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Evaluation of subfoveal choroidal thickness and choroidal flow area in children with unilateral amblyopia

Unilateral ambliyopili çocuklarda subfoveal koroid kalınlığı ve koroidal akım alanının değerlendirilmesi

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ABSTRACT

Aim: This study aimed to assess alterations in subfoveal choroidal thickness and choriocapillaris flow area in children diagnosed with hyperopic anisometropic, strabismic, and deprivation amblyopia, and to compare these findings with those obtained from fellow healthy eyes and age-matched control subjects.

Materials and Methods: This prospective study included 48 children with unilateral amblyopia and 20 healthy control subjects matched for age and sex, all aged between 12 and 18 years. Subfoveal choroidal thickness measurements were obtained using enhanced depth imaging optical coherence tomography (EDI-OCT), while choriocapillaris flow parameters were assessed by optical coherence tomography angiography (OCTA). Differences among the study groups were analyzed using the Kruskal–Wallis test, with subsequent post hoc comparisons when applicable. Correlation analyses were performed to investigate the relationship between best-corrected visual acuity and choroidal parameters.

Results: Both subfoveal choroidal thickness and choriocapillaris flow area were significantly greater in amblyopic eyes than in the contralateral non-amblyopic eyes as well as in the healthy control eyes ($p < 0.05$). In contrast, no statistically meaningful difference was identified between the fellow eyes of patients with amblyopia and the control group. Furthermore, visual acuity showed a moderate positive association with subfoveal choroidal thickness ($r = 0.622$) and choriocapillaris flow area ($r = 0.596$), with both correlations reaching statistical significance ($p < 0.05$).

Conclusions: Increased subfoveal choroidal thickness and enlarged choriocapillaris flow area in amblyopic eyes suggest that choroidal structural and vascular alterations may play a role in the pathophysiology of amblyopia. These parameters may represent potential biomarkers for the evaluation of amblyopia and for predicting treatment response in future studies.

Keywords: Choroidal thickness, amblyopia, anisometropia, strabismus

ÖZ

Amaç: *Bu çalışma, hipermetropik anizometropik, şaşılık ve deprivasyon ambliyopisi tanısı almış çocuklarda subfoveal koroid kalınlığı ve koriokapillaris akım alanındaki değişiklikleri değerlendirmeyi ve bu bulguları sağlam fellow gözler ile kontrol olgularından elde edilen bulgularla karşılaştırmayı amaçlamıştır.*

Gereç ve Yöntem: *Bu prospektif çalışmaya, yaş ve cinsiyet açısından eşleştirilmiş, 12–18 yaş aralığında olan tek taraflı ambliyopisi bulunan 48 ambliyopik olgu (21 hipermetropik anizometropik, 15 şaşılık ambliyopisi ve 12 deprivasyon ambliyopisi) ile 20 sağlıklı kontrol olgusu dahil edildi.*

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Subfoveal koroid kalınlığı ölçümleri enhanced depth imaging optik koherens tomografi (EDI-OKT) kullanılarak elde edilirken, koriokapillaris akım parametreleri optik koherens tomografi anjiyografi (OKT-A) ile değerlendirildi. Çalışma grupları arasındaki farklar Kruskal–Wallis testi kullanılarak analiz edildi ve uygun durumlarda post hoc karşılaştırmalar yapıldı. En iyi düzeltilmiş görme keskinliği ile koroidal parametreler arasındaki ilişkinin incelenmesi amacıyla korelasyon analizleri gerçekleştirildi.

Bulgular: *Subfoveal koroid kalınlığı ve koriokapillaris akım alanı, ambliyopik gözlerde hem karşı taraf non-ambliyopik gözlere hem de sağlıklı kontrol gözlerine kıyasla anlamlı olarak daha yüksek bulundu ($p < 0,05$). Buna karşılık, ambliyopisi olan hastaların sağlam diğer gözleri ile kontrol grubu arasında istatistiksel olarak anlamlı bir fark saptanmadı. Ayrıca, görme keskinliği ile subfoveal koroid kalınlığı ($r = 0,622$) ve koriokapillaris akım alanı ($r = 0,596$) arasında orta düzeyde pozitif bir korelasyon bulundu ve her iki korelasyon da istatistiksel olarak anlamlıydı ($p < 0,05$).*

Sonuç: *Ambliyopik gözlerde artmış subfoveal koroid kalınlığı ve genişlemiş koriokapillaris akım alanı, koroidal yapısal ve vasküler değişikliklerin ambliyopinin patofizyolojisinde rol oynayabileceğini düşündürmektedir. Bu parametreler, ambliyopinin değerlendirilmesinde ve gelecekteki çalışmalarda tedavi yanıtının öngörülmesinde potansiyel biyobelirteçler olarak kullanılabilir.*

Anahtar Sözcükler: *Koroid kalınlığı, ambliyopi, anizometropi, şaşılık*

INTRODUCTION

During the critical stages of visual development, inadequate or abnormal sensory input may lead to amblyopia, a condition characterized by reduced best-corrected visual acuity (BCVA). Reported to affect 0.8% to 3.3% of children globally, amblyopia represents a major public health issue due to its potential to cause permanent visual impairment if left untreated. Clinically, amblyopia is defined as reduced best-corrected visual acuity (BCVA) in one or both eyes that cannot be attributed to structural ocular abnormalities and results from abnormal visual experience during the critical period of visual development. Current clinical guidelines emphasize that amblyopia is commonly diagnosed based on an interocular visual acuity difference of two or more lines on a standardized visual acuity chart, or visual acuity below age-adjusted normal limits (1).

Clinically, amblyopia arises from several distinct etiologies, most commonly uncorrected refractive error, ocular misalignment, or obstruction of the visual axis (2). Hyperopic anisometropic amblyopia develops when unequal refractive errors lead to chronic retinal image defocus in one eye, whereas strabismic amblyopia is associated with constant or intermittent ocular deviation and subsequent suppression of the deviating eye (3,4). Deprivation amblyopia, although less common, represents the most severe form and results from prolonged visual axis occlusion during early life, such as congenital cataract or ptosis (4). While these subtypes differ in etiology and clinical course, they share a final common pathway of impaired visual development.

Studies examining the pathogenesis of amblyopia have consistently reported abnormalities in higher visual processing centers, particularly the visual cortex and lateral geniculate nucleus (4). In parallel, a growing body of literature has investigated whether amblyopia is accompanied by structural or vascular changes within the retina and choroid. Using OCT, several studies have evaluated central macular thickness in amblyopic eyes (5–7), while OCTA-based analyses have focused on vascular density in the superficial and deep retinal plexuses (3,8–10). Despite these investigations, the significance of retinal and choroidal involvement in amblyopia remains unclear.

Although several previous studies have evaluated retinal thickness and vascular density in amblyopic eyes using OCT and OCT angiography, the involvement of the choroidal vasculature remains incompletely understood. In particular, limited data exist regarding choriocapillaris flow characteristics and their relationship with choroidal structural changes in different amblyopia subtypes. Moreover, most previous studies have focused primarily on anisometropic amblyopia, whereas comparative analyses including strabismic and deprivation amblyopia are scarce. Therefore, the present study aimed to evaluate both subfoveal choroidal thickness and choriocapillaris flow area in children with different types of unilateral amblyopia and to compare

these findings with those of fellow eyes and healthy controls.

MATERIALS and METHODS

Approval for this prospective, cross-sectional study was obtained from the Ethics Committee of Afyonkarahisar Health Sciences University (2011-KAEK-2). Participants were prospectively and consecutively enrolled from the Pediatric Ophthalmology and Strabismus Unit between May 2020 and February 2021. All enrolled subjects were between 12 and 18 years of age. The amblyopia cohort consisted of 21 patients with hyperopic anisometropic amblyopia, 15 patients with strabismic amblyopia associated with esotropia, and 12 patients with deprivation amblyopia, in the amblyopia group, both amblyopic eyes and their fellow eyes were included to enable intra-individual comparisons. As these eyes originate from the same subjects, paired statistical methods were applied to account for inter-eye correlation. In the control group, only the right eye of each subject was included to ensure independence of observations. Imaging was performed at the first clinical visit prior to the initiation of any amblyopia treatment. The control group comprised 20 age-matched emmetropic individuals with no ocular abnormalities, and only the right eyes were selected for analysis. Comprehensive medical information, including demographic data and systemic health status, was collected for all participants. Ocular alignment was evaluated using cover–uncover and alternate cover tests to identify manifest deviations, and in patients with strabismus, the magnitude of ocular misalignment at near and distance was quantified with the prism cover test. Cycloplegia was achieved through the administration of 1% cyclopentolate hydrochloride (Sikloplejin® 1%, Abdi İbrahim İlaç San. ve Tic. A.Ş.), applied twice at 5-minute intervals. Objective refractive measurements were obtained 45 minutes after instillation using an autorefractometer. Following appropriate refractive correction, best-corrected visual acuity (BCVA) was assessed with a Snellen chart, recorded in decimal form, and converted to logarithm of the minimum angle of resolution (logMAR) values. All participants underwent slit-lamp biomicroscopy for anterior segment assessment as well as dilated fundus examination. Individuals presenting with nystagmus, media opacities affecting image quality, or structural abnormalities involving the optic nerve head, macula, or retinal vasculature were excluded.

All OCT and OCTA imaging was performed during morning hours (09:00–12:00) to limit circadian effects. During image acquisition and analysis, scans with poor fixation, motion artifacts, or segmentation errors were excluded to minimize potential measurement bias. Choroidal thickness was measured using enhanced depth imaging OCT (SD-OCT device Heidelberg Engineering GmbH, Heidelberg, Germany) and defined as the distance from the outer border of the retinal pigment epithelium to the choroidoscleral interface. All measurements were performed by the same experienced examiner who was masked to the clinical grouping of the subjects to reduce potential measurement bias (Figure-1). Measurements were obtained manually at the subfoveal region as well as at points located 500 µm temporal, nasal, superior, and inferior to the foveal center. Evaluation of the choriocapillaris flow area was performed using OCT angiography with the AngioVue OCTA system (Optovue Inc., Fremont, CA, USA). Images were acquired using a 6 × 6 mm macular scan protocol, with analyses focused on the automatically segmented choriocapillaris slab positioned directly beneath the RPE–Bruch's membrane complex. Scans exhibiting inadequate image quality (signal strength index < 7) or prominent motion-related artifacts were excluded. Segmentation accuracy was verified manually when required, and no clinically relevant segmentation errors necessitating adjustment were observed. The choriocapillaris flow area, expressed in square millimeters (mm²), was automatically calculated using the device's proprietary software and subsequently included in the statistical analyses (Figure-2).

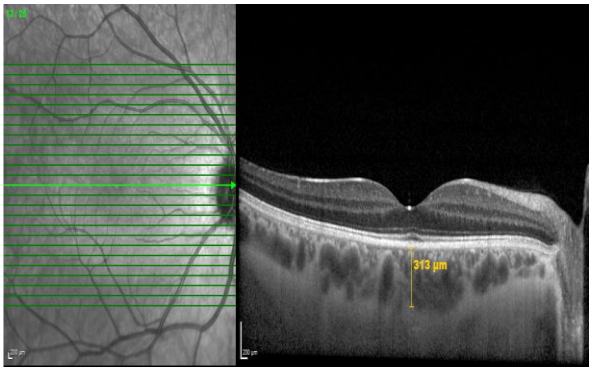

Figure-1. Subfoveal Choroidal Thickness

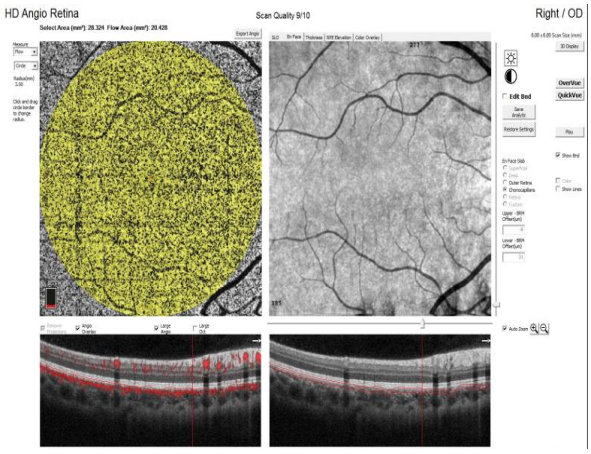

Figure-2. Choroidal Flow Area

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics software (version 22.0; IBM Corp., Chicago, IL, USA). Descriptive statistics were used to summarize the data. The normality of continuous variables was assessed using the Shapiro–Wilk test. Amblyopic eyes, fellow eyes, and control eyes were analyzed as separate groups to evaluate differences in choroidal parameters. For variables that did not follow a normal distribution, comparisons among groups were performed using the Kruskal–Wallis test. Because amblyopic and fellow eyes originated from the same individuals, paired statistical tests were used for intra-individual comparisons to account for inter-eye correlation. Comparisons involving control eyes were conducted using independent group analyses. When overall group differences were statistically significant, pairwise comparisons were performed using Dunn's multiple comparison test with Bonferroni correction. Continuous variables were expressed as mean ± standard deviation or median (interquartile range), as appropriate. Spearman's rank correlation analysis was used to evaluate the relationship between best-corrected visual acuity and choroidal parameters. Correlation analyses were performed using pooled data from amblyopic eyes. A p value < 0.05 was considered statistically significant. A post hoc power analysis was performed using G*Power software (Heinrich Heine University Düsseldorf, Düsseldorf, Germany) based on subfoveal choroidal thickness as the primary outcome measure. With an alpha error probability of 0.05, the achieved statistical power was greater than 99%.

RESULTS

The values of all parameters and their comparison between groups are given in Table-1. The study groups were comparable in terms of age, and no statistically significant difference in mean age was observed between the groups ($p > 0.05$). Comparative analyses revealed a statistically significant variation in subfoveal choroidal thickness among the study groups ($p < 0.05$). Eyes affected by anisometropic, strabismic, and deprivation amblyopia demonstrated increased subfoveal choroidal thickness when compared with both their fellow non-amblyopic eyes and the healthy control eyes ($p < 0.05$). In contrast, no statistically meaningful difference in subfoveal choroidal thickness was identified between the fellow eyes of amblyopic patients and the control group ($p = 0.260$). Similarly, choriocapillaris flow area measured by OCT angiography differed significantly across groups ($p < 0.05$). Amblyopic eyes in all three subtypes exhibited larger choriocapillaris flow areas relative to both control eyes and fellow healthy eyes ($p < 0.05$), whereas comparable values were observed between the fellow eyes and controls ($p = 0.390$). While no significant differences were identified among the groups in nasal, superior, or inferior choroidal thickness**,** temporal choroidal thickness was found to be significantly increased in anisometropic amblyopic eyes compared with all other groups ($p < 0.05$). Overall, both choroidal thickness **and** choriocapillaris flow area were significantly increased across all amblyopia subgroups relative to the control group and the fellow healthy eyes ($p < 0.05$). When pooled amblyopic eyes were analyzed, a significant positive correlation was observed between BCVA and both SFCT ($r = 0.622$) and CCFA ($r = 0.596$) ($p < 0.05$).

Table-1. Comparison of Clinical and Choroidal Parameters Between Groups

Parameter	Anisometropic (Amblyopic) (12/9)	Anisometropic (Healthy) (12/9)	Strabismic (Amblyopic) (9/6)	Strabismic (Healthy) (9/6)	Deprivation (Amblyopic) (6/6)	Deprivation (Healthy) (6/6)	Healthy Control (12/8)	p value
Age (years)	13.46 ±1.76	12.85 ± 2.17	14.26 ±2.02	13.41 ± 2.43	13.2 ±1.74	14.65 ± 2.23	13.66 ±2.36	p=0.765
VA (LogMAR)	0.44	0.0	0.44	0.0	0.78	0.0	0.0	p<0.05
AL (mm)	22.99±1.23	23.02±1.07	23.01±0.25	23.04±1.08	23.01±1.24	22.98±1.18	23.04±1.16	p=0.390
SFCT (µm)	323.66±12.34	281.12±11.20	317.64±13.30	284.24±10.56	320.75±14.26	270.52±16.51	271.49±13.21	p<0.05
Temporal CT (µm)	290.78±13.36	265.67±14.42	276.88±15.56	263.67±17.78	278.56±18.24	255.67±16.54	257.23±12.98	p<0.05
Nasal CT (µm)	192.28±12.56	187.34±21.12	189.17±15.34	184.12±13.36	188.23±23.34	185.13±14.41	176.23±12.67	p=0.436
Inferior CT (µm)	245.21±12.26	243.26±26.03	242.65±12.56	239.26±13.23	249.34±12.34	243.21±16.45	253.21±14.65	p=0.578
Superior CT (µm)	260.23±24.21	265.43±12.34	267.45±23.21	264.23±17.86	271.21±13.46	262.14±15.51	264.28±12.45	p=0.542
CCFA (mm^2)	21.57±4.26	19.42±3.39	21.53±4.56	19.78±3.29	21.77±4.54	19.21±5.57	19.43±3.26	p<0.05

VA: Visual Acuity; AL: Axial Length; SFCT: Subfoveal Choroidal Thickness; CT: Choroidal Thickness; CCFA: Choriocapillaris Flow Area. p values were calculated using the Kruskal–Wallis test. (n: girl/boy)

DISCUSSION

The choroid is a highly vascular structure responsible for supplying the outer retinal layers. In addition to its nutritive role, the choroid has been proposed to play a part in emmetropization. Wallman et al. first demonstrated that the choroid can dynamically modulate ocular refraction by up to approximately 7 diopters in response to myopic and hyperopic defocus, highlighting its potential role in refractive regulation (11). In the present study, subfoveal choroidal thickness and choriocapillaris flow area were found to be significantly increased in amblyopic eyes of children with hyperopic anisometropic, strabismic, and deprivation amblyopia. These findings suggest that amblyopia may be associated not only with retinocortical alterations but also with structural and vascular changes at the choroidal level. Earlier investigations have consistently shown that subfoveal choroidal thickness is increased in eyes with hyperopic anisometropic amblyopia when compared with unaffected fellow eyes. Notably, Nishi et al. (12), Mori et al. (13), and Tenlik et al. (14) each reported a significant thickening of the subfoveal choroid in amblyopic eyes. Subsequent studies that evaluated mixed amblyopia subtypes, including anisometropic and strabismic forms, also identified similar increases in subfoveal choroidal thickness relative to control eyes (15–18). Distinct from the majority of prior reports, the present study incorporated patients with deprivation amblyopia and demonstrated that subfoveal choroidal thickness was significantly elevated across all amblyopia subgroups when compared with both fellow healthy eyes and controls. In contrast, Karaca et al. (19) described increased choroidal thickness in the fellow eyes of amblyopic patients, a finding that was not replicated in our study population. In a study including 31 patients with amblyopia, Zha et al. (20) reported increased choroidal thickness in the subfoveal as well as nasal and superior choroidal regions. In contrast, although subfoveal choroidal thickness was also increased in our cohort, a statistically significant difference among groups was observed only in the temporal choroidal region in anisometropic amblyopic eyes. Such variation across studies may be explained by heterogeneity in study design, demographic characteristics, or differences in imaging and measurement techniques. Regarding axial length, our findings did not reveal a significant difference between amblyopic eyes and their healthy fellow counterparts. This contrasts with the results of Hui et al. (21) and Kara et al. (15), who reported shorter axial lengths in amblyopic eyes and identified an inverse relationship between axial length and choroidal thickness. Differences in age range, refractive profiles, and sample size may underlie these discrepant observations. Studies evaluating choriocapillaris flow area in amblyopia are relatively limited. With the advancement of OCT angiography technology, noninvasive assessment of choroidal microcirculation has become feasible. In line with our findings, Huang et al. (22) and Cao et al. (23) reported increased choriocapillaris flow area in amblyopic patients, supporting the hypothesis that choroidal vascular alterations may accompany amblyopia. The significant positive correlation observed between visual acuity and both choroidal thickness and

choriocapillaris flow area suggests that greater visual impairment may be associated with more pronounced choroidal alterations. Several studies (3, 24, 25, 26) have investigated retinal vascular density using OCTA in amblyopic eyes in order to elucidate the pathogenesis of amblyopia. In addition, another study by Köksaldı et al. (27) examined the relationship between amblyopia and the choroid, evaluating whether there is a difference in the choroidal vascularity index between amblyopic and healthy eyes. Another limitation of this study is the relatively small studies have reported a reduction in choroidal thickness following amblyopia treatment (28,29), suggesting that choroidal changes may be dynamic and potentially reversible. However, the findings of the present study should be interpreted with caution given its cross-sectional design. Although increased choroidal thickness and choriocapillaris flow area were observed in amblyopic eyes, these alterations cannot be interpreted as direct structural or vascular consequences of amblyopia. Instead, they may represent associations related to underlying ocular characteristics. In particular, refractive error magnitude and axial length are known to influence choroidal parameters and may act as potential confounding factors. While our findings suggest a possible association between amblyopia and choroidal structural and vascular alterations, further longitudinal studies with larger cohorts are required to clarify whether these parameters could serve as reliable biomarkers of amblyopia severity.

Despite its strengths, the present study is subject to certain limitations. Despite the high post hoc statistical power, the relatively small and uneven subgroup sizes should still be considered when interpreting subgroup comparisons and amblyopic and fellow eyes originated from the same subjects, which may introduce intra-subject correlation and should be considered when interpreting the results. The relatively limited sample size and the cross-sectional nature of the study design did not allow for longitudinal assessment or follow-up analysis. Another limitation of this study is that axial length–related magnification correction (e.g., Bennett's formula) was not applied for OCTA measurements. Although axial length values were comparable between the groups, magnification effects may still influence quantitative OCTA parameters. This study is the relatively small and uneven distribution of patients among amblyopia subtypes. In particular, the number of patients with deprivation amblyopia was limited, which may have reduced the statistical power for subgroup comparisons. In addition, the sample size may have influenced the ability to detect subtle regional differences in choroidal parameters. Therefore, the results should be interpreted with caution, and larger studies with more balanced subgroup distributions are needed to confirm these findings. Future studies using statistical approaches designed for clustered ocular data may further clarify these findings.

CONCLUSION

This study demonstrates that amblyopic eyes exhibit significant alterations in choroidal thickness and choriocapillaris flow **area**, highlighting the potential involvement of the choroidal vasculature in the pathophysiology of amblyopia. Taken together, the present results indicate that alterations in choroidal parameters could provide clinically meaningful information for the diagnostic assessment of amblyopia and may have value in anticipating therapeutic outcomes in future investigations.

Consent for publication: Not applicable

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The author(s) declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article

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