Radial peripapillary capillary density in superior segmental optic hypoplasia measured with OCT angiography.

Maiko Abe

Tohoku University Graduate School of Medicine

Kazuko Omodaka

Tohoku University Graduate School of Medicine

Tsutomu Kikawa

Topcon Corporation

Toru Nakazawa (✉ ntoru@oph.med.tohoku.ac.jp)

Tohoku University Graduate School of Medicine <https://orcid.org/0000-0002-5591-4155>

Research article

Keywords: optical coherence tomography angiography, diagnosis, radial peripapillary capillary density, superior segmental optic hypoplasia

Posted Date: November 14th, 2019

DOI: <https://doi.org/10.21203/rs.2.17299/v1>

License: This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background: To investigate the diagnostic power of radial peripapillary capillary (RPC) density, measured with optical coherence tomography angiography (OCT-A), in patients with superior segmental optic hypoplasia (SSOH), a disease which is important to differentiate from glaucoma.

Methods: Forty subjects with SSOH and 40 age- and axial length-matched control subjects were retrospectively registered for this study. SSOH was defined as intraocular pressure (IOP) less than 21 mmHg with the presence of two of the following: superior rim thinning, superior entrance of the central retinal artery, scleral halo, and pale optic disc; as well as non-progressive visual field loss. RPC density was measured with swept-source OCT-A (Triton, Topcon) in the overall, quadrants, and 12 clock-wise sectors. RPC density was compared in normal and SSOH subjects with Welch's t-test. Diagnostic power was assessed with the area under the receiver operating characteristics curve.

Results: Overall cpRNFLT was significantly different in the normal ($106.7 \pm 9.5 \mu\text{m}$) and SSOH ($77.2 \pm 13.7 \mu\text{m}$, $p < 0.001$) subjects. RPC density in the overall area ($p < 0.001$) and superior ($p < 0.001$), nasal ($p < 0.001$), and inferior ($p < 0.001$) quadrants was significantly lower in the SSOH group, but not in the temporal ($p = 0.756$) quadrant. The diagnostic power of RPC density was highest in the superior quadrant (AUC = 0.928) and the 1 o'clock sector (0.896).

Conclusions: Low RPC density was found in the three non-temporal quadrants of the optic nerve head. Measuring RPC density with OCT-A may help the diagnosis of SSOH and may improve the management of glaucoma.

Introduction

Superior segmental optic hypoplasia (SSOH) is a congenital anomaly of the optic nerve head (ONH) characterized by superior entry of the central retinal vessels, superior peripapillary scleral halo, and reduced circumpapillary retinal nerve fiber layer thickness (cpRNFLT) with non-progressive inferior-sector visual field defects. In Asia, normal-tension glaucoma (NTG) is the primary subtype of open-angle glaucoma (1) making it important to differentiate SSOH from NTG (2). Previously, it was reported that SSOH could be identified based on the location of cpRNFLT loss (3) and structural abnormalities in the extension of the retinal pigment epithelium (RPE) over the nasal disc margin (4), both measured with spectral-domain optical coherence tomography (OCT). Thus, both fundus photography and OCT may be useful in the clinical treatment of SSOH.

We previously showed that tissue mean blur rate (MT), representing blood flow (BF) in the ONH, decreases in SSOH (5). MT is also correlated with deep-ONH BF, but not surface-ONH BF (6). Recently, OCT angiography (OCT-A) has become available clinically and is increasingly important for visualizing vessels both in the retina and ONH. The density of radial peripapillary capillaries (RPCs), a network of surface nerve fiber layers, has been shown to have diagnostic power for glaucoma (7). However, until now, there have been no reports on changes in RPC density or the diagnostic power of RPC density in

SSOH. This study is thus the first to assess the microvasculature of the peripapillary retina and investigate whether vascular parameters are useful for diagnosing SSOH.

Methods

Eighty eyes of 80 patients (normal: 40 eyes; SSOH: 40 eyes) were included. SSOH was diagnosed by glaucoma specialists after a careful differential diagnosis for glaucoma (4). SSOH diagnosis was based on the presence of more than two of the following four symptoms: superior rim thinning, superior entrance of the central retinal artery, scleral halo, and pale optic disc; combined with non-progressive visual field loss (in an average of 6.3 ± 4.8 visual field tests), peripheral visual field defects in the V-4 target of the Goldmann visual field test, and intraocular pressure (IOP) less than 21 mmHg. Mean deviation measurements used reliable data from Humphrey field analyzer (HFA) standard automated perimetry. RPC density was measured with OCT-A (Triton, Topcon), as previously described (7), overall, in the superior, temporal, inferior, and nasal quadrants, and in 12 clock-wise sectors. cpRNFLT was measured with swept-source OCT.

This study adhered to the tenets of the Declaration of Helsinki, and the protocols were approved by the institutional review board of the Tohoku University Graduate School of Medicine (study 2017-1-290). Clinical findings and other characteristics, including age, sex, axial length, and IOP, were compared in the two study groups with the Mann-Whitney U test. The area under the receiver operating characteristic curve (AUC) was calculated for differentiating normal subjects and SSOH patients based on OCT-A parameters. All statistical analyses were performed with JMP software (Pro version 13.1.0, SAS Institute Japan Inc., Tokyo, Japan).

Results

There were no differences between the groups in age (normal: 39.5 ± 8.2 , SSOH: 41.2 ± 18.0 , $p = 0.326$), axial length (24.6 ± 0.8 , 25.1 ± 1.3 , $p = 0.088$), or IOP (14.0 ± 2.2 , 14.1 ± 2.5 , $p = 0.749$). Figure 1 shows representative SSOH and normal subjects; RPC density in the superior to nasal quadrants is clearly lower in the SSOH subject (Fig. 1). Table 1 shows differences in RPC density between the normal and SSOH groups. There were significant differences in overall RPC density and in the superior, nasal, and inferior (all: $p < 0.001$), but not temporal ($p = 0.756$) quadrants. RPC density was significantly lower in the 1, 2, 4, 5, 7, 9, 11, and 12 o'clock sectors. Table 2 shows the diagnostic power of RPC density. The highest area under the curve was in the superior quadrant (AUC = 0.928, Fig. 1E), with a cutoff value of 42.14% (83% sensitivity and 88% specificity). The 1 o'clock sector had the highest AUC (0.896, Fig. 1F), with a cutoff value of 34.8% (80% sensitivity and 83% specificity).

Discussion

We found that the power of RPC density to differentiate SSOH patients and controls was strong, especially in the superior, nasal, and inferior areas. Previously, we used laser speckle flowgraphy to show

that SSOH, a congenital anomaly, causes reduced microcirculation in the ONH (5), that the quadrant MBR ratios in the ONH have a strong power to differentiate SSOH and NTG (indicating that SSOH has a fundamentally different pathogenesis from NTG) (5), and that the structure of the deep layers of the ONH, around the lamina cribrosa, are correlated to MT, but not RPC density (6). Here, we found that the density of the peripapillary retinal microvasculature decreased in SSOH, but that the pattern of RPC loss was distinctly different from that reported for cpRNFLT (3). RPC density in the 9 o'clock sector, outside the temporal area, was significantly lower, but RPC density in the 3 o'clock sector was not significantly different in the SSOH and normal subjects. On the other hand, cpRNFLT was not significantly different in the 9 o'clock sector (normal: 67.6 ± 9.9 , SSOH: 70.3 ± 19.4 , $p = 0.431$), but was in the 3 o'clock sector (normal: 63.6 ± 12.7 , SSOH: 57.8 ± 26.9 , $p < 0.001$). Thus, the location of changes in RPC density and cpRNFLT is on horizontally opposite sides of the ONH. This may be due to lower initial RPC density in the nasal ONH, higher RPC density in the temporal ONH, and the location of the major retinal central vessel in the superior and inferior ONH. These findings suggest that OCT-A might have the potential to diagnose SSOH.

Limitations of this cross-sectional study include a small size and differing methods of calculating RPC density for devices from different companies. However, we excluded patients with high myopia and applied a method (8) to compensate for optical magnification of the eye, and excluded the major central retinal vessels by using image processing with a Laplacian of Gaussian filter with noise reduction. Thus, we are the first to demonstrate the potential of RPC density measurement for SSOH diagnosis.

In conclusion, we found that RPC density decreased in SSOH, and that changes in microcirculation were indicative of SSOH. However, it remains unclear whether these changes are congenital or secondary to retinal nerve fiber layer degeneration. In addition to cpRNFLT and the extension of the RPE over the nasal disc margin (4), OCT-A may be a new, non-invasive, objective instrument for SSOH diagnosis.

Declarations

Ethics approval and consent to participate:

This retrospective study was approved by the institutional review board of Tohoku University Graduate School of Medicine (study 2019–1–165). Written patient's informed consent was not required because the ethics committee allowed us to obtain data retrospectively from patients' records under insured medical treatment and approved to carry out by opt-out method. No patient was individually identified in this study.

Consent for publication:

Not applicable.

Availability of data and materials

Not applicable.

Competing interests:

The authors declare that they have no competing interests except for co-author TK. Co-author TK is employed by Topcon Corporation, a commercial company but has no conflicts of interest associated with the content of this article.

Funding:

This manuscript was supported in part by a JST grant from JSPS KAKENHI Grants-in-Aid for Scientific Research (B) (T. N. 26293372), by the JST Center for Revitalization Promotion and KAKENHI Grants-in-Aid for young scientists (B) (K. O. 17K16957) and by the Public Trust Suda Memorial Fund for Glaucoma Research.

Authors' contributions:

MA and KO contributed to data collection. KO and TN contributed to manuscript writing. TK contributed to technical support.

Acknowledgements:

The authors thank Mr. Tim Hilts for editing this manuscript. Co-author TK is employed by Topcon Corporation, a commercial company. This retrospective study was approved by the institutional review board of Tohoku University Graduate School of Medicine (study 2017–1–290).

References

1. Iwase A, Suzuki Y, Araie M, Yamamoto T, Abe H, Shirato S, et al. The prevalence of primary open-angle glaucoma in Japanese: the Tajimi Study. *Ophthalmology*. 2004;111(9):1641–8.
2. Yamamoto T, Sato M, Iwase A. Superior segmental optic hypoplasia found in Tajimi Eye Health Care Project participants. *Jpn J Ophthalmol*. 2004;48(6):578–83.
3. Yagasaki A, Sawada A, Manabe Y, Yamamoto T. Clinical features of superior segmental optic hypoplasia: hospital-based study. *Jpn J Ophthalmol*. 2019;63(1):34–9.
4. Hayashi K, Tomidokoro A, Konno S, Mayama C, Aihara M, Araie M. Evaluation of optic nerve head configurations of superior segmental optic hypoplasia by spectral-domain optical coherence tomography. *Br J Ophthalmol*. 2010;94(6):768–72.
5. Aizawa N, Kunikata H, Omodaka K, Nakazawa T. Optic disc microcirculation in superior segmental optic hypoplasia assessed with laser speckle flowgraphy. *Clin Exp Ophthalmol*. 2014;42(7):702–4.
6. Kiyota N, Kunikata H, Shiga Y, Omodaka K, Nakazawa T. Relationship between laser speckle flowgraphy and optical coherence tomography angiography measurements of ocular microcirculation. *Graefes Arch*

7.Kiyota N, Kunikata H, Shiga Y, Omodaka K, Nakazawa T. Ocular microcirculation measurement with laser speckle flowgraphy and optical coherence tomography angiography in glaucoma. Acta Ophthalmol. 2018;96(4):e485-e92.

8.Iwase A, Sekine A, Suehiro J, Tanaka K, Kawasaki Y, Kawasaki R, et al. A New Method of Magnification Correction for Accurately Measuring Retinal Vessel Calibers From Fundus Photographs. Invest Ophthalmol Vis Sci. 2017;58(3):1858–64.

Tables

Table 1. Comparison of RPC density in normal and SSOH subjects

RPC (%)			
	Normal	SSOH	p
	(n = 40)	(n = 40)	
Average	46.1±3.3	39.6±4.7	< 0.001***
Superior	50.3±7.1	36.6±7.1	< 0.001***
Nasal	37.6±5.7	31.5±8.1	< 0.001***
Inferior	50.7±5.8	44.0±10.2	< 0.001***
Temporal	45.9±5.6	46.3±6.6	0.756
Superior	11 56.6±8.4	49.6±10.7	0.002**
	12 43.0±11.7	30.5±13.3	< 0.001***
	1 51.5±11.2	30.3±12.9	< 0.001***
Nasal	2 42.7±9.5	33.6±13.7	< 0.001***
	3 31.6±8.1	29.0±10.9	0.238
	4 38.7±7.8	32.0±11.7	0.004**
Inferior	5 45.9±9.9	36.8±12.5	< 0.001***
	6 44.9±8.5	41.3±13.6	0.158
	7 61.3±9.0	54.9±11.3	0.007**
Temporal	8 46.5±8.3	47.2±8.6	0.700
	9 38.2±7.3	41.9±8.1	0.039*
	10 52.7±8.9	50.0±10.7	0.226

Table 2. Diagnosis power of localized RPC density in normal and SSOH subjects.

		AUC of RPC (%)
Average		0.879
Superior		0.928
Nasal		0.744
Inferior		0.706
Temporal		0.520
Superior	11	0.692
	12	0.769
	1	0.896
Nasal	2	0.729
	3	0.637
	4	0.693
Inferior	5	0.709
	6	0.614
	7	0.669
Temporal	8	0.513
	9	0.628
	10	0.563

Figures

Figure 1

Representative normal and SSOH subjects and the regional diagnostic power of RPC density for SSOH. A, B: Fundus photography. C, D: RPC density measured with OCT-A. A, C: Normal subject. B, D: SSOH subject. E: Receiver operating characteristic (ROC) curve for superior-quadrant cpRNFLT. F: ROC curve for the 1 o'clock sector of cpRNFLT.