

REDUCED TEMPORAL RETINAL VASCULAR DENSITY AS AN EARLY FINDING IN SICKLE CELL RETINOPATHY



A small study may suggest a way to screen for early disease in patients with sickle cell disease.

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Sickle cell disease (SCD) is the most prevalent structural hemoglobinopathy in the world. It is associated with multisystemic vascular occlusive events that can affect the retinal microvasculature.

Sickle cell retinopathy (SCR) is the most severe ocular complication of SCD. It is classified either as nonproliferative (NPSCR), with features including peripheral venous tortuosity, salmon-patch hemorrhages, iridescent spots and black sunbursts, or as proliferative (PSCR). Goldberg proposed a five-stage grading system for PSCR.¹ Without early detection and treatment, SCR can lead to irreversible vision loss.²

Macular thinning and lower vascular density have been proposed as preclinical alterations preceding SCR development.³ Because these abnormalities are not detected in routine observations, imaging exams are crucial for SCR screening.

We performed a study to analyze the characteristics of the macula and temporal retina in children with SCD.

MATERIALS AND METHODS

This single-center, retrospective study included children less than 18 years old with SCD. Exclusion criteria were high refractive errors (> 6.00 D), media opacities, and retinopathy other than SCR. Approval was obtained from the relevant institutional research committee.

We collected clinical and laboratory data and performed ophthalmologic evaluation including BCVA, slit-lamp observation, and fundoscopy.

Macular OCT and OCT angiography (OCTA) imaging

with the Cirrus HD-OCT 5000 with Angioplex (Carl Zeiss Meditec) was performed. Scan protocols included collecting 6x6-mm images centered at the fovea and 3x3-mm images through the temporal macula. Macular thickness, foveal avascular zone (FAZ), and superficial vessel density (SVD) were automatically generated.

Deep vascular density (DVD) was calculated with ImageJ using the method described by Parodi et al.⁴ Vascular density (VD) was expressed as the ratio between vessel pixels and total area (Figure).

AT A GLANCE

- A small retrospective study found that the temporal region is the area of the retina most susceptible to damage in sickle cell disease (SCD).
- The study suggests that temporal retinal thinning and reduced vascular density may predict the presence of retinopathy in children with SCD.
- The study authors suggest that temporal centered OCT angiography should be a part of screening for children with SCD.

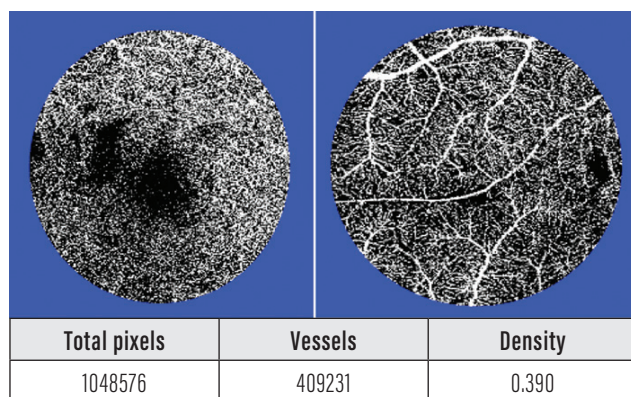


Figure. A deep vascular density (DVD) image generated by ImageJ. On the left is the fovea-centered image; on the right, the temporal retina. At bottom, the output calculated by ImageJ (here, for deep foveal capillary density).

Statistical analysis was performed using SPSS Statistics 23.0 (IBM). Mann-Whitney tests were used to compare eyes with and without SCR. Statistical significance was defined as $P < .05$.

RESULTS

Our study included 15 children with SCD; eight had SCR and seven had no SCR. For two children, information could be retrieved from only one eye due to lack of cooperation. Hence, data for 28 eyes were included in the study.

Patients' mean age was 12 ± 4 years. Demographic and laboratory data are presented in Tables 1 and 2, respectively. BCVA was 6/7.5 bilaterally in both the SCR and the no-SCR groups.

Fourteen of 28 eyes (50%) were classified as having NPSCR, and none had PSCR.

OCT data are shown in Table 3. There were no differences regarding foveal thickness between the SCR and no-SCR groups.

The temporal retina tended to be thinner than the fovea, with a thickness of $196.5 \pm 18.1 \mu\text{m}$ at 6 mm temporal to the macula. Mean temporal thickness was lower in eyes with retinopathy ($185.3 \pm 16.2 \mu\text{m}$ vs $205.2 \pm 13.2 \mu\text{m}$, respectively, $P < .01$). This difference was more pronounced in the temporal subfield of the displaced scan in the temporal retina ($184.3 \pm 16.3 \mu\text{m}$ vs $196.4 \pm 10.7 \mu\text{m}$, $P = .04$).

OCTA results are presented in Table 4. Mean FAZ appeared to be larger in the SCR group (0.36 ± 0.11 vs $0.30 \pm 0.1 \text{ mm}^2$, $P = .46$).

Mean foveal VD values were lower in the SCR group than in the no-SCR group, both SVD ($37.1 \pm 1.4\%$ vs $43.3 \pm 1.7\%$, $P = .01$) and DVD ($39.1 \pm 1.2\%$ vs $44.3 \pm 2.2\%$, respectively, $P = .01$). In SCR eyes, the temporal SVD ($27.6 \pm 3.7\%$ vs 37.1 ± 2.3 , $P < 0.01$) and DVD ($32.3 \pm 2.6\%$ vs $38.3 \pm 2.1\%$, $P < .01$) mean values were also lower.

DISCUSSION

SCR can lead to serious visual impairment if not recognized and treated early. Recent work has led to the detection of certain retinal alterations that can predict

TABLE 1. DEMOGRAPHIC INFORMATION

	No SCR (n = 7)	SCR (n = 8)
Age, years (range)	11 $\pm$ 2 (9-15)	12 $\pm$ 3.6 (8-17)
Sex		
Male	3	3
Female	5	4
Race		
Black	7	8
SCD Genotype		
HbSS	4	4
HbSC	2	2
HbS// β -thalassemia	1	2
Medication		
Folic Acid	6	7
Hydroxyurea	2	4
Transfusion		
Yes	1	2
No	6	6
Other Manifestations		
Yes	5	6
• Vaso-occlusive crisis	2	2
• Dactylitis	2	2
• Aplastic crisis	1	1
• Femoral head avascular necrosis	0	1
No	2	2

Abbreviations: SCD, sickle cell disease; SCR, sickle cell retinopathy.

TABLE 2. GENERAL OPHTHALMIC EVALUATION FINDINGS (N = 28)

	No SCR (n = 14)	SCR (n = 14)
Spherical Equivalent		
OD	+0.50	+0.50
OS	+0.50	+0.90
BCVA		
	6/7.5	6/7.5
Anterior Segment		
No alternations	11	11
Sclerotic jaundice	3	3
Retinopathy		
Nonproliferative	-	14
Proliferative	-	0

Abbreviations: OD, right eye; OS, left eye; SCR, sickle cell retinopathy.

TABLE 3. OCT DATA: MACULAR AND TEMPORAL RETINA THICKNESS			
	No SCR (n = 14)	SCR (n = 14)	P Value
Macular Thickness (μm)			
Fovea	232.4 ±13.7	221.5 ±15.4	.12
Temporal	303.5 ±26.7	305.4 ±8.2	.76
Nasal	322.7 ±18.1	323.2 ±9.3	.90
Inferior	325.4 ±10.9	315.6 ±14.3	.06
Superior	326.9 ±17.3	329.2 ±7.8	.8
Temporal Retina (μm)			
6 mm	205.2 ±13.4	185.3 ±16.2	< .01
Temporal	196.4 ±10.7	184.3 ±16.3	.04
Inferior	215.3 ±9.2	211.4 ±12.8	.473
Superior	214.7 ±15.2	208.7 ±15.8	.341
Abbreviations: SCR, sickle cell retinopathy.			

TABLE 4. OCTA DATA: VESSEL DENSITY AND FOVEAL AVASCULAR ZONE			
	No SCR (n = 14)	SCR (n = 14)	P Value
Fovea			
Superficial Capillary Plexus (%)	43.3. ±1.7	37.1 ±1.4	.01
Deep Capillary Plexus (%)	44.3 ±2.2	39.1 ±1.2	.01
6 mm Temporal			
Superficial Capillary Plexus (%)	37.1 ±2.3	27.6 ±3.7	< .01
Deep Capillary Plexus (%)	38.3 ±2.1	32.3 ±2.6	< .01
Foveal Avascular Zone (mm²)			
	0.30 ±.01	0.36 ±.01	.46
Abbreviations: SCR, sickle cell retinopathy.			

the development of proliferative disease, improving early diagnosis and treatment.⁵⁻⁷

In this study in children with SCD, mean foveal SVD and DVD values were lower in eyes with SCR than in eyes with no SCR. However, no difference was seen between the groups regarding foveal thickness. Mean temporal retinal thickness and VD in both plexuses were also lower in eyes with SCR, adding information to previous reports.⁸

This finding suggests that the temporal macula may be more susceptible to damage due to the small caliber of terminal arterioles. The authors believe that reduced VD could be reliable markers of early retinal damage.

Because these alterations are commonly asymptomatic and most often undetectable in routine ophthalmologic examination, OCTA could be helpful in screening for SCR.

It is important to highlight that screening should start early, but there is also a need to establish parameters for OCTA data in healthy children to further help in identifying those at risk for SCR. We propose that temporal retina scans should be part of regular evaluation of children with SCD.

Our results are encouraging and, despite the small sample size, may provide a basis for prospective clinical trials to define the role of OCTA in SCR screening. ■

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