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OCT ANGIOGRAPHY OF THE PERIPAPILLARY RETINA IN PRIMARY OPEN-ANGLE GLAUCOMA

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Резюме

Целью данного исследования было изучение топографической взаимосвязи между уменьшенным парапапиллярным микроциркуляторным руслом сетчатки, оцененным с помощью оптической когерентной томографической ангиографии (ОКТА), и дефектом слоя нервных волокон сетчатки (СНВС) в глазах с первичной открытоугольной глаукомой (ПОУГ) и локализованный дефект СНВС.

Методы. Оценивали перипапиллярное кровообращение сетчатки с помощью ОКТА с центром на диске зрительного нерва в 98 глазах с ПОУГ и локализованным дефектом СНВС и в 45 здоровых контрольных глазах. Сосудистое нарушение определяли при ОКТА по наличию признака, указывающего на снижение микроциркуляторного русла. Частоты ВИ сравнивали между группами ПОУГ и контрольной, и определяли топографическую корреляцию между сосудистыми нарушениями и дефектом СНВС, выявленным на фотографиях глазного дна, в группе ПОУГ.

Результаты. Сосудистое нарушение наблюдали как участок пониженной плотности микрососудистой сети сетчатки на 100% глаз с ПОУГ. сосудистое нарушение точно совпадал с дефектом СНВС, очевидным на фотографиях глазного дна без красного, как по расположению, так и по протяженности (коэффициент корреляции Пирсона = 0,997 и 0,988 соответственно, все P <0,001). Ни один из контрольных глаз не показал сосудистое нарушение в ОСТА.

Выводы. У больных ПОУГ в месте дефекта СНВС выявлено снижение парапапиллярного микроциркуляторного русла сетчатки по данным ОКТ. Это открытие позволяет предположить, что уменьшение микроциркуляторного русла сетчатки, вероятно, является вторичной потерей или закрытием капилляров в области глаукоматозной атрофии СНВС.

Ключевые слова: первичная открытоугольная глаукома, ОКТ-ангиография, СНВС.

Хулоса

Мақсад: Бирламчи очиқ бурчакли глаукома (БОБГ) билан оғриган кўзларда оптик когерент томография ангиографияси (ОКТ-А) ва ретинал нерв толаси қатлами (RNFL) нуқсони билан баҳоланган парапапилляр ретинал микроваскулатуранинг пасайиши ўртасидаги топографик алоқани, локал RNFL нуқсони ўрганиш

Тадқиқот усуллари: перипапилляр ретинал қон айланиши локал RNFL нуқсони бўлган 98 БОБГ кўзларида ва 45 соғлом назорат кўзларида курув нерви диски ОКТ-А ёрдамида баҳоланди. ОКТ-А да қон томирларининг шикастланиши

микротомирларнинг камайганлигини кўрсатадиган белги мавжудлиги билан аниқланди. шикастланиши частоталари БОБГ ва назорат гуруҳлари ўртасида таққосланди ва БОБГ гуруҳида қизил рангсиз фундус фотосуратларида аниқланган ва RNFL нуқсони ўртасидаги топографик корреляция аниқланди.

Натижалар: қон томирларининг шикастланиши 100% БОБГ кўзларида ретинанинг микроваскуляр тармоғининг зичлиги пасайган ҳудуд сифатида кузатилди. қон томирларининг шикастланиши жойлашуви ва ҳажми бўйича қизил рангсиз фундус фотосуратларида аниқ кўринадиган RNFL нуқсонига тўғри келди (Пирсон корреляция коэффициенти = 0,997 ва 0,988, барча П <0,001). Назорат қилувчи кўзларнинг ҳеч бири ОКТ-А да қон томирларининг шикастланишини кўрсатмади.

Хулоса: БОБГ билан оғриган беморларда RNFL нуқсони жойлашган жойда ОКТ-А томонидан аниқланган ретинанинг парапапилляр микроваскуляциясининг пасайиши аниқланди. Ушбу топилма шуни кўрсатадики, ретинал микроваскуляциясининг пасайиши глаукоматоз RNFL атрофияси ҳудудида капиллярларнинг иккиламчи йўқолиши ёки ёпилиши бўлиши мумкин.

Калит сўзлар: бирламчи очиқ бурчакли глаукома, ОКТ ангиографияси, RNFL

Summary

Purpose: The purpose of this study was to investigate the topographic relationship between the decreased parapapillary retinal microvasculature as assessed by optical coherence tomography angiography (OCTA) and retinal nerve fiber layer (RNFL) defect in eyes with primary open-angle glaucoma (POAG) and a localized RNFL defect.

Methods: The peripapillary retinal circulation was evaluated using the OCTA centered on the optic nerve head in 98 POAG eyes having a localized RNFL defect and 45 healthy control eyes. A vascular impairment (VI) was identified in OCTA by the presence of a sign indicating decreased microvasculature. The frequencies of VI were compared between the POAG and control groups, and the topographic correlation between the VI and the RNFL defect identified in red-free fundus photographs was determined in the POAG group.

Results: The VI was observed as an area of decreased density of the microvascular network of the retina in 100% of the POAG eyes. The VI exactly coincided with the RNFL defect evident in red-free fundus photographs in terms of both the location and extent (Pearson's correlation coefficient = 0.997 and 0.988, respectively, all $P < 0.001$). None of the control eyes exhibited VI in OCTA.

Conclusions: Decreased parapapillary microvasculature of the retina determined by OCTA was found at the location of RNFL defect in POAG patients. This finding suggests that the decreased retinal microvasculature is likely secondary loss or closure of capillaries at the area of glaucomatous RNFL atrophy.

Key words: primary open-angle glaucoma, OCT angiography, RNFL

Introduction. Ocular blood flow is thought to have an important role in the pathology of glaucoma.[1,2] In particular, vascular dysfunction in the optic nerve head (ONH) has been proposed as a contributing factor to the development and progression of glaucoma.[3] With fluorescein angiography, filling defects in the ONH have been reported in eyes with glaucomatous neuropathy.[8] However, fluorescein angiography is difficult to perform in a clinical setting as it is invasive and time

consuming. Alternative imaging methods have been widely investigated, but it has been a challenge to identify clinically feasible ones until recently with the advent of optical coherence tomography angiography (OCTA).

Studies have shown that peripapillary retinal blood flow and retinal vessel caliber are reduced in glaucoma patients compared with healthy subjects, using laser Doppler flowmetry, Doppler optical coherence tomography (OCT), and measurements of retinal vessel caliber. [4] Decreased retinal perfusion has also been demonstrated angiographically in glaucoma patients using fluorescein angiography. These findings have raised the interest in the potential role of decreased ocular perfusion as an etiopathogenic factor for the glaucomatous optic neuropathy (GON), together with epidemiologic or clinical data that demonstrated the association of low blood pressure [5,6] or nocturnal blood pressure dips with glaucoma. In contrast, Quigley et al. [7,11] demonstrated that the density of capillaries remained constant across a wide range of neural tissue losses within the optic nerve head (ONH) in both experimental and human glaucoma eyes. In addition, Cull et al. showed that the ONH blood flow measured by laser speckle flowgraphy increased during the earliest stage of glaucoma followed by a linear decline that was strongly correlated with thickness reduction of the retinal nerve fiber layer (RNFL) thickness. [10] These findings suggest that the reduced retinal perfusion could simply result from ONH degeneration and a consequently diminished metabolic demand. It therefore remains unclear whether the decreases in retinal and ONH blood flows in glaucoma are the cause or result of GON. [10]

We hypothesized that determination of the topographic relationship between the structural damage of peripapillary retina and the decreased density of peripapillary microvasculature may give a clue to determine the causal relationship between the decreased microvasculature/retinal circulation and GON. If decreased retinal vascularity is an effect of primary vascular change (e.g., reduction of large retinal vessel caliber due to lack of autoregulation or local vasospasm), the area of decreased vessel density would follow the territory of the retinal vessels. On the contrary, if it is the result of the GON (i.e., capillary dropout at the area of RNFL defect), the decreased vessel density would be observed only at the area of RNFL defect. Therefore, we performed this study to characterize the OCTA findings of the retinal layer in POAG eyes having localized RNFL defect compared with healthy control eyes.

Purpose. To investigate the topographic relationship between the decreased parapapillary retinal microvasculature as assessed by optical coherence tomography angiography (OCTA) and retinal nerve fiber layer (RNFL) defect in eyes with primary open-angle glaucoma (POAG) and a localized RNFL defect.

Material and methods. The peripapillary retinal circulation was evaluated using the OCTA centered on the optic nerve head in 98 POAG eyes having a localized RNFL defect and 45 healthy control eyes. A vascular impairment (VI) was identified in OCTA by the presence of a sign indicating decreased microvasculature. The frequencies of VI were compared between the POAG and control groups, and the topographic correlation between the VI and the RNFL defect identified in red-free fundus photographs was determined in the POAG group.

Results and discussions. The segmentation depth from the internal limiting membrane to the outer border of the inner plexiform layer was 98.3 ± 13.5 μm in POAG eyes and 113.6 ± 11.1 μm in healthy eyes. The VI was identified in 98 of the 98 POAG eyes (100%). It was observed as an area of decreased microvessel density of the parapapillary area. The VI was identified as a well-demarcated wedge-shaped area whose appearance was similar to that of the RNFL defect evident in the red-free fundus photographs. None of the eyes in the control group exhibited reduced vascularity in the OCTA images.

In the 98 POAG eyes, the VI exhibited nearly complete topographic correlations with the RNFL defect in terms of both the circumferential location (Pearson's correlation coefficient = 0.997, $P < 0.001$) and the extent (Pearson's correlation coefficient = 0.988, $P < 0.001$.

The interobserver ICCs (95% CIs) in measuring the circumferential location and extent of the VI and the localized RNFL defect were 0.990 (0.985–0.993) and 0.961 (0.943–0.974) for VI and 0.996 (0.993–0.997) and 0.995(0.993–0.997) for RNFL defect, respectively.

This study investigated the peripapillary retinal circulation using OCTA in POAG eyes and healthy control eyes. Decreased microvascular density (i.e., VI) of parapapillary retina was identified in 100% of the POAG eyes at the location of glaucomatous damage, whereas none of the healthy control eyes exhibited reduced vascularity.

The retinal microvasculature was evaluated using the en face image of a slab that included the inner retinal layer. Therefore, the defined slab included deeper layers in the periphery in cases where the inner retinal layer was thinner than the juxtapapillary area. This could result in visualizing not only the radial peripapillary capillaries but also the inner vascular plexus. However, in our experience, including retinal layers that are below the inner plexiform layer does not substantially affect the visualization of the retinal vasculature. In addition, the en face image obtained using our method provided better contrast between the areas of decreased and intact vascularity than the enface image obtained from the RNFL only.

Localized attenuation of the microvascular network was found in the parapapillary retina by OCTA in virtually all of the POAG patients. This finding is in line with Liu et al. and Akagi et al., reporting that focal retinal vessel defects had a hemifield concordance with the location of functional deterioration: eyes with superior VF loss had a decreased inferior parapapillary vessel density. However, hemifield concordance between the retinal vessel defect and the VF defect does not necessarily indicate that the location and extent of the two changes coincide each other. In the present study, we examined the topographic relationship of the localized VI with structural glaucomatous damage (i.e., RNFL defect), and found that VI almost perfectly coincided with the localized RNFL defect identified using red-free photography.

Studies have suggested that vascular factors can play a pathogenic role in glaucoma. It is of great interest to know whether the decreased peripapillary retinal vasculature identified by OCTA is one manifestation of compromised ocular perfusion that may contribute to the development of GON. In the present study, we identified a universal presence of inner-retinal hypoperfusion, which coincided with the RNFL defect identified via red-free photography. This finding suggests that the decreased density of retinal

microvasculature probably represents the closure or degeneration of capillaries that occurs along with the RNFL loss. If it was due to the primary reduction of retinal perfusion, the area of VI should not necessarily coincide with the RNFL defect. Rather, it should have followed the territory of the retinal arterial branches, as was demonstrated in cases of branched retinal arterial occlusion. However, the present study did not definitively address the causal relationship between the decreased blood flow and GON. A longitudinal study is needed to clarify whether the decreased capillary density of the peripapillary retina is the result or cause of GON.

The decreased vascularity in the area of an RNFL defect found in the present study is in line with the other OCTA studies that have found correlations between the density of retinal vessels and the thickness of the inner retinal layer or the RNFL. It appears that the capillaries within the RNFL or the inner retina become involuted as the neural tissue degenerates. This finding has also been demonstrated within the ONH neural tissue in eyes with glaucoma. Quigley et al. demonstrated that the loss of capillary volume was proportional to the loss of neural tissue within the ONH in both experimental and human glaucoma eyes.

One limitation of the current study was the absence of blood flow quantification. The current version of commercially available OCTA devices does not provide software for measuring the blood flow index. However, the interobserver agreement was found to be nearly perfect in determinations of the location and extent of VI. In addition, these parameters were successfully used in this study to demonstrate the topographic correlation with the RNFL defect. The second limitation is that only eyes with a localized RNFL defect were included. Thus, the results of the current study are not directly applicable to eyes with diffuse RNFL atrophy. In other words, it remains to be elucidated whether the relationship between the decreased vascularity and the RNFL damage in such eyes is different from that in eyes with localized RNFL defect.

Conclusion. a decreased parapapillary retinal microvasculature was universally identified using OCTA in POAG eyes with a localized RNFL defect, with an excellent topographic relationship with the area of RNFL defect. The finding suggests that the decreased microvasculature identified in OCTA probably represents the secondary loss or closure of capillaries, which occur along with the glaucomatous RNFL loss. Further longitudinal studies are required to confirm the relationship between the development of an RNFL defect and decreases in the retinal microvasculature

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