

Access this article online
Quick Response Code:

Website: www.e-tjo.org
DOI: 10.4103/tjo.tjo_2_22

Change of intraocular blood flow during treatment for thyroid eye disease

Masashi Mimura^{1*}, Yuko Nishikawa¹, Keiko Inagaki¹, Yohei Sato¹, Yasushi Fujita¹, Don O. Kikkawa^{2,3}

Abstract:

To report a sequential observational study of changes in the retinal and choroidal blood flow during medical and surgical treatments for a thyroid eye disease (TED) patient, using optical coherence tomography angiography (OCTA) and laser speckle flowgraphy (LSFG). A 28-year-old man with a history of Graves' disease diagnosed 8 months prior was presented in the active phase of TED. His clinical activity score (CAS) was 6, but without diplopia or visual loss. Intraocular pressure measurement was OD 20 mmHg and OS 24 mmHg. Thyrotropin receptor antibody (TRAb) and thyroid-stimulating antibody levels were 18.8 IU/L and 4347%. Magnetic resonance imaging revealed enlargement of both extraocular muscles and fat compartments in both orbits. The patient underwent IV pulsed steroid therapy (1 g/day, 3 days) followed by an oral prednisone for 1 month. His CAS score decreased to 4. Bilateral orbital fat decompression decreased his final CAS score to 1 in both eyes. Intraocular blood flow was measured using laser speckle flowgraphy (LSFG), and OCTA was performed. Retinal blood flow increased slightly, but choroidal blood flow showed a robust increase. Choroidal blood flow measured using both LSFG and OCTA was negatively correlated with the CAS score and TRAb. In our case report, the ocular perfusion, especially choroidal blood flow, may decrease in active TED, which may be reversed by medical and surgical treatment.

Keywords:

Laser speckle flowgraphy, optical coherence tomography angiography, thyroid eye disease

¹Department of Ophthalmology, Osaka Medical and Pharmaceutical University, Takatsuki, Japan, ²Department of Ophthalmology, Division of Oculofacial Plastic and Reconstructive Surgery, Shiley Eye Institute, University of California San Diego, San Diego, CA, USA, ³Department of Surgery, Division of Plastic Surgery, University of California San Diego, San Diego, CA, USA

*Address for correspondence:

Dr. Masashi Mimura,
Department of Ophthalmology, Osaka Medical College, 2-7 Daigakumachi, Takatsuki, Osaka 569-8686, Japan.
E-mail: opt119@osaka-med.ac.jp

Submission: 07-12-2021
Accepted: 03-01-2022
Published: 28-02-2022

Introduction

Thyroid eye disease (TED) is an autoimmune disease targeting the orbital and peri-orbital soft tissues. Resulting inflammation may increase intra-orbital pressure causing venous congestion and in rare instances, compress the optic nerve, resulting in compressive optic neuropathy.^[1] Optical coherence tomography angiography (OCTA) is a novel instrumental that analyzes intraocular microvascular changes layer by layer. Recent reports have been focused on the retinal perfusion on TED patients to demonstrate early subclinical signs of the disease.^[2-9] However, controversy exists as

to whether the perfusion is decreased^[2,3] or increased.^[4,6] This discrepancy may be due to cross-sectional studies comparing the TED patients and controls, and also that vascular perfusion may vary based on the systemic condition of the patient, intraocular pressures (IOP), and inflammatory status of the orbit. In addition, results can differ depending on the scanning area, i.e., disk or macula, and even vary based on the type of commercial OCTA used.^[10,11] Laser speckle flowgraphy (LSFG) has also been used to measure intraocular perfusion.^[12-14] This is a novel device that measures sequential perfusion changes, taking the IOP and blood pressure into account, which is suitable for monitoring the tissue circulation at the same site in the same eye at various intervals.^[12]

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Mimura M, Nishikawa Y, Inagaki K, Sato Y, Fujita Y, Kikkawa DO. Change of intraocular blood flow during treatment for thyroid eye disease. Taiwan J Ophthalmol 2022;12:97-100.

We report a sequential observational study in a single patient examining changes in intraocular perfusion using both OCTA and LSFG during medical and surgical treatment for TED with particular attention to how treatment affects globe perfusion.

Case Report

A 28-year-old man with a history of Graves' disease diagnosed 8 months prior was referred with active TED. His clinical activity score (CAS) was 6 [Figure 1a]. Visual acuity was 20/20 OU. Exophthalmometry measured OD 20.5 mm and OS 21.5 mm. IOP was OD 20 mmHg and OS 24 mmHg. Thyrotropin receptor antibody (TRAb) was 18.8 IU/L (normal range: <2.0 IU/L), and thyroid-stimulating antibody was 4347% (normal range: <120%). He was euthyroid. Magnetic resonance imaging revealed enlargement of fat and extraocular muscles in both orbits [Figure 2a]. He was a habitual 1 pack per day smoker. His medical history was otherwise unremarkable.

One month after presentation, he underwent three courses of pulsed IV steroids (1 g/day for 3 days) with an oral steroid taper over the following month. After the IV pulsed steroids, his CAS score decreased to 4. Bilateral orbital fat decompression was then performed with 4cc of fat removal from each orbit through transconjunctival approach^[15,16] that finally decreased his CAS score to 1 in both eyes [Figure 1b and 2b and c].



Figure 1: 28-year-old male patient with thyroid eye disease at pre-(a) and post-(b) treatment

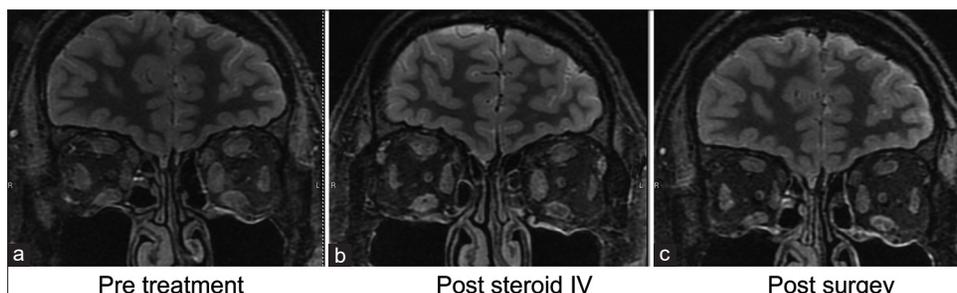


Figure 2: MRI of orbits at pretreatment (a), poststeroid pulsed therapy (b), and postorbital decompression surgery (c)

During the time course of treatment described above, corresponding measurements were made. Intraocular blood flow was analyzed using LSFG (LSFG, LSFG-NAVI, and LSFG Analyzer software; Softcare Co., Ltd., Fukuoka, Japan) and enhanced depth imaging OCT (EDI-OCT; RS 3000 Advance2; NIDEK Co., Ltd., Tokyo, Japan). LSFG measurements were performed in a sitting position with heart rate monitoring along with IOP and blood pressure measurement.^[12] Relative blood flow velocity was calculated using first-order speckle statistics quantified as mean blur rate (MBR). MBR of the vascular areas in the optic nerve head (MBR-V), reflecting retinal blood flow, and MBR of the tissue areas in the parafovea (MBR-T), reflecting choroidal blood flow, were automatically calculated using the LSFG analyzer software [Figure 3]. OCTA imaging was also performed in the sitting position. Signal density of radial peripapillary capillary plexus (RPCP; ILM to ILM+104 mm), reflecting retinal blood flow, and that of choroidal plexus (CP; RPE/BM+4 mm to RPE/BM+125 mm), reflecting choroidal blood flow, were automatically measured on the images obtained using a spectral domain-OCT in 3 mm × 3 mm areas in the optic nerve [Figure 4]. All measurements were repeated three times, and the mean value was used for the analyses.

The choroidal blood flow measured using both LSFG and OCTA was negatively correlated with the CAS score and TRAb. Retinal blood flow, conversely, did not change during the treatment [Figure 5]. Using LSFG, the MBR-V (retinal perfusion) increased OD 18.5% (38.17 initial vs. 45.4 end) and OS 1.9% (34.3 initial vs. 34.9 end). MBR-T (choroidal perfusion) increased OD 51.6% (4.2 initial vs. 6.3 end) and OS 45.2% (4.73 initial vs. 6.87 end). Regarding OCTA, the density of signal of RPCP increased slightly by OD 1.6% (19.07 initial vs. 21.68 end) and OS 15.2% (9.67 initial vs. 18.12 end). CP increased remarkably, with OD 563.5% (3.24 initial vs. 21.47end) and OS 1618.9% (1.06 initial vs. 18.22 end). During all visits, the mean IOP was stable, showing OD 21.9 ± 3.8 mmHg and OS 20.7 ± 3.4 mmHg.

Discussion

The current case report shows that ocular blood flow is correlated with the orbital inflammation in TED. The

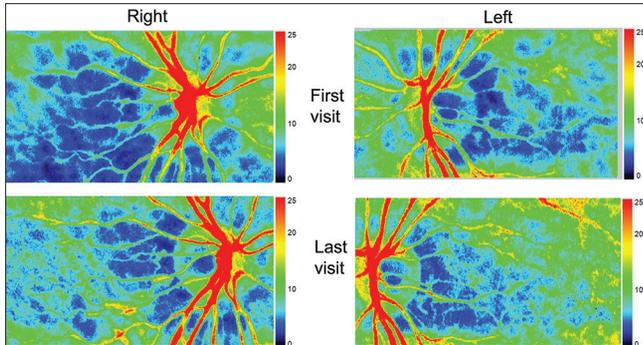


Figure 3: Serial perfusion map photos by laser speckle flowgraphy of the patient at pretreatment (upper row) and posttreatment (lower row)

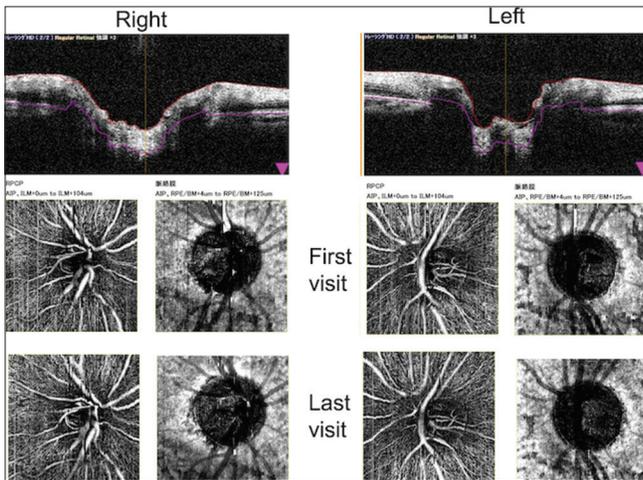


Figure 4: Serial perfusion map photos by optical coherence tomography angiography of the patient at pretreatment (upper row) and posttreatment (lower row)

choroidal blood flow showed more increase than retinal blood flow in response to treatment for active TED. Our impression is that ocular perfusion is affected by the orbital inflammation.

We hypothesize that the differential response of retinal and choroidal blood flows may arise from several reasons. First, the choroidal blood supply is from the smaller artery, short posterior ciliary artery compared to the larger central retinal artery. Second, the optic nerve sheath may provide additional protection to the central retinal artery from both orbital pressure and inflammation. Thus, the choroidal perfusion may be more sensitive to external orbital pressure in patients with active TED.^[17] One additional factor influencing choroidal circulation is sympathetic innervation that may be affected by thyroid hormone, but our patient was euthyroid.^[5,18]

The current case shows that both medical and surgical therapy contribute to the recovery of the ocular blood flow. Blood flow was noted to dramatically increase after steroid pulse therapy, indicating that the relief of the orbital pressure increased ocular blood flow, overcoming the pharmaceutical vessel contraction caused by steroids.^[19] Orbital decompression can also contribute to blood flow recovery. In the current study, decompression occurred after steroid therapy when the inflammation was reduced. After orbital decompression, blood flow additionally recovered indicating that choroidal blood supply may be very sensitive to orbital pressure.^[20,21]

With less severe orbital compartment syndrome, such as the current case, a decrease in choroidal blood flow can be seen before developing compressive optic neuropathy and diminished retinal arterial flow.^[2] This

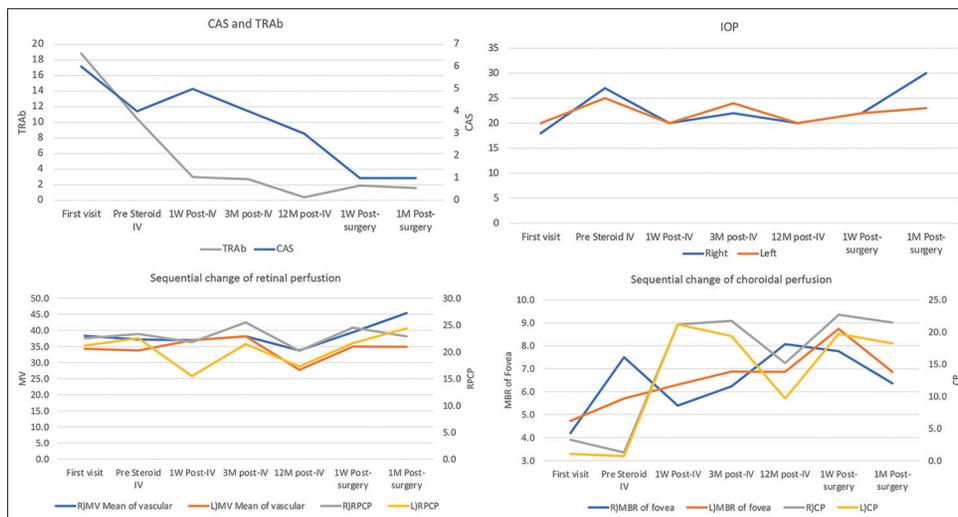


Figure 5: Graphs showing the sequential change of clinical activity score and thyrotropin receptor antibody (upper left), of intraocular pressure (upper right), choroidal perfusion (lower right), and retinal perfusion (lower left), at various times: Pretreatment, after intravenous steroid pulse infusion therapy, and after orbital decompression

means that the occult reduction in choroidal blood flow may occur with effects on vision before objective visual disturbances. In other words, monitoring choroidal flow of TED patients may assist in the evaluation of orbital pressure increases. This may also approximate orbital inflammation quantitatively, which can be another parameter to evaluate TED severity along with CAS and VISA scores. We are now accumulating data in additional patients for further study.

This study has some limitations. First, this is a preliminary case report that needs to accumulate various data to confirm our result. Second, potential artifacts may occur, especially in OCTA, which can influence the result. Despite these limitations, these two novel methods showed similarities with respect to ocular perfusion in TED globe, suggesting future potential utility.

Conclusion

Orbital pressure in TED patients can decrease blood supply, especially choroidal perfusion. OCTA and LSFG are simple and noninvasive methods to evaluate the ocular perfusion quantitatively. Its usefulness and role in evaluating TED require further study.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that their names and initials will not be published, and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Ethical approval

The protocols used in this study were approved by the Ethics Committee of Osaka Medical College (approval number: 2019–2810).

Financial support and sponsorship

Nil.

Conflicts of interest

The authors declare that there are no conflicts of interests of this paper.

References

- Meyer P, Das T, Ghadiri N, Murthy R, Theodoropoulou S. Clinical pathophysiology of thyroid eye disease: The cone model. *Eye (Lond)* 2019;33:244-53.
- Jamshidian Tehrani M, Mahdizad Z, Kasaei A, Fard MA. Early macular and peripapillary vasculature dropout in active thyroid eye disease. *Graefes Arch Clin Exp Ophthalmol* 2019;257:2533-40.
- Mihailovic N, Lahme L, Rosenberger F, Hirscheider M, Termühlen J, Heiduschka P, et al. Altered retinal perfusion in

- patients with inactive graves ophthalmopathy using optical coherence tomography angiography. *Endocr Pract* 2020;26:312-7.
- Ye L, Zhou SS, Yang WL, Bao J, Jiang N, Min YL, et al. Retinal microvasculature alteration in active thyroid-associated ophthalmopathy. *Endocr Pract* 2018;24:658-67.
- Wu Y, Tu Y, Bao L, Wu C, Zheng J, Wang J, et al. Reduced retinal microvascular density related to activity status and serum antibodies in patients with graves' ophthalmopathy. *Curr Eye Res* 2020;45:576-84.
- Akpolat C, Kurt MM, Yılmaz M, Ordulu F, Evliyaoglu F. Analysis of foveal and parafoveal microvascular density and retinal vessel caliber alteration in inactive graves' ophthalmopathy. *J Ophthalmol* 2020;2020:7643737.
- Özkan B, Koçer ÇA, Altıntaş Ö, Karabaş L, Acar AZ, Yüksel N, et al. Choroidal changes observed with enhanced depth imaging optical coherence tomography in patients with mild Graves orbitopathy. *Eye (Lond)* 2016;30:917-24.
- Louidice P, Pellegrini M, Marinò M, Mazzi B, Ionni I, Covello G, et al. Choroidal vascularity index in thyroid-associated ophthalmopathy: A cross-sectional study. *Eye Vis (Lond)* 2021;8:18.
- Yu L, Jiao Q, Cheng Y, Zhu Y, Lin Z, Shen X. Evaluation of retinal and choroidal variations in thyroid-associated ophthalmopathy using optical coherence tomography angiography. *BMC Ophthalmol* 2020;20:421.
- Shiuhara H, Sakamoto T, Yamashita T, Kakiuchi N, Otsuka H, Terasaki H, et al. Reproducibility and differences in area of foveal avascular zone measured by three different optical coherence tomographic angiography instruments. *Sci Rep* 2017;7:9853.
- Yilmaz H, Karakurt Y, Icel E, Ugurlu A, Ucak T, Tasli NG, et al. Normative data assessment of vessel density and foveal avascular zone metrics using angioscan software. *Curr Eye Res* 2019;44:1345-52.
- Sugiyama T, Araie M, Riva CE, Schmetterer L, Orgul S. Use of laser speckle flowgraphy in ocular blood flow research. *Acta Ophthalmol* 2010;88:723-9.
- Kohmoto R, Sugiyama T, Ueki M, Kojima S, Maeda M, Nemoto E, et al. Correlation between laser speckle flowgraphy and optical coherence tomography angiography measurements in normal and glaucomatous eyes. *Clin Ophthalmol* 2019;13:1799-805.
- Calzetti G, Fondi K, Bata AM, Luft N, Wozniak PA, Witkowska KJ, et al. Assessment of choroidal blood flow using laser speckle flowgraphy. *Br J Ophthalmol* 2018;102:1679-83.
- Cheng AM, Wei YH, Tighe S, Sheha H, Liao SL. Long-term outcomes of orbital fat decompression in Graves' orbitopathy. *Br J Ophthalmol* 2018;102:69-73.
- Ediriwickrema LS, Korn BS, Kikkawa DO. Orbital decompression for thyroid-related orbitopathy during the quiescent phase. *Ophthalmic Plast Reconstr Surg* 2018;34:S90-7.
- Jampol LM, Goldbaum M, Rosenberg M, Bahr R. Ischemia of ciliary arterial circulation from ocular compression. *Arch Ophthalmol* 1975;93:1311-7.
- Kawarai M, Koss MC. Sympathetic vasoconstriction in the rat anterior choroid is mediated by alpha1-adrenoceptors. *Eur J Pharmacol* 1998;363:35-40.
- Hirooka K, Saito W, Namba K, Takemoto Y, Mizuuchi K, Uno T, et al. Relationship between choroidal blood flow velocity and choroidal thickness during systemic corticosteroid therapy for Vogt-Koyanagi-Harada disease. *Graefes Arch Clin Exp Ophthalmol* 2015;253:609-17.
- Norris JH, Ross JJ, Kazim M, Selva D, Malhotra R. The effect of orbital decompression surgery on refraction and intraocular pressure in patients with thyroid orbitopathy. *Eye (Lond)* 2012;26:535-43.
- Nik N, Fong A, Derdzakyan M, Adamopoulou C, Sise A, Khanifar A, et al. Changes in choroidal perfusion after orbital decompression surgery for graves' ophthalmopathy. *J Ophthalmic Vis Res* 2017;12:183-6.