• Clinical Research •

Assessment of iris volume in glaucoma patients with type 2 diabetes mellitus by AS-OCT

Ying Su[1,2,3,4], *Qing-Shu Ge*[2,3,4], *Zong-Yi Li*[2,3,4], *Qian-Wen Bu*[2,3,4], *Die Hu*[2,3,4], *Long-Fang Zhou*[2,3,4], *Xiao-Jing Pan*[2,3,4]

[1]School of Clinical Medicine, Weifang Medical University, Weifang 261021, Shandong Province, China
[2]Eye Institute of Shandong First Medical University, Qingdao Eye Hospital of Shandong First Medical University, Qingdao 266071, Shandong Province, China
[3]State Key Laboratory Cultivation Base, Shandong Provincial Key Laboratory of Ophthalmology, Qingdao 266071, Shandong Province, China
[4]School of Ophthalmology, Shandong First Medical University, Qingdao 266071, Shandong Province, China
Co-first authors: Ying Su and Qing-Shu Ge
Correspondence to: Xiao-Jing Pan. Eye Institute of Shandong First Medical University; Qingdao Eye Hospital of Shandong First Medical University; State Key Laboratory Cultivation Base, Shandong Provincial Key Laboratory of Ophthalmology; School of Ophthalmology, Shandong First Medical University, Qingdao 266071, Shandong Province, China. panxjcrystal@163.com
Received: 2023-02-16 Accepted: 2023-03-06

Abstract

● **AIM:** To examine the change of iris volume measured by CASIA2 anterior segment optical coherence tomography (AS-OCT) in glaucoma patients with or without type 2 diabetes mellitus (T2DM) and explore if there is a correlation between hemoglobin A1c (HbA1c) level and iris volume.

● **METHODS:** In a cross-sectional study, 72 patients (115 eyes) were divided into two groups: primary open angle glaucoma (POAG) group (55 eyes) and primary angle-closure glaucoma (PACG) group (60 eyes). Patients in each group were separately classified into patients with or without T2DM. Iris volume and glycosylated HbA1c level were measured and analyzed.

● **RESULTS:** In the PACG group, diabetic patients' iris volume was significantly lower than those of non-diabetics (P=0.02), and there was a significant correlation between iris volume and HbA1c level in the PACG group (r=-0.26, P=0.04). However, diabetic POAG patients' iris volume was noticeably higher than those of non-diabetics (P=0.01), and there was a significant correlation between HbA1c level and iris volume (r=0.32, P=0.02).

● **CONCLUSION:** Diabetes mellitus impact iris volume size, as seen by increased iris volume in the POAG group and decreased iris volume in the PACG group. In addition, iris volume is significantly correlated with HbA1c level in glaucoma patients. These findings imply that T2DM may compromise iris ultrastructure in glaucoma patients.

● **KEYWORDS:** glaucoma; diabetes mellitus; iris volume; glycosylated hemoglobin; optical coherence tomography
DOI:10.18240/ijo.2023.05.11

Citation: Su Y, Ge QS, Li ZY, Bu QW, Hu D, Zhou LF, Pan XJ. Assessment of iris volume in glaucoma patients with type 2 diabetes mellitus by AS-OCT. *Int J Ophthalmol* 2023;16(5):743-747

INTRODUCTION

Glaucoma is the main cause of permanent blindness worldwide, and it is a major public health issue[1]. Glaucoma affected 64.3 million people in 2013, which will increase to 111.8 million in 2040[2]. Primary open angle glaucoma (POAG) and primary angle-closure glaucoma (PACG) are two different types of glaucoma based on the anatomy[3]. PACG, which has a narrow anterior chamber angle, is three times more likely to induce significant bilateral vision impairment than POAG[4]. Traditional risk factors for atrial angle closure include anatomical features such as a small anterior chamber, a short eye axis, the thickness of the lens, and anterior displacement of the lens location[5]. In addition, the iris volume and the position of the entire iris relative to the meshwork are two factors that determine how close the anterior chamber angle is to apposition[6-7]. The findings of recent research strongly suggest that the iris contributes substantially to the progression of angle closure[8-10].

Diabetes mellitus (DM) is another prevalent cause of vision loss in people, and it can cause raised intraocular pressure (IOP) by interfering with the function of the trabecular meshwork[11-12]. Some studies have found that DM can protect against glaucoma[13-15], while others have found that DM can aggravate glaucoma[16-17]. The exact relationship between the two still remains a matter of debate. In PACG patients, POAG patients, and normal subjects, a large iris volume is

an important factor for a small anterior chamber angle[18-19]. According to population-based studies, diabetic patients are more likely to develop primary angle closure than non-diabetics[20-22]. However, the change in iris volume in glaucoma patients with DM remains unknown.

CASIA2 anterior segment optical coherence tomography (AS-OCT) is a novel type of AS-OCT. All eyes were scanned using a three-dimensional angle analysis scan, which is a volume scan with 16 and 13 mm length and depth measurements, respectively[23]. The three-dimensional angle analysis is carried out on 16 AS-OCT pictures from 16 distinct three-dimensional angles[24]. As a result, the present study used CASIA2 AS-OCT to evaluate the change of iris volume in glaucoma patients with or without type 2 diabetes mellitus (T2DM) and whether there was a correlation between iris volume and glycosylated hemoglobin A1c (HbA1c) level.

SUBJECTS AND METHODS

Ethical Approval This study was performed in accordance with the principles of the Declaration of Helsinki and with the approval of the Ethics Committee of Qingdao Eye Hospital [No.(2022)25]. All of the subjects signed informed consent.

Subjects The study was performed on 115 eyes of 72 patients who were diagnosed with POAG or PACG at Qingdao Eye Hospital. The patients were divided into two groups. The first group consisted of 55 POAG eyes, including diabetic POAG, which comprised 25 eyes, and POAG without T2DM, which comprised 30 eyes. The second group consisted of PACG patients with or without T2DM, each contained 30 eyes. Patients with diabetic glaucoma in each group made up the primary case group, and patients without T2DM in each group comprised the matched comparison group.

Individuals with T2DM aged 40 to 80 were eligible for inclusion. Exclusion criteria were as follows: 1) severe systemic disease except T2DM; 2) any history of ocular surgery or laser treatment; 3) any eye trauma history; 4) inability to fixate for eye examination; 5) episodes of acute angle closure and large dislocation.

Clinical Examinations All subjects underwent a standardized ophthalmic examination. Venous blood samples were collected for the level of HbA1c assessed at Qingdao Eye Hospital. Thorough ophthalmological examinations were conducted, including visual acuity, autorefraction, slit lamp examination, IOP, and ocular biometric measurement, and examined by CASIA2 AS-OCT. IOP measurement was performed using a non-contact tonometer Canon TX-20P. The IOLMaster 700 (Carl Zeiss Meditec AG, Jena, Germany) was used to measure ocular biometry, including central cornea thickness (CCT), lens thickness (LT), axial length (AL), and anterior central chamber depth (ACD). All subjects were examined by a skilled physician.

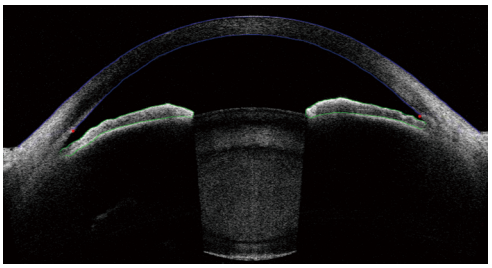

Figure 1 CASIA2 anterior segment optical coherence tomography (AS-OCT) cross-sectional image with scleral spur, corneal boundaries, and iris boundaries Scleral spurs were manually identified (denoted in red). The software built-in to the OCT automatically detected the boundaries of the cornea and iris (shown in blue and green, respectively).

CASIA2 anterior segment optical coherence tomography imaging AS-OCT images of the enrolled eyes were performed with the CASIA2 AS-OCT (Tomey, Nagoya, Japan). To ensure that no lid artifacts were present in the images, the operator gently held the subjects' eyelids while avoiding pressing the eyeball. During imaging, participants were asked to fixate on an internal target for 3s. Each eye's image quality was assessed in order to choose a high-quality image with a clearly visible scleral spur, angle, and iris. All subjects were examined by an experienced physician in the specialized examination room with the same lighting condition (300 lx).

After the image was centered and focused, the instruments started taking measurements automatically using software integrated into the device and measurement tools provided by the manufacturers. For each scan, the anterior and posterior boundaries of the cornea and iris were automatically detected by the internal software of CASIA2 AS-OCT. With the high scan speed of the device, an entire 360° image of the cornea and iris is obtained, providing a global assessment of corneal, anterior chamber, and iris volume (Figure 1).

The open angle distance at 500 μm (AOD500) and the trabecular iris space area at 500 μm (TISA500) were also obtained. Specifically, the AOD500 was the perpendicular distance measured from the corneal endothelium to the surface of the iris at 500 μm from the scleral spur. The TISA500 was a trapezoidal surface defined by AOD500, the anterior iris surface, the corneoscleral wall, and the distance between the iris surface and the scleral spur[24].

Statistical Analysis Data was analyzed using SPSS version 26 (IBM Corp, Armonk, NY, USA). Continuous variables were reported as means and standard deviations and compared using a Student's *t*-test. The correlation between quantitative variables was assessed using the Pearson correlation coefficient. $P<0.05$ was considered significant.

RESULTS

Demographic and Clinical Data of Study Participants The mean ages of the study and the control groups in the POAG

Table 1 Demographic characteristics and clinical data of study participants

Characteristics	POAG group (*n*=55)			PACG group (*n*=60)		
	POAG+DM (*n*=25)	Non-diabetic (*n*=30)	*P*[a]	PACG+DM (*n*=30)	Non-diabetic (*n*=30)	*P*[a]
Number of cases (patients/eyes)	17/25	16/30	-	20/30	19/30	-
Age (y)	61.00±10.18	59.56±12.47	0.72	66.60±7.15	65.21±7.67	0.56
Gender (male/female)	12/5	12/4	-	7/13	8/11	-
HbA1c (%)	7.92±1.10	5.39±0.43	<0.01	7.34±0.78	5.67±0.39	<0.01
IOP (mm Hg)	19.88±7.31	18.06±6.92	0.35	20.47±8.98	21.89±10.55	0.58
AL (mm)	24.32±1.35	24.50±1.72	0.67	22.73±0.82	22.62±0.81	0.61
ACD (mm)	3.10±0.40	3.24±0.33	0.17	2.36±0.36	2.42±0.40	0.57
LT (mm)	4.59±0.27	4.38±0.37	0.02	5.12±0.39	4.81±0.31	0.001
CCT (μm)	528.08±39.54	513.97±29.84	0.14	543.10±32.83	560.47±45.96	0.10

POAG: Primary open angle glaucoma; PACG: Primary angle-closure glaucoma; DM: Diabetes mellitus; IOP: Intraocular pressure; AL: Axial length; ACD: Anterior chamber depth; LT: Lens thickness; CCT: Central corneal thickness; HbA1c: Glycosylated hemoglobin A1c. [a]Student's *t*-test.

Table 2 Comparison between the parameters of two groups in the CASIA2 AS-OCT examination

Parameters	POAG group (*n*=55)			PACG group (*n*=60)		
	POAG+DM (*n*=25)	Non-diabetic (*n*=30)	*P*[a]	PACG+DM (*n*=30)	Non-diabetic (*n*=30)	*P*[a]
Cornea volume (mm^3)	88.61±8.11	86.17±7.89	0.26	69.02±11.08	73.28±11.32	0.15
Anterior chamber volume (mm^3)	147.99±32.60	151.14±31.25	0.72	77.81±27.20	81.93±20.13	0.51
Iris volume (mm^3)	37.67±4.72	34.55±4.12	0.01	29.36±4.50	32.55±5.50	0.02
AOD500 (mm)	0.39±0.23	0.41±0.19	0.68	0.26±0.18	0.21±0.12	0.19
TISA500 (mm^2)	0.14±0.09	0.16±0.07	0.56	0.10±0.08	0.08±0.05	0.14

POAG: Primary open angle glaucoma; PACG: Primary angle-closure glaucoma; DM: Diabetes mellitus; AOD500: Angle opening distance at 500 μm; TISA500: Trabecular iris space area at 500 μm. [a]Student's *t*-test.

group were 61.00±10.18 and 59.56±12.47y, respectively (*P*=0.72). Male/female ratios were 12/5 and 12/4 for the study and control groups in the POAG group, respectively. The mean HbA1c level of diabetic POAG patients during OCT measurements was 7.92±1.10. In the PACG group, the mean age of the study and control groups was 66.60±7.15 and 65.21±7.67y, respectively (*P*=0.56). Male/female ratios were 7/13 and 8/11 in the study and control groups of PACG patients, respectively. Additionally, diabetic PACG patients' mean HbA1c level was 7.34±0.78. In the POAG and PACG groups in IOP, AL, ACD, and CCT, there were no statistically significant differences between the study and control groups (all *P*>0.05). Despite the fact that there were statistically significant differences in the LT between the POAG and PACG patients' study and control groups (*P*=0.02 and *P*=0.001, respectively; Table 1).

CASIA2 Anterior Segment Optical Coherence Tomography Imaging CASIA2 AS-OCT-based measurements in each group were investigated (Table 2). There were no significant differences in corneal volume, anterior chamber volume, AOD500, and TISA500 in the two groups other than iris volume (all *P*>0.05). In the POAG group, the value of the iris volume of the diabetic POAG patients was higher (diabetic: 37.67±4.72, non-diabetic: 34.55±4.12, *P*=0.01). In the PACG group, there was a significant difference in the iris volume, which was 29.36±4.50 in the diabetic eyes and 32.55±5.50 in the non-diabetic eyes (*P*=0.02).

Table 3 Pearson's correlation test

Parameters	POAG group (*n*=55)		PACG group (*n*=60)	
	r	*P*	*r*	*P*
Iris volume (mm^3)	0.32	0.02	-0.26	0.04

POAG: Primary open angle glaucoma; PACG: Primary angle-closure glaucoma.

Correlations The result is summarized in Table 3. Our results showed that HbA1c level was weakly significantly correlated to iris volume in the POAG and PACG group (*r*=0.32, *P*=0.02 and *r*=-0.26, *P*=0.04, respectively).

DISCUSSION

In our study, we used the CASIA2 AS-OCT, which has a fast scan speed and allows 360° imaging of the iris, to perform a comprehensive three-dimensional assessment of iris volume. Based on these collected statistics, we compared and analyzed the iris volume of non-diabetic and diabetic patients in the POAG and PACG groups individually. To the best of our knowledge, this is the first study to assess iris volume in glaucoma patients with T2DM. It was discovered that diabetic PACG patients' iris volume was smaller than those of non-diabetic PACG patients. The difference is that the iris volume of POAG from T2DM patients was found to be larger than that of non-diabetic POAG patients.

One possible explanation for the iris volume reduction in PACG patients results from ischaemic damage. In our study, there have been significant thickening changes in terms of lens thickness changes in diabetic POAG and PACG patients

compared to the non-diabetic glaucoma population. Previous literature has reported a thicker lens in diabetics than in non-diabetics, consistent with our analysis of glaucoma patients[21,25-26]. PACG eyes had higher level of vascular endothelial growth factor members (vascular endothelial growth factor B, vascular endothelial growth factor C) and receptor (vascular endothelial growth factor receptor-2), suggesting that PACG has a compensatory mechanism to protect the iris vasculature from ischaemic damage[27]. During hyperglycemia, extra glucose in the lens is changed into sorbitol. Poorly permeable sorbitol builds up in the lens. The influx of water from the aqueous humor into the lens as a result of the difference in osmotic pressure that occurs when blood glucose levels drop leads to lenticular swelling[21,26,28-29]. Hyperglycemia causes thicker lenses, iris compression, and decreased iris blood volume. It is expected to result in PACG patients' compensatory mechanisms failing, iris thinning, and iris volume reduction.

The iris is the only tissue in the anterior chamber with a vasculature network, and intra-iris vascular blood flow diffuses from the iris interstitium through the microvascular endothelium to the anterior chamber for fluid exchange with atrial fluid. The decreased iris volume may be due to the diabetic PACG patients' altered iris microvascular structure, according to previous studies that showed how hyperglycemia can alter the iris' ultrastructure by triggering signaling pathways[16,30-32].

As for the increased iris volume in POAG, the possibility is that it may take some time for the microstructure to transform into macroscopic volume. Meng *et al*[31] assessed the iris volume of 117 diabetic patients aged 40 to 80 using swept-source AS-OCT and it was concluded that larger iris volume was significantly correlated with shorter duration of DM. It has been demonstrated that in patients with long-term diabetic conditions, the iris muscle cells and nerves undergo degenerative change[33-35]. We hypothesized that diabetic duration was related to iris volume in POAG patients. In glaucoma patients, short duration of DM increases iris volume, whereas long duration of DM decreases iris volume. More research is needed to confirm the link between iris volume and diabetic duration in glaucoma patients.

Furthermore, in the POAG groups, HbA1c level was significantly positively associated with iris volume, while in the PACG groups, HbA1c level was significantly negatively associated with iris volume, implying that glycemic control affects iris volume in glaucoma patients.

Additionally, we are aware of some of the limitations of our study. First, the relatively small sample size, which could be explained by the stringent inclusion and exclusion criteria, could be seen as a potential limitation. Second, the inclusion of both eyes in some glaucoma patients might be biased because ophthalmic variables are typically similar between the eyes of the same person. Third, the diabetic duration was not available in this study. Further investigation with diabetic duration would aid in determining the change in iris volume in glaucoma diabetic patients.

In conclusion, we found that T2DM increased iris volume in POAG patients, which may narrow the anterior chamber angle, and decreased iris volume in PACG patients, which affects the iris blood supply. These suggest that T2DM appears to be a risk factor for glaucoma patients. These findings, if confirmed in a larger longitudinal study, should prompt researchers to reconsider the pathophysiologic role of T2DM in the natural history of glaucoma.

ACKNOWLEDGEMENTS

Foundation: Supported by Natural Science Foundation of Shandong Province (No.ZR2020MH172).

Conflicts of Interest: Su Y, None; **Ge QS,** None; **Li ZY,** None; **Bu QW,** None; **Hu D,** None; **Zhou LF,** None; **Pan XJ,** None.

REFERENCES

1 Kang JM, Tanna AP. Glaucoma. *Med Clin North Am* 2021;105(3):493-510.

2 Tham YC, Li X, Wong TY, Quigley HA, Aung T, Cheng CY. Global prevalence of glaucoma and projections of glaucoma burden through 2040:a systematic review and meta-analysis. *Ophthalmology* 2014; 121(11):2081-2090.

3 Mohammadi M, Mohammadi SS, Tabatabaei SM, Eslami Y, Zarei R, Zandvakil N, Fakhraie G, Safizadeh M, Farshchi MR, Moghimi S. Comparison of vascular density and structural patterns between primary open angle glaucoma and primary angle closure glaucoma. *J Glaucoma* 2022;31(8):645-650.

4 Kondkar AA. Updates on genes and genetic mechanisms implicated in primary angle-closure glaucoma. *Appl Clin Genet* 2021;14:89-112.

5 Song PG, Wang JW, Bucan K, Theodoratou E, Rudan I, Chan KY. National and subnational prevalence and burden of glaucoma in China: a systematic analysis. *J Glob Health* 2017;7(2):020705.

6 Yang HF, Yu PK, Cringle SJ, Sun XH, Yu DY. Microvascular network and its endothelial cells in the human iris. *Curr Eye Res* 2018;43(1):67-76.

7 Yao W, Zhu JY Cao GF. Research progress of the iris mechanism in primary angle - closure glaucoma. *Guoji Yanke Zazhi (Int Eye Sci)* 2022;22(2):240-243.

8 Guo JM, Li M, Xu XL, Zhang H, Wang JM. Anterior segment changes after pharmacologic mydriasis using Pentacam and optical coherence tomography in angle closure suspects. *Int J Ophthalmol* 2015;8(5):980-984.

9 You SQ, Liang ZQ, Yang KY, Zhang Y, Oatts J, Han Y, Wu HJ. Novel discoveries of anterior segment parameters in fellow eyes of acute primary angle closure and chronic primary angle closure glaucoma. *Invest Ophthalmol Vis Sci* 2021;62(14):6.

10 Nongpiur ME, Verma S, Tun TA, Wong TT, Perera SA, Aung T. Plateau iris and severity of primary angle closure glaucoma. *Am J*

Ophthalmol 2020;220:1-8.

11 Drinkwater JJ, Davis TME, Davis WA. Incidence and predictors of vision loss complicating type 2 diabetes: the Fremantle Diabetes Study Phase II. *J Diabetes Complicat* 2020;34(6):107560.

12 Lavaju P, Shah S, Sharma S, Maskey R. Diabetes Mellitus and the risk of Primary open angle glaucoma. *Nepal J Ophthalmol* 2017;9(18):17-23.

13 Hou HY, Moghimi S, Baxter SL, Weinreb RN. Is diabetes mellitus a blessing in disguise for primary open-angle glaucoma? *J Glaucoma* 2021;30(1):1-4.

14 Akkaya S, Can E, Öztürk F. Comparison of optic nerve head topographic parameters in patients with primary open-angle glaucoma with and without diabetes mellitus. *J Glaucoma* 2016;25(1):49-53.

15 Hou HY, Shoji T, Zangwill LM, Moghimi S, Saunders LJ, Hasenstab K, Ghahari E, Manalastas PIC, Akagi T, Christopher M, Penteado RC, Weinreb RN. Progression of primary open-angle glaucoma in diabetic and nondiabetic patients. *Am J Ophthalmol* 2018;189:1-9.

16 Luo XY, Tan NYQ, Chee ML, Shi Y, Tham YC, Wong TY, Wang JJ, Cheng CY. Direct and indirect associations between diabetes and intraocular pressure: the Singapore epidemiology of eye diseases study. *Invest Ophthalmol Vis Sci* 2018;59(5):2205-2211.

17 Rim TH, Lee SY, Bae HW, Seong GJ, Kim SS, Kim CY. Increased risk of open-angle glaucoma among patients with diabetes mellitus: a 10-year follow-up nationwide cohort study. *Acta Ophthalmol* 2018; 96(8):e1025-e1030.

18 Huang WB, Li XY, Gao XB, Zhang XL. The anterior and posterior biometric characteristics in primary angle-closure disease: data based on anterior segment optical coherence tomography and swept-source optical coherence tomography. *Indian J Ophthalmol* 2021;69(4):865-870.

19 Mak H, Xu GH, Leung CKS. Imaging the iris with swept-source optical coherence tomography: relationship between iris volume and primary angle closure. *Ophthalmology* 2013;120(12):2517-2524.

20 Saw SM, Wong TY, Ting S, Foong AWP, Foster PJ. The relationship between anterior chamber depth and the presence of diabetes in the tanjong pagar survey. *Am J Ophthalmol* 2007;144(2):325-326.

21 Wiemer NGM, Dubbelman M, Kostense PJ, Ringens PJ, Polak BCP. The influence of diabetes mellitus type 1 and 2 on the thickness, shape, and equivalent refractive index of the human crystalline lens. *Ophthalmology* 2008;115(10):1679-1686.

22 Senthil S, Garudadri C, Khanna RC, Sannapaneni K. Angle closure in the Andhra pradesh eye disease study. *Ophthalmology* 2010; 117(9):1729-1735.

23 Jin GM, Xiao B, Zhou YJ, Wang YY, Li XP, Zheng DY. Agreement of corneal curvature and central corneal thickness obtained from a swept-source OCT and Pentacam in ectopia lentis patients. *Int J Ophthalmol* 2020;13(8):1244-1249.

24 Chen XX, Wang XL, Tang YZ, Sun XH, Chen YH. Optical coherence tomography analysis of anterior segment parameters before and after laser peripheral iridotomy in primary angle-closure suspects by using CASIA2. *BMC Ophthalmol* 2022;22(1):144.

25 Pierro L, Brancato R, Zaganelli E, Guarisco L, Calori G. Correlation of lens thickness with blood glucose control in diabetes mellitus. *Acta Ophthalmol Scand* 1996;74(6):539-541.

26 Li HY, Luo GC, Guo J, Liang Z. Effects of glycemic control on refraction in diabetic patients. *Int J Ophthalmol* 2010;3(2):158-160.

27 Seet LF, Narayanaswamy A, Finger SN, Htoon HM, Nongpiur ME, Toh LZ, Ho H, Perera SA, Wong TT. Distinct iris gene expression profiles of primary angle closure glaucoma and primary open angle glaucoma and their interaction with ocular biometric parameters. *Clin Exp Ophthalmol* 2016;44(8):684-692.

28 Gabbay KH. The sorbitol pathway and the complications of diabetes. *N Engl J Med* 1973;288(16):831-836.

29 Kocatürk T, Zengin MÖ, Cakmak H, Evliçoglu GE, Dündar SO, Omürlü IK, Unübol M, Güney E. The ocular biometric differences of diabetic patients. *Eur J Ophthalmol* 2014;24(5):786-789.

30 Miao H, Hou XR, Hwang DK, Tao Y. Vascular endothelial growth factor, basic fibroblast growth factor, and pigment epithelium-derived factor expression in the neovascular iris in retinal diseases. *J Ophthalmol* 2018;2018:8025951.

31 Meng J, Han X, Wang W, Gong X, Li WT, Xiong K, Li YT, Zhang XL, Liang XL, Huang JJ, Huang WY. Analysis of Iris volume using swept-source optical coherence tomography in patients with type 2 diabetes mellitus. *Acta Ophthalmol* 2022;100(2):e553-e559.

32 Stanaway SERS, Gill GV. Protein glycosylation in diabetes mellitus: biochemical and clinical considerations. *Pract Diab Int* 2000;17(1):21-25.

33 Ishikawa S, Bensaoula T, Uga S, Mukuno K. Electron-microscopic study of iris nerves and muscles in diabetes. *Ophthalmologica* 1985; 191(3):172-183.

34 Fujii T, Ishikawa S, Uga S. Ultrastructure of iris muscles in diabetes mellitus. *Ophthalmologica* 1977;174(4):228-239.

35 Demirtas Ö, Pekel G, Pekel E, Cetin EN. Iris thickness measurements in patients with diabetic retinopathy. *Eur J Ophthalmol* 2022;32(1): 491-496.