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EVALUATION OF CLINICAL AND FUNCTIONAL INDICATORS OF OCT ANGIOGRAPHY AND PERIMETRY IN PATIENTS WITH PRIMARY OPEN-ANGLE GLAUCOMA

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Резюме

Цель. Оценить взаимосвязь между измерениями плотности сосудов с помощью оптической когерентной томографической ангиографии (ОКТ-А) и потери полей зрения при первичной открытоугольной глаукоме (ПОУГ).

Объект и методы исследования. Были обследованы 31 здоровых лиц, 48 пациентов с подозрением на ПОУГ и 74 пациента с ПОУГ.

Результаты. По сравнению с глазами с ПОУГ, нормальные глаза демонстрировали более плотную микрососудистую сеть в пределах RNFL. Плотность сосудов была выше в нормальных глазах, за которыми следуют глаза с подозрением на глаукому, легкую глаукому и глаукому средней и тяжелой степени для wiVD (55,5, 51,3, 48,3, 41,7% соответственно) и cpVD (62,8, 61,0, 57,5, 49,6% соответственно) (P< 0,001 для обоих). Связь между тяжестью повреждения поля зрения (MD) с cpVD и wiVD была сильнее (R2 = 0,54 и R2 = 0,51 соответственно), чем связь между MD поля зрения и RNFL (R2 = 0,36) и площадью ободка (R2 = 0,36). p 2=0,19) (P<0,05 для всех). Многомерный регрессионный анализ с поправкой на вмешивающиеся факторы показал, что каждый 1%-й спад cpVD был связан с уменьшением MD на 0,64 dB , а каждый 1%-ный спад wiVD был связан с уменьшением MD на 0,66 dB . Кроме того, было обнаружено, что связь между плотностью сосудов и тяжестью повреждения поля зрения является значимой даже после учета эффекта структурной потери.

Выводы. Снижение плотности сосудов было в значительной степени связано с тяжестью повреждения поля зрения независимо от структурной потери. ОКТ-А — многообещающая технология лечения глаукомы, потенциально улучшающая понимание роли сосудов в патофизиологии заболевания.

Ключевые слова: первичная открытоугольная глаукома, ОКТ-ангиография, компьютерная периметрия, корреляционный анализ.

Хулоса

Мақсад. Бирламчи очиқ бурчакли глаукомада (БОБГ) қон томир зичлиги ва кўриш майдонини йўқотишнинг оптик когерент томографик ангиографияси (ОКТ-А) ўртасидаги боғлиқликни баҳолаш.

Тадқиқот объекти ва усуллари. 31 соғлом одам, БОБГга шубҳа қилинган 48 бемор ва БОБГ билан касалланган 74 бемор текширилди.

Натижалар. БОБГ кўзлари билан солиштирганда, оддий кўзлар RNFL ичида зичроқ микроваскуляр тармоқни кўрсатди. Қон томирлари зичлиги оддий кўзларда юқори бўлган, ундан кейин глаукомага шубҳа қилинган, енгил глаукома ва ўртача ва

оғир глаукома кўзларида wiVD (мос равишда 55,5, 51,3, 48,3, 41,7%) ва cpVD (мос равишда 62,8, 61,0, 57,5,49%). иккаласи учун 0,001). Кўриш майдонининг шикастланишининг (MD) cpVD ва wiVD билан жиддийлиги ўртасидаги боғлиқлик кўриш майдони MD ва RNFL (P2 = 0,36) ва жант майдони (P2 = 0,19) ўртасидаги боғлиқликка қараганда кучлироқ еди (мос равишда P2 = 0,54 ва P2 = 0,51).) (барчаси учун П<0,05). Кўп ўзгарувчан регрессия таҳлили, чалкашликлар учун созланган, cpVD нинг ҳар 1% пасайиши MDда 0,64 dB йўқотиш билан боғлиқлигини ва wiVDнинг ҳар 1% пасайиши MDда 0,66 dB йўқотиш билан боғлиқлигини кўрсатди. Бундан ташқари, томир зичлиги ва кўриш майдонининг шикастланишининг оғирлиги ўртасидаги боғлиқлик структуравий йўқотиш таъсирини назорат қилгандан кейин ҳам муҳим еканлиги аниқланди.

Хулоса. Томир зичлигининг пасайиши структуравий йўқотишдан қатъи назар, визуал майдоннинг шикастланишининг жиддийлиги билан сезиларли даражада боғлиқ еди. ОКТ-А глаукомани даволашда истиқболли технология бўлиб, касалликнинг патофизиологиясида қон томир ролини тушунишни потенциал равишда кучайтиради.

Калит сўзлар: бирламчи очиқ бурчакли глаукома, ОКТ ангиографияси, ҳисобланган периметрия, корреляция таҳлили.

Summary

Purpose. To assess the relationship between optical coherence tomographic angiography (OCT-A) measurements of vascular density and visual field loss in primary open-angle glaucoma (POAG).

Object and methods of research. 31 healthy individuals, 48 patients with suspected POAG and 74 patients with POAG were examined.

Results. Compared to POAG eyes, normal eyes demonstrated a denser microvascular network within the RNFL. Vessel density was higher in normal eyes followed by glaucoma suspects, mild glaucoma and moderate to severe glaucoma eyes for wiVD (55.5, 51.3, 48.3, 41.7% respectively) and for cpVD (62.8, 61.0, 57.5, 49.6% respectively) (P<0.001 for both). The association between the severity of visual field damage (MD) with cpVD and wiVD was stronger (R2=0.54, and R2=0.51 respectively) than the association between visual field MD and RNFL (R2=0.36) and rim area (R2=0.19) (P<0.05 for all). Multivariate regression analysis, adjusted for confounders, showed that each 1% decrease in cpVD was associated with 0.64 dB loss in MD and each 1% decrease in wiVD, was associated with 0.66 dB loss in MD. In addition, the association between vessel density and the severity of visual field damage was found to be significant even after controlling for the effect of structural loss.

Conclusions. Decreased vessel density was significantly associated with severity of visual field damage independent of the structural loss. OCT-A is a promising technology in glaucoma management, potentially enhancing the understanding of vascular role in the pathophysiology of the disease.

Key words: primary open-angle glaucoma, OCT angiography, computed perimetry, correlation analysis.

Introduction. Glaucoma is a progressive optic neuropathy with unknown etiology characterized by degeneration of retinal ganglion cells (RGC) and their axons

resulting in a characteristic appearance of the optic disc and visual field loss. [1,2] There is increasing evidence that optic nerve blood flow impairment and microcirculatory deficiency may have a role in the pathogenesis of glaucoma. Although the details of this relationship have not been established precisely. This is in part due to the instrumentation that has been available and their difficulty of accurately measuring ocular blood flow. [6]

In contrast to ocular blood flow, objective, accurate, and quantitative measurements of the optic nerve head and macula can be obtained with optical coherence tomography (OCT), and they have become the standard for structural evaluation in glaucoma research and clinical practice. However, structural measurements have only moderate correlation with visual field loss. [3]

It recently has become possible to obtain non-invasive images to characterize retinal vasculature with OCT angiography (OCT-A) [4.5]. OCT-A provides reproducible quantitative assessment of the microvasculature in the optic nerve head, peripapillary retina, and macula. [8] Recent studies using OCT-A have suggested that this new technology might be useful in the diagnosis, staging, and monitoring of glaucoma. [7,9,10] These measurements also may clarify the role of microcirculation and optic nerve blood flow in the pathogenesis of glaucoma.

The current study evaluates the relationship between OCT-A retinal vessel density parameters with functional measurements and compare it to standard spectral domain OCT (SD-OCT) structural measurements.

Purpose. To evaluate the association between vessel density measurements using optical coherence tomography angiography (OCT-A) and severity of visual field loss in primary open-angle glaucoma (POAG).

Material and methods. This was an observational cross-sectional study including 153 eyes from 31 healthy, 48 glaucoma suspect, and 74 primary open angle glaucoma (POAG) patients.

All participants completed a comprehensive ophthalmologic examination, including best corrected visual acuity (BCVA), slit-lamp biomicroscopy, intraocular pressure (IOP) measurement with Goldmann applanation tonometry, gonioscopy, dilated fundus examination, stereoscopic optic disc photography, ultrasound pachymetry, and standard automated perimetry (SAP) in both eyes. Only participants over 18 years of age with open angles on gonioscopy, and spherical refraction within ± 10 D were included.

Healthy subjects were required to have an IOP of 21 mmHg or less with no history of elevated IOP, normal appearing optic discs, intact neuroretinal rims and retinal nerve fiber layer (RNFL), and normal visual field test results defined as a Pattern Standard Deviation (PSD) within the 95% confidence limits, and Glaucoma Hemifield Test (GHT) result within normal limits. Glaucoma suspects had either an IOP ≥ 22 mmHg and/or suspicious appearing optic discs without evidence of repeatable glaucomatous visual field damage.

Results and discussions. Glaucoma was defined by the presence of repeatable abnormal SAP results with a GHT outside normal limits or PSD outside the 95% normal limits. Glaucoma patients were additionally classified into 2 groups based on the severity of their visual field damage; mild glaucoma was defined as visual field mean deviation (MD) higher than −6 dB and moderate to severe glaucoma as a visual field MD lower than −6 dB.22 To ensure

comparability of age across study groups, only subjects ≥ 45 years were included.

Eyes with history of intraocular surgery (except for glaucoma surgery or uncomplicated cataract surgery), secondary causes of glaucoma, non-glaucomatous optic neuropathies, vascular or non-vascular retinopathies, and other ocular or systemic diseases known to impair the visual field were excluded from the investigation.

Two blood pressure (BP) measurements obtained in a resting, seated position were taken at least 5 minutes apart using an instrument. Mean arterial pressure (MAP) was calculated as MAP= 1/3 systolic BP + 2/3 diastolic BP and mean ocular perfusion pressure (MOPP) was defined using the following equation: MOPP = 2/3 MAP-IOP.

Results and discussion. The study population consisted of 31 healthy subjects (mean age 69.0 ± 7.7 years, SAP MD 0.3 ± 1.3 dB), 48 glaucoma suspects (mean age 71.4 ± 9.4 years, SAP MD −0.6 ± 1.5 dB), 46 mild glaucoma patients (mean age 72.9 ± 10.7 years, SAP MD −3.0 ± 1.8 dB) and 28 moderate to severe glaucoma patients (mean age 75.7 ± 10.7 years, SAP MD −13.6 ± 6.6 dB). Healthy subjects tended to be younger than glaucoma suspects and glaucoma patients, but this difference was not statistically significant (ANOVA P=0.063). Healthy eyes generally appeared to have denser capillary networks in the RNFL layer compared to eyes with early glaucomatous optic nerve damage and trend of a sparser microvascular network could be detected with advancing stages of the disease. Vessel density measurements were lower in more severe disease. Specifically, the mean wiVD in moderate to severe glaucoma eyes was significantly lower (41.7 ± 5.5 %,) than in mild glaucomatous eyes (48.3 ± 4.2 %), glaucoma suspects (51.3 ± 4.6 %) and healthy eyes (55.5 ± 3.2 %) (ANOVA P<0.001, Tukey HSD P<0.05 for all comparisons). Mean cpVD values were also significantly lower in moderate to severe glaucoma eyes (49.6 ± 6.9 %,) followed by mild glaucoma (57.5 ± 4.4), glaucoma suspects (61.0 ± 4.7 %) and healthy eyes (62.8 ± 3.9 %), (ANOVA P<0.001, Tukey HSD P<0.05 for all pairwise comparison except between healthy and glaucoma suspect eyes. (P=0.322). Standard structural and functional measurements also showed statistically significant differences among groups (P<0.001).

Significant differences were found comparing strength of the associations between MD and both OCT-A vascular parameters with the association between MD and RNFL and rim area measurements (P≤0.05 for all pairwise comparisons). The association between MD and RNFL thickness was also significantly stronger than between MD and rim area (P=0.001). The associations between wiVD and cpVD with MD were similar (P=0.500). The strongest associations with visual field PSD were with wiVD, cpVD (R2=0.39 and 0.36 respectively), and RNFL (R2=0.37) followed by rim area (R2=0.23). Significant differences were found between the associations of PSD with wiVD and rim area (P=0.026) and between RNFL thickness and rim area (P=0.035). The linear associations between visual field mean sensitivity were strongest with cpVD (R2=0.55) followed by wiVD (R2=0.53), RNFL thickness (R2=0.37) and rim area (R2=0.19). After converting mean sensitivity from logarithmic (dB) to linear units (1/lambert), a similar pattern was found; Association with mean sensitivity (1/lambert), were highest for wiVD and cpVD (R2=0.44 for both) followed by RNFL

thickness (R2=0.34) and rim area (R2=0.18).

The strength of the associations between visual field MD with structural and OCT-A measures also were compared using a curvilinear quadratic model. The associations between OCT-A and visual field MD were significantly stronger than the associations between visual field MD and RNFL and rim area (P<0.05 for all pairwise comparisons using bootstrapping procedure).

Results from univariate regression analysis for visual field MD as the dependent variable are summarized. Multivariate linear regression analysis, while controlling for the potentially confounding effect of age, IOP, CCT, and axial length, showed that each 1% decrease in cpVD, was associated with 0.64 dB loss in MD (P<0.001), and each 1% decrease in wiVD, was associated with 0.66 dB loss in MD (P<0.001).

Multivariate regression analysis that controlled for the effect of potential confounders (age, IOP, CCT and axial length) and also adjusted for the effect of RNFL thickness, showed that wiVD was independently associated with visual field MD. Similar results were found when cpVD was included in the model instead of wiVD. The association between RNFL with MD was no longer statistically significant when vessel density was included in the model. The multivariate regression analysis also was completed using rim area instead of RNFL thickness, and the results were similar; Each 1% decrease in wiVD, was associated with 0.71 dB loss in MD (P<0.001) and the association between rim area and MD were no longer significant (P=0.285) when wiVD was included in the model.

For completeness, associations between clinical and ophthalmic features and OCTA vessel density also were evaluated. OCT-A vessel density was significantly associated with RNFL and rim area measurements (P<0.001). As structural measurements, such as RNFL, optic nerve head rim and cup area have been shown to be associated with disc size, we also evaluated the association of ONH area on OCT-A vascular measurements. There were no statistically significant correlations between disc area with wiVD and cpVD measurements in healthy eyes (R2=0.005, P=0.696, and R2=0.009, P=0.614, respectively). For this reason, disc area was not controlled for in the multivariable analyses. In addition, we did not find a significant association between MOPP and cpVD (R2=0.003, P=0.49) or wiVD (R2=0.000, P=0.85).

Results of the present study demonstrate a significant relationship between vessel density and severity of visual field damage. Qualitatively, the OCT-A vessel density map showed sparser peripapillary vascular networks in more severe glaucoma. Quantitatively, lower vessel density values, were associated with more advanced stages of glaucomatous visual field damage. The principal finding of the study was a relatively strong association between cpVD, wiVD, and visual field loss expressed as MD (R2=0.54 and 0.51, respectively, P<0.001 for both) suggesting that reduced OCT-A vessel density is associated with more severe glaucoma. Our results also suggest the vascular-functional correlations were stronger than the standard structural (RNFL and rim area)-function relationships whether comparing linear or non-linear fitted models. Moreover, multivariate analyses indicated an independent relationship between reduced vessel density and visual field loss, even after adjusting for the severity of structural

damage measured by rim area and RNFL thickness.

Conclusion. In our study, SAP MD, PSD and MS measured in a logarithmic scale reported in decibels and also MS converted to a linear scale reported in 1/lambert were significantly associated with vessel density measurements (P<0.001 for all). The associations between cpVD, wiVD and MD (R2=0.54 and 0.51, respectively) were higher than their association with PSD (R2=0.36 and 0.39 respectively, P<0.001). Reports comparing the strength of the association between OCT based vascular measurements and different visual field summary measures are inconsistent. Hwang et al7 showed that total retinal blood flow measured by Doppler-OCT was highly correlated with MD, but its relationship with PSD did not reach statistical significance. Another Doppler-OCT based study33 investigating hemispheric retinal blood flow measurements in eyes having glaucomatous visual field damage confined to a single hemifield, reported significant differences in blood flow measurements between the affected and unaffected retinal hemispheres in glaucoma patients compared to healthy age-matched subjects, but failed to find an association between hemispheric retinal blood flow measurements and visual field mean retinal sensitivity measured as 1/lambert in the corresponding hemifield.

OCT-A vessel density measurements are significantly associated with severity of visual field damage. These associations are generally stronger than standard structural measures such as RNFL and rim area. Moreover, OCT-A vessel density measurements are still significantly associated with severity of visual field loss even after adjusting for standard structural measurements. For these reasons, OCT-A is a promising technology that will allow clinical monitoring of vascular changes in glaucoma, and it could potentially allow further understanding on the pathophysiology of the disease, specifically its underlying vascular mechanism.

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