ORIGINAL RESEARCH

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Evaluation of Central Macular Thickness and Perifoveal Ganglion Cell Complex Thickness with Optical Coherence Tomography in Cases with Primary Open Angle Glaucoma and Ocular Hypertension

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ABSTRACT Objective: Evaluation of central macular thickness (CMT) and perifoveal ganglion cell complex thickness (GCC) through spectral-domain optical coherence tomography (SD-OCT) in cases with primary open angle glaucoma (POAG) and ocular hypertension (OHT). **Material and Methods:** In this study, 150 eyes of 75 patients with POAG, 144 eyes of 72 patients with OHT and 142 eyes of 71 healthy cases were included. All cases undergone a complete ophthalmologic examination, visual field examination with standard automated perimetry, and CMT and GCC thickness measurements with RTVue-100 SD-OCT device. In CMT and GCC analysis, average, inferior-half and superior-half thickness values were evaluated. **Results:** No statistically significant difference was detected between the groups in terms of age and gender ($p>0.05$). CMT was found as 227.4±21.6 μm, 235.7±20.3 μm, 238.5±17.8 μm, GCC average thickness was found as 91.6±9.6 μm, 98.1±6.5 μm, 98.2±6.8 μm, GCC superior-half thickness as 91.2±9.6 μm, 97.4±6.6 μm, 97.4±6.8 μm and GCC inferior-half thickness as 92.1±10.3 μm, 98.9±6.8 μm, 99.0±7.3 μm in POAG, OHT and control groups, respectively. In the POAG group, the GCC average, superior-half and inferior-half thickness and CMT values were significantly lower than those of the OHT and control groups. No significant difference was detected between the OHT and control groups. GCC and CMT analyses are correlated. **Conclusions:** In distinguishing POAG cases from OHT and healthy cases, GCC and CMT analyses are rather effective and reliable. GCC and CMT analyses may be used as adjuvant methods to visual field testing in the diagnosis and treatment follow-up of patients with POAG. GCC and CMT analyses are not reliable in distinguishing OHT cases from normal cases.

Keywords: Glaucoma; glaucoma, open-angle; ocular hypertension; tomography, optical coherence

Glaucoma is a chronic progressive optical neuropathy which is one of the leading causes of blindness worldwide. Since the nerve fiber damage that occurs in glaucoma is irreversible, early diagnosis is very important in the prevention of such damage.[1] In the follow-up of patients with glaucoma, standard automated perimetry is considered as the gold standard, however this method does not give way to the detection of the defect before 40% of the ganglion cell axons are damaged.[2-3] Therefore, new methods are investigated for early diagnosis and follow-up of patients with glaucoma.

Optical coherence tomography (OCT) is a high-resolution non-invasive method that provides cross-sectional imaging of the tissues. Glaucoma primarily affects the ganglion cells and the nerve fiber layer of the retina. In recent years, in addition to visual field (VF), spectral-domain optical coherence tomography (SD-OCT) has also been used in order to measure retinal nerve fiber layer (RNFL), ganglion cell complex thickness (GCC) and central macular thickness (CMT) which are well accepted in the current diagnosis

and treatment follow-up of glaucoma patients.[4,5] GCC includes RNFL, ganglion cell layer and inner plexiform layer. OCT provides objective evaluation of RNFL and GCC, and has become an important imaging method in the diagnosis and follow-up of glaucoma.

In this study, we studied the CMT and GCC thickness by using SD-OCT in cases with primary open angle glaucoma (POAG) and ocular hypertension (OHT). We investigated the reliability of CMT and GCC analyses in distinguishing cases with POAG and OHT from healthy cases. In addition, we aimed to evaluate the correlation between these two tests.

MATERIAL AND METHODS

Cases diagnosed or followed up in our clinic between November 2011-May 2012 were studied retrospectively. 150 eyes of 75 POAG patients, 144 eyes of 72 OHT patients and 142 eyes of 71 patients who referred to our clinic for routine check up without any glaucoma diagnosis as the control group were included in the study. The patients were informed of the clinical study and informed consent was obtained.

All cases included in the study were given visual acuity with Snellen chart, biomicroscopic anterior and posterior segment examination, intraocular OP measurement with Goldmann applanation tonometry, gonioscopic examination and central corneal thickness (CCT) measurement with ultrasound pachymetry. Corrected IOP values were recorded according to the central corneal thickness measurements of the cases by using linear correction formula. Mean deviation (MD) and pattern standard deviation (PSD) values were examined by using SITA-Standard 24-2 threshold testing in Humphrey Field Analyzer II 750 (Zeiss Humphrey Systems) computerized automated perimetry. False-positive and false-negative test results below 30% and fixation losses below 20% were deemed reliable. Additionally, in all cases, best corrected visual acuity was ≥0.7, spherical refraction was ±5D, cylindrical refraction was ±2D and the angle was open in gonioscopy (Grade 3-4 in Shaffer classification).

Those cases that complied with the parameters above were divided into 3 groups. Group 1 consisted of patients diagnosed with POAG who had optic disc and visual field defects associated with glaucoma and IOP measurements above 21 mmHg in the lack of anti-glaucomatous treatment. Optical disc examination revealed out the presence of one or more of the findings of; increase in cup/disc ratio or vertical cup ratio, asymmetrical cup/disc ratio between the two eyes, thinning in neuro-retinal rim, fading in optical disc, incisura of the veins getting out of the papilla, being pushed to the nasal area and peripapillary atrophy. Results of the visual field test showed defects such as nasal step, arcuate scotoma or temporal wedge. One or more of these findings were diagnosed as glaucoma. Group 2 consisted of OHT patients with no optic disc damage associated with glaucoma in fundus examination, normal visual fields and IOP measurements above 21 mmHg in repeated measurements without treatment, whereas Group 3 was the control group involving those patients with no eye pathologies, having IOP measurements below 21 mmHg and normal optic discs and visual fields. Before OCT, pupil dilatation was provided through tropicamide eye drops. MM6 (6 mm diameter macular thickness map) and GCC analyses were made with RTVue-100 (Optovue, Inc., Fremont, CA) SD-OCT device. In the GCC analysis, average thickness, superior-half and inferior-half thickness measurements were made. In the MM6 analysis, only CMT measurement was made.

Exclusion criteria were history of previous eye surgery (excluding cataract surgery without complications at least 6 months ago), narrow or closed angle view in gonioscopic examination, fundus pathology (disc abnormality, macular pathology, retinal vascular diseases, etc.), pathologies that destroy transparency of ocular media (cataract, corneal pathologies, etc.), secondary glaucoma (pseudoexfoliation, inflammation, trauma and situations that cause high IOP due to lens), low compatibility to the study and test results with low reliability. The study was conducted in accordance with the tenets of the Declaration of Helsinki by obtaining written consent from all patients, with the approval of the local ethical review board.

Statistics: SPSS 15.0 for Windows program was used for statistical analysis. Descriptive statistics were represented as numbers and percentages for categorical variables whereas they were represented as median and standard deviation for numerical variables. As the comparison of the numerical variables in two independent groups did not provide normal distribution conditions, Mann Whitney U test was used whereas in more than two groups Kruskal Wallis test was used. The subgroup analysis of comparisons involving more than two groups was conducted with Mann Whitney U test and interpreted with Bonferroni Correction. The intergroup categorical variable rate was tested with Chi-square analysis. As the correlations among numerical variables did not provide parametrical test conditions, they were analyzed with Spearman's correlation analysis. The statistical significance alpha level was accepted as $p<0.05$.

RESULTS

The age, gender and central corneal thickness distribution of the groups are shown (Table 1). No statistically significant difference was detected between the groups in terms of age and gender (p=0.443). The values of central corneal thickness did not differ between the group 1 and 3 (p=0,194); on the other hand there was a significant difference between the group 1 and 2 (p=0,002).

The visual field MD and PSD values, GCC average, superior-half and inferior-half thickness and CMT values of the groups are shown (Table 2). MM6 and GCC analysis images of 1 case from Group 1 and 2 case from Group 2 are presented (Figure 1,2,3,4). In MM6 analysis; values of foveal, parafoveal and perifoveal thicknesses are shown (Figure 1,3). In the GCC analysis, thickness and significance maps and thickness values are shown. In the significance map, areas with normal thickness are shown in green, areas with thinness are shown in yellow and red color (Figure 2,4). In the POAG group, the MD value was found to be significantly lower compared to the OHT and control groups whereas the PSD value was higher statistically ($p<0.001$). No statistically significant difference was found between the OHT and control groups ($p>0.05$). In the POAG group, a statistically significant difference was found compared to the OHT and control groups in terms of GCC average, superior-half and inferior-half thickness and CMT values ($p<0.001$).

The paired comparisons of the groups in terms of GCC average, superior-half and inferior-half

TABLE 1: Age, gender, central corneal thickness distribution of the groups.

		POAG (Group1)	OHT (Group2)	Control Group	p*
Age (Avg.±SD)		58.3±7.5	57.3±7.4	56.5±7.3	0.443
Gender (n, %)	Female	49 (65.3)	48 (66.7)	47 (66.2)	0.985
	Male	26 (34.7)	24 (33.3)	24 (33.8)	
CCT		549.5±36.3	559.6±25.8	555.4±38.7	0.010

POAG: Primary Open Angle Glaucoma, OHT: Ocular Hypertension, CCT: Central Corneal Thickness, p: p value. Kruskal Wallis test*

TABLE 2: Visual field (MD, PSD), GCC (average, superior-half and inferior-half) thickness and CMT values of the groups.

	POAG (Goup 1) Avg.±SD	OHT (Group2) Avg.±SD	Control Group Avg.±SD	p*
VF MD (dB)	-2.24 ± 2.96	-0.85 ± 1.29	-0.68 ± 1.88	<0.001
VF PSD (dB)	3.11± 2.42	1.66 ± 0.46	1.44 ± 0.28	<0.001
Average (GCC)	91.6±9.6	98.1±6.5	98.2±6.8	<0.001
Superior-half (GCC)	91.2±9.6	97.4±6.6	97.4±6.8	<0.001
Inferior-half (GCC)	92.1±10.3	98.9±6.8	99.0±7.3	<0.001
CMT	227.4±21.6	235.7±20.3	238.5±17.8	<0.001

POAG: Primary Open Angle Glaucoma, OHT: Ocular Hypertension, VF: visual field, MD: mean deviation, PSD: pattern standard deviation, dB: decibel, GCC: Ganglion cell complex, CMT: central macular thickness, p: p value. Kruskal Wallis test*

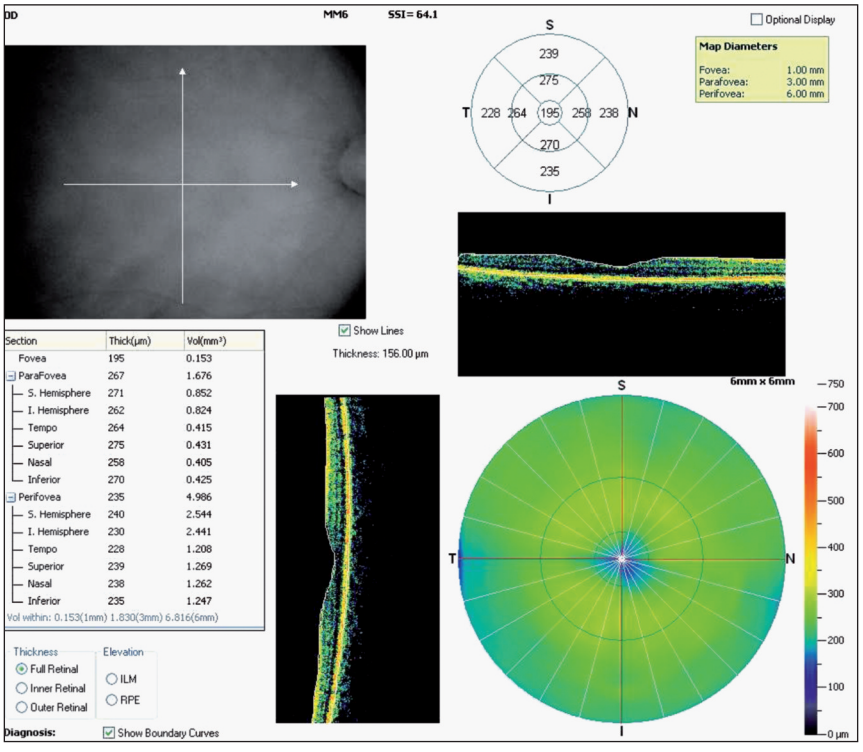

FIGURE 1: 6 × 6 mm macula analysis image of right eye of the POAG patient.
Thickness values of the fovea, perifoveal and parafoveal regions are shown.

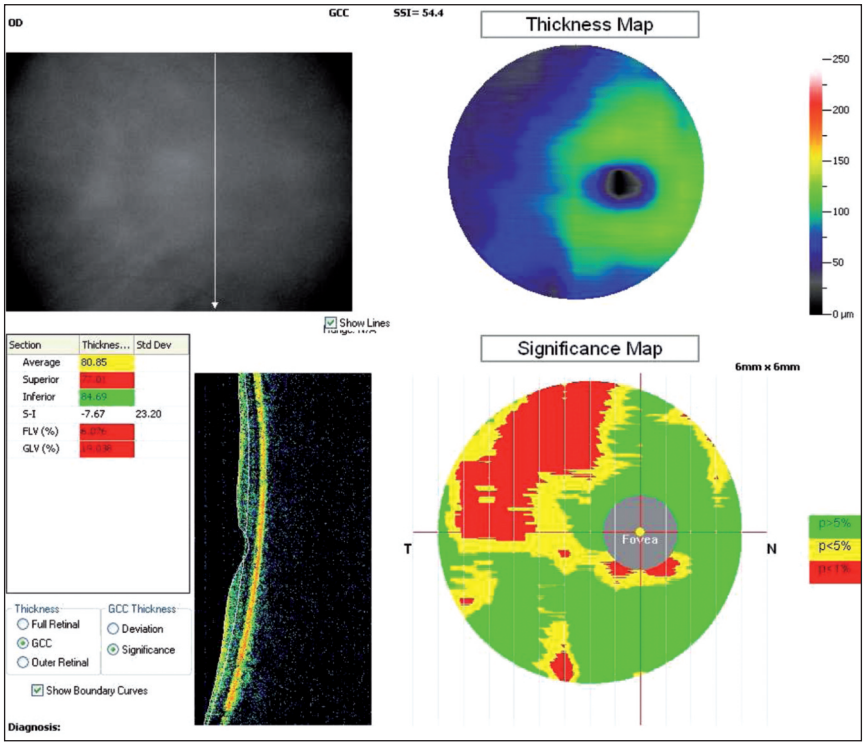

FIGURE 2: Ganglion cell complex image of right eye of the POAG patient.
Average, superior and inferior ganglion cell complex thickness with focal and general volume loss values are shown. In the significance map, the areas which have normal thickness are shown with green color while the thinner areas with yellow and red color.

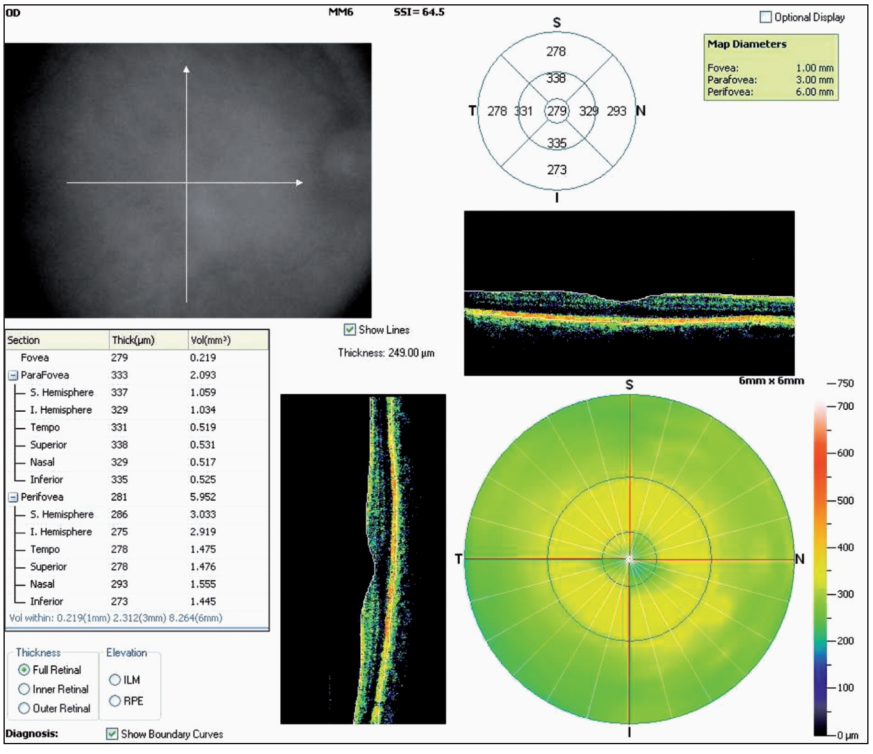

FIGURE 3: 6x6 mm macula analysis image of the right eye of the OHT patient.
Thickness values of the fovea, perifoveal and parafoveal regions are shown.

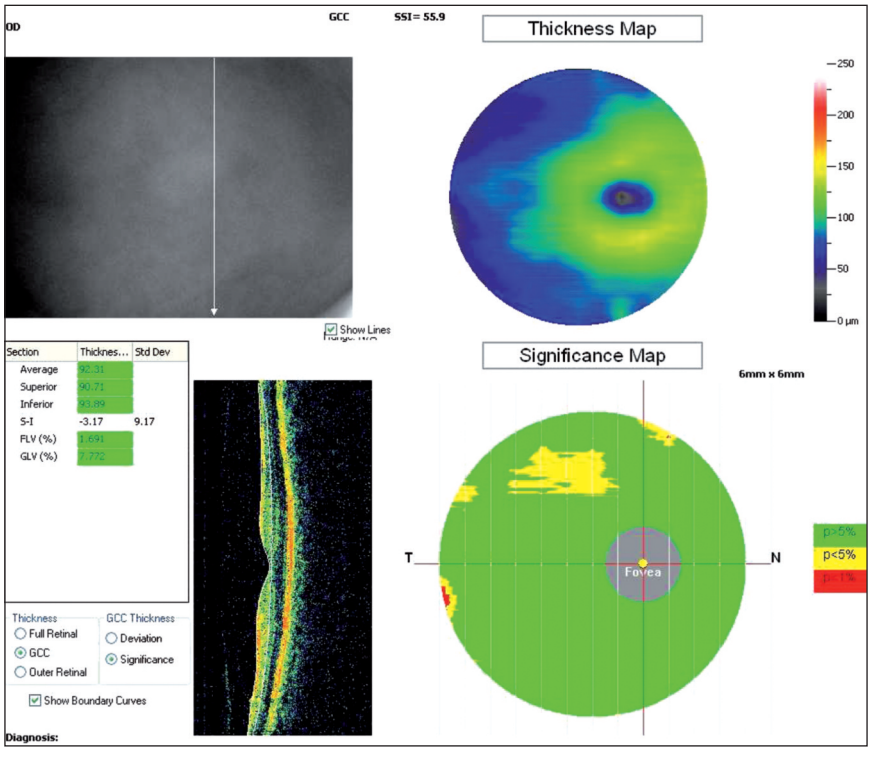

FIGURE 4: Ganglion cell complex image of the right eye of the OHT patient.
Average, superior and inferior ganglion cell complex thickness with focal and general volume loss values are shown. In the significance map, the areas which have normal thickness are shown with green color while the thinner areas with yellow and red color.

TABLE 3: Paired comparison of the groups in terms of GCC average, superior-half and inferior-half thickness and CMT values.

	GCC Average	GCC superior-half	GCC inferior-half	CMT
	p	p	p	p
POAG - OHT	<0.001	<0.001	<0.001	<0.001
POAG - Control	<0.001	<0.001	<0.001	<0.001
OHT - Control	0.946	0.815	0.839	0.077

POAG: Primary Open Angle Glaucoma, OHT: Ocular Hypertension, GCC: Ganglion cell complex, CMT: central macular thickness, p: p value. Bonferroni regulation p<0,017.

thickness and CMT values are shown (Table 3). The GCC average, superior-half and inferior-half and CMT value averages were significantly lower in the POAG group than the OHT and control groups statistically (p<0.001). The difference between the averages of the OHT and control groups was not statistically significant (p values 0.946, 0.815, 0.839, 0.077).

The evaluation of the correlation between the GCC average, superior-half and inferior-half thickness and CMT is shown (Table 4). In all groups, a positively significant correlation was detected between the CMT values and the GCC average, superior-half and inferior-half thickness values statistically (p<0.001).

DISCUSSION

OCT is a non invasive method that provides high resolution cross sectional imaging of tissues.[6] Spectral domain OCT, differently from the Time domain OCT, includes a spectrometer.[7] Very high-velocity and high-resolution 2 dimensional images are obtained through the use of SD-OCT. RTVue-100 SD-OCT renders 965 A-scan images in 0.39 seconds.[8]

As the nerve fiber damage due to glaucoma is irreversible, early diagnosis is very important in preventing such damage. In standard automated perimetry which is considered as the gold standard in the follow-up of patients with glaucoma, early defects can only be observed when the rate of damage in the ganglion cell axons reaches about 40%.[2-3] Ganglion cell complex is made up of 3 layers, namely retinal nerve fiber layer, ganglion cell layer and inner plexiform layer. GCC makes about 35% of the macular thickness. Ganglion cell loss in glaucoma primarily takes place in the zone surrounding the fovea. This area is considered as the ideal zone for detecting early cell loss due to its high cell density.[9]

Studies have shown that in distinguishing glaucoma cases from healthy ones and in the early diagnosis of glaucoma, SD-OCT is rather reliable.[10] There exist different views among researchers about the effectiveness of OCT in distinguishing OHT cases from healthy ones. In this regard, Garas et al[5] claim that OCT is effective and reliable whereas Schulze et al assume the contrary.[11] In histological studies, it is reported that ganglion cell density has close correlation with standard perimetric findings.[12] It is shown that GA and GCC are correlated.[13] In the most recent studies, it has been shown that RNFL and GCC analyses conducted by RTVue-100 SD-OCT device may be used in the diagnostic evaluation of glaucoma and OHT patients.[5] It has been emphasized that in the early detection of glaucoma, GCC is at least as reliable as RNFL and there is a highly significant correlation between them.[14-16] Parlak et al. showed that perifoveal GCC thickness is lower in glaucomatous eyes compared to normal eyes and that this could be a guiding parameter in the early diagnosis and follow-up of glaucoma.[17]

Studies have shown that in the OCT of glaucoma patients, there is a correlation between RNFL

TABLE 4: Evaluation of the correlation between GCC average, superior-half and inferior-half thickness and CMT

	CMT	
GCC	r	p
Average	0.385	<0.001
Superior-half	0.379	<0.001
Inferior-half	0.368	<0.001

GCC: Ganglion cell complex, CMT: central macular thickness, p: p value, r: r value. Spearman Corelation analysis.

thinning and decreased macular thickness.[18,19] Huang et al. stated in their study that in glaucoma patients, GCC measurement provides more significant results than macular thickness measurements.[20] Tanito et al reported significant thinning in the CMT of POAG patients both at the early stage and the advanced stage.[21] Guedes et al. showed that in glaucomatous eyes, both CMT and RNFL went through statistically significant thinning.[22] Mederios et al. stated that CMT values of glaucoma cases were thinner than those of normal individuals.[19] Wollstein et al. evaluated peripapillary RNFL and CMT measurements.[23] They showed that both tests were effective and correlated with each other in detecting glaucomatous damage.

In our study, the GCC average, superior-half and inferior-half and CMT value averages were significantly lower in the POAG group than those of the OHT and control groups. The difference between the averages of the OHT and control groups was not statistically significant.

In conclusion, although CMT and GCC analyses are rather reliable in the diagnostic evaluation of patients with POAG, they are not as effective in distinguishing OHT patients from normal cases. In distinguishing POAG cases from normal cases, CMT and GCC analyses may be used as adjuvant examination methods besides peripapillary RNFL analysis.

Conflict of Interest

Authors declared no conflict of interest or financial support.

Authorship Contributions

Idea and Concept of Study: *Semra Tiryaki Demir;* ***Design of Study:*** *Selam Yekta Şendül, Burcu Dirim;* ***Consultancy:*** *Cemile Üçgül Atılgan;* ***Data Collection and Processing:*** *Erdem Ergen;* ***Analysis and Comments:*** *Ali Olgun, Dilek Güven;* ***References Crosshatching:*** *Selam Yekta Şendül, Semra Tiryaki Demir;* ***Article Writing:*** *Semra Tiryaki Demir, Çağrı Türker.*

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