ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

Relationship between optic nerve head topography and nerve fiber layer thickness with central corneal thickness in patients with primary open-angle glaucoma

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SUMMARY
Introduction/Objective In patients with primary open-angle glaucoma (POAG) we explored the relationship between the optic nerve head (ONH) topography parameters and the retinal nerve fiber layer (RNFL) thickness with the central corneal thickness (CCT).
Methods This retrospective study included 97 patients (97 eyes) with primary open-angle glaucoma. Patients were divided into a thin CCT < 540 μm (45 eyes) and a thick CCT ≥ 540 μm (52 eyes) group, using ultrasonic pachymeter. Topographic measurements of the ONH parameters and RNFL thickness was performed using optical coherence tomography (OCT). The outcomes were compared with the thin and thick CCT and correlated with the thin CCT of the subjects.
Results There were significantly lower mean intraocular pressure ($p < 0.0001$) and CCT ($p < 0.0001$) in patients with thin CCT compared to patients with thick CCT. Statistically significant differences of ONH parameters were found in thin cornea group compared to thick cornea group in: cup/disc area ratio ($p < 0.03$), vertical cup/disc ratio ($p < 0.01$) and rim volume ($p < 0.01$). Statistically significant differences of RNFL thickness were found in thin cornea group compared to thick cornea group in: average ($p < 0.001$), superior ($p < 0.03$), inferior ($p < 0.03$) and nasal ($p < 0.01$). Significant positive correlation was found between thin CCT and OCT parameters in: optic disc area ($r = 0.429$, $p = 0.003$), cup/disc area ratio ($r = 0.287$, $p = 0.05$), horizontal cup/disc ratio ($r = 0.472$, $p < 0.001$), vertical cup/disc ratio ($r = 0.578$, $p < 0.001$), average RNFL ($r = 0.796$, $p < 0.001$), superior RNFL ($r = 0.665$, $p < 0.001$), inferior RNFL ($r = 0.650$, $p < 0.001$), nasal RNFL ($r = 0.611$, $p < 0.001$) and temporal RNFL thickness ($r = 0.601$, $p < 0.001$).
Conclusion POAG patients with thin cornea will probably develop larger glaucoma changes than those with a thicker cornea. Ultrasonic pachymetry measurements of CCT and OCT analysis of ONH topography parameters and RNFL thickness provide significant information in early diagnosis and monitoring progression of POAG.
Keywords: intraocular pressure; ultrasonic pachymetry; optical coherence tomography

INTRODUCTION

Primary open angle glaucoma (POAG) is the disorder of the structural and functional changes of the optic nerve [1].

Glaucoma changes of the optic nerve may manifest as a morphological damage in the optic nerve head (ONH) as well as a decrease in the thickness of the retinal nerve fiber layer (RNFL) [2].

Optical coherence tomography (OCT) is a method usually used for evaluation of the structural glaucoma damage [3, 4]. OCT is non-contact and high-resolution device which provides a cross-sectional image, good for quantitative evaluation of the ONH and RNFL [5]. It is a repeatable time-saving procedure.

Central corneal thickness (CCT) is a risk factor for the development of POAG and a predictive factor for conversion ocular hypertension (OHT) to POAG [1]. It has been reported that thick cornea provides falsely elevated intraocular pressure (IOP), which may cause a false POAG diagnosis, whereas thin cornea provides an opposite result, which hides the risk of developing POAG [6]. Herendon et al. [7] reported that CCT was an important parameter of glaucoma ONH structural change. Hewitt et al. [8] also found that, in glaucoma eyes, thin CCT was related to increased vertical cup/disc ratio (VCDR).

The aim of this study was to determine whether thin CCT is associated with specific ONH topography parameters and RNFL thickness, measured by OCT in POAG patients.

METHODS

The is a retrospective study on documented 97 patients (97 eyes) with POAG at the Family Čivčić Ophthalmology practice in Belgrade.

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The research was done in accordance with the Helsinki Declaration and with the approval of the local Committee on Ethics.

Exclusion criteria were: myopia ≥ -6 D, secondary glaucoma, POAG advanced glaucoma stage, drusen of the optic nerve head and other anomalies of the optic nerve head, other ocular diseases, history of previous ocular surgeries and laser treatments, trauma, systemic comorbidities that may affect the visual field, patients with unreliable visual field (defined as false-negative errors > 33%, false-positive errors > 33%, and fixation losses > 20%), mean deviance (MD) ≥ -10 dB.

In all participants we examined best corrected visual acuity (BCVA), slit-lamp biomicroscopy, IOP measurement using Goldmann applanation tonometry, gonioscopy, a dilated fundus evaluation using indirect ophthalmoscopy with 90 D lens, and a 24-2 threshold test using a standard automated perimetry AP-1000 Tomey (Tomey, Nagoya, Japan). In addition, CCT was measured with ultrasonic pachymeter SP-100 Tomey (Tomey). ONH analysis (disc, cup and rim area, cup and rim volume, cup/disc (C/D) ratio, horizontal and vertical C/D ratio) with RNFL measurements (average and four quadrants RNFL thickness), was performed using spectral domain OCT (SOCT Copernicus Plus, Optopol Technology, Zawiercie, Poland).

POAG patients were classified into two groups according to their median CCT: thin CCT < 540 µm (45 eyes) and thick CCT ≥ 540 µm (52 eyes).

Demographic and clinical characteristics and OCT parameters were compared with the two groups according to the CCT value, using unpaired t-test (Microsoft Excel, Office 2010, Microsoft Corporation, Redmond, WA, USA). Pearson's correlation coefficients (r) were calculated to assess the associations between thin CCT and optic disc morphological parameters. Statistical analysis of Pearson 's correlation coefficients were performed by JASP version 0.12.2 (Jeffrey's Amazing Statistics Program, Amsterdam, the Netherlands). The significance level was set at p value of < 0.05.

RESULTS

This study included 97 eyes of 97 patients with medically controlled POAG. Of these, 39 (40.21%) patients were male and 58 (59.79%) patients were female. The average age of the examined population was 57.18 ± 13.05 (range 26–78) years. Demographic and clinical characteristics of patients with POAG were compared with the two groups according to the CCT value (Table 1). There was statistically significant difference in the mean IOP and CCT between the groups (p < 0.0001). IOP with the prescribed therapy was significantly higher in patients with thick CCT compared to patients with thin CCT (17.92 ± 2.40 mmHg *vs*. 15.62 ± 2.39 mmHg, p < 0.0001). CCT was significantly higher in patients with thick CCT compared to patients with thin CCT (569.65 ± 22.06 µm *vs*. 512.44 ± 20.39 µm, p < 0.0001). We found no statistically significant difference between the groups in terms of age, gender, and MD (p = 0.053, p = 0.65, p = 0.007).

Table 2 shows a comparison of ONH parameters obtained by OCT between two studied groups. There were statistically significant differences between thin CCT and thick CCT in these stereometric parameters: cup/disc area ratio (0.48 ± 0.15 *vs*. 0.42 ± 0.11, p < 0.03), VCDR (0.71 ± 0.12 *vs*. 0.69 ± 0.10, p < 0.01) and rim volume (0.12 ± 0.06 mm³ *vs*. 0.15 ± 0.05 mm³, p < 0.01). ONH parameters showed that cup/disc area ratio and VCDR were significantly larger and rim volume significantly smaller in POAG patients with thin CCT compared to patients with thick CCT.

The average and quadrant RNFL thickness were compared between the thin CCT and thick CCT. Statistically significant differences were found in thin cornea group compared to thick cornea group in: average (102.88 ± 11.04 µm *vs*. 110.32 ± 10.83 µm, p < 0.001), superior (118.42 ± 16.76 µm *vs*. 125.57 ± 15.82 µm, p < 0.03), inferior (118.44 ± 19.38 µm *vs*. 126.59 ± 16.93 µm, p < 0.03) and nasal (78.33 ± 12.39 µm *vs*. 84.15 ± 11.16 µm, p < 0.01) RNFL thickness (Table 3). The average and quadrants (superior, inferior, nasal) RNFL thickness were significantly lower in thin cornea group compared to thick cornea group in POAG patients.

There was no statistically significant difference in optic disc area (p = 0.45), horizontal cup/disc ratio (p = 0.15), cup area (p = 0.18), cup volume (p = 0.21), rim area (p = 0.11) and temporal RNFL thickness (p = 0.31) between the two groups (Table 2 and 3).

Table 4 gives the correlation coefficient between OCT parameters (ONH parameters and RNFL thickness) and thin CCT. There was a positive correlation with all OCT parameters. Statistical significance was found in: optic disc area (r = 0.429, p = 0.003), and cup/disc area ratio (r = 0.287, p = 0.05). High statistical significance was found in: horizontal cup/disc ratio (r = 0.472, p < 0.001), VCDR (r = 0.578, p < 0.001), average RNFL (r = 0.796, p < 0.001), superior RNFL (r = 0.665, p < 0.001), inferior RNFL (r = 0.650, p < 0.001), nasal RNFL (r = 0.611, p < 0.001) and temporal RNFL thickness (r = 0.601, p < 0.001).

DISCUSSION

OCT provide objective and reliable data of ONH and RNFL with a high reproducibility in glaucoma and healthy eyes [9].

CCT has been demonstrated as an important risk factor for development and progression of ocular hypertensive to primary open-angle glaucoma patients [10]. The Ocular Hypertension Treatment Study (OHTS) discovered that the risk for development of glaucoma is larger in eyes with thin CCT and lower in eyes with thick CCT [10]. Our study showed a significantly lower mean IOP (p < 0.0001) and CCT (p < 0.0001) in POAG patients with thin cornea compared to patients with thick cornea. Patil et al. [11] demonstrated that the mean CCT in the normal group (554.38 ± 17.67 µm) and the glaucoma group (554.15 ± 16.39 µm) was similar and was significantly lower than the mean CCT in the OHTN group

Table 1. Demographic and clinical characteristics of patients with primary open-angle glaucoma

Parameters	CCT < 540 µm (n = 45) $\bar{x}$ ± SD	CCT ≥ 540 µm (n = 52) $\bar{x}$ ± SD	p
Age (years)	59.93 ± 12.81	54.80 ± 12.91	0.053
Gender (M/F), n	17/28	22/30	0.65
Mean IOP (mmHg)	15.62 ± 2.39	17.92 ± 2.40	< 0.0001
CCT (µm)	512.44 ± 20.39	569.65 ± 22.06	< 0.0001
MD (dB)	-3.72 ± 1.57	-3.22 ± 1.1	0.077

M/F – male/female; IOP – intraocular pressure; CCT – central corneal thickness; p – unpaired t-test; MD – mean deviation

Table 2. Optic nerve head topography parameters classified by central corneal thickness (CCT)

Optic nerve head parameters	CCT < 540 µm (n = 45) $\bar{x}$ ± SD	CCT ≥ 540 µm (n = 52) $\bar{x}$ ± SD	p
Optic disc area (mm²)	1.72 ± 0.4	1.78 ± 0.36	0.45
Cup/disc area ratio	0.48 ± 0.15	0.42 ± 0.11	< 0.03
Horizontal cup/disc ratio	0.67 ± 0.13	0.63 ± 0.12	0.15
Vertical cup/disc ratio	0.71 ± 0.12	0.69 ± 0.10	< 0.01
Cup area (mm²)	0.84 ± 0.33	0.76 ± 0.27	0.18
Cup volume (mm³)	0.21 ± 0.13	0.18 ± 0.10	0.21
Rim area (mm²)	0.87 ± 0.29	0.97 ± 0.31	0.11
Rim volume (mm³)	0.12 ± 0.06	0.15 ± 0.05	< 0.01

p – unpaired t-test

Table 3. Retinal nerve fiber layer (RNFL) thickness classified by central corneal thickness (CCT)

RNFL thickness	CCT < 540 µm (n = 45) $\bar{x}$ ± SD	CCT ≥ 540 µm (n = 52) $\bar{x}$ ± SD	p
Average (µm)	102.88 ± 11.04	110.32 ± 10.83	< 0.001
Superior (µm)	118.42 ± 16.76	125.57 ± 15.82	< 0.03
Inferior (µm)	118.44 ± 19.38	126.59 ± 16.93	< 0.03
Temporal(µm)	63.15 ± 9.81	71.47 ± 11.03	0.31
Nasal (µm)	78.33 ± 12.39	84.15 ± 11.16	< 0.01

p – unpaired t-test

Table 4. Optical coherence tomography parameters in relationship to thin central corneal thickness (CCT)

OCT parameters	Correlation coefficient (r)	p
Optic disc area (mm²)	0.429	0.003
Cup/disc area ratio	0.287	0.05
Horizontal cup/disc ratio	0.472	< 0.001
Vertical cup/disc ratio	0.578	< 0.001
Cup area (mm²)	0.227	0.126
Cup volume (mm³)	0.118	0.429
Rim area (mm²)	0.268	0.069
Rim volume (mm³)	0.108	0.472
Average RNFL (µm)	0.796	< 0.001
Superior RNFL (µm)	0.665	< 0.001
Inferior RNFL (µm)	0.650	< 0.001
Nasal RNFL (µm)	0.611	< 0.001
Temporal RNFL (µm)	0.601	< 0.001

OCT – optical coherence tomography; RNFL – retinal nerve fiber layer; r – Pearson's correlation coefficient

(568.18 ± 30.52 µm, p < 0.01). Bulut et al. [12] found that the CCT in the POAG group (545.6 ± 29.7 µm) and the healthy control group (551.9 ± 26.2 µm) was significantly higher than the CCT in the normal tension glaucoma group (519.0 ± 25.7 µm, p < 0.001). Marić et al. [13] found in patients with suspected glaucoma significantly lower mean CCT in adults than in children (547 ± 35 µm *vs.* 578 ± 35, p < 0.032).

In the current study ONH parameters showed that the cup/disc area ratio and VCDR were significantly larger and rim volume significantly smaller in POAG patients with thin CCT compared to patients with thick CCT. Anton et al. [14] and Dagdalen and Dirican [9] showed that rim parameters were significantly smaller and C/D ratio significantly greater in glaucomatous eyes than in normal and OHT eyes.

Several studies using OCT showed that the mean RNFL thickness and superior and inferior sector thickness are valuable measurement parameters in the differentiation of glaucoma. Kaushik et al. [15] found that the RNFL in ocular hypertensives with CCT ≤ 555 µm was thinner than in those with thicker corneas. Anton et al. [14] and Dagdalen and Dirican [9] discovered that mean RNFL thickness and superior and inferior RNFL thickness were thinner in eyes with glaucoma, than in eyes with ocular hypertension and normal eyes. Chen et al. [16] found that the most RNFL thickness (except at the nasal quadrant) were significantly lower in preperimetric glaucoma eyes compared to normal eyes. Bulut et al. [12] discovered that the mean RNFL thickness were thinner in normal tension glaucoma group than in POAG and healthy control group. In the present study, the average and quadrants (superior, inferior, nasal) RNFL thickness were significantly lower in thin cornea group compared to thick cornea group in POAG patients.

In our study a significant positive correlation was found between thin CCT and OCT parameters in: optic disc area (p = 0.003), cup/disc area ratio (p = 0.05), horizontal cup/disc ratio (p < 0.001), VCDR (p < 0.001), average RNFL (p < 0.001), superior RNFL (p < 0.001), inferior RNFL (p < 0.001), nasal RNFL (p < 0.001) and temporal RNFL thickness (p < 0.001). In the recent study Öztürker [17] found a significant positive correlation between thin CCT and inferior RNFL thickness (r = 0.353, p < 0.005) in patients with POAG. Wangsupadilok and Orapiriyakul [18] found a significant positive correlation between CCT and RNFL thickness in all quadrants and average RNFL thickness, with highest correlation for average RNFL thickness (r = 0.487, p = 0.001) in POAG patients.

CONCLUSION

POAG patients with thin cornea will probably develop larger glaucoma changes than those with a thicker cornea. Ultrasonic pachymetry measurements of CCT and OCT analysis of ONH topography parameters and RNFL thickness, provide significant information in the early diagnosis and monitoring progression of POAG. It is necessary to perform a larger prospective study in the future to confirm these findings.

Conflict of interest: None declared.

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Повезаност топографских параметара главе оптичког нерва и дебљине слоја нервних влакана ретине са централном дебљином рожњаче код болесника са примарним глаукомом отвореног угла

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САЖЕТАК

Увод/Циљ Истраживали смо повезаност између топографских параметара главе оптичког нерва (ГОН) и дебљине слоја нервних влакана ретине (СНВР) са централном дебљином рожњаче (ЦДР) код болесника са примарним глаукомом отвореног угла.

Методе У ову ретроспективну студију укључено је 97 болесника (97 очију) са примарним глаукомом отвореног угла. Болесници су подељени на групу са тањом рожњачом (ЦДР < 540 *μm*, 45 очију) и дебљом рожњачом (ЦДР ≥ 540 *μm*, 52 ока), које су мерене ултразвучном пахиметријом. Топографска мерења параметара ГОН и дебљине СНВР рађена су оптичком кохерентном томографијом (ОКТ). Резултати су упоређивани са тањом и дебљом ЦДР и корелирани са тањом ЦДР учесника студије.

Резултати Утврђене су статистички значајно ниже вредности интраокуларног притиска ($p < 0,0001$) и ЦДР ($p < 0,0001$) код болесника са танком ЦДР у поређењу са болесницима са дебљом ЦДР. Код параметара ГОН добили смо статистички значајну разлику у групи са танком рожњачом у поређењу са групом са дебљом рожњачом код површине односа *cup/disc* ($p < 0,03$), вертикалног односа *cup/disc* ($p < 0,01$) и волумена *rim* ($p < 0,01$). Пронађена је статистички значајна разлика код дебљине СНВР у групи са танком рожњачом у поређењу са групом са дебљом рожњачом код средње ($p < 0,001$), горње ($p < 0,03$), доње ($p < 0,03$) и унутрашње ($p < 0,01$) дебљине СНВР. Утврђена је статистички значајна позитивна корелација танке ЦДР и параметара оптичке кохерентне томографије код површине *optic disc* ($r = 0,429$, $p = 0,003$), површине односа *cup/disc* ($r = 0,287$, $p = 0,05$), хоризонталног односа *cup/disc* ($r = 0,472$, $p < 0,001$), вертикалног односа *cup/disc* ($r = 0,578$, $p < 0,001$), средње дебљине СНВР ($r = 0,796$, $p < 0,001$), горњег СНВР ($r = 0,665$, $p < 0,001$), доњег СНВР ($r = 0,650$, $p < 0,001$), унутрашњег СНВР ($r = 0,611$, $p < 0,001$) и спољашњег СНВР квадранта ($r = 0,601$, $p < 0,001$).

Закључак Болесници са примарним глаукомом отвореног угла и тањом рожњачом вероватно ће развити веће глаукомне промене од оних са дебљом рожњачом. Ултразвучном пахиметријом мерена ЦДР и оптичком кохерентном томографијом анализирани топографски параметри ГОН и дебљина СНВР пружају значајне информације у раној дијагнози и праћењу прогресије код примарног глаукома отвореног угла.

Кључне речи: интраокуларни притисак; ултразвучна пахиметрија; оптичка кохерентна томографија