Spectral-Domain Optical Coherence Tomography Findings as Prognostic Factors in Patients with Acute Central Serous Chorioretinopathy

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ABSTRACT

Purpose: To determine the value of predictive factors for transition to chronic central serous chorioretinopathy (CSC) in patients with acute CSC.

Materials and Methods: The records of 46 patients with acute CSC were retrospectively evaluated. After exclusion, 24 eyes of 24 patients were analyzed. The relationship between anatomical& functional recovery and the height of subretinal fluid (SRF) in the center of the fovea, the outer nuclear layer thickness (ONLT), the existence of pathology in retinal pigment epithelium (RPE), the volume of subretinal fluid (SRFV), and base width of subretinal fluid (SRFBW) were evaluated through spectral-domain optical coherence tomography (SD-OCT).

Results: The mean age of the patients was 46.2 ± 8.8 years (33-54 years). The mean duration of symptoms was 35.0 ± 13.7 days (15-60 days). Sixteen (66.7%) out of the 24 eyes had complete resorption of the serous retinal detachment. The mean BCVA was improved from 0.36 ± 0.25 (0.7 to 0.0) to 0.15 ± 0.29 (1.0 to 0.0) (p= 0.028). 16 of the eyes (66.7%) had total resorption of SRF, 6 of them (25.0%) had partial improvement, and 2 (8.3%) had an increase in SRF. There was a significant relationship between change in SRFH and baseline SRFBW (R:-0.596, p=0.041), and there was also a significant relationship between the change in SRFV and baseline SRFBW (R:0.621, p=0.026). Multiple regression analysis revealed that none of the parameters was independently related to the SRFH change, According to the ROC analyses, the most sensitive factors for having persistent SRF were age (AUC=0.494) and SRFBW (AUC=0.481). In anatomical parameters, it was found that having a defect in the RPE and having a large SRFBW were helpful parameters to determine the tendency of progression to the chronic form of CSC.

Conclusion: The RPE defects and large SRFBW determined by SD-OCT may be useful in predicting the high probability of chronic CSC.

Keywords: Acute central serous chorioretinopathy, Spectral-domain optic coherence tomography, Predictive factors, Chronic central serous chorioretinopathy.

INTRODUCTION

Central serous chorioretinopathy (CSC) is a common chorioretinal disease that is seen especially in healthy males between 25 and 55 years. It is typical to have a well-circumscribed serous retinal detachment on fundus examination and optical coherence tomography (OCT). Fundus fluorescein angiography (FFA) reveals one or more leaking points.[1-3] The underlying pathology of CSC is not described yet. Several factors such as defects in the pump function of retinal pigment epithelium (RPE), impairment of the RPE barrier function, dilatation in the choriocapillaris, choroidal vascular hyperpermeability, increased choroidal thickness, and excessive activation of the mineralocorticoid receptor pathway have been reported as responsible in the pathophysiology of CSC.[4]

Although visual acuity generally returns to normal after the resolution of the subretinal fluid (SRF), the disease becomes chronic and results in permanent vision loss in some patients. In addition, one or more recurrences occur in 40-50% of patients with spontaneous recovery.[5] The main reason for severe vision loss is related to RPE and outer nuclear layer atrophy, persistent or recurrent pigment epithelial detachment (PED), and choroidal neovascularization.[6-8]

A significant decrease in outer nuclear layer thickness (ONLT) has been reported in resistant SRF patients,

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and there is a correlation between the severity of outer nuclear layer thinning and visual loss.[9,10] In the light of this information, using the term 'a disease that needs to be followed up and treated carefully if necessary' instead of 'a benign disease' for CSC would be more appropriate. The general approach is to follow patients with acute CSC without treatment until 3 to 6 months and apply treatment if it becomes chronic. However, there might be permanent vision loss in some patients, especially when the chronic stage has arisen, and it would be better to define and treat those with a high possibility of resistant SRF. Unfortunately, there is no adequate information about the predictive factors that may show the tendency to chronicity in acute CSC patients. This study aimed to evaluate the predictive value of spectral-domain optical coherence tomography (SD-OCT) findings in patients with acute CSC in terms of the tendency to have persistent SRF.

MATERIALS and METHODS

Forty-six patients diagnosed with acute CSC in Balıkesir University Faculty of Medicine between April 2019 and April 2021 were evaluated. The study followed the tenets of the Declaration of Helsinki, and it was approved by the local ethical committee. (Approval reference number:2020/150) Informed consent was obtained from all participants. Patients with a history of previous CSC, any active or previous retinal disease, a spherical equivalent of more than ± 6 diopters, and any media opacity that may decrease the signal strength of SD-OCT images, with glaucoma, and with any other vision-threatening ocular disease were excluded. After exclusion, 24 eyes of 24 naive patients were scanned retrospectively. None of the participants received treatment other than observation.

The diagnosis of CSC was made through decreased visual acuity in the last 3 months with or without micropsia or metamorphopsia, serous retinal detachment determined by SD-OCT, and detection of leakage points which were characteristic for CSC by FFA. The signal strength above 6/10 in SD-OCT was accepted as reliable. The absence of SRF in SD-OCT examination and absence of active leakage in FFA at the 6th month was accepted as complete resorption. Through FFA, occult choroidal neovascular membranes and polypoidal choroidal vasculopathy were also excluded. Indocyanine green angiography was not performed in any patient since no polypoidal choroidal vasculopathy was suspected.

A complete ophthalmologic examination including best-corrected visual acuity (BCVA), intraocular pressure (with Goldmann applanation tonometer), slit-lamp biomicroscopy, non-contact fundus examination (SuperField lens; Volk Optical Inc, Mentor, Ohio, USA), SD-OCT (Cirrus HD-OCT; Carl Zeiss Meditec, Dublin, CA), fundus photography, and FFA (Visucam 224; Carl Zeiss Meditec, Dublin, CA) was performed at the baseline examination. All SD-OCT images were obtained through a dilated pupil with a high-definition 5-line raster scan protocol (length 6 mm, spacing 0.075 mm). The BCVA measurements, fundus examination, and OCT examination of the patients were performed at each visit, during the follow-up period. During the six months, patients were examined monthly.

Two authors (M.K and G.S.V), who were masked to the information on BCVA and symptom duration, independently evaluated SD-OCT images, and a retinal specialist (***) acted as arbiter in cases of disagreement between the two authors. The subretinal fluid height (SRFH) (Figure 1a) in the center of the fovea, the ONLT, the presence of bulges or detachments in the RPE, the

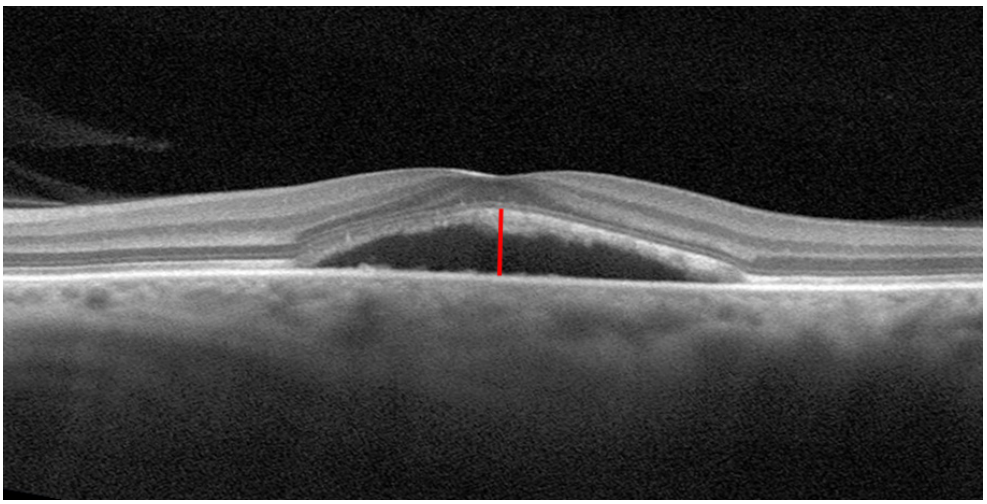

Figure 1a: *The demonstration of subretinal fluid height (SRFH) in central serous chorioretinopathy.*

subretinal fluid volume (SRFV), and the base width of the subretinal fluid (SRFBW), (Figure 1b) were measured and the relationship of these parameters with anatomical and functional recovery were examined. By using the digital caliper tool built into the SD-OCT system, retinal thicknesses were measured by an experienced observer, who was blinded to the groups. At the center of the fovea, we measured the ONLT which is defined as the distance between the external limiting membrane and apex of the RPE layer. (Figure 2) Calculation of SRFV was carried out as described in previous studies.[11,12] Briefly, using the SD-OCT's internal segment switching tool, the cursor line in the RPE was brought to the end of the photoreceptor outer segment. Macular volume except SRF was determined and used to examine the macular volume of the eye. The SRFV was calculated by subtracting corrected macular volume from the macular volume automatically given by SD-OCT. (Figure 3)

Eyes with total resrption of subretinal fluid were accepted as group 1 and eyes with persitent subretinal fluid were accepted as group 2 and 2 groups were compared for all parameters.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for Social Sciences for Windows V.20 (SPSS, Inc, Chicago, Illinois, USA). The BCVA in Snellen was transformed to logMAR. The normality of the data distribution was evaluated by the Shapiro-Wilk test. For the difference between the parameters in the first and last examination, and eyes with spontenous resorption and eyes with persitent subretinal fluid, paired t-test was used for dependent groups, and the chi-square test was used for nonparametric values. The relationship between the parameters at the first examination and the anatomical and functional changes were evaluated by Pearson correlation analysis. ROC analysis was used to determine the

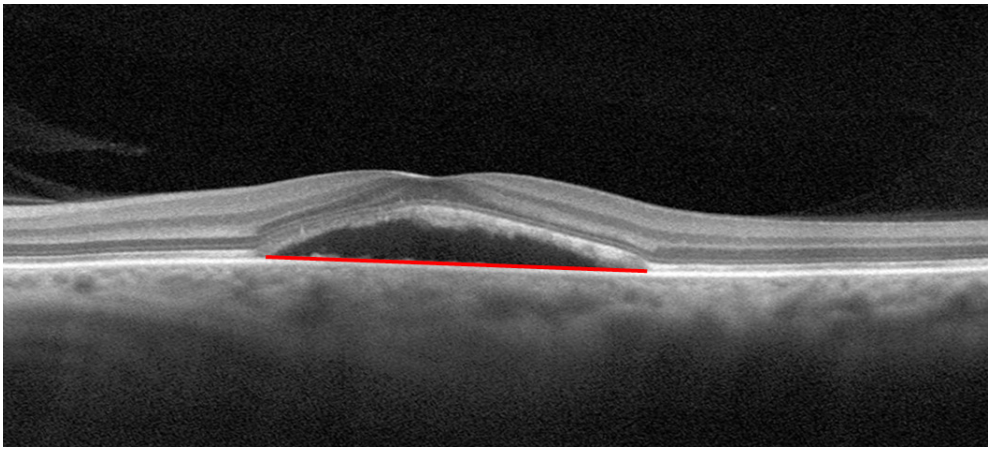

Figure 1b: *The demonstration of subretinal fluid base width (SRFBW) in central serous chorioretinopathy.*

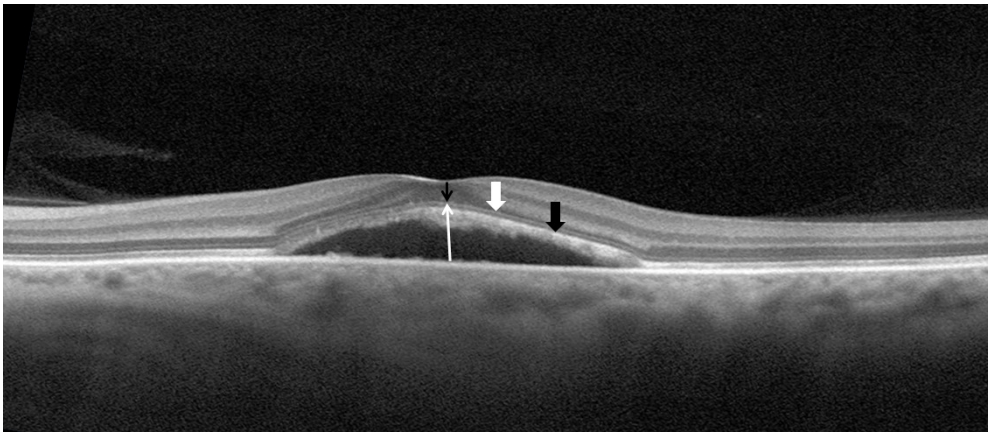

Figure 2: *SD-OCT image of an eye with central serous chorioretinopathy. The thick-black arrow shows the ONL thickness at the fovea. The thin-white arrow shows the OL thickness at the central fovea. The thick-white arrow shows ELM line and the thick-black arrow shows the IS/OS junction.*

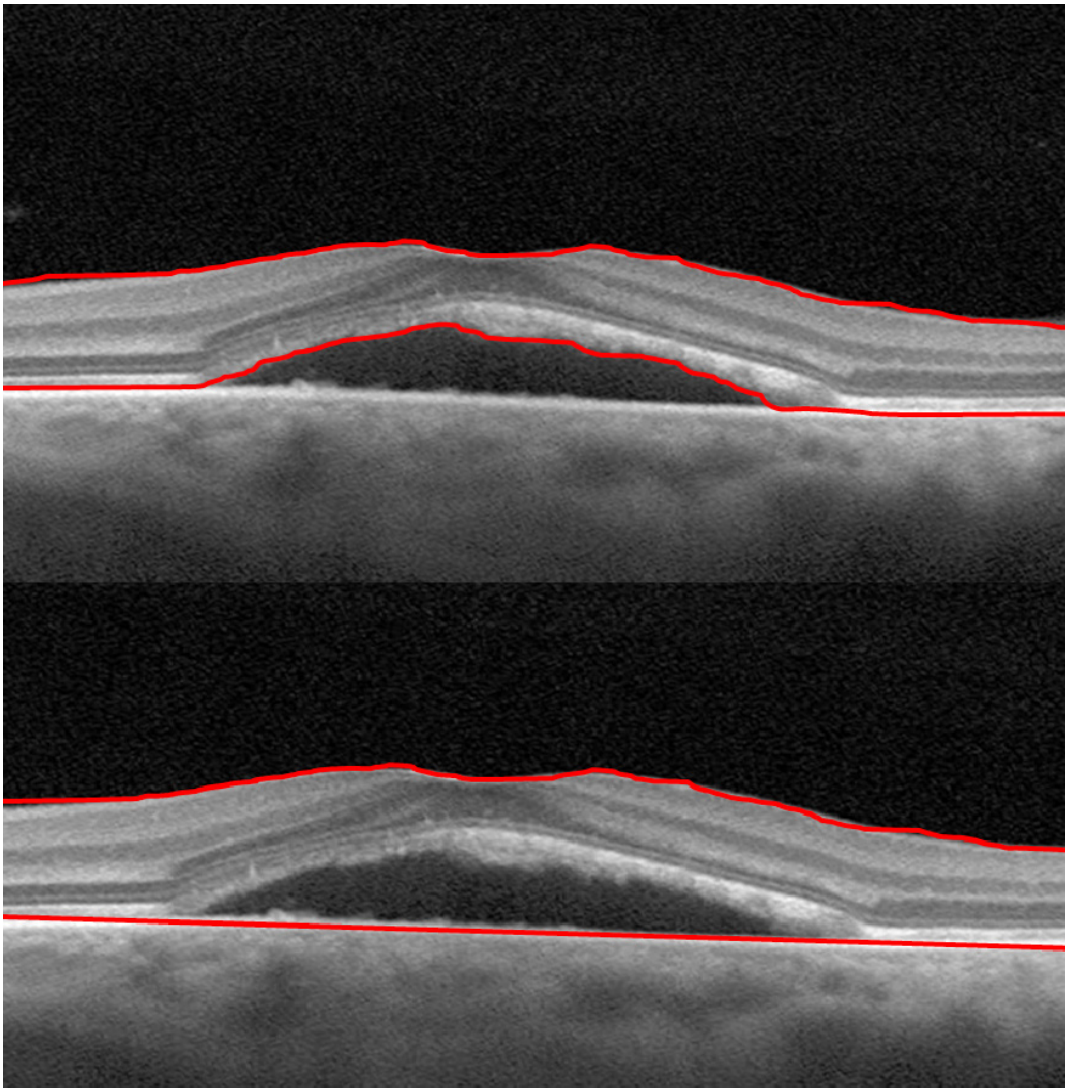

Figure 3: *Determining of the subretinal fluid volume (SRFV): The cursor line on the RPE (b) was moved to the tips of the outer segments of photoreceptors (a), and the SRFV was calculated by subtracting the modified macular volume from the total macular volume.*

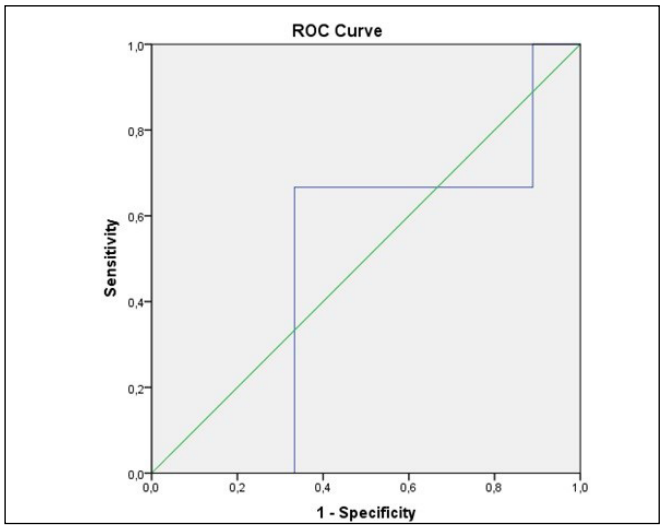

Figure 4: *ROC curve analysis graphic for sensitivity and specifity of subretinal fluid base width in determining the tendency of chronicity.*

sensitivity of parameters evaluated in terms of chronicity (Figure 4). P-value <0.05 was accepted as statistically significant ratio.

RESULTS

The mean age of the patients was 46.2 ± 8.8 years (33-54 years). Twenty-one patients were male and 3 were female. The mean duration of symptoms was 35.0 ± 13.7 days (15-60 days). The mean BCVA at the first examination was 0.36 ± 0.25 (0.7 to 0.0) and 0.15 ± 0.29 (1.0 to 0.0) at the final examination (p= 0.028). Of the 24 eyes, 18 (75.0%) had improvement in BCVA, 4 had no change (16.7%), 2 had worsened (8.3%) at the 6th-month follow-up. Functional and anatomical data at the beginning and the 6th month are summarized in Table 1. Of the eyes, 16 (66.7%) had total resorption of SRF, 6 (25.0%) had partial improvement, and 2 (8.3%) had an increase in SRF. There was no difference between eyes with spontaneous resorption and eyes with

Table 1: *Average values of visual acuity and SD-OCT parameters at the first and 6th-month examination.*

	Baseline	6th month	p value
BCVA (logMAR)	0.36 ± 0.25	0.26 ± 0.38	0.339
SRFH (µm)	246.6 ± 155.7	161.4 ± 126.6	0.199
SRFV (µm^3)	12405 ± 11998	7025 ± 8424	0.212
ONLT (µm)	104.6 ± 40.1	111.3 ± (46.2)	0.432
SRFBW (µm)	2205.7 ± 1140.0	1678.0 ± 972.0	0.321

persistent subretinal fluid in terms of age, gender, or any prognostic factor. In the logistic regression analysis, a factor that was significantly associated with the chronicity of the disease could not be detected.

There was no significant relationship between the change in BCVA (between baseline and 6th-month visit) and age, duration of symptoms, and baseline BCVA, ONLT, SRFH, SRFV, SRFBW. However, there was a significant relationship between change in SRFH and baseline SRFBW, and there was also a significant relationship between the change in SRFV and baseline SRFBW. Table 2 demonstrates the correlation of change in SRFH and SRFV with all parameters.

At the baseline examination, RPE was normal in six eyes (25%), ten eyes (41.7%) had a bulge in RPE, and eight eyes (33.3%) had bulges and PED. The mean SRFBW was 1423 ± 637 µm (990-2155 µm) in those who have normal RPE and 2466 ± 1174 µm (819-3984 µm) in those with bulge and/or PED (p= 0.014). The mean BCVA at the 6th-month visit was 0.03 ± 0.06 (1,0 to 0,0) in patients with healthy RPE, and it was 0.34 ± 0.42 (1.0 to 0.0) in patients with any RPE defect at the baseline examination (p=0.059).

According to the ROC analyses, the most sensitive factors for having persistent SRF were age and SRFBW. (Table 3)

CONCLUSION

In recent years, especially with the advancement of SD-OCT, permanent disturbances of anatomical structures were

Table 2: *Linear regression analysis findings showing the relationship of subretinal fluid height and volume with baseline parameters.*

	Age	Duration of symptoms	BCVA (logMAR)	ONLT (µm)	SRFH (µm)	SRFV (µm^3)	SRFBW (µm)
Change in SRFH	R:0.163 p:0.613	R:0.436 p:0.156	R:0.179 p:0.578	R:0.388 p:0.213	R:0.781 p:0.003*	R:0.739 p:0.006*	R:-0.596 p:0.041*
Change in SRFV	R:0.241 p:0.450	R:0.408 p: 0.188	R:0.014 p:0.966	R:0.215 p:0.502	R:0.813 p:0.001*	R:0.802 p:0.002*	R:0.621 p:0.026*

Table 3: *Multiple regression analysis results showing the relationship between the change in subretinal fluid height and the parameters studied.*

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	1333.803	599.651		2.224	0.090
	Age	-18.720	7.868	0.816	-2.379	0.076
	Duration of symptomes	1.976	4.064	0.133	0.486	0.652
	Initial BCVA	-450.233	267.074	-0.693	-1.686	0.167
	ONLT	-1.103	1.000	-0.218	-1.103	0.332
	SRFH	-0.634	1.326	-0.487	-0.479	0.657
	SRFV	0.029	0.021	1.730	1.410	0.231
	SRFBW	-0.123	0.096	-0.690	-1.281	0.269

Dependent Variable: change in SRFH

Table 4: *Multiple regression analysis results showing the relationship between the change in subretinal fluid volume and the parameters studied.*

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	89251.476	31837.526		2.803	0.049
	Age	-1314.487	417.723	-0.825	-3.147	0.035
	Duration of symptoms	213.379	215751	0.207	0.989	0.379
	Initial BCVA	-26353.920	14179.893	-0.584	-1.859	0.137
	ONLT	-31.830	53.081	-0.091	-0.600	0.581
	SRFH	-96.147	70.381	-1.064	-1.366	0.244
	SRFV	2.975	1.100	2.537	2.704	0.054
	SRFBW	-11.103	5.080	-0.900	-2.185	0.094
Dependent Variable: change in SRFV						

Table 5: *ROC analysis results showing the sensitivity and specificity powers of the parameters examined in SD-OCT in terms of showing the tendency to become chronic.*

	Age	ONL	SRFH	SRFV	SRFBW
AUC	0.494	0.407	0.407	0.444	0.481

observed in CSC patients. More severe visual loss occurs if SRF persists.[13,14] Ozdemir et al. divided 67 patients into 6 groups according to the duration of the symptoms, with one-month intervals. While there was no difference between the eyes whose symptom duration ranged from one day to one month and those between one to two months, and more than two months. There was a significant thinning in ONLT in those with complaints for more than two months, and the loss was positively correlated with the duration of symptoms, and it was observed that functional loss occurs in patients SRF with more than 2 months[14] Matsumoto et al. divided the eyes into two groups according to the visual acuity level after spontaneous resorption. The VA was less than 1.0 (decimal) in 24 out of 67 eyes, and it was 1.0 (decimal) or better after improvement in 43 eyes. The ONLT was 74.6 µm in patients with visual acuity below 1.0 (decimal) and 103.2 µm in patients with 1.0 (decimal) and above. They stated that, although the disease seemed to improve anatomically, some patients suffered a permanent functional loss due to photoreceptor cell loss.[9]

Since anatomical deterioration might begin even in patients who were accepted as acute CSC,[15] should we consider early treatment with acute CSC? However, there is no evidence-based and globally accepted treatment for CSC. Conventional laser therapy has been used in patients with CSC with a single focus away from the foveal center. Although satisfying results have been reported, it is well known that it has side effects such as paracentral scotoma and idiopathic choroidal vascularization.[16] Mohabati et al. evaluated the risk of transition to chronic disease in patients with acute CSC. They reported that the recurrence of SRF was occurred in 24% of untreated cases and in 4% of treated cases and early PDT may decrease the risk of recurrences.[22] In the light of these findings, it could be claimed that leaving acute CSC patients without treatment should be questioned. Is it possible to detect the predictive factors that could determine the tendency of becoming chronic instead of treating all patients as there is no established treatment modality? In this study, it was aimed to evaluate the SD-OCT findings that may be determinative in terms of having refractory SRF. There was no relationship between functional improvement and any parameter in this study, but the SRFBW was associated with anatomical improvement. The improvement in SRFH and SRFV was significantly more limited in those with broad-based serous detachment. Also, as the width of the base increases, the decrease in SRFH becomes less. We also found in ROC analysis that the most sensitive parameter related to the tendency of persistent SRF was SRFBW. This may be related to the more significant RPE damage in eyes with a broad base. So indeed, the SRFBW in eyes without RPE defect was 1423.8±637.5 µm, and 2466.3 ± 1174.6 µm in those with RPE defect (819.0 µm-3984.0 µm), (p=0.014). However, the rate of eyes with total resorption of the SRF was same in eyes with and without RPE defects. The SRF was resorbed entirely in 4 (66.7%) of 6 eyes without RPE defect, and in 18 eyes with RPE defect, 12 (66.7%) had complete spontaneous resorption (p = 974).

It has previously been reported that the presence of PED may promote the risk of chronic CSC. Ohkuma et al. demonstrated a significantly increased risk of chronic CSC in the presence of a small flat PED but not with a dome-shaped PED. Chan et al. reported that the presence of PED at the baseline was a negative predictive factor of visual improvement.[24] Choronopulos et al. reported that a flat-irregular PED was associated with either chronic or recurrent CSC, whereas the absence of a PED correlated positively with acute CSC.[25] Daruich et al were also stated that a higher degree of RPE alteration at leakage sites was an independent factor for longer acute CSC episodes.[26] Our results seem reasonable to claim that the patients with larger SRFBW have more RPE dysfunction. This may indicate a more common choroidal circulation deficiency in these patients, but to prove this hypothesis these findings must be supported with OCT angiography.

Our study has some limitations, the most important weakness of this study was the small size of our cohorts and retrospective design of the study. The functional retina tests as visual field or multifocal electroretinography were not carried out. The choroidal thickness was not evaluated, because the technical problems occured in Enhanced Depth Imaging (EDI-Mode) OCT during study. Furthermore, as a tertiary center, the cases recorded in our database do not directly reflect the exact incidence of CSC and constitute a selection bias.

In conclusion, there is no consensus on the treatment of acute CSC patients according to the current knowledge. The spontaneous recovery rate is very high in acute CSC patients, it is inappropriate to treat all patients. We believe that the predictive factors for chronic CSC are important to determine the patients who need early treatment. Currently, there is no predictive factor to show which cases will become chronic, but prospective studies with larger cases will reveal objective criteria that could determine which patients with acute CSC should be treated or which should be observed.

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