ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH

DOI: 10.5336/ophthal.2019-72059

Optical Coherence Tomography Angiography Findings in Obese Women

Obez Kadınlarda Optik Koherens Tomografi Bulguları

Erel İÇEL[a], Turgay UÇAK[a], Hayati YILMAZ[a], Nurdan Gamze TAŞLI[a], Adem UĞURLU[a], Adem TÜRK[b]

[a]Erzincan Binali Yıldırım University Faculty of Medicine, Department of Ophthalmology, Erzincan, TURKEY
[b]Karadeniz Technical University Faculty of Medicine, Department of Ophthalmology, Trabzon, TURKEY

ABSTRACT Objective: Microvascular changes accompanying obesity can result in various complications in many organs. The aim of this study is to investigate the retinal microvascular changes in obese women by using optical coherence tomography angiography (OCTA), which has become increasingly common in recent years. **Material and Methods:** The study included a total of 61 female volunteers, 30 were obese volunteers with a body mass index (BMI) of over 30 kg/m² with no accompanying systemic disease and 31 were non-obese volunteers. Results of OCT and OCTA examinations of the participants' both eyes were compared. **Results:** The mean age of the participants was 42.7 ± 10 years in the obese group and 41.36 ± 10.73 in the non-obese group (p=0.615). In the obese group, OCTA examinations revealed that retinal vessel density (VD) in superficial capillary plexus and deep capillary plexus was found to be lower in both eyes, compared to those of non-obese group (p<0.05 for all). There was no significant difference between the two groups in terms of foveal avascular zone (FAZ) measurements. Similarly, no significant difference was observed between the two groups in terms of peripapillary retinal nerve fiber layer thickness, central macular thickness, and central macular volume measurements. **Conclusion:** It was observed in the OCTA examinations that superficial and deep retinal layer VD is lower in obese women and the FAZ measurements are not affected. optical coherence tomography angiograph method was found to be beneficial in revealing the changes occurred in microvascular structures accompanying obesity.

Keywords: Obesity; retina; optical coherence tomography angiography

ÖZET Amaç: Obeziteye eşlik eden mikrovasküler değişiklikler birçok organda çeşitli komplikasyonlara sebep olabilmektedir. Bu çalışmanın amacı kullanımı son senelerde giderek yaygınlaşan optik koherens tomografi anjiografi (OKTA) cihazı eşliğinde obez kadınlarda ortaya çıkan retinal mikrovasküler değişiklikleri araştırmaktı. **Gereç ve Yöntemler:** Eşlik eden herhangi bir sistemik rahatsızlığı bulunmayan, beden kitle indeksi (BKİ) değeri > 30 kg/m² olan 30 obez ile obez olmayan 31 kadın gönüllü çalışmaya dahil edildi. Katılımcıların her iki gözlerine ait OKT ve OKTA incelemeleri karşılaştırıldı. **Bulgular:** Katılımcıların yaş ortalamaları obez grupta 42.7±10, obez olmayan grupta 41,36±10,73 yıl idi (p=0,615). OKTA incelemelerinde yüzeyel ve derin kapiller pleksusta retina damar dansitesinin obez kadınların her iki gözlerinde de obez olmayan kadınlara göre daha düşük olduğu görüldü (hepsi için p<0,05). Foveal avasküler zon (FAZ) ölçümleri açısından ise her iki grup arasında anlamlı bir farklılık yoktu. Yine iki grup arasında retina sinir lifi tabakası kalınlığı, santral makular kalınlık, santral makular hacim ölçümleri açısından da anlamlı bir farklılık mevcut değildi. **Sonuç:** OKTA incelemesinde obez kadınlardaki yüzeyel ve derin tabakada yer alan retina damar dansitesinin daha düşük olduğu, FAZ ölçümlerinin ise etkilenmediği saptanmıştır. Obeziteye eşlik eden mikrovasküler yapılardaki değişiklikleri ortaya koymada OKTA başarılı bulunmuştur.

Anahtar Kelimeler: Obezite; retina; optik koherens tomografi anjiografi

Being defined as the exceed of optimal body mass index (BMI), obesity is a serious health problem that is gradually increasing throughout the world and may result in morbidity and mortality.[1] Molecular, genetic, environmental, and behavioral factors are held responsible for its etiology.[2] BMI is calculated by dividing the weight by the square of the height (kg/m²). The upper limit is 25 kg/m² in adults. Those with a BMI value of 25-30 kg/m² and of >30 kg/m² are considered as overweight, and obese, respectively.[3]

Correspondence: Erel İÇEL
Erzincan Binali Yıldırım University Faculty of Medicine, Department of Ophthalmology, Erzincan, TURKEY/TÜRKİYE
E-mail: dr_erel@hotmail.com

Peer review under responsibility of Turkiye Klinikleri Journal of Ophthalmology.

Received: 30 Oct 2019 ***Received in revised form:*** 03 Jan 2020 ***Accepted:*** 08 Jan 2020 ***Available online***: 13 Jan 2020

Obesity is known to be an important risk factor for chronic diseases such as diabetes, hypertension, dyslipidemia, osteoarthritis, cardiovascular diseases, stroke, sleep apnea syndrome and various types of cancer.[4] The ocular effects are not clearly defined, but it has been reported to be associated with several diseases such as glaucoma, cataract, age-related macular degeneration (ARMD) and diabetes-induced retinopathy.[5,6]

Previous studies have reported that obesity affects the microvascular bed in the body and as an indication of this, there is a relationship between the increased BMI and the narrower retinal arteriolar and wider venular calibers.[7,8] In a study by Viljanen et al., constriction of retinal arteriolar and expansion of venular calibers in obese patients who underwent bariatric surgery was reported to improve.[8]

Optical coherence tomography (OCT) and optical coherence tomography angiography (OCTA) are common methods used for the diagnosis and follow-up of retinal diseases. OCTA makes repetitive OCT scans in a specific retinal area and provides a detailed examination of the retinal vessels based on the movements of the erythrocyte through vessels.[9] With this feature, OCTA is a new, fast (compared to classical angiography techniques), and non-invasive imaging technique that does not require staining during screening which is used to reveal vascular changes in various ocular pathologies.[10] In recent studies, it has been shown that this method can provide significant diagnostic opportunities particularly in ocular pathologies such as age-related maculopathy, diabetic retinopathy, and glaucoma.[11,12]

To the best of our knowledge, OCTA findings of obese cases have not been previously reported. The purpose of this study was to investigate the probable retinal microvascular and morphological changes in obese female population.

MATERIAL AND METHODS

This is a prospective study and it was approved by the local ethics committee (Date:18.10.2018 No:33216249-604.01.02-E.46279). Written informed consent was obtained from all participants. The study was performed in concordance with the principles of the 2008 Declaration of Helsinki.

Emmetropic patients older than 28 and younger than 65 years of age, those with a BMI value of 30 kg/m² for at least five years, and those who had no additional ocular disease were included in the study. The control group consisted of healthy non-obese emmetropic individuals who applied to ophthalmology clinic for routine examination. Before the participants were included in the study, detailed internal, cardiological, rheumatological, psychiatric examinations of were done and required blood tests (glucose, thyroid parameters, cholesterol levels etc.) were requested. The exclusion criteria were the presence of any systemic disease like diabetes mellitus, primary or secondary hypertension, coronary artery disease, acute or chronic infection that may affect the measurements, sleep apnea syndrome, liver or kidney diseases, malignancy, pregnancy, alcohol use or smoking. Patients who have any ocular pathology were excluded from the study.

Detailed ophthalmological examination was performed on all participants, including best corrected visual acuity, intraocular pressure, biomicroscopic examination and fundus examination. For all cases, OCTA images were obtained by a single physician by using AngioScan OCT Angiography software on the RS-3000 Advance OCT (Nidek, Japan) device. The light source of this device has a wavelength of 880 nm and has seven microns optical resolutions on the Z axis, 20 microns on the XY axis, and a scanning speed of 53,000 A-scans per second. The fovea is focused on by using OCTA prototype internal fixation lamp and 3x3 mm macula cubes each consisting of 256 B-scans are generated. Nidek has a new version of software for angioscan. With this device the macular, peripapillary vascular density (VD) and foveal avascular zone (FAZ) can be automatically calculated. In the deep capillary plexus, FAZ area was calculated manually because this measurement in this field cannot be done automatically with this device.

FAZ and VD measurements in the superficial capillary plexus (SCP) and deep capillary plexus (DCP) were measured in both eyes of all participants. OCTA images showing FAZ measurements in SCP and DCP layers are shown in Figure 1a and Figure

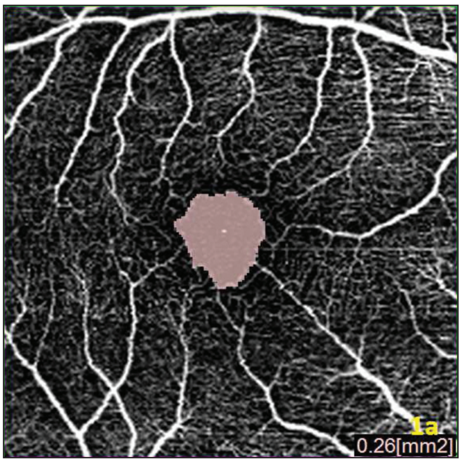

FIGURE 1a: OCTA image showing FAZ measurement in SCP layer.

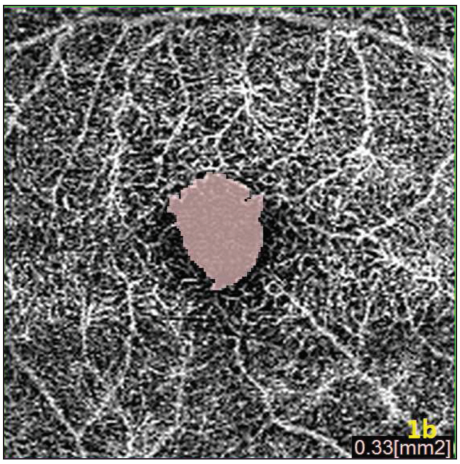

FIGURE 1b: OCTA image showing FAZ measurement in DCP layer.

1b. If SSI quality was <7/10, the scan was repeated. Retinal nerve fiber layer thickness (RNFLT), central macular thickness (CMT) and central macular volume (CMV) were measured through OCT analysis. Participants were divided into two groups as obese and non-obese according to BMI values. The height and weight measurements were performed using the same measuring devices in order to provide equivalence.

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS version 13.0.1 software (SPSS, Chicago, IL; license no:9069728, KTU Trabzon). The data were expressed as mean and standard deviation. One-Sample Kolmogorov-Smirnov test was used to determine whether the data was distributed normally. Differences in the groups were analyzed using the Independent Samples *t*-Test. P <0.05 was considered statistically significant.

RESULTS

The study included 30 obese female volunteers with BMI values over 30 kg/m² and 31 non-obese female volunteers. The mean age of the obese group was 42.7±10 (min-max: 28-65) while the mean age of the non-obese group was 41.36±10.73 (min-max: 28-65) (p=0.615). The mean height of the obese group was 162.37±5.9 cm (147-173 cm) while it was 161.74±5.17 cm (152-170 cm) in the non-obese group (p=0.661). The mean weight of the obese group was 91.14 ± 10.12 kg (min-max: 75-120 kg), while the mean weight of the non-obese group was 59.93±10.23 (min-max: 43-84) kg (p<0.0001). The mean BMI of the obese group was 34.57±3.09 kg/m² (min-max: 30.8-41.8 kg/m²) while it was 22.85±3.71 kg/m² (min-max: 17.4-30 kg/m²) in non-obese group (p<0.0001). Based on these values, there was no significant difference between the two groups in terms of age and height, whereas weight and BMI values were found to be statistically significantly different.

The FAZ and retinal VD measurements in SCP and DCP, which were obtained by the OCTA device, are presented in Table 1 separately for the right and left eyes. There was no significant difference between the groups regarding the FAZ measurements in SCP and DCP layers, retinal VD measurements were found to be lower in the obese group. There was no significant difference between the two groups in terms of RNFL, CMT and CMV values. The results are given in Table 1.

DISCUSSION

The purpose of this study was to compare FAZ and retinal VD measurements in SCP and DCP of obese patients with non-obese healthy group. Retinal VD measurement results of obese patients were found to be significantly lower in SCP and DCP layers. To the best of our knowledge, this is the first study in which OCTA measurements of obese patients were compared with the healthy group.

TABLE 1: OCTA analysis findings of the cases included in the study according to groups.

Parameters	Obese (n=30)	Non-obese (n=31)	P values
FAZ SCP (mm^2)			
OD	0.39 ± 0.16	0.35 ± 0.09	0.194
OS	0.38 ± 0.17	0.35 ± 0.1	0.474
FAZ DCP (mm^2)			
OD	0.55 ± 0.14	0.51 ± 0.14	0.286
OS	0.54 ± 0.18	0.5 ± 0.11	0.193
Retinal vessel density SCP (%)			
OD	29.29 ± 3.86	33.16 ± 4.32	<0.0001
OS	29 ± 3.94	32.42 ± 3.77	0.001
Retinal vessel density DCP (%)			
OD	35.24 ± 4.12	38.67 ± 4.17	0.002
OS	33.69 ± 4.12	38.77 ± 4.25	<0.0001
RNFL (µm)			
OD	107.5 ± 9.77	111.19 ± 9.18	0.133
OS	107.23 ± 10.25	111.61 ± 10.17	0.099
CMT (µm)			
OD	264.27 ± 22.91	260.19 ± 13.87	0.403
OS	263.9 ± 22	264.06 ± 16.55	0.974
CMV (mm^3)			
OD	9.09 ± 0.44	9.22 ± 0.59	0.315
OS	9.09 ± 0.59	9.27 ± 0.55	0.211

FAZ: Foveal avascular zone, SCP: Superficial capillary plexus, DCP: Deep capillary plexus, RNFL: Retinal nerve fiber layer, CMT: Central macular thickness, CMV: Central macular volume.

OCT-A, an enhancement of spectral-domain optical coherence tomography (SD-OCT), provides exhaustive knowledge of the retinal and choroidal microvascular composition. It can provide valuable data with structural details of the retina.[1,13] It is an effective method that can provide an understanding of pathogenesis and detect early changes in diseases in which retina is affected.[14,15]

Obesity, which is becoming gradually common in the world, is a serious and complex medical condition associated with behavioral, genetic, psychological and metabolic factors.[16] Therefore, investigation of its effects on ocular tissue is important to prevent possible pathologies. In a study in the literature, a negative correlation was reported between obesity and visual activity.[17] Obesity, a multifactorial condition, is one of the well-known causes of microvascular diseases and the basis of this relationship can be revealed by examining vascular tissue.[18] An examination of this relationship is also important in terms of determining the ocular effects of obesity, which has not been fully understood yet.

Studies previously published in the literature have shown that obesity can trigger ocular complications such as ARM or diabetic retinopathy by affecting retinal microvascular structures.[19] In a study by Karti et al. including obese children, RNFL loss on the optic disc due to obesity was determined.[20] In another study, Koca et al. reported similar changes in the optic disc in the obese children.[21] Zarei et al. reported in their study that RNFL thickness of the optic disc decreased in patients with metabolic syndrome.[22] In a study by Zhi et al. including diabetic obese mice, retinal thickness and retinal blood flow were found to decrease compared to normal mice. They have reported that the reduced retinal thickness is particularly between the nerve fiber layer (NFL) and the inner plexiform layer (IPL). Although there was no significant decrease in retinal VD in this study, the decrease in retinal blood flow was found to be significant.[23] In compatible with the literature, RNFL thicknesses in both eyes were found to be lower in obese patients included in our study, however, this difference was not statistically significant compared to non-obese group.

In obese study group, retinal VD was observed to significantly decrease in SCP and DCP layers. There was no statistically significant difference between the groups in terms of FAZ measurements. However, it was observed that FAZ measurements were higher in obese patients, although not significant.

High BMI values have been reported to cause retinal dysfunction by affecting the retinal vascular structure.[18] Furthermore, the relationship between obesity and ARM has been reported in many studies.[5,19] In the literature, it was reported that this relationship may be due to the systemic oxidative stress developed secondary to hyperleptinemia caused by obesity.[24] Studies on this subject have reported that obesity is a risk factor for retinal diseases such as retinal vein occlusion and diabetic retinopathy.[25,26] In the light of this information, it was thought that the microvascular injury caused by obesity-related oxidative stress affects the retinal vascular structure of the patients and accordingly affect the RNFL thickness levels as well as FAZ and retinal vein density measurements in SCP and DCP layers. Vascular density measurements in superficial and deep layers were found to be lower in obese patients and may be considered as early signs of ocular complications in these cases. Although in this study is not statistically significant, elevated FAZ measurements in obese patients may be a sign of macular status.

There are some limitations in the present study. The number of participants was relatively small and only female volunteers were included. Although, all systemic evaluations of participants were done, systemic blood pressure, thyroid parameters, HbA1c levels which are the factors that may affect measurements such as blood flow, CMT, CMV, have not been reported. The fact that FAZ measurement in the deep layer is not performed automatically is another limiting factor.

CONCLUSION

This study has revealed that retinal VD of obese patients, which were evaluated by using OCTA method first time in the literature, decreased significantly and FAZ measurements were found to be increased compared to the healthy group. The pathologies that obesity may cause as a result of retinal microvascular changes can be detected in the early period non-invasively via OCTA examination.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Erel İçel;* ***Design:*** *Turgay Uçak;* ***Control/Supervision:*** *Erel İçel, Adem Türk;* ***Data Collection and/or Processing:*** *Erel İçel, Nurdan Gamze Taşlı, Hayati Yılmaz, Adem Uğurlu;* ***Analysis and/or Interpretation:*** *Adem Uğurlu, Turgay Uçak;* ***Literature Review:*** *Erel İçel, Nurdan Gamze Taşlı;* ***Writing the Article:*** *Erel İçel, Turgay Uçak;* ***Critical Review:*** *Adem Türk;* ***References and Fundings:*** *Erel İçel;* ***Materials:*** *Erel İçel.*

REFERENCES

1. Rohde K, Keller M, la Cour Poulsen L, Blüher M, Kovacs P, Böttcher Y, et al. Genetics and epigenetics in obesity. Metabolism. 2019;92:37-50. [Crossref] [PubMed]
2. Upadhyay J, Farr O, Perakakis N, Ghaly W, Mantzoros C. Obesity as a disease. Med Clin North Am. 2018;102(1):13-33. [Crossref] [PubMed]
3. Schwartz MW, Seeley RJ, Zeltser LM, Drewnowski A, Ravussin E, Redman LM, et al. Obesity pathogenesis: an endocrine society scientific statement. Endocr Rev. 2017;1;38(4): 267-96. [Crossref] [PubMed] [PMC]
4. Chooi YC, Ding C, Magkos F. The epidemiology of obesity. Metabolism. 2019;92: [Crossref] [PubMed]
5. Seddon JM, Reynolds R, Yu Y, Daly MJ, Rosner B. Risk models for progression to advanced age-related macular degeneration using demographic, environmental, genetic, and ocular factors. Ophthalmology. 2011;118(11): 2203-11. [Crossref] [PubMed] [PMC]
6. Vainio H, Kaaks R, Bianchini F. Weight control and physical activity in cancer prevention: international evaluation of the evidence. Eur J Cancer Prev. 2002;11 Suppl 2:S94-100.
7. Boillot A, Zoungas S, Mitchell P, Klein R, Klein B, Ikram MK, et al. Obesity and the microvasculature: asystematic review and meta-analysis. PLoS One. 2013;8(2):e52708. [Crossref] [PubMed] [PMC]

8. Viljanen A, Soinio M, Cheung CY, Hannukainen JC, Karlsson HK, Wong TY, et al. Effects of bariatric surgery on retinal microvascular architecture in obese patients. Int J Obes (Lond). 2019;43(9):1675-80. [Crossref] [PubMed]

9. Babiuch AS, Khan M, Hu M, Kaiser PK, Srivastava SK, Singh RP, et al. Comparison of OCT angiography review strategies to ıdentify vascular abnormalities in the avatar study. Ophthalmol Retina. 2018;2(6):606-12. [Crossref] [PubMed] [PMC]

10. Ang M, Tan ACS, Cheung CMG, Keane PA, Dolz-Marco R, Sng CCA, et al. Optical coherence tomography angiography: a review of current and future clinical applications. Graefes Arch Clin Exp Ophthalmol. 2018;256(2):237-45. [Crossref] [PubMed]

11. Jia Y, Wei E, Wang X, Zhang X, Morrison JC, Parikh M, et al. Optical coherence tomography angiography of optic disc perfusion in glaucoma. Ophthalmology. 2014;121(7):1322-32. [Crossref] [PubMed] [PMC]

12. Jia Y, Bailey ST, Hwang TS, McClintic SM, Gao SS, Pennesi ME, et al. Quantitative optical coherence tomography angiography of vascular abnormalities in the living human eye. Proc Natl Acad Sci U S A. 2015;112(18):E2395-402. [Crossref] [PubMed] [PMC]

13. Cicinelli MV, Cavalleri M, Consorte AC, Rabiolo A, Sacconi R, Bandello F, et al. Swept-source and spectral domain optical coherence tomography angiography versus dye angiography in the measurement of type 1 neovascularization. Retina. 2020;40(3):499-506. [Crossref] [PubMed]

14. Dimitrova G, Chihara E. Implication of deep-vascular-layer alteration detected by optical coherence tomography angiography for the pathogenesis of diabetic retinopathy. Ophthalmologica. 2019;241(4):179-82. [Crossref] [PubMed]

15. Rosen RB, Andrade Romo JS, Krawitz BD, Mo S, Fawzi AA, Linderman R, et al. Earliest evidence of preclinical diabetic retinopathy revealed using OCT Angiography (OCTA) perfused capillary density. Am J Ophthalmol. 2019;203:103-15. [Crossref] [PubMed] [PMC]

16. Fernández-Sánchez A, Madrigal-Santillán E, Bautista M, Esquivel-Soto J, Morales-González Á, Esquivel-Chirino C, et al. Inflammation, oxidative stress, and obesity. Int J Mol Sci. 2011;12(5):3117-32. [Crossref] [PubMed] [PMC]

17. Bergman B, Nilsson-Ehle H, Sjöstrand J. Ocular changes, risk markers for eye disorders and effects of cataract surgery in elderly people: a study of an urban Swedish population followed from 70 to 97 years of age. Acta Ophthalmol Scand. 2004;82(2):166-74. [Crossref] [PubMed]

18. Yumusak E, Ornek K, Durmaz SA, Cifci A, Guler HA, Bacanli Z, et al. Choroidal thickness in obese women. BMC Ophthalmol. 2016;16(1):48. [Crossref] [PubMed] [PMC]

19. Cheung N, Wong TY. Obesity and eye diseases. Surv Ophthalmol. 2007;52(2):180-95. [Crossref] [PubMed] [PMC]

20. Karti O, Nalbantoglu O, Abali S, Tunc S, Ozkan B. The assessment of peripapillary retinal nerve fiber layer and macular ganglion cell layer changes in obese children: a cross-sectional study using optical coherence tomography. Int Ophthalmol. 2017;37(4):1031-8. [Crossref] [PubMed]

21. Koca S, Keskin M, Saricaoglu MS, Bilge Koca S, Duru N, Şahin Hamurcu M, et al. Optic nerve parameters in obese children as measured by spectral domain optical coherence tomography. Semin Ophthalmol. 2017;32(6):743-7. [Crossref] [PubMed]

22. Zarei R, Anvari P, Eslami Y, Fakhraie G, Mohammadi M, Jamali A, et al. Retinal nerve fibre layer thickness is reduced in metabolic syndrome. Diabet Med. 2017;34(8):1061-6. [Crossref] [PubMed]

23. Zhi Z, Chao JR, Wietecha T, Hudkins KL, Alpers CE, Wang RK, et al. Noninvasive imaging of retinal morphology and microvasculature in obese mice using optical coherence tomography and optical microangiography. Invest Ophthalmol Vis Sci. 2014;20;55(2):1024-30. [Crossref] [PubMed] [PMC]

24. Yamagishi SI, Amano S, Inagaki Y, Okamoto T, Takeuchi M, Inoue H, et al. Pigment epithelium-derived factor inhibits leptin-induced angiogenesis by suppressing vascular endothelial growth factor gene expression through anti-oxidative properties. Microvasc Res. 2003;65(3):186-90. [Crossref]

25. Wong TY, Larsen EKM, Klein R, Mitchell P, Couper DJ, Klein BEK, et al. Cardiovascular risk factors for retinal vein occlusion and arteriolar emboli: the atherosclerosis risk in communities & cardiovascular health studies. Ophthalmology. 2005;122(4):540-7. [Crossref] [PubMed]

26. Zhang L, Krzentowski G, Albert A, Lefebvre PJ. Risk of developing retinopathy in diabetes control and complications trial type 1 diabetic patients with good or poor metabolic control. Diabetes Care. 2001;24(7):1275-9. [Crossref] [PubMed]