## Change in choroidal vascularity in acute central serous chorioretinopathy

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Purpose: This study aims to compare the effect of laser photocoagulation or observation on choroidal vascularity in acute central serous chorioretinopathy (CSCR). Methods: A retrospective analysis of 30 patients with acute CSCR treated either with laser photocoagulation (16 eyes) or sham laser (14 eyes) was performed. Demographic details, visual acuity (VA) assessment, and other relevant clinical data were considered from baseline to the 3rd and 6th month follow-up visits. Participants with chronic CSCR and missing follow-up or inadequate data were excluded. Choroidal analysis including choroidal thickness and choroidal vascularity index (CVI) assessment was done for each visit using Spectral Domain (SD) Optical Coherence Tomography (OCT) images. Results: In laser arm group, there was a statistically significant change in VA, contrast sensitivity and central macular thickness (CMT) and neurosensory detachment (NSD) (P < 0.05) at the 3rd and 6th month visits. However, there was no statistically significant difference in subfoveal choroidal thickens (SFCT) and CVI (P > 0.05) at both the visits. In sham laser group, similarly, there was a significant improvement in VA, contrast sensitivity, CMT, and CVI (P < 0.05) at the 3<sup>rd</sup> and 6<sup>th</sup> month visits. There was significant reduction in NSD at the 3<sup>rd</sup> month; however, it was not statistically significant at the 6<sup>th</sup> month visit. SFCT did not change significantly at both the visits. There was no significant difference for the changes in parameters between the groups at the 6<sup>th</sup> month. Regression analysis showed no significant correlation with final VA with any of the baseline parameters. Conclusion: Early laser photocoagulation does lead to change in choroidal morphology, though insignificant, in comparison to observation. The present data, yet again, support no additional benefit of early laser photocoagulation in acute CSCR.



Key words: Central serous chorioretinopathy, choroid, choroidal vascularity

Choroidal hyperpermeability is an established proposed mechanism for central serous chorioretinopathy (CSCR).<sup>[1,2]</sup> Recent studies have reported that increased choroidal thickness in eyes with acute CSCR as well as in the fellow eyes when compared with healthy eyes.[3-7] Recently, the concept of measuring choroidal vascular index (CVI) (ratio of luminal area to total choroidal area) using OCT images has been reported in various diseases including CSCR.[6,8,9] We reported increase in CVI in acute CSCR which was significantly more compared to chronic CSCR and age-matched healthy participants.<sup>[9,10]</sup> As conventionally reported, acute presentation of CSCR does not need any intervention. In a recent randomized trial, we reported no benefit of early laser photocoagulation, that is, within 2 months of presentation, in acute CSCR.[11] We found no significant difference between the early laser group and observation group in terms of resolution of subretinal fluid, change in retinal sensitivity, change in visual acuity (VA), and contrast VA at 6-month follow-up.

Maruko *et al.* reported slight decrease in choroidal thickness after laser photocoagulation along with the resolution of serous subretinal fluid, though, the change was insignificant.<sup>[12]</sup> Change in the choroidal vascularity may be a parameter to understand the response to laser photocoagulation or natural recovery in eyes with acute CSCR. In the present study, we were interested in understanding the changes in choroidal vascularity between

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the observation group and early laser photocoagulation group of our previous prospective study cohort.

## Methods

The present retrospective study included 30 eyes of 30 patients underwent either early focal (16 eyes) or sham laser (14 eyes) photocoagulation in eyes with acute CSCR. This study was conducted at a tertiary eye care center in India to compare the effect of early focal laser photocoagulation with that of sham laser photocoagulation for the treatment of acute CSCR with focal leak. The informed consent was taken from all the patients and ethical approval was obtained from Institutional review board.

## **Inclusion criteria**

Subjects diagnosed with acute CSCR and with complete visits during the acute phase along with natural history (baseline to the 6<sup>th</sup> month visit) and eyes with visible choroidal outer boundaries on spectral domain OCT (SD-OCT) in both groups from previous data.

#### **Exclusion criteria**

(i) History of prior treatment for CSCR; (ii) absence of any leak on fundus fluorescein angiography (FFA); (iii) subfoveal leak on

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FFA; (iv) diffuse leak on FFA, retinal pigment epithelium (RPE) atrophy, or any other signs of chronic CSC; (v) vitreoretinal/ macular disorders other than CSC currently or in the past; (vi) any intraocular procedure in the last 6 months; (vii) currently on steroid therapy; (viii) any media opacity likely to cause attenuation of signal strength in OCT; (ix) history of malignant hypertension; (x) pregnancy; (xi) currently, on any systemic medication such as pioglitazones which can cause macular edema; (xii) evidence of glaucoma; and (xiii) spherical equivalent  $\geq \pm 6$  D. Participants with poor visibility of choroidal boundaries were excluded from the study.

All the participants underwent a comprehensive ophthalmic examination including best-corrected VA (BCVA) tested using Snellen charts, slit-lamp biomicroscopy, intraocular pressure measurement using Goldmann applanation tonometer, and dilated fundoscopic examination. BCVA was assessed using early treatment diabetic retinopathy study (ETDRS) letter count and low-contrast VA (LCVA) was assessed using COMPlog.

## Fundus fluorescein angiography

FFA was performed using fluorescein sodium 20% on Navilas<sup>®</sup> system (OD-OS GmbH, Teltow, Germany) to determine the site of leakage at baseline, and at 3 and 6 months from baseline.

#### Laser photocoagulation

Participants in laser group were treated with navigated laser photocoagulation as per the protocol reported before. In sham laser group, only the laser beam was turned on, but not the source and fundus photographs were obtained.

#### Spectral domain optical coherence tomography

The SD-OCT scans were obtained using Cirrus high-definition (HD)-OCT (Carl Zeiss Meditec, Inc., Dublin, CA, USA) after dilatation of pupil with 0.8% tropicamide and 5% phenylephrine eye drops at both the visits. The scanning protocol included HD 5-line raster, HD single line raster, enhanced depth imaging, and macular cube. Central macular thickness (CMT) was determined automatically and analyzed by OCT software, by generating images using the Macular Cube 512 × 128 scan over 6 mm × 6 mm area, the cube being composed of 128 horizontal examination lines of 512 A-scans each. The CMT was obtained from the 1-mm central retinal thickness area as described in the ETDRS fields corresponding to the CMT. The subfoveal choroidal thickness (SFCT) was obtained using the EDI-OCT technique previously described by Spaide et al. The vertical distance between the hyperreflective line of Bruch's membrane and the innermost hyperreflective line of the chorioscleral interface was taken, and the average of the two scans (vertical and horizontal) was considered as the SFCT. The height of neurosensory detachment (NSD) was measured by the vertical distance between the outermost hyperreflective margin of the detached neurosensory retina at the fovea and the hyperreflective line of the RPE.

#### Choroidal vascularity index calculation

The CVI calculation of the single HD scan, passing through fovea, was done using previously reported algorithm.<sup>[13]</sup> Briefly, choroidal stroma and vessel area analysis involved (i) automated binarization of a HD horizontal 6-mm OCT B-scan and (ii) automated segmentation of the binarized choroid layer as reported previously. The task of automated binarization in turn involved (a) preprocessing, (b) exponential and nonlinear enhancement, and (c) thresholding.

#### Statistical analysis

Statistics for Windows, Version 24 (IBM Corp. Released 2016, IBM SPSS) was used to analyze the results. The BCVA and LCVA were converted to logarithm of the minimum angle of resolution equivalent for statistical analysis. The change in BCVA, LCVA, CMT, NSD, SFCT, and CVI from baseline, 3<sup>rd</sup> and 6<sup>th</sup> month follow-up visits, was analyzed using paired samples *t*-test to compare the means (within the group and between the group). *P* <0.05 was considered as statistically significant. Correlation between the variables was estimated using Pearson's correlation.

## Results

In the present study, laser group had 16 eyes of 16 participants (53.3%), of which 13 were male and 3 were female. Sham laser group had 14 eyes of 14 paricipants (46.6%), of which 13 were male and only 1 female. Baseline characteristics of both the groups are shown in Table 1.

#### Laser group

There was a statistically significant change in BCVA, LCVA, CMT, and NSD (P < 0.05) at the 3<sup>rd</sup> and 6<sup>th</sup> month visits. However, there was no statistically significant difference in SFCT and CVI (P > 0.05) at both the visits [Table 1 and Fig. 1].

#### Sham laser group

Similarly, there was a statistically significant improvement in BCVA, LCVA, CMT, and CVI (P < 0.05) at the 3<sup>rd</sup> and 6<sup>th</sup> month visits. Whereas, there was significant reduction in NSD at the 3<sup>rd</sup> month; however, it was not statistically significant at the 6<sup>th</sup> month visit [Fig. 2]. SFCT did not change significantly at both the visits [Table 1].

Comparison between the groups for change in parameters at 6 months showed no statistical significance with any of the parameters [Table 2].



**Figure 1:** Laser arm, optical coherence tomography of the left eye of a 32-year-old female using spectral domain optical coherence tomography at baseline, 3 months, and 6 months, (a-c), respectively. (d-f) Images show choroid segmentation using an automated algorithm. (g-i) are the binarized images, which is used to calculate the choroidal vascularity index (0.57, 0.57, and 0.57, respectively)

	Mean±SD (P)					
	Laser arm			Sham laser		
	Baseline	3 <sup>rd</sup> month	6 <sup>th</sup> month	Baseline	3 <sup>rd</sup> month	6 <sup>th</sup> month
BCVA (logMAR)	0.26±0.21	-0.16±0.26 (0.028)	-0.18±0.26 (0.012)	0.32±0.22	-0.27±0.19 (0.000)	-0.28±0.23 (0.001)
LCVA (logMAR)	0.70±0.30	-0.44±0.33 (0.000)	-0.53±0.35 (0.000)	0.65±0.39	-0.51±0.34 (0.000)	-0.56±0.43 (0.001)
CMT (µm)	576.19±227.29	-300.40±245.11 (0.000)	-316.12±196.47 (0.000)	541.07±288.95	-271.08±232.01 (0.002)	-302.42±292.48 (0.002)
NSD (µm)	391.73±227.61	-316.50±249.30 (0.000)	-335.73±214.30 (0.000)	371.71±286.30	-256.25±136.45 (0.033)	-125.75±235.51 (0.364)
SFCT (µm)	264.47±52.07	-4.50±56.47 (0.770)	8.20±62.46 (0.619)	260.00±65.87	16.45±42.19 (0.225)	-13.14±78.22 (0.540)
CVI (µm)	0.58±0.02	0.00±0.03 (0.356)	0.01±0.03 (0.211)	0.55±0.02	0.02±0.02 (0.012)	0.02±0.03 (0.020)

#### Table 1: Baseline, 3rd, and 6th month visit characteristics of laser arm and sham laser groups

BCVA: Best-corrected visual acuity, LCVA: Low-contrast visual acuity, CMT: Central macular thickness, NSD: Neurosensory detachment, SFCT: Subfoveal choroidal thickness, CVI: Choroidal vascularity index, SD: Standard deviation, LogMAR: Logarithm of the minimum angle of resolution

Table 2: Comparison between the groups for change inparameters at 6 months				
Between	Mean±SD (	Mean±SD (significant)		
the group comparison	Laser arm Sham laser		between the groups in regards the change in different parameters ( <i>P</i> )	
Mean change in BCVA (Mean±SD) (logMAR)	-0.18±0.26 (0.012)	-0.28±0.23 (0.001)	0.154	
Mean change in LCVA (logMAR)	-0.53±0.35 (0.000)	-0.52±0.44 (0.374)	0.463	
Mean change in CMT (µm)	-316.12±196.47 (0.000)	-302.42±292.48 (0.002)	0.441	
Mean change in NSD (µm)	-335.73±214.30 (0.000)	-332.85±324.45 (0.001)	0.431	
Mean change in SFCT (µm)	8.20±62.46 (0.619)	-13.14±78.22 (0.540)	0.116	
Mean change in CVI (µm)	0.01±0.03 (0.211)	-0.01±0.16 (0.337)	0.248	

BCVA: Best-corrected visual acuity, LCVA: Low-contrast visual acuity, CMT: Central macular thickness, NSD: Neurosensory detachment, SFCT: Subfoveal choroidal thickness, CVI: Choroidal vascularity index, SD: Standard deviation, LogMAR: Logarithm of the minimum angle of resolution

## Correlations

To evaluate the correlation of BCVA at final visit with baseline parameters, Pearson's correlation was performed [Table 3a] which showed no significant correlation with any of the



**Figure 2:** Sham laser, optical coherence tomography of the right eye of a 40-year-old male using spectral domain optical coherence tomography at baseline, 3 months, and 6 months, (a-c), respectively. (d-f) Images show choroid segmentation using an automated algorithm. (g-i) are the binarized images, which is used to calculate the choroidal vascularity index (0.56, 0.58, and 0.59, respectively)

baseline parameters. Similarly, CVI at the final visit with baseline parameters showed no significant correlation with any baseline parameters in laser arm group, but in sham laser group, only baseline SFCT was closely correlating with final CVI (<0.05) [Table 3b].

## Discussion

In our previous study, we reported increased CVI in acute CSCR compared to fellow eye and age-matched healthy participants.<sup>[9,10]</sup> CVI could be a parameter demonstrating the choroidal vessel congestion, which is the primary pathogenic mechanism for CSCR. Therefore, CVI could also be a useful to understand the effect of therapeutic intervention. The present

## Table 3a: Correlation of baseline parameters with final visit best-corrected visual acuity of both the groups

6 <sup>th</sup> month BCVA	Lase	er arm	Sham laser		
	Correlation	Significance	Correlation	Significance	
Baseline BCVA	-0.155	0.565	0.14	0.633	
Baseline LCVA	-0.099	0.716	0.021	0.945	
Baseline CMT	-0.352	0.181	-0.085	0.773	
Baseline NSD	-0.385	0.156	-0.064	0.827	
Baseline SFCT	0.36	0.188	-0.299	0.299	
Baseline CVI	0.406	0.119	0.12	0.683	

BCVA: Best-corrected visual acuity, LCVA: Low-contrast visual acuity, CMT: Central macular thickness, NSD: Neurosensory detachment, SFCT: Subfoveal choroidal thickness, CVI: Choroidal vascularity index

#### Table 3b: Correlation of baseline parameters with final visit choroidal vascularity index of both the groups

6 <sup>th</sup> month BCVA	Laser arm		Sham laser		
	Correlation	Significance	Correlation	Significance	
Baseline BCVA	-0.061	0.821	0.123	0.689	
Baseline LCVA	-0.191	0.478	-0.089	0.784	
Baseline CMT	0.105	0.698	-0.013	0.966	
Baseline NSD	0.15	0.595	0.04	0.897	
Baseline SFCT	0.298	0.28	0.58	0.038	
Baseline CVI	-0.086	0.75	0.211	0.489	

BCVA: Best-corrected visual acuity, LCVA: Low-contrast visual acuity, CMT: Central macular thickness, NSD: Neurosensory detachment, SFCT: Subfoveal choroidal thickness, CVI: Choroidal vascularity index

# study shows the change in CVI in acute CSCR with or without intervention.

Interestingly, there was a slight increase in CVI, though it is statistically insignificant, in sham laser group, which could be because of persistent choroidal congestion in the absence of any intervention. Such increase was not noted in laser arm; rather a slight decrease in choroidal thickness and CVI was noted. There was an increase in CVI in both the groups at 6 months, which may be suggestive of reappearance of choroidal congestion, however, which was not associated with the recurrence of subretinal fluid. This probably could be associated with recurrence in subretinal fluid in the future in sham group. However, this cannot be answered with the present study data.

One of the limitations of our study is the small sample size for the present analysis. Due to poor visibility of choroidal boundaries, we could not include all the eyes of our previous cohort. As the change in CVI is very small, therefore, study with larger sample size in two groups would be required to evaluate the significance." However, our study provides the change in CVI in a prospective manner, which is one of the main strengths of our study. We did not evaluate the CVI changes at 1 month; it is possible the change in CVI could have been more significant at 1 month from baseline.

## Conclusion

Our study provides a change in choroidal vascularity in eyes with acute CSCR with or without laser intervention. Early laser photocoagulation does lead to change in choroidal morphology though insignificant, in comparison to observation. The present data, yet again, support no additional benefit of early laser photocoagulation in acute CSCR. However, further, prospective evaluation of larger sample of acute CSCR may expand our understanding about the changes in choroidal morphology with different treatment modalities.

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Nil.

## **Conflicts of interest**

There are no conflicts of interest.

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