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Gender-related Influences on Superficial Papillary Microcirculation Measured with Optical Coherence Tomography Angiography in Patients with Glaucoma

Surina Wang [a], Carmen Mendez-Hernandez [a], Paula Arribas-Pardo [b], Liseth Salazar Quiñones [a], Cristina Fernandez-Perez [c], and Julian Garcia-Feijoo [a]

[a]Department of Ophthalmology, Hospital Clinico San Carlos, Instituto de Investigaciones Oftalmológicas Ramón Castroviejo, Departamento de Inmunología, Oftalmología y ORL, Facultad de Medicina, Universidad Complutense, Madrid, Spain; [b]Department of Ophthalmology, Hospital Gomez Ulla, Madrid, Spain; [c]Clinical Research and Methodology Unit, Facultad de Medicina, Hospital Clínico San Carlos Universidad Complutense de Madrid, Instituto de Investigación Sanitaria San Carlos (IdISSC), Madrid, Spain

ABSTRACT

Purpose: To evaluate the optic nerve head (ONH), macular vessel density, and retinal nerve fiber layer (RNFL) thickness differences between the genders.

Material and methods: In this prospective case-control cross-sectional study 111 healthy subjects and 130 primary open-angle glaucoma (OAG) patients were examined with optical coherence tomography angiography (OCT-A (RS-3000 Advance (Nidek, Gamagori, Japan))). The vessel density in the peripapillary and macular area as well as the RNFL thickness was evaluated.

Results: Men appeared to have less RNFL thickness compared with women in early glaucomatous group, *being significant at the whole circumpapillary retinal nerve fiber layer (cpRNFL) thickness and inferior and nasal quadrants*: (cpRNFL) (71.01 ± 9.32 vs 77.64 ± 9.95 µm; *P = .001), superior quadrant (89.10 ± 16.63 vs 92.97 ± 17.53 µm; P = .284)*, inferior quadrant (83.03 ± 19.17 vs 95.07 ± 21.70 µm; *P = .006*), temporal quadrant (57.11 ± 10.36 vs 61.78 ± 11.37 µm; *P = .043*), nasal quadrant (54.81 ± 11.42 vs 60.73 ± 11.62 µm; *P = .016*). *Circumpapillary (wcpVD) and macular (wmVD) vessel density values were lower in men than women in the early stage OAG group, being wmVD significantly lower*: wcpVD (15.53 ± 2.45% vs 16.81 ± 3.17%, *P = .032*) and wmVD values (12.51 ± 2.21 vs 13.63 ± 2.28%, *P = .019*), but not in the moderate OAG group (wcpVD 14.46 ± 2.20% vs 16.61 ± 3.10%, *P* = .056 and wmVD 12.61 ± 2.40% vs 12.74 ± 2.54%, *P* = .870). There were no significant differences between men and women for RNFL thickness and the vessel density parameters in normal group.

Conclusion: Both, the thickness of the nerve fiber layer and peripapillary and macular vessel density are lower in men than in women with glaucoma, more markedly in early stage glaucomatous patients.

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Introduction

Glaucoma is a chronic and progressive optic neuropathy with resulting deterioration of visual function. It is one of the leading causes of blindness in the world.[1] Elevated intraocular pressure (IOP) plays an important role in development and progression of glaucoma. Other risk factors include low central corneal thickness, advanced age, exfoliation, or diabetes.[2,3] Currently, many studies have suggested that reduced blood flow of the optic nerve head (ONH) has also been considered as a risk factor for the pathogenesis of glaucoma.[4–6]

Regarding open-angle glaucoma (OAG), gender alone is usually not considered as a risk factor. However, many publications have shown results, from their study sample, that propose some differences in the prevalence and incidence of OAG between genders.[7,8] Mitchell et al. found that the prevalence of glaucoma was higher in women after adjusting the age[7] but Leske et al. showed higher prevalence in men.[8] Ever since, many studies have focused on the relationship between hormonal factors and glaucoma. Hulsman et al. examined the relationship between the age at menopause and OAG, considering that women with early menopause have a higher risk of OAG.[9] Another study analyzed the influence of early menarche on OAG risk showing that women with later menarche had an increased OAG risk.[10] Therefore, in a review, Tehrani considered that endogenous estrogen had a protective effect in the development of glaucoma.[11] However, until now, the level of endogenous estrogen on the blood flow of ONH or the blood flow of ONH difference between men and women is unknown.

Currently, a new extension of optical coherence tomography (OCT) has been developed: optical coherence tomography angiography (OCT-A). This non-invasive, easy to manage instrument, was designed to evaluate vascular alterations in the retina and ONH and quantify vessel density. Nowadays, many published studies using OCT-A have shown a decreased peripapillary vessel density at the ONH and macula in glaucomatous eyes.[12–14] Both, vessel density quantifying method and retinal nerve fiber layer (RNFL) thickness have similar diagnostic capacity.[15,16]

CONTACT Carmen Mendez-Hernandez cdmendezh@gmail.com Ophthalmology Department, Hospital Clinico San Carlos, C/Profesor Martín Lagos s/n. 28009 Madrid, Spain

Subject classification codes: glaucoma

To date, there is a lack of studies comparing peripapillary and macular vessel density as well as RNFL thickness between men and women.[17]

This study was designed to evaluate ONH and macular vessel density and RNFL differences between the genders in glaucoma patients using the RS-3000 Advance OCT-A device.

Material and methods

Study population

In this prospective observational case-control cross-sectional study 111 healthy subjects and 130 OAG patients from the Ophthalmology Department of our hospital were included. The study protocol was approved by the Institutional Review Board of Hospital Clinico San Carlos of Madrid and followed Helsinki declaration guidelines. All subjects signed an informed consent form after the study protocol and its purpose were explained to them in detail.

All participants underwent an ophthalmologic examination, including visual acuity, refraction, slit-lamp biomicroscopy, IOP measurement with Goldmann applanation tonometry, gonioscopy, ultrasound pachymetry, and dilated fundus examination. Perimetry was done and analyzed for glaucoma patients, not for healthy subjects. Only one eye randomly selected per subject was included in the final analysis.

Inclusion criteria were (1) greater than 45 years of age, (2) open-angles on gonioscopy and (3) visual acuity of 20/40 or better and a sphere between ±5 diopters and a cylinder between ±3 diopters.

Specific inclusion criteria for the glaucoma group were: (1) history of primary open-angle glaucoma; (2) documented glaucoma damage at the optic disc or (3) repeatable glaucomatous perimetric damaged.

Specific inclusion criteria for healthy subjects were (1) IOP <21 mmHg; (2) no history of elevated IOP; (3) Normal aspect of the optic disc.

Glaucoma was defined by the presence of repeatable abnormal standard automated perimetry (SAP) results with mean defect (MD) or loss variance (LV) outside the 95% normal limits. OAG patients were divided into 2 groups based on the severity of their visual field damage; early glaucoma was defined as visual field MD lower than 6 decibels (dB), and moderate glaucoma was defined as a visual field MD between 6 dB and 12 dB.

Patients with other types of glaucoma (such as angle-closure glaucoma, neovascular glaucoma, or normal tension glaucoma), non-glaucomatous optic neuropathies, retinopathies, macular, neuroophthalmological or retinal disease, systemic diseases (for example, neurological diseases such as dementia), or a history of arterial hypotension, were not included. In order to report systemic disorders patients were asked which medication they were taking using a standardized questionnaire in which the following questions were included: have you been diagnosed with high blood pressure, diabetes, or hypercholesterolemia? If yes, when were you diagnosed and what medication are you currently taking? Women using post-menopausal hormone treatments were not included.

Eyes with intraocular surgery (except cataract surgery) or recently undergoing cataract surgery (<1 year) were excluded.

Scan protocol

All participants were examined with the Nidek´s RS-3000 Advance OCT (Nidek, Gamagori, Japan), which automatically calculates the peripapillary and macular vessel densities, to collect SD-OCT and OCT-A images.

All the scans were obtained by the same operator without pupil dilation in a dark room. The scanning was repeated if the SSI quality was <7/10. Poor OCT image quality due to segmentation errors secondary to extensive peripapillary changes that make OCT-A unreadable were not included.

The RNFL thickness as well as vessel density in the peripapillary and macular area were evaluated.

Spectral domain optical coherence tomography

The Spectral Domain (SD-OCT) provides a scan of 2.1 mm depth in tissue, 20 μm transversal and 7 μm axial resolution, set a 3D image only needs 1.6 s.[18] It optimizes every time to improve the image quality. Automated measurements of circumpapillary retinal nerve fiber layer thickness (cpRNFL) raster scanning over a 4.5 × 4.5 mm^2 area centered on the optic disc were taken. The following parameters were used to evaluate cpRNFL: (1) average thickness of the entire 360° around the optic nerve head; and average thickness in the (2) superior quadrant; (3) temporal quadrant; (4) inferior quadrant; and (5) nasal quadrant using the TSNIT chart.

Optical coherence tomography angiography

The OCT-A RS-3000 Advance is an advance developed technology of OCT which includes a system that provides a noninvasive method for obtaining 3D tomographic images of the posterior pole (ONH and retinal vasculature). The OCT-A allows scans at various retinal layers and provides the vessel density map and an automated measurement of the vascular density in the scanned region. We obtained the following measurements: circumpapillary vessel density of the whole image (wcpVD), percentage of vessel density at the optic nerve head (iVD), and macular capillary density of the whole image (wmVD). For this study, the imaging of scanning over a 4.5 × 4.5 mm^2 areas centered on the optic disc and on the foveal center was used. The measurement of vascular density in the external RNFL layer, from the internal limiting membrane (ILM) to the inner plexiform layer/inner nuclear layer +8 μm was considered.

Statistical analysis

The Kolmogorov–Smirnov test was used to confirm the normal distribution of the quantitative data. Parameters were normally distributed. Data were compared between men and women in each group (normal, early stage glaucoma, moderate stage glaucoma) using the Student's t-test. The Chi-square test was used to determine if there were differences in hypertension (HTA), diabetes, and hypercholesterolemia between men and women. Data are presented as means ± standard deviation (SD). Relationships between parameters were examined through Pearson correlation. Gender, maximum IOP, i.e., IOP before starting the antiglaucomatous treatment recorded in the patient's medical record, IOP at study visit, and age influence on vessel density were analyzed using multiple regression analysis. All statistical tests were performed using the software package IBM SPSS (version 21.0; IBM Corp., Somers, NY, USA). *Bonferroni adjustment was applied in the stratified analysis so significance was set at $p < .02$.*

Results

A total of 250 eyes were included in this study. Of these eyes, 9 were excluded due to poor quality images. Therefore, data from 241 eyes were analyzed. Table 1 summarizes the demographic, clinical, and ocular characteristics of men and women in the normal and OAG groups. 111 normal subjects, 91 OAG eyes in early stage and 39 OAG eyes in moderate stage were analyzed. None of OAG patients had a severe stage.

There were no significant differences in age, arterial hypertension, diabetes mellitus, hypercholesterolemia, visual field MD, maximum IOP, study visit IOP, disc or cup area, and horizontal or vertical cup-to-disc (C/D) ratio measurements between men and women in the control or in any glaucoma group (Table 1).

Circumpapillary retinal nerve fiber layer thickness

The RNFL thickness and the differences between groups are shown in Table 2.

Significant differences between normal subjects and glaucoma patients in the whole cpRNFL and all quadrants were found. *Men appeared to have significant less RNFL thickness compared with women in early glaucomatous group in whole cpRNFL, inferior, and nasal quadrants but not in the superior and temporal quadrants.* No differences in RNFL thickness were found between men and women in the control or moderate stage glaucomatous group (Table 2).

Optical coherence tomography angiography

The results of vessel density are shown in Table 2. Significant differences between normal subjects and glaucoma patients in the wcpVD, iVD, and wmVD were found. Similar to the RNFL thickness, there were no significant differences between men and women for all the vessel density parameters (wcpVD, iVD, and wmVD), $p > .02$ in normal group. On the other hand, wcpVD and wmVD values were lower in men than women in the early stage OAG group, but not in the moderate OAG group, *being the macular capillary density significantly lower in men in the early OAG group.*

The correlation between cpRNFL and wcpVD, iVD, and wmVD parameters is shown in Figures 1–3. *Vessel density was significantly correlated with RNFL thickness wcpVD ($r = 0.796$, $p < .0001$), wmVD ($r = 0.455$, $p < .0001$), and iVD ($r = 0.486$, $p < .0001$.)*

No correlation was found between refractive error, maximum, or study visit IOP values and vessel density parameters. Age showed a negative correlation with circumpapillary ($r = -0.350$, $p < .0001$) and macular vessel density ($r = -0.289$, $p < .0001$).

Multiple regression analysis was used to determine gender influence on vessel density values. In the first regression model (RM1), the effect of gender on optic nerve head, circumpapillary, and macular vessel density was analyzed. In the other two models, the effect of gender on vessel density has been adjusted by age (RM2) and IOP (maximum IOP and study visit IOP) (RM3). The results of the three regression models are shown in Table 3. In all regression models, women show a non-significant increase in vessel density compared to men. Adjusting the regression model by age, women present a significant increase of 1.2% and 0.7% in circumpapillary and macular vessel density, respectively, compared to men.

Discussion

Studies evaluating gender differences in glaucoma patients are still scarce

Previous studies demonstrated that consensus on gender predilection for OAG is unclear.[19,20] Different studies have shown different prevalence between men and women in white population: the Rotterdam study showed higher prevalence in men[19] in contrast to the greater prevalence among women shown in the Blue Mountains Eye study.[7]

Actually, we might consider that the age-adjusted prevalence of POAG might be higher in men especially among black population.[21]

Some studies suggest that female sexual hormones may be protective against glaucoma.[10,22]

Higher IOP has been demonstrated after menopause. It could be explained in part by the effect of estradiol on the smooth muscle tone and vascular resistance. Receptors are located in the ciliary body and the outflow system, and therefore it could influence IOP, by reducing the aqueous production and increasing the aqueous outflow.[23,24]

In our study, we found less thickness of the global and sectoral nerve fiber layer between men and women in patients with early glaucoma.

In the moderate glaucoma group, men's mean RNFL thickness was two microns lower than women's, although this difference was not significant. It is known that the RNFL thickness decreases with age. Although the age difference between men and women in each of the diagnostic groups was not significant, men in the early OAG group were 2 years older than women while in the group of moderate OAG, men were 3 years younger. It is estimated that the overall thickness of the RNFL decreases about 0.23 microns each year[25,26] so that the lower thickness of RNFL found in men in the early glaucoma stage group would not be justified by the age difference between men and women. It might be possible that in the group of patients with moderate glaucoma, no matter men had two microns less in RNFL thickness, that difference might have not been significant because of the number of subjects included in this group.

The results obtained with OCT-A showed higher peripapillary and macular vessel density in control group than in glaucoma patients.

Table 1. Demographic, clinical, and ocular characteristics.

	Normal Group				Glaucoma Group (n = 130)							
						Early Stage (n = 91)			Moderate Stage (n = 39)			
	Total (n = 111)	Men (n = 51)	Women (n = 60)	*P* value (men & women)	Total (n = 130)	Men (n = 48)	Women (n = 43)	*P* value (men & women)	Men (n = 21)	Women (n = 18)	*P* value (men & women)	*P* value (normal & glaucoma)
Age	63.14 ± 13.68	61.35 ± 10.48	65.97 ± 13.95	0.055$^{\#}$	71.46 ± 9.78	72.50 ± 8.57	70.51 ± 10.87	0.333$^{\#}$	69.90 ± 10.29	72.72 ± 9.88	0.399$^{\#}$	<0.001$^{\#}$
HTA (yes/no)	37/74	17/34	20/40	1.000$^{\&}$	49/81	21/27	15/28	0.388$^{\&}$	5/16	8/10	0.173$^{\&}$	0.481$^{\&}$
DM (yes/no)	19/92	12/39	7/53	0.098$^{\&}$	35/95	11/37	9/34	0.819$^{\&}$	7/14	8/10	0.477$^{\&}$	0.069$^{\&}$
HC (yes/no)	40/71	19/32	21/39	0.805$^{\&}$	38/92	17/31	13/30	0.599$^{\&}$	4/17	4/14	0.807$^{\&}$	0.260$^{\&}$
MD (dB)	/	/	/	/	4.77 ± 2.50	3.26 ± 1.62	3.77 ± 1.56	0.125$^{\&}$	7.34 ± 1.18	8.17 ± 1.83	0.095$^{\#}$	/
Maximum IOP	/	/	/	/	24.24 ± 4.10	24.67 ± 4.18	24.03 ± 4.87	0.584$^{\#}$	23.82 ± 2.90	24.10 ± 2.28	0.799$^{\#}$	/
Study visit IOP	12.90 ± 1.45	13.14 ± 1.15	12.7 ± 1.64	0.113$^{\#}$	16.25 ± 2.59	16.13 ± 2.91	16.50 ± 2.51	0.574$^{\#}$	16.17 ± 2.12	16.15 ± 2.54	0.988$^{\#}$	<0.001$^{\#}$
Disc area (mm^2)	2.16 ± 0.35	2.13 ± 0.35	2.19 ± 0.35	0.395$^{\#}$	2.13 ± 0.44	2.08 ± 0.38	2.10 ± 0.50	0.826$^{\#}$	2.30 ± 0.47	2.13 ± 0.36	0.220$^{\#}$	0.601$^{\#}$
Cup area (mm^2)	0.53 ± 0.34	0.44 ± 0.30	0.62 ± 0.35	0.005$^{\#}$	1.15 ± 0.49	1.06 ± 0.46	1.07 ± 0.39	0.924$^{\#}$	2.13 ± 0.36	1.15 ± 0.54	0.049$^{\#}$	<0.001$^{\#}$
Horizontal C/D	0.52 ± 0.15	0.47 ± 0.14	0.55 ± 0.14	0.02$^{\#}$	0.74 ± 0.14	0.71 ± 0.14	0.73 ± 0.12	0.451$^{\#}$	0.82 ± 0.13	0.72 ± 0.18	0.052$^{\#}$	<0.001$^{\#}$
Vertical C/D	0.44 ± 0.13	0.41 ± 0.12	0.47 ± 0.13	0.05$^{\#}$	0.70 ± 0.13	0.69 ± 0.12	0.69 ± 0.11	0.964$^{\#}$	0.78 ± 0.11	0.72 ± 0.18	0.174$^{\#}$	<0.001$^{\#}$

HTA (Arterial hypertension); DM (Diabetes mellitus); HC (hypercholesterolemia); MD (Mean defect); C/D (cup to disc ratio); IOP (intraocular pressure), Maximum IOP (IOP before starting antiglaucomatous medical treatment), Study visit IOP (IOP at the visit study).

$^{\&}$Chi-square.

$^{\#}$t-Student test.

Table 2. Comparison of cpRNFL (μm) and vessel density (%) between men and women in normal, early, and moderate stage glaucomatous groups.

	Normal Group				Glaucoma Group							
						Early Stage (n = 91)			Moderate Stage (n = 39)			
	Total (n = 111)	Men (n = 51)	Women (n = 60)	*P* value (men &women)	Total (n = 130)	Men (n = 48)	Women (n = 43)	*P* value (men&women)	Men (n = 21)	Women (n = 18)	*P* value (men& women)	*P* value (normal & glaucoma)
Whole cpRNFL	100.85 ± 9.30	101.48 ± 12.70	100.31 ± 8.08	0.510#	73.15 ± 11.07	71.01 ± 9.32	77.64 ± 9.95	0.001#	69.97 ± 12.52	71.83 ± 13.51	0.658#	<0.001#
Superior cpRNFL	127.10 ± 15.00	129.02 ± 15.45	125.47 ± 14.55	0.215#	88.98 ± 18.72	89.10 ± 16.63	92.97 ± 17.53	0.284#	82.77 ± 18.92	86.37 ± 24.88	0.611#	<0.001#
Temporal cpRNFL	70.33 ± 9.70	69.70 ± 9.61	70.87 ± 9.83	0.532#	59.40 ± 10.76	57.11 ± 10.36	61.78 ± 11.37	0.043#	58.19 ± 9.46	61.23 ± 11.04	0.359#	<0.001#
Inferior cpRNFL	131.61 ± 14.53	132.65 ± 16.13	130.72 ± 13.08	0.489#	86.93 ± 22.23	83.03 ± 19.17	95.07 ± 21.70	0.006#	84.75 ± 25.99	80.39 ± 22.64	0.584#	<0.001#
Nasal cpRNFL	74.37 ± 13.95	74.57 ± 14.38	74.20 ± 13.69	0.891#	57.29 ± 12.16	54.81 ± 11.42	60.73 ± 11.62	0.016#	54.18 ± 11.44	59.294 ± 14.4	0.226#	<0.001#
wcpVD (%)	22.36 ± 3.85	22.46 ± 4.58	22.27 ± 3.13	0.800#	15.87 ± 2.86	15.53 ± 2.45	16.81 ± 3.17	0.032#	14.46 ± 2.20	16.61 ± 3.10	0.056#	<0.001#
iVD (%)	18.67 ± 4.90	19.65 ± 4.93	17.86 ± 4.75	0.056#	12.86 ± 4.79	12.67 ± 4.42	14.04 ± 4.97	0.168#	10.48 ± 4.93	13.36 ± 4.46	0.065#	<0.001#
wmVD (%)	15.00 ± 2.45	14.65 ± 3.09	15.05 ± 2.61	0.472#	12.93 ± 2.34	12.51 ± 2.21	13.63 ± 2.28	0.019#	12.61 ± 2.40	12.74 ± 2.54	0.870#	<0.001#

cpRNFL = circumpapillary retinal nerve fiber layer thickness, wcpVD = circumpapillary vessel density of the whole image, i. VD = percentage of vessel density at the optic nerve head, wmVD = macular capillary density of the whole image.
All above measurements are represented by mean ±SD.
#t-Student test

Men with glaucoma had less vessel density at the optic nerve head and macula being clinically relevant in patients with early glaucoma stage. Even more macular vessel density was significantly lower in men in early glaucoma patients and statistical significance was close to 0.02 in the differences in peripapillary vascular density (mean density of men 15.53 ± 2.45 vs mean density of women 16.81 ± 3.17, P = .032).

It is possible that the number of patients included in the moderate glaucoma group was not sufficient to reach a significant difference in peripapillary and macular vessel density between men and women since statistical significance was *also* close to 0.02 in the differences in peripapillary vascular density (mean density of men 13.16 ± 2.00% versus mean density of women 14.69 ± 2.82%, *P* = .056). *The sample size estimation to reach a statistically significant difference is 53 patients (α = 0.05, β = 0.20, 80% of power).*

Some studies have reported macular vessel density changes in glaucoma.[27,28] The peripapillary vessel density parameters appear to have better diagnostic capacity in glaucoma than macular vessel density[16,29,30] which would partly justify finding no differences between men and women in macular vascular density *in this group*.

Macular vessel density has been shown to be reduced in glaucomatous eyes compared with healthy eyes.[31,32]RNFL damage in early glaucoma may be more evident in the retina farther from the peripapillary area.[33]Therefore, the ONH vessel density as well as the RNFL thickness may not identify early glaucomatous changes.

Little is known about gender-specific differences in ocular blood flow and its regulation and *scarce* data about gender differences in optic nerve head blood flow are currently available.[34] *Faster blood flow velocity at the optic nerve in women than in men have been found but most of the studies have been done using laser Doppler velocimetry in the retrobulbar vessels or Laser speckle flowgraphy in order to measure blood vessel velocities.*[34–37] To our knowledge, there are not any studies analyzing *ocular perfusion density* differences between men and women.

We found a decrease in the vessel density in the glaucomatous eyes, which was correlated with RNFL thickness. Besides, RNFL thickness had a stronger correlation with ONH vessel density than with macular vessel density. It is still unclear whether vascular changes are a primary or secondary consequence in glaucoma. Reduced retinal perfusion leads to faster retinal ganglion cell death, but on the other hand, OCT-A may detect lower metabolic demands or vascular dropout due to retinal ganglion cell dysfunction. Moghimi et al.[38] found that OCT-A parameters were associated significantly with the rate of RNFL decline in patients with mild to moderate POAG followed up over time. Patients with lower baseline circumpapilar and macular vessel density tended to progress significantly faster than those with higher values.

Our results agree with other studies in which vessel density measured with OCT-A or optic disc blood flow measured using noninvasive techniques such as Laser Doppler flowmetry, laser speckle flowgraphy, and OCT-A was significantly lower in glaucoma patients.[12,39,40] *These data suggest that OCT-A measurements have good correlation with the severity of structure loss in glaucoma.*

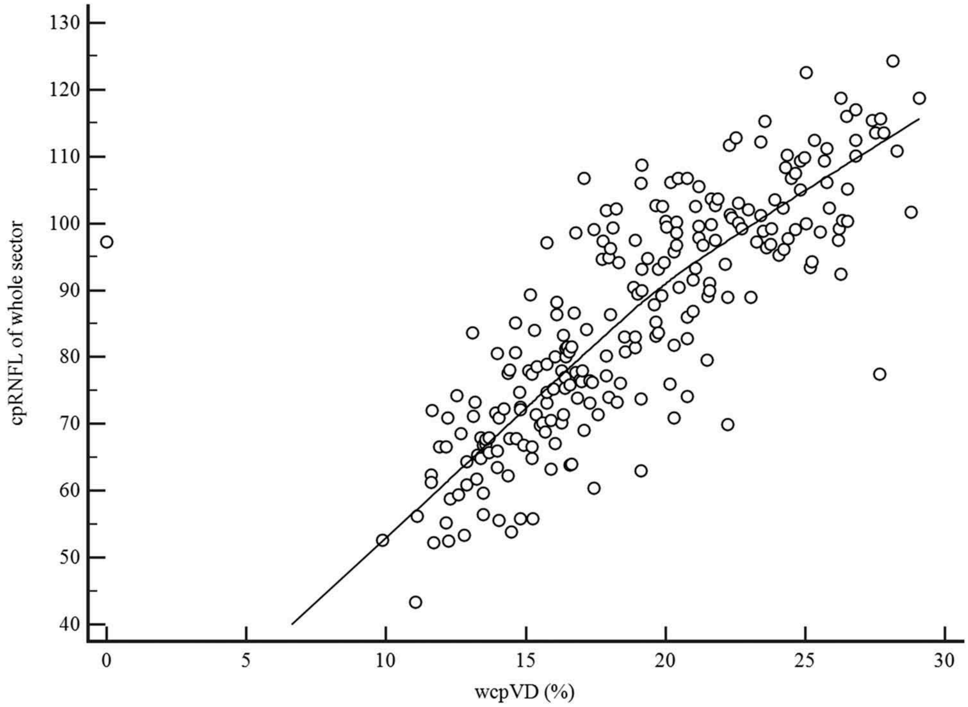

Figure 1. Correlation between the whole cpRNFL and the circumpapillary vessel density of the whole image (wcpVD). Pearson's correlation coefficient 0.796, $p < .0001$.

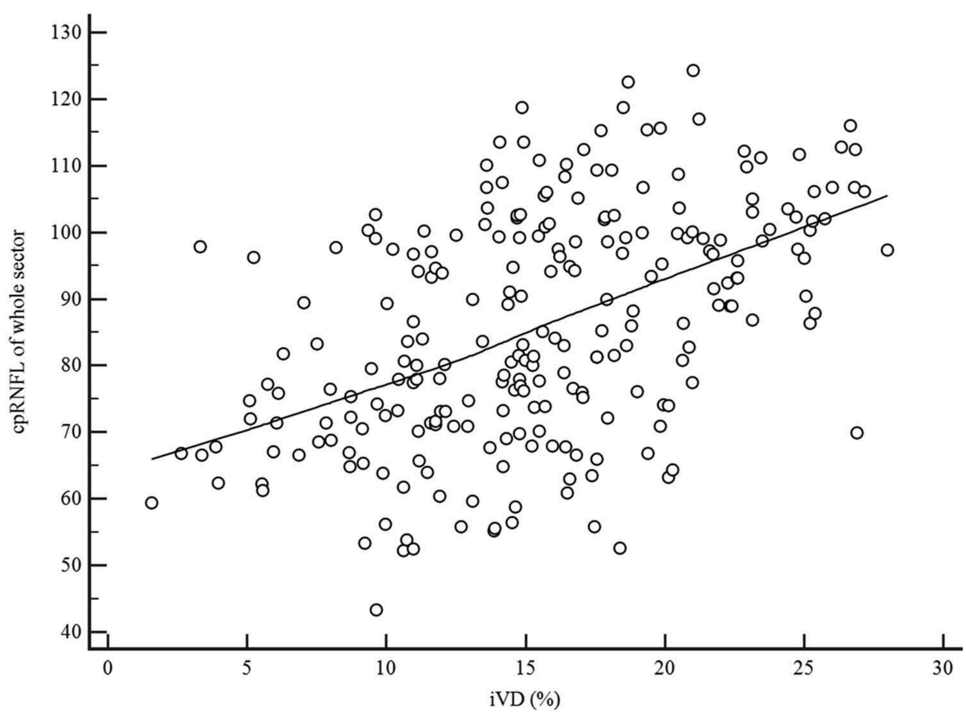

Figure 2. Correlation between the whole cpRNFL and the percentage of vessel density at the optic nerve head (iVD). Pearson's correlation coefficient 0.486, $p < .0001$.

Optic nerve ischemia and reduced ocular blood flow have been shown to be associated with the development and progression of glaucoma.[41–43] In the present study, sex-related differences were only shown in early-stage glaucoma patients, when vascular changes could precede the loss of RNFL and have a causative role. Vascular factor could play a more important role in this phase of the disease and women, due to the protective effect of estrogen, would have less alteration in vascular density.[44–47] As this is a cross-sectional study, our results did not answer this question.

This study has limitations. This was a preliminary study, carried out with an OCT-A which was lended during a limited period of time in order to carry out research studies. For that reason, the number of patients included

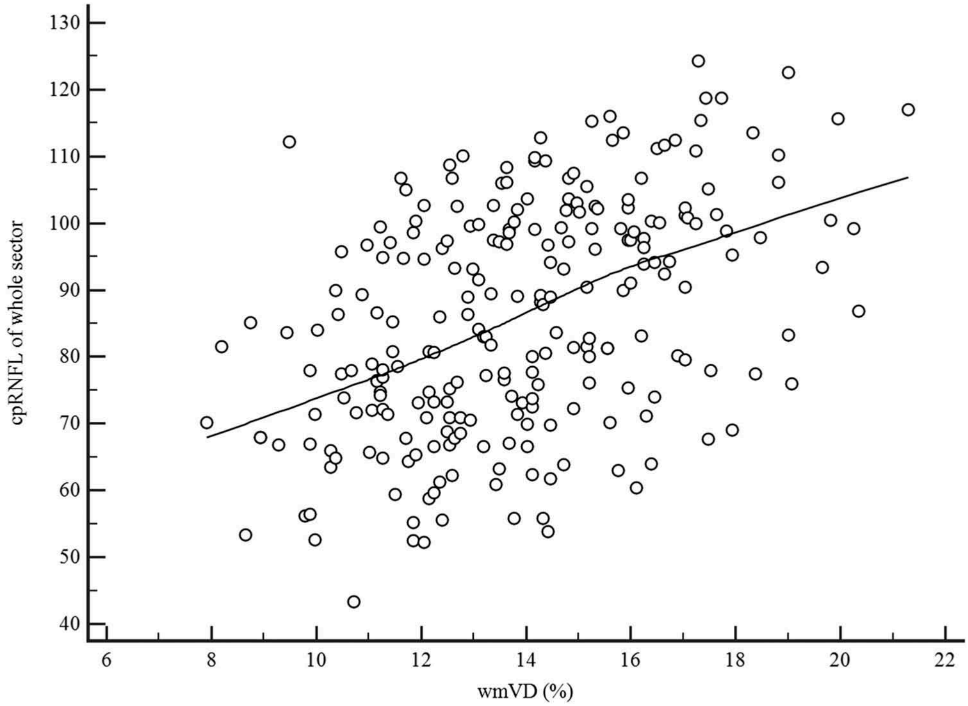

Figure 3. Correlation between the whole cpRNFL and the macular capillary density of the whole image (wmVD). Pearson's correlation coefficient 0.455, $p < .0001$.

Table 3. Multiple regression analysis to determine gender influence on vessel density at the optic nerve head and circumpapillary and macular vessel density.

	RM1			RM2			RM3		
	β slope	95% CI	p	β slope	95% CI	p	β slope	95% CI	p
wcpVD (%)	0.957	−0.180 ~ 2.094	0.099	1.230	0.181 ~ 2.280	0.022	0.768	−0.423 ~ 1.960	0.203
wmVD (%)	0.638	−0.018 ~ 1.294	0.057	0.758	0.130 ~ 1.387	0.018	0.630	−0.355 ~ 1.615	0.207
iVD (%)	0.605	−0.823 ~ 2.033	0.405	0.601	−8.34 ~ 2.036	0.410	1.504	−1.83 ~ 3.192	0.080

RM1: gender.
RM2: gender + age.
RM3: gender + IOP (maximum IOP, study visit IOP).
iVD: iVD: vessel density at the optic nerve head; wcpVD: circumpapillary vessel density; wmVD: macular vessel density.
β: β slope; 95% CI: 95% Confidence Interval; RM: Regression Model.

in the moderate glaucoma group was low which may have influenced that no significant differences were found between men and women in vessel density and RNFL thickness in this group. We did not include ocular hypertensive patients or patients with advanced stage glaucoma; therefore it was not possible to determine if differences in vascularization between men and women are present in these stages of the disease.

In conclusion, the thickness of the nerve fiber layer and peripapillary and macular vessel density is lower in men than in women with open-angle glaucoma, more markedly in the group of early glaucoma.

Long-term studies *using OCT-A* including a greater number of glaucoma patients *might improve our knowledge about the vascular differences between men and women.*

Declaration of interest

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ORCID

Surina Wang http://orcid.org/0000-0002-5342-5796
Carmen Mendez-Hernandez http://orcid.org/0000-0003-3413-5248
Paula Arribas-Pardo http://orcid.org/0000-0003-1973-5798
Liseth Salazar Quiñones http://orcid.org/0000-0002-2712-9109
Cristina Fernandez-Perez http://orcid.org/0000-0001-9853-6257
Julian Garcia-Feijoo http://orcid.org/0000-0002-7772-5718

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