Santral Seröz Koryoretinopatide Fotodinamik Tedavinin Koroidal Vasküler İndekse Etkisi

Effect of Photodynamic Therapy on Choroidal Vascularity Index in Central Serous Chorioretinopathy

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ÖZ

Amaç: Santral seröz koryoretinopatide (SSKR) düşük fluens fotodinamik tedavi sonrası (FDT) koroidal vasküler indeks (KVİ) üzerindeki değişimlerini değerlendirmek.

Gereç ve Yöntemler: Altı aydan uzun şikayetleri olan ve kronik SSKR tanısı konularak düşük fluens FDT tedavisi uygulanan hastaların dosyaları retrospektif olarak incelendi. Tedavi öncesi ve tedavi sonrası arttırılmış derinlikli görüntülemeli (EDI) - optik koherens tomografi (OKT) görüntüleri olanlar çalışmaya alındı. 1500 µm'lik subfoveal alan segmente edilerek incelendi. Koroidal vasküler indeks; EDI-OKT'de koroidal damarların lümen boşluğu alanının (LA) tüm koroidal alana (TKA) oranlaması olarak bulundu.

Bulgular: On dokuz hastanın 23 gözü çalışmaya alındı. Ortalama yaş 43,21±7,4, bulundu ve hastaların 10'u (%52,6) erkekti. Koroidal vasküler indeks tedavi öncesi % 65,4 iken tedavi sonrası 1. haftada % 64,82, 1. ayda % 62,42, 6. ayda % 62,97 saptandı. Tedavi öncesi ile tedavi sonrası karşılaştırıldığında 1. ay ve 6. ayda koroidal vasküler indekste anlamlı azalma saptandı ($p<0,05$). Tedavi öncesi subfoveal koroid kalınlığı değeri 457,65±108,15 µm iken; 1. haftada 443,30±108,38 µm , 1. ayda 416,60±89,71 µm ve 6. ayda 411,47±101,29 µm bulundu. Tedavi sonrası tüm koroid kalınlığı ölçümleri tedavi öncesine göre anlamlı azalmıştı ($p<0,05$).

Sonuç: SSKR'de fotodinamik tedavi sonrası koroidal vasküler indekste anlamlı azalma saptanmıştır. Koroidal vasküler indeks SSKR'de tedaviye cevabı izlemede faydalı bir gösterge olabilir.

Anahtar Kelimeler: Santral seröz koryoretinopati, fotodinamik tedavi, optik koherens tomografi.

ABSTRACT

Purpose: To evaluate the changes in choroidal vascular index (CVI) after low fluence photodynamic therapy (PDT) in central serous chorioretinopathy (CSC).

Materials and Methods: Patients with complaints of longer than 6 months who were diagnosed as CSC and underwent low fluence PDT was reviewed retrospectively. Patients with enhanced depth imaging (EDI) - optical coherence tomography (OCT) images before and after treatment were included in the study. Subfoveal area of1500 µm was evaluated after segmentation. CVI was defined as ratio of lumen area (LA) to total choroidal area (TCA) as measured on EDI-OCT images.

Results: Twenty-three eyes of 19 patients were included to the study. The mean age was 43.21 ± 7.4, and 10 (52.6%) of the patients were male. Choroidal vascularity index was 65.4% before treatment, 64.82% on week 1, 62.42% at month 6, and 62.97% at month 6 after treatment. A significant decrease in choroidal vascular indecency was detected at months 1 and 6 after treatment when compared with those obtained before treatment ($p<0.05$). The subfoveal choroidal thickness was 457.65 ± 108.15 µm before treatment whereas 443.30 ± 108.38 µm on week 1, 416.60 ± 89.71 µm at month 1 and 411.47 ± 101.29 µm at month 6. The choroidal thickness measurements at all time points after treatment were significantly lower than those obtained before treatment ($p <0.05$).

Conclusion: There was a significant decrease in choroidal vascular index after PDT in CSC. The choroidal vascular index may be a useful biomarker to monitor treatment response in CSC.

Key Words: Central serous chorioretinopathy, photodynamic therapy, optical coherence tomography.

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INTRODUCTION

Central serous chorioretinopathy (CSC) is a disorder that often involves macular region and leads serous detachment in neurosensory retina, which is generally accompanied by focal detachment in retinal pigment epithelium.[1] It is classified into acute, chronic and recurrent types. The cases with complaints and findings longer than 6 months are termed as chronic type.[2] In chronic CSC, photocoagulation, low fluence photodynamic therapy (PDT) or medical therapy are treatment modalities which may be used during course of disease in selected cases.[1,2]

In particular, enhanced depth imaging (EDI) function in spectral domain optical coherence tomography (SD-OCT) devices allow better understanding of role of choroid in CSC.[3,4] It was shown that choroid thickness was increased in eyes with CSC and contralateral eyes on EDI-OCT when compared to healthy individuals[5,6] Choroid involves blood vessel and stroma. Choroid thickness as determined by EDI-OCT does not only provide information about thickness of blood vessels but also provides thickness of stromal structures and blood vessels within choroid as a whole. Sonada et al. calculated the area of choroid lumen in eyes with age-related macular degeneration (AMD) on EDI-OCT images by using a digital software.[7] By a similar method, Agrawal et al. estimated ratio of lumen area to total choroidal area which was termed as choroidal vascularity index (CVI).[8] In another study by same authors, it was shown that the choroidal vascularity index was increased in acute CSC and contralateral eyes of these patients, proposing that the index could be a more relevant marker for monitoring changes in choroidal vessels .[9]

In our study, it was aimed to assess effects of low fluence photodynamic therapy on choroidal vascularity index calculated on EDI-OCT images in chronic CSC.

MATERIAL AND METHOD

The study included patients with complaints longer than 6 months who were diagnosed as chronic central serous chorioretinopathy according to ophthalmological examination; underwent low fluence photodynamic therapy; and had pretreatment and post-treatment EDI-OCT images. The study was approved by local Ethics Committee and conducted in accordance to Helsinki Declaration. The patients with higher degrees of myopia and hypermetropia (>-6 D or >+3 D), those with history of previous intraocular surgery, and those with poor EDI-OCT images were excluded. The thorough ophthalmological examination including best-corrected visual acuity, slit-lamp examination, intraocular pressure measurements and fundoscopy in addition to EDI-OCT imaging studies were performed before treatment and on week 1 and at months 1 and 6 after treatment in all patients.

In all patients, fluorescein angiography (FA) and indocyanine green angiography (ICA) were performed to establish definitive diagnosis. Low fluence photodynamic therapy (25 j/cm^2, 83 second) was administered to choroidal leakage area on ICA.

The enhanced depth imaging (EDI) function of Spectralis OCT device (Heidelberg Engineering, Heidelberg, Germany) was used for choroidal imaging. Subfoveal choroidal thickness (SFCT) was manually measured on OCT section involving foveal area by using device's scale. Subfoveal choroidal thickness was measured as distance between pigment epithelium and outer margin of choroid.

Image processing: The EDI-OCT section involving fovea was used for binarization. The open-access Fiji software was used to create and measure binary images.[10] The image segmentation was performed using a method described by Agrawal et al.[9] A subfoeval area of 1500 µm (areas of 750 µ in size from each side) were selected (Figure 1). Choroid- sclera junction was set off by converting it to binary image via Niblack auto-local threshold device. The area between choroid-sclera junction and retinal pigment epithelium was selected by polygon device in the software. The areas of dark pixels (lumen area) and light pixels (stromal area) were calculated within selected area. The choroidal vascularity index was calculated via dividing lumen area (LA) by total choroidal area (TCA).

Statistical analyses were performed by SPSS version 21.0 (Statistical Package for Social Sciences). The normal distribution of data was assessed by Kolmogorov-Smirnov test. Results are presented as mean ± standard deviation. The values before and after treatment were assessed by paired sample t test. Variation coefficient was used to compare choroidal vascularity index with distribution of subfoveal choroidal thickness. A p value<0.05 was considered as statistically significant.

FINDINGS

The study included 23 eyes of 19 patients underwent low fluence PDT with diagnosis of chronic CSC. Of the patients, 10 (52.6%) were men while 9 (47.4%) were women. Mean age was 43.21 ± 7.4 years (27-55). There was bilateral involvement in 4 patients. In addition, serous detachment was present in all eyes before treatment. At month 6, subretinal fluid was completely regressed in all eyes.

It was found that mean best corrected visual acuity was 0.38±0.26 logMAR before treatment whereas 0.33±0.28 logMAR on week 1, 0.31±0.29 logMar at month 1 and 0.30±0.30 logMAR on month 6. Although there was improvement in vision at month 6 after treatment, no significant difference was detected when compared to baseline (p>0.05). Table 1 presents pretreatment and post-treatment luminal, stromal and total choroidal areas, choroidal vascularity indexes and subfoveal choroid thicknesses.

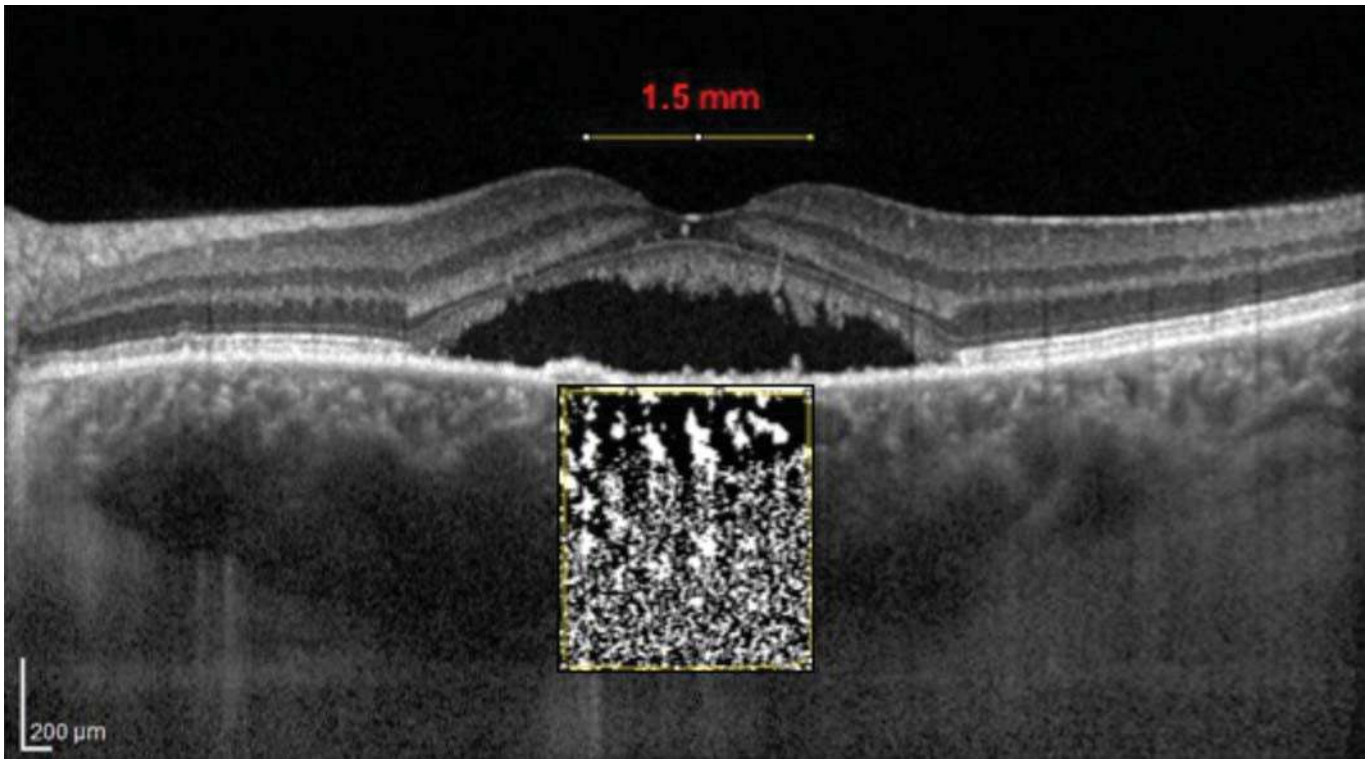


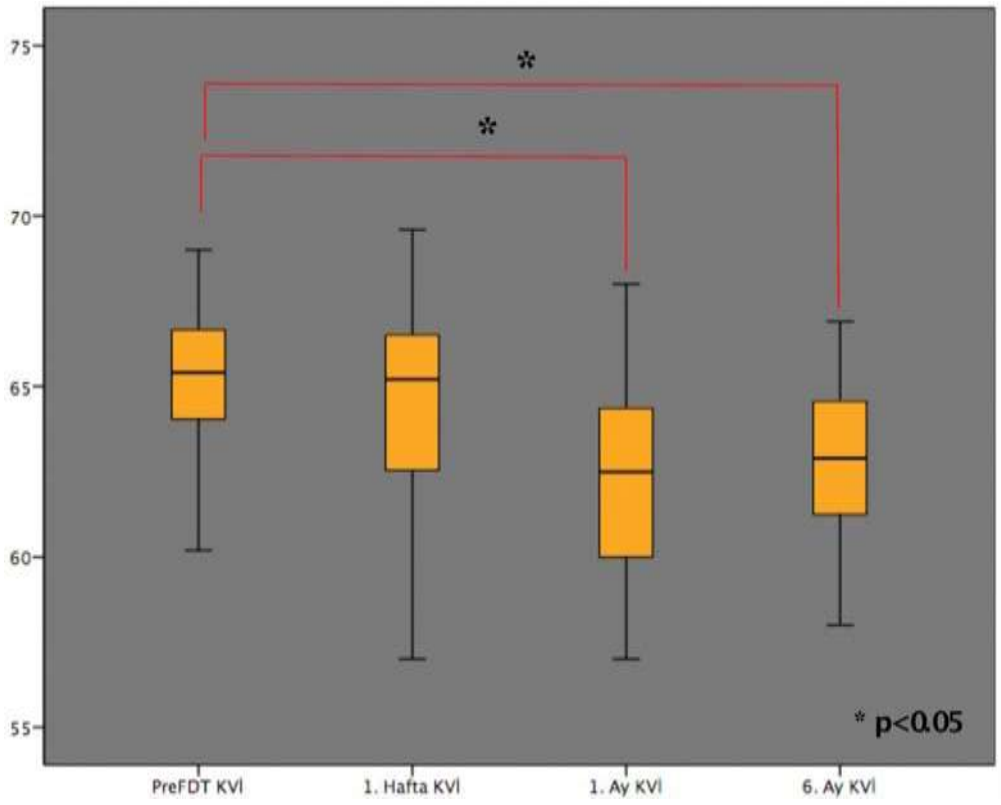
Figure 1: *Choroidal area calculated by binarization on EDI-OCT*

Table 1: *Stromal thickness, total choroidal area, choroidal vascularity index and subfoveal choroidal thickness values before treatment and on week one and month 6 after treatment*

	PRETREATMENT	POST-TREATMENT		
		1. HAFTA	1. AY	6. AY
LA (mm^2)	1.41 ± 0.35	1.34 ± 0.32*	1.26 ± 0.28*	1.24 ± 0.25*
SA (mm^2)	0.76 ± 0.22	0.77 ± 0.21	0.76 ± 0.19	0.74 ± 0.19
TCA (mm^2)	2.17 ± 0.56	2.11 ± 0.50	2.02 ± 0.47*	1.98 ± 0.43*
KVİ (%)	65.42 ± 2.46	64.82 ± 3.40	62.42 ± 2.82*	62.97 ± 3.07*
SFCT (µm)	457.65 ± 108.15	433.30 ± 108.38*	416.60 ± 89.71*	411.47 ± 101.29*

LA: Lumen area. SA: Stromal area. TCA: Total choroidal area. CVI: Choroidal vascularity index,
SFCT: Subfoveal choroidal thickness
* Those with significant difference when compared to pretreatment values ($p<0.05$)

It was found that lumen area was 1.41±0.35 mm^2 before treatment while it was 1.34 ±0.32 mm^2, 1.26 ±0.28 mm^2, 1.24 ±0.25 mm^2 on week 1 and months 1 and 6 after treatment, respectively. The lumen area showed significant decrease in all time points after treatment when compared to pretreatment values ($p<0.05$). Stromal area was found to be 0.76±0.22 mm^2 before treatment while it was 0.77±21 mm^2, 0.76±0.19 mm^2 and 0.74 ±0.19 mm^2 on week 1 and at months 1 and 6 after treatment, respectively. The changes in stromal area after treatment did not reach statistical significance ($p>0.05$). It was found that total choroidal area was 2.17±0.56 mm^2 before treatment whereas 2.11±0.50 mm^2, 2.02±0.47 mm^2 on 1.98±0.43 mm^2 on week 1 and at months 1 and 6 after treatment, respectively. Only reductions detected in total choroidal area at months 1 and 6 significantly differed when compared to pretreatment values ($p<0.05$). The choroidal vascularity index was 65.42±2.46% before treatment whereas 64.82±3.40% on week 1, 62.42±2.82% at month 1 and 62.97±3.07% at month 6 (Graphic 1). Although choroidal vascularity index was decreased in all time points after treatment, the decrease reached statistical significance only at months 1 and 6 ($p<0.05$). Subfoveal choroidal thickness was 457.65±108.15 µm before treatment whereas 433.30±108.38 µm on week 1, 416.60±89.71 µm at month1 and 411.47±101.29 µm at month 6 after treatment. SFCTT showed significant decrease in all time points after treatment when compared to pretreatment values ($p<0.05$). The variation coefficient was 3.7 for CVI and 25.01 for SFCTT before treatment



Graphic 1: *Pre- and post-treatment distribution of choroidal vascularity index*

whereas 4.8 for CVI and 24.6 for SFCT at month 6 after treatment, indicating less variation in CVI when compared to SFCT.

DISCUSSION

The enhanced depth imaging (EDI) function in optical coherence tomography has allowed to measure thickness of choroid in a cross-sectional manner and to assess its structure.[11] In previous studies, it was shown that the choroid was thickened on EDI-OCT in serous chorioretinopathy where choroidal vascular hyper-permeability and venous dilatation play role in pathophysiology.[5,6] It is well-known that choroid consists of blood vessels and interstitial stroma. The interstitial tissue involves pigment cells, smooth muscle cells, neurons, inflammatory cells and connective tissue. Thus, measurements on EDI-OCT by B-mode only allow measuring and assessing all these structures collectively. Sonoda et al. created binary EDI-OCT images by a digital software (Fiji, İmage J) and were able to measure choroidal lumen area and interstitial area separately.[7] In their study, authors showed that there was significant decrease in choroidal lumen area and interstitial area after photodynamic therapy in patients with AMD.[7] In addition, they reported that the method had high levels of repeatability and reproducibility. Authors found no change in lumen and interstitial area in the intact eyes of cases included during follow-up[7]

Agrawal et al. defined choroidal vascularity index by using similar approach.[8] Authors calculated percent choroidal vascularity index through dividing dark-colored lumen area by total choroidal area. In that study, it was shown that CVI ranged from 60.7% to 70.27% mean 65.61%) in 345 healthy individuals. In same individuals, it was found that SFCT ranged from 40.24 to 519.48 μm. In healthy individuals, it was shown that even CVI measured in a single EDI-OCT section from subfoveal area reflects condition of choroid in whole macular region.[12]

It was seen that no significant difference was detected in choroidal thickness while lumen area and CVI were significantly decreased in eyes with AMD when compared to contralateral normal eyes.[13]

Agrawal et al. assessed CVI in CSC and found that CVI was 70% in acute phase while 65.44 in CSC regressed, 67.00% in normal appearing contralateral eyes and 65.18% in normal individuals[8] In our study, CVI was 65.4% in eyes with chronic CSC before treatment whereas 62.9% at month 6 after treatment. It is thought that initial lower CVI values may be due to ethnic differences and the fact that our patients were in chronic phase. The fact that reduction in CVI following PDT became more prominent at months 1 and 6 might have resulted from decreased calibration of choroidal vessels and remodeling.

The number of variables influencing on subfoveal choroid thickness is higher when compared to CVI.[8] In multivariate regression analysis, younger age, shorter axial length, higher intraocular pressure, higher lumen area and lower systolic blood pressure were associated with SFCT while CVI was associated with SFCT alone.[8]

In our study, a significant decrease was shown in CVI at months 1 and 6 after treatment while a significant decrease was shown in lumen area in all time points after treatment. In addition, no significant difference was detected in stromal area after treatment. Despite significant decrease in choroidal thickness, CVI appeared as a feasible marker due to substantial number of factors affecting on choroidal changes, higher variation coefficient of choroid thickness and higher distribution of SFCT in our study.

CVI has been investigated in some inflammatory disorders other than exudative AMD and CSC such as diabetes mellitus.[14,15,16] It was shown that CVI aas decreased by relief in disease activity during follow-up in Vogt-Koyonagi-Harada disease.[14] In patients with panuveitis, it was found that the CVI was decreased by 6.2% during follow-up despite lack of change in choroidal thickness measured on EDI-OCT.[15] When patients with diabetes mellitus were compared to healthy controls, no significant difference was detected in choroidal thickness, total choroidal area, stromal area, and lumen area while CVI was found to be decreased in patients with DM.[16] In addition, decrease in CVI was detected in patients with retinopathy, proposing that this might be due to narrowing in choroid at capillary level.

Although mean visual acuity showed slight improvement following PDT when compared to baseline, no significant difference was observed in our study. It is thought that inadequate functional recovery despite anatomical improvement as assessed by CVI and choroid thickness might be due to treatment of cases during chronic phase.

This study has some limitations including smaller sample size, duration of follow-up limited to 6 months, lack of FA or ICG images, limited size of area examined (1500 μm), lack of a control group and assessment of images by a single researcher.

In conclusion, a significant decrease was seen in CVI in CSC after treatment. Clinical assessment of choroidal vascularity index can be a useful marker for follow-up and monitoring treatment response central in serous chorioretinopathy and similar disorders involving choroid.

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