0-2 mm and 2-6 mm all layers (anterior, mid stroma and posterior) (p <0.001) and of total area of the layers anterior and mid-stoma (p <0.001 and p = 0.016; respectively). (TABLE 6)

The ROC curve (AUC ROC) constructed to determine the capacity of each variable to distinguish between glaucomatous and healthy subjects is provided in figure 2. The variables identified as showing most discriminating capacity were corneal densities recorded for the anterior, mid-stroma and full thickness layers of the 0 to 2 mm central ring.

Multiple linear regression analysis was used to assess the association between the dependent variable total corneal density and the independent variables age, gender, CCT and Km in both the control and POAG groups. (TABLE 7). In the control group, this model showed that after adjusting for age, for each year of age, total corneal density increased by 0.315 GSU (slope: 0.315; p<0.001; 95% CI [0.246-0.384]). Similarly, for each micron of CCT increase, corneal density increased by 0.024 GSU (slope: 0.024; p=0.030; 95% CI [0.002-0.045]). In the POAG group, for each 1 year increase in age, total corneal density increased by 0.370 GSU (slope: 0.370; p<0.001; 95% CI [0.255-0.486]).

Also by multiple linear regression, we examined the relationship between CAE (TABLE 8) and PEA (TABLE 9) as dependent variables, and age, gender, CCT, and Km as independent factors. For CAE as the dependent variable in the control group, this model showed, after adjusting for age, for every one year increase in age, total corneal density decreased by 0.040 GSU (slope: -0.040; p= 0.023; 95% CI [-0.076-(-0.005)]). Likewise, in the POAG group each diopter increase in Km was associated with an increase in CAE of 0.651 microns (slope: 0.651; p<0.001; 95% CI [0.308-0.994]).

Similarly, when we assessed the effects of the predictors on PAE in the control group, each year of age increase was associated with an increase in PAE of 0.134 microns (slope: 0.134; p= 0.009; 95% CI [0.034-0.235]). Further, in this model, each micron of CCT increase was associated with an increase in PAE of 0.046 microns (slope 0.046; p= 0.004; 95% CI [0.014-0.077]). In the POAG group, CCT was also found to affect PEA, as each micron increase in this variable was associated with a reduction in PEA of 0.054 units (slope: -0.054; p= 0.021; 95% CI [-0.100-(-0.008)].

DISCUSSION

Patients with POAG have characteristic features associated with glaucomatous damage (eg, defects in the visual field, loss of retinal nerve fiber layer thickness). Corneal topographic, and more recently, densitometry alterations have been also observed. However, there is scarce information available on corneal densitometry in both healthy subjects and glaucoma patients.

In the present study, mean corneal density in our control group of 125 healthy Caucasian individuals was 25.59 ±7.52 GSU. In contrast, mean total corneal densities of 16.46 ± 1.85 GSU have been reported by Garzon et al. for 338 Caucasian subjects, and of 19.74 ± 3.89 GSU by Dhubhghaill et al. for 445 Belgian subjects. The higher value obtained here could be explained by the younger age of the study participants of those studies (62.32.39 ±6.61 and 48 ±15.3 years, respectively) compared to our controls (64.16 ±1.34 years). [17,18]

When we compared anterior chamber parameters (volume, depth and angle), the only significant differences found between healthy controls and POAG patients was a greater angle in the patients (p = 0.006). Sekeroglu et al. in their study in patients with pseudoexfoliative glaucoma (GPE) observed a smaller ACD, ACV along with a smaller ACA in the GPE group (29.87 ± 10.92 vs. 31.33 ± 12.12; p = 0.401). [9] In contrast, in our study, the POAG group showed a higher ACA than controls (38.48 ± 9.41 vs. 34.70 ± 9.26; p = 0.006). These differences can be explained by the anatomical differences that characterize both types of glaucoma.

In a search of normative corneal densitometry data for adults with POAG, we only found one study from Turkey in which data obtained when POAG was diagnosed were 20.03 ± 5.42 GSU compared to 28.46 ±7.45 recorded in our POAG group. This difference could be attributed to the corneal modifications induced by phacoemulsification or filtering surgeries in our patients as the participants of the Turkish study were naive patients. [19]

In addition to changes in corneal structure derived from surgical procedures, the impacts of topical treatments on corneal density are remarkable. In the study by Sen et al., a decrease in corneal density was noted from the third trimester of treatment with latanoprost (p=0.08). [19] In our study, the POAG pool was not divided according to treatment as these were long-term patients, so we cannot draw firm conclusions. In future work, it would be interesting to prospectively examine corneal density classification by groups of drugs.

Tekin et al. described in healthy subjects correlation between corneal densitometry, endothelial cell density and the percentage of hexagonal cells and argued that densitometry could serve as a marker of corneal endothelial status. [20] In a similar specular microscopy study, Yu et al. compared corneal endothelial cell density in patients with POAG who had or not received treatment and healthy controls. Their results indicated a lower endothelial density in glaucoma patients than healthy subjects and in treated patients than untreated patients. These findings were attributed to mechanical damage due to elevated IOP and the toxicity of some topical glaucoma treatments. [21]

Our results indicate significantly higher corneal densitometry variables in POAG patients than in healthy subjects. Most differences were observed in the anterior layer and full corneal thickness followed by the mid-stroma and finally the posterior layer. According to the segments examined, differences in corneal density were detected in the central 0-2 mm and 2-6 mm rings in all layers except the posterior layer.

Our topographic data also revealed significantly higher CAE (p=0.004) and PEA (p=0.042) in POAG. In the multiple linear regression analysis for both parameters separately, age emerged as a confounding factor for both parameters (PEA and CAE) in the control group, but not in POAG.

No differences were found between the two study groups in the K and CCT measurements, as in the studies by Kistos et al. or Saenz-Frances et al., although reports exist in the literature of such differences in POAG. In this last study comparing the corneal characteristics of healthy subjects and POAG patients using the Pentacam Scheimpflug device, significant differences were detected in mean corneal thickness (p=0.005) and in thickness across the central 0 to 6 mm ring. [22-24]

We observed positive correlation between age and corneal densitometry, such that corneal density increased with age (r = 0.623; p <0.001). However, no significant correlation was noted with other parameters such as keratometry (Kmax, Kmin or Km) (p>0.01) or with severity of glaucoma as reflected by the mean defect. (TABLE 5) In Figure 1, it may be observed that patients with more severe glaucoma showed the higher total corneal density. Probably, the lack of significance can be attributed to the small sample size as a limitation of this study.

It should be noted that no other study has related by multiple linear regression total corneal densitometry with independent variables such as age, gender, CCT or Km. In the present study, we found that age was a confounding factor for densitometry measurements in both the control (slope: 0.315; p<0.001; 95% CI [0.246-0.384]) and POAG groups (slope: 0.370; p<0.001; 95% CI [0.255-0.486]).

The diagnostic capacity of total corneal densitometry (whole area full thickness) was found to be intermediate (AUC 0.617; p=0.005). After determining differences between groups in both topographic and densitometry variables, the factor showing the best discriminatory capacity for glaucoma was total corneal density of the 0-2 mm ring (AUC=0.679; p<0.001). Further, all the densitometry variables except values for the 10-12 mm ring anterior layer, 6-10 mm and 10-12 mm middle layer, 6-10 mm, 10-12 mm ring posterior layer, whole area posterior layer and 10-12 mm ring full thickness showed significant diagnostic capacity.

Although the diagnosis of POAG is clinical and based on the tests mentioned earlier, our study shows that corneal density values differ between healthy subjects and POAG patients, and that they have some discriminating capacity. Thus, besides for diagnostic purposes, these parameters might be also useful for patient follow up, given the importance of these properties in corneal transparency and their influence on IOP measurements. [14] These results support the use of these new variables in clinical practice. In this preliminary study, it is not possible to determine the influence of other variables such as previous surgeries, previous treatments or the impact increased corneal density could have on the mean defect or visual acuity.

The limitations of our study are its small sample size, especially the size of the groups arising from patient stratification by severity of glaucoma. In addition, there were several confounding factors such as age. Further work is needed to prospectively address corneal densitometry in POAG patients and the effects of hypotensive drugs or the different types of glaucoma filtering surgery. In the POAG group, we included patients with moderate and advanced glaucoma who had had prior surgery. In future studies it should be clarified whether this factor could lead to changes in corneal density or if it is a primary alteration.

In conclusion, our findings indicate corneal densitometry differences in healthy subjects and patients with POAG besides known differences in other corneal properties. Some corneal density measurements showed a good diagnostic capacity for POAG suggesting a possible role of densitometry as a complementary test in the diagnostic and prognostic support of glaucoma. Further work is still needed however to determine if this corneal property is a primary or secondary alteration in patients with POAG.

DECLARATION OF INTEREST

The authors report no conflicts of interest.

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TABLE 7. Multiple linear regression analysis for the dependent variable total corneal density (full thickness)

TABLE 8. Multiple linear regression analysis for the dependent variable CAE.

TABLE 9. Multiple linear regression analysis for the dependent variable PEA

FIGURES

FIGURE 1. Graphic representation of mean defect (MD) in each group according to glaucoma severity. X-axis = severity of glaucoma (early MD <6, moderate MD = 6-12, advanced MD> 12). Y-axis = MD values.

FIGURE 2. ROC curve (AUC ROC) used to determine the glaucoma discriminating capacity of each variable examined

TABLE 1. Demographic and clinical characteristics of the patients and controls

VARIABLE	Controls n=125	POAG n=75	P*
Age (years)	64.16 (±1.34)	72.20 (±1.38)	p=0.063
Sex (% male)	35.2	42.66	p=0.290+
Eye (% right eyes)	48	60	p=0.100+
IOP (mmHg)	16.37 (±3.35)	16.38 (±3.10)	p=0.978*
CCT (µm)	559.39 (±48.36)	557.04 (±42.4)	p=0.720*
MD (dB)	-	MEAN ± SD	-
Early (n=25)	-	2.85 (±1.23)	-
Moderate (n=25)	-	8.26 (± 1.90)	-
Advanced (n=25)	-	15.66 (±3.46)	-

TABLE 2. Corneal characteristics with Pentacam HR

VARIABLE	**Controls** **n=125**	**POAG** **n=75**	**p** *
Km (D)	46.75 (±33.15)	44.40 (±2.32)	p=0.432
K max (D)	44.41 (±1.79)	44.97 (±2.57)	p=0.099
Kmin (D)	43.08 (±1.90)	43.68 (±2.34)	p=0.061
AEA (µm)	1.14 (±3.85)	1.77 (±3.75)	p=0.258
CAE (µm)	**1.08** (±**2.98)**	**2.46** (±**3.43)**	**p=0.004**
PEA (µm)	**11.83** (±**8.83)**	**14.36** (±**8.22)**	**p=0.042**
CPE (µm)	6.04 (±6.43)	6.69 (±6.24)	p=0.485

TABLE 3. Pentacam HR anterior segment parameters

VARIABLE	Controls n=125	POAG n=75	p *
ACD (mm)	2.86 (±0.69)	3.04 (±0.86)	p=0.139
ACV(mm^3)	153.12 (±38.38)	153.29 (±38.34)	p=0.976
ACA (degrees)	**34.70 (±9.26)**	**38.48 (±9.41)**	**p=0.006**

TABLE 4. Pentacam HR corneal densitometry measurements

VARIABLE	Controls n=125	POAG n=75	p *
Anterior 120 µm			
0-2 mm	**31.26 (±17.13)**	**38.80 (±18.15)**	**p=0.004**
2-6 mm	**30.61 (±16.91)**	**37.87 (±17.4)**	**p=0.004**
6-10 mm	**37.43 (±15.43)**	**43.05 (±14.34)**	**p=0.01**
10-12 mm	42.35 (±14)	44.22 (±14.89)	p=0.383
Total area	**34.78 (±14.55)**	**40.82 (±14.68)**	**p=0.005**
Mid stroma			
0-2 mm	**17.72 (±3.82)**	**20.18 (±4.52)**	**p<0.001**
2-6 mm	**17.31 (±4.22)**	**19.65 (±5.5)**	**0.002**
6-10 mm	27.51 (±10.46)	29.93 (±9.72)	0.099
10-12 mm	32.12 (±10.10)	31.58 (±8.99)	0.695
Total area	**23.1(±6.21)**	**25.14 (±6.11)**	**0.024**
Posterior 60 µm			
0-2 mm	14.74 (±10.30)	15.04 (±2.75)	0.763
2-6 mm	**13.86 (±3.03)**	**14.82 (±3.11)**	**0.034**
6-10 mm	22.49 (±7.67)	23.78 (±6.62)	0.210
10-12 mm	26.71 (±7.49)	25.41(±6.19)	0.185
Total area	18.73 (±4.56)	19.51 (±3.88)	0.197
Full thickness			
0-2 mm	**20.97 (±6.83)**	**24.64 (±7.69)**	**0.001**
2-6 mm	**20.62 (±7.07)**	**24.12 (±7.92)**	**0.002**
6-10 mm	**29.21 (±10.35)**	**32.25 (±9.44)**	**0.035**
10-12 mm	33.78 (±9.91)	33.90 (±9.43)	0.932
Total area	**25.59 (±7.52)**	**28.46 (±7.45)**	**0.01**

TABLE 5. Correlations between total full thickness corneal density and other variables.

VARIABLE	Pearson correlation	p *
Early (MD<6)	0.007	p=0.972
Moderate (MD 6-12)	0.016	p=0.904
Advanced (MD>12)	0.056	p=0.789
Age (years)	**0.623**	**p<0.001**
Kmin (D)	-0.083	p=0.357
Kmax (D)	-0.042	p=0.638
Km (D)	-0.004	p=0.966

TABLE 6. Receiver operating characteristics curves (ROC) and areas under the curve (AUCs) reflecting the capacity of each variable to distinguish between glaucomatous and healthy eyes.

VARIABLE	AUC ROC	P*	SENSITIVITY	SPECIFICITY
CCT	0.503	0.960	0.760	0.680
Kmin	0.555	0.164	0.400	0.288
Kmax	0.557	0.146	0.627	0.472
Km	0.562	0.116	0.560	0.408
ACD	0.554	0.194	0.600	0.440
ACV	0.508	0.830	0.613	0.504
ACA	0.607	0.011	0.640	0.408
AEA	0.511	0.760	0.227	0.152
CAE	0.561	0.121	0.293	0.120
PEA	**0.613**	**0.006**	**0.613**	**0.392**
CPE	**0.587**	**0.031**	**0.653**	**0.464**
Ant Dens 0-2 mm	**0.673**	**0.000**	**0.627**	**0.272**
Ant Dens 2-6 mm	**0.674**	**0.000**	**0.573**	**0.232**
Ant Dens 6-10 mm	**0.621**	**0.004**	**0.867**	**0.608**
Ant Dens 10-12 mm	0.535	0.359	0.587	0.480
Anterior total area	**0.646**	**0.000**	**0.507**	**0.248**
Stromal Dens 0-2 mm	**0.676**	**0.000**	**0.587**	**0.296**
Stromal Dens 2-6 mm	**0.652**	**0.000**	**0.813**	**0.552**
Stromal Dens 6-10 mm	0.578	0.064	0.827	0.624
Stromal Dens 10-12 mm	0.502	0.862	0.760	0.664
Stromal total area	**0.601**	**0.016**	**0.800**	**0.600**
Post Dens 0-2 mm	**0.657**	**0.000**	**0.773**	**0.512**
Post Dens 2-6 mm	**0.620**	**0.005**	**0.680**	**0.472**
Post Dens 6-10 mm	0.565	0.123	0.800	0.648
Post Dens 10-12 mm	0.528	0.579	0.493	0.440
Posterior total area	0.563	0.127	0.800	0.640
Full thickness 0-2 mm	**0.679**	**0.000**	**0.600**	**0.240**
Full thickness 2-6 mm	**0.669**	**0.000**	**0.733**	**0.392**
Full thickness 6-10 mm	**0.593**	**0.027**	**0.840**	**0.648**

Full thickness 10-12 mm	0.514	0.662	0.720	0.640
FULL THICKNESS TOTAL AREA	**0.617**	**0.005**	**0.893**	**0.680**

TABLE 7. Multiple linear regression analysis for the dependent variable total corneal density (full thickness)

Total corneal densitometry	Coefficient	Confidence Interval (95%)	Significance
CONTROL			
Age	**0.315**	**[0.246-0.384]**	**p<0.001**
Gender	-1.211	[-3.390-0.967]	p=0.273
CCT	**0.024**	**[0.002-0.045]**	**p=0.030**
Km	-0.016	[-0.048-0.014]	p=0.291
POAG			
Age	**0.370**	**[0.255-0.486]**	**p<0.001**
Gender	-2.701	[-5.575-0.173]	p=0.065
CCT	0.016	[-0.017-0.050]	p=0.326
Km	0.269	[-0.369-0.908]	p=0.404

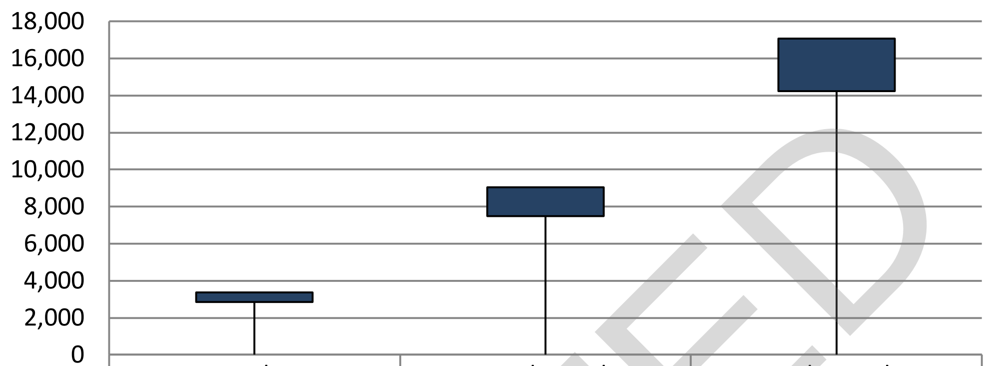
TABLE 8. Multiple linear regression analysis for the dependent variable CAE.

CAE	Slope	Confidence Interval (95%)	Significance
CONTROL			
Age	**-0.040**	**[-0.076-(-0.005)]**	**p= 0.023**
Gender	0.115	[-0.996-1.227]	p= 0.838
CCT	0.001	[-0.009-0.012]	p= 0.778
Km	0.002	[-0.013-0.019]	p= 0.725
POAG			
Age	0.008	[-0.053-0.070]	p= 0.781
Gender	-1.075	[-2.616-0.465]	p= 0.168
CCT	-0.002	[-0.021-0.015]	p= 0.747
Km	**0.651**	**[0.308-0.994]**	**p<0.001**

TABLE 9. Multiple linear regression analysis for the dependent variable PEA

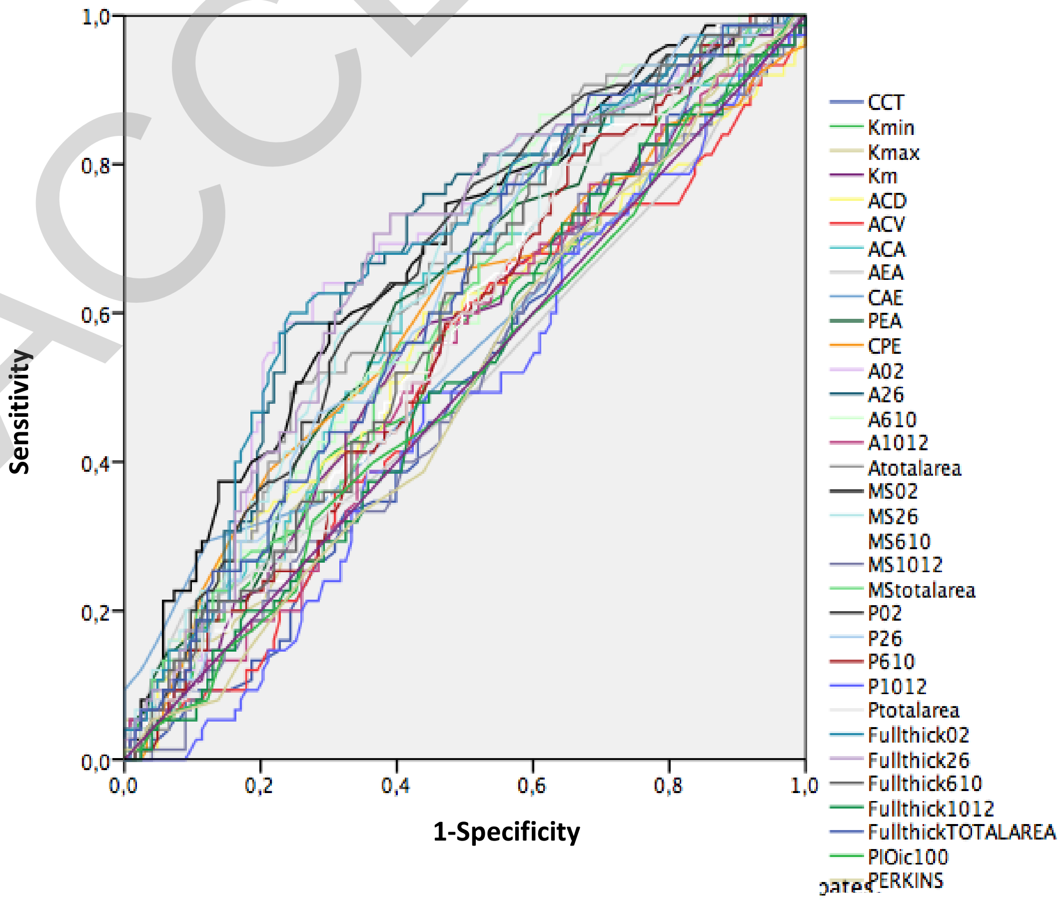
PEA	Slope	Confidence interval (95%)	Significance
CONTROL			
Age	**0.134**	**[0.034-0.235]**	**p= 0.009**
Gender	1.198	[-1.965-4.361]	p= 0.455
CCT	**0.046**	**[0.014-0.077]**	**p= 0.004**
Km	0.008	[-0.037-0.054]	p= 0.720
POAG			
Age	0.108	[-0.048-0.264]	p= 0.172
Gender	-0.308	[-4.201-3.585]	p= 0.875
CCT	**-0.054**	**[-0.100-(-0.008)]**	**p= 0.021**
Km	0.106	[-0.759-0.972]	p= 0.807

FIGURE 1



	Early	Moderated	Advanced
p75	3,366	9,055	17,092
Upper limit	5	0	22
Lower limit	0	0	0
p25	2,856	7,481	14,228

ROC CURVE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0,0
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0,2
0,4
0,6
0,8
1,0
1-Specificity
CCT
Kmin
Kmax
Km
ACD
ACV
ACA
AEA
CAE
PEA
CPE
A02
A26
A610
A1012
Atotalarea
MS02
MS26
MS610
MS1012
MStotalarea
P02
P26
P610
P1012
Ptotalarea
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Fullthick26
Fullthick610
Fullthick1012
FullthickTOTALAREA
PIOic100
PERKINS