Research Square

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# Retrobulbar hemodynamic characteristics of glaucoma suspects assessed by color Doppler imaging

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**Research Article**

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# Abstract

Background/Aims

To evaluate retrobulbar haemodynamic parameters in glaucoma suspects using colour Doppler imaging (CDI) and other eye characteristics such as intraocular pressure (IOP), structural optic nerve parameters and ocular perfusion pressure (OPP).

Methods

A descriptive cross-sectional, single-centre study was conducted among glaucoma suspects. Doppler ultrasound was used to assess haemodynamic parameters such as peak systolic velocity (PSV), end-diastolic velocity (EDV), and resistance index (RI) in the ophthalmic artery (OA), central retinal artery (CRA), and nasal and temporal short posterior ciliary arteries (nSPCA and tSPCA). IOP, systemic blood pressure (BP), OPP, and optical coherence tomography (OCT) parameters were recorded. A secondary analysis was performed to compare retrobulbar haemodynamic parameters between glaucoma suspects with and without DM2.

Results

A total of 134 eyes from 73 patients were included. The mean age was 59.5 years, and the majority of participants were female (65.7%). The prevalence of type 2 diabetes mellitus and systemic hypertension was 27.3% and 24.7%, respectively. Mean PSV, EDV and RI where 38.54 ± 11.16, 8.72 ± 2.88 and 0.77 ± 0.06 for OA; 13.86 ± 3.50, 4.70 ± 1.30 and 0.66 ± 0.06 for CRA; 11.29 ± 3.50, 4.69 ± 1.23 and 0.57 ± 0.07 for nSPCA; and 11.71 ± 3.36, 4.79 ± 1.17 and 0.58 ± 0.07 for tSPCA. Eyes of patients with DM2 exhibited decreased velocities and increased RI when compared to eyes of the non-DM2 patients.

Conclusion

This study characterized PSV, EDV, and RI values in the retrobulbar circulation of a glaucoma suspect cohort, providing hemodynamic information in a population for which such data were previously unavailable.

**PRECIS**

Colour Doppler imaging successfully characterized retrobulbar blood flow velocities and resistance indices in glaucoma suspects. Furthermore, participants with type 2 diabetes exhibited significantly decreased vascular velocities and increased resistance compared to non-diabetic individuals.


# INTRODUCTION

Glaucoma is a chronic, progressive, and irreversible optic neuropathy characterized by visual field loss and, consequently, impaired quality of life [1]. It represents the leading cause of irreversible blindness and

the second leading cause of blindness worldwide, affecting more than 85 million people, with an estimated prevalence of approximately 111.8 million by 2040 [2,3]. Based on the drainage angle of the eye, it is categorized into open-angle and angle-closure glaucoma. The prevalence of primary open-angle glaucoma over the last 20 years is approximately 2.4%, a figure that has unfortunately remained unchanged even though the population continues to increase [4]. Given the nature of this disease, timely diagnosis is essential; therefore, early detection of glaucoma suspects is crucial.

A glaucoma suspect is defined as a patient with open anterior chamber angles who present one or more of the following characteristics: ocular hypertension with a normal optic nerve, retinal nerve fibre layer (RNFL), and visual fields; optic nerve cupping or RNFL suspicious for glaucomatous damage; or visual fields suggestive of glaucomatous damage in the absence of clinical signs of optic neuropathy or retinopathy [5].

Several theories have been proposed to explain the pathogenesis of glaucomatous optic neuropathy, the most widely accepted being the mechanical and vascular theories [6]. The vascular theory posits that glaucomatous damage results primarily from ischemia secondary to impaired blood flow, due to altered ocular perfusion pressure and/or dysfunctional vascular auto-regulation [7]. Various techniques allow assessment of ocular blood flow, including laser Doppler flowmetry, laser Doppler velocimetry, Doppler optical coherence tomography, laser speckle flowgraphy and colour Doppler ultrasound, [8].

Colour Doppler ultrasound is an objective diagnostic modality that enables the evaluation of both vascular anatomy and blood flow by measuring erythrocyte velocity in major ophthalmic vessels, such as the ophthalmic artery (OA), central retinal artery (CRA), and nasal and temporal short posterior ciliary arteries (nSPCA and tSPCA) [9]. Hemodynamic parameters obtained from retrobulbar circulation include peak systolic velocity (PSV), end-diastolic velocity (EDV), mean flow velocity (MFV), mean systolic velocity (Sm), mean diastolic velocity (Dm), and resistance index (RI) [10].

Reduced blood flow velocities combined with increased vascular resistance in the retrobulbar circulation are considered indicators of decreased optic nerve head perfusion and consequent ischemia. Numerous studies have reported reduced PSV and EDV, along with increased RI, in the retrobulbar circulation of glaucomatous eyes [11–19]. However, there is very limited information concerning retrobulbar circulation changes in glaucoma suspects and related risk factors as diabetes.

Several clinical practice guidelines indicate that type 2 diabetes mellitus (DM2) is a risk factor for developing glaucoma [20]. The prevalence of DM2 in the Mexican population reaches 17% according to the national health survey [21]. Moreover, diabetic retinopathy (DR) in patients with DM2 reports a prevalence of 33.6% [22]. Eyes with DR show alterations in retrobulbar circulation when compared to healthy eyes. These changes include reduced PSV and EDV, along with increased RI in retrobulbar arteries [23].

Retrobulbar circulation can also be altered by intrinsic ocular factors, such as intraocular pressure (IOP), optic disc size and RNFL thickness. Eyes with higher IOP show differences in retrobulbar circulation

when compared to eyes with controlled IOP, mostly in CRA and SPCA [24,25]. RNFL thinning has been proposed as a consequence of ischemia [12], and larger optic disc size is typically associated with lower retrobulbar blood flow velocities [26]. Calvo et al. reported alterations in retrobulbar arterial velocities and resistance indices in Caucasian ocular hypertensive glaucoma suspects who converted to glaucoma during a two-year follow-up period [27]. Furthermore, two epidemiological studies conducted in Hispanic populations – LALES and Proyecto VER – have demonstrated that reduced ocular perfusion pressure (OPP) is associated with up to a fourfold increased risk of developing glaucoma [28,29]. To date, there is no available information regarding retrobulbar haemodynamic parameters in Hispanic glaucoma suspects, with or without ocular hypertension.

To our knowledge, no published study has evaluated retrobulbar hemodynamic parameters in Hispanic glaucoma suspects, with or without ocular hypertension. The aim of this study was to describe retrobulbar haemodynamic parameters in Hispanic glaucoma suspects using colour Doppler imaging (CDI), as well as their IOP, structural optic nerve parameters and OPP. As an exploratory secondary analysis, retrobulbar haemodynamic parameters were compared between glaucoma suspects with and without DM2.

# MATERIALS AND METHODS

A descriptive cross-sectional, single-centre study was conducted at the Asociación para Evitar la Ceguera I.A.P. (Mexico City, Mexico) between March and November 2025.

We reviewed clinical records; sociodemographic data and clinical variables were collected prior to examination. Inclusion criteria required all patients to have undergone optical coherence tomography (OCT) of the optic nerve (Cirrus HD-OCT 6000 (Carl Zeiss Meditec, Dublin, CA, USA)) and a complete ophthalmological evaluation by a glaucoma specialist (SSBU), who confirmed the diagnosis of glaucoma suspect according to the European Glaucoma Association Guidelines (6th edition) [1]. Patients with the following conditions were excluded: primary or secondary glaucoma; non-glaucomatous optic neuropathies; thyroid eye disease; history of cataract surgery, laser iridotomy or trabeculoplasty, ocular trauma, retinal artery or vein occlusion, and diabetic retinopathy.

The variables that were taken into consideration were: age, gender, IOP, optic nerve clinical findings (optic nerve disc size and cupping) and OCT findings (optic disc size, vertical cup-to-disc ratio (VCD) and average RNFL thickness). Retrobulbar hemodynamic parameters were evaluated in an exploratory secondary analysis comparing glaucoma suspects with and without DM2.

All participants provided written informed consent. The study adhered to the Declaration of Helsinki, ensuring confidentiality, anonymity, and ethical principles of beneficence, nonmaleficence, and justice. The research committee and research ethics committee evaluated and approved the study (CONBIOETICA-09-CEI-006-20170306).

Patients were examined in the supine position after instillation of topical anaesthesia (tetracaine). Blood pressure was measured before Doppler evaluation, and after 5 minutes in the supine position to calculate mean arterial pressure (MAP) and OPP. MAP was calculated as follows: systolic blood pressure + twice the diastolic blood pressure, all divided by three. OPP was calculated as the difference between MAP and the IOP according to the following formula corrected for supine position [30]:

OPP = 115/130(MAP) − IOP.

Colour Doppler ultrasound was performed using an ACUSON NX3 Elite system (Siemens Healthineers, Erlangen, Germany) with a 16.5-MHz probe by ophthalmologists specialized in ocular ultrasound (CBR, SSBU). Transpalpebral evaluation was performed for each artery in which PSV, EDV and RI could be adequately evaluated. OA was studied at the intersection with the optic nerve, CRA was measured 1–3 mm beyond the posterior pole of the eyeball, and SPCAs were found 3–5 mm behind the posterior pole. The measurement angles for each vessel were taken into consideration and they did not exceed 60 degrees [31]. Ultrasound acquisition was conducted in accordance with ALARA safety principles [32].

Data were recorded and entered into a database for statistical analysis using Stata version 19 (StataCorp, College Station, TX, USA). Normality was assessed using the Kolmogorov–Smirnov test. Descriptive statistics included frequencies, percentages, means, standard deviations, and percentiles.

# RESULTS

A total of 134 eyes from 73 patients were included. The mean age of the study population was 59.5 years, and the majority of participants were female (65.7%). The prevalence of DM2 and systemic hypertension was 27.3% and 24.7%, respectively. The mean MAP was 88.5 ± 12.7 mmHg (Table 1).

Intraocular pressure values were within the normal range, with a maximum of six eyes (4.5%) presenting IOP values greater than 21mmHg. The mean OPP was 63.0 ± 11.6mmHg, with only 2 patients with OPP lower than 40 mmHg (Table 1).

The retrobulbar vascular parameters evaluated included PSV, EDV, and RI. The mean values of these parameters are shown in Table 2 (Supplementary figures).

PSV and EDV mean values of all evaluated arteries were numerically lower, whereas mean RI values were numerically higher, than the previously published values shown in Table 2. More than 30% of PSV measurements in all four arteries studied were below the minimum published range, with the CRA exhibiting the highest proportion of reduced PSV values (65.7%). Regarding EDV, the OA and tSPCA showed the highest proportion of values below the lower published limit, at 38.0% and 59.7%, respectively. Increased RI values were observed in up to nearly 30% of cases when compared to the published reference, predominantly affecting the nSPCA.

Demographic and ocular characteristics of glaucoma suspects with and without type 2 diabetes mellitus are shown in Table 3. No significant difference was observed between the two groups ($p > 0.05$)

Eyes of patients with DM2 exhibited decreased velocities (EDV of AO and ACR, and PSV of ACR) and increased AO RI when compared to eyes of the non-DM2 patients (Table 4). Patients with or without systemic hypertension showed no differences in retrobulbar parameters.

# DISCUSSION

Colour Doppler ultrasound is a useful tool in the evaluation of the retrobulbar vasculature, allowing us to measure velocities and resistances of retrobulbar arteries. The main advantages of this technique include its non-invasive nature, absence of contrast agents and ionizing radiation, and lack of interference from ocular media opacities [33,34].

An impaired optic nerve blood flow, characterized by decreased velocities and elevated vascular resistance, have been associated with reduced optic nerve head perfusion, potentially leading to ischemic damage and development of glaucomatous optic neuropathy, as proposed in the vascular theory of glaucoma [35,36].

Retrobulbar circulation findings in glaucomatous eyes include reduced PSV and EDV, and increase in RI, regardless of the type of glaucoma [11–19]. It has also been found that the severity of visual field defects was proportional to the retrobulbar blood flow diminishing [37,38]. Furthermore, alterations in retrobulbar circulation exhibits differences according to the severity of the disease, with more marked alterations in advanced cases [39,40].

However, information about retrobulbar alterations in glaucoma suspects is scarce, with only one prospective study that followed glaucoma suspects with ocular hypertension that converted to glaucoma, and a cross-sectional study that compared ocular hypertensive patients with glaucoma patients. Calvo et al. demonstrated that Caucasian ocular hypertensive glaucoma suspects who developed glaucoma during a two-year follow-up exhibited alterations in retrobulbar arterial velocities and resistance indices. [27], and Nicolela et al. reported differences in PSV of the CRA between ocular hypertension and glaucoma [41]. Nevertheless, this last study didn't include a control group (healthy eyes).

The principal findings in our present study were the characterization of PSV, EDV and RI values in a glaucoma suspects cohort. Our findings suggest differences when compared to previous publications; however, proper comparison cannot be made mainly because equipment and study population differ greatly [42].

Kurysheva et al. demonstrated that Doppler-derived hemodynamic parameters in preperimetric glaucoma are more reliable than structural parameters obtained by OCT for early glaucoma detection [43]. Furthermore, To et al. reported that 10.8% of glaucoma suspects reported a change in diagnostic to

primary open-angle glaucoma within four years of follow-up [44]. Consequently, identifying haemodynamic characteristics similar to those observed in established glaucoma may allow for closer surveillance and earlier diagnosis.

According to our study aim, which was to assess IOP, structural optic nerve parameters and OPP; the majority of the study population presented normal range values of IOP and OPP. Regarding disc size we found that almost 24% of the cohort had a disc size outside normal limits (> 2.5 mm). Previous studies have suggested that larger optic disc size is associated with decreased retrobulbar blood flow velocities. [26].

Gherghel et al found that mean OPP correlated positively with EDV in the OA and CRA in patients with deteriorating glaucoma, suggesting that alterations in ocular blood flow regulation may contribute to the progression in glaucomatous damage [45]. Kaskan et al found that OPP negatively correlated with changes in the nSPCA RI of DM2 patients with open angle glaucoma (OAG), suggesting that mechanisms influencing the systemic vasculature may also affect localized ocular blood vessels more strongly in OAG patients with DM2 [46].

Reduced OPP has been linked to a substantially higher risk of glaucoma, with two epidemiological studies in Hispanic populations reporting up to a fourfold increase in risk. [28,29]. In the present cohort, only 2 participants exhibited OPP values below 40mmHg.

Liu et al. found that an increase in IOP altered mostly CRA and SPCA velocities and resistance indeces [24]. However, it is worth mentioning that the study group included acute angle-closure glaucoma and IOP greater than 40mmHg.

Numerous studies have reported alterations in retrobulbar hemodynamic parameters in patients with diabetes mellitus, particularly in eyes with diabetic retinopathy. These changes comprise decreased PSV and EDV, together with elevated RI across the retrobulbar circulation [23,47–52]. In our study, patients with DM2 demonstrated similar alterations in retrobulbar circulation.

The inclusion of patients with DM2 could be considered as a study limitation, due to the fact that these eyes can show alterations in retrobulbar blood flow velocities. However, this reflects the characteristics of a real-world clinical population, and excluding these patients would have reduced the external validity of our findings. The cross-sectional design of this study limits the ability to establish temporal or causal relationships. Longitudinal follow-up of these patients would provide more comprehensive information on changes in retrobulbar hemodynamic parameters over time. Future longitudinal studies are warranted to determine whether these retrobulbar hemodynamic alterations can predict functional progression in glaucoma suspects.

This study characterized PSV, EDV, and RI values in the retrobulbar circulation of a Hispanic glaucoma suspect cohort, providing hemodynamic information in a population for which such data were previously unavailable.

The hemodynamic values observed suggest differences from those reported in previous publications; however, direct comparison is constrained because equipment and study populations differ substantially.

These results should be interpreted in light of the study's limitations. The cross-sectional design precludes establishing temporal or causal relationships. Longitudinal follow-up of these patients would provide more comprehensive information on changes in retrobulbar hemodynamic parameters over time. Future longitudinal studies are warranted to determine whether these retrobulbar hemodynamic alterations can predict functional progression in glaucoma suspects.

# CONCLUSIONS

Findings support the relevance of impaired optic nerve head perfusion at the suspect stage of glaucoma (consistent with the vascular theory) and suggest that hemodynamic assessment may complement structural evaluation, given evidence that Doppler-derived parameters can be more reliable than structural OCT parameters for early detection.

In addition, glaucoma suspects with DM2 in this cohort demonstrated alterations in retrobulbar circulation similar to those previously described in diabetic eyes, comprising decreased PSV and EDV together with elevated RI.

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# TABLES

Tables 1 and 2 are available in the Supplementary Files section.

Tables 3 and 4 are not available with this version.

## Supplementary Files

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- Table1JOG.pdf
- Table2JOG.pdf