Risk Factors for Retinal Thinning in Sickle Cell versus Control Eyes: Analysis of a Prospective Study Using SDOCT Imaging

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Summary

- Sickle cell eyes showed progressive macular thinning over time in contrast to control eyes
- Risk factors for increased rates of retinal thinning in sickle cell eyes = age, HgbSC and SThal subtypes, progression of sickle cell retinopathy stage, thicker baseline retina, hypertension, acute chest syndrome, diabetes mellitus, stroke
- Protective risk factor = hydroxyurea usage, associated with a decreased rate of retinal thinning

SDOCT Imaging Revealed Sickle Cell Retinopathy is Associated with Retinal Thinning

TABLE 4. Comparison of Spectral-domain Optical Coherence Tomography Subfield Measurements for Sickle Cell Eyes With Control Eyes (Analysis of Variance)

Subfield Location	SDOCT Thickness (μm): Control Eyes, Mean ± SE	SDOCT Thickness (μm): Sickle Cell (All Subtypes) Eyes, Mean ± SE	ANOVA *P* Value
Central	262.8 ± 2.42	253.7 ± 1.05	.002*
Nasal inner	339.8 ± 2.26	332.1 ± 1.07	.009
Superior inner	338.4 ± 2.23	331.4 ± 1.13	.021
Temporal inner	325.0 ± 2.08	313.3 ± 1.20	<.001*
Inferior inner	335.9 ± 2.30	328.6 ± 1.11	.017
Nasal outer	310.2 ± 2.08	308.3 ± 0.93	.461
Superior outer	294.6 ± 1.88	292.7 ± 0.89	.428
Temporal outer	281.7 ± 1.78	273.1 ± 1.28	.012
Inferior outer	287.1 ± 1.89	284.5 ± 0.90	.286

ANOVA = analysis of variance; SDOCT = spectral-domain optical coherence tomography.

P values < .006 (ie, 0.05/9) are considered significant based on Bonferroni correction and are indicated by an asterisk (*).

- 513 sickle (260 patients) and 75 control eyes
- SDOCT measurements were significantly lower in sickle cell eyes compared with control eyes; Hgb SS eyes worse than other subtypes.
- SDOCT measurements of inner ETDRS subfields were inversely correlated with age ($p<.001$), stage ($p=0.016$) and systemic diseases.

Lim JI, Cao D. Analysis of Retinal Thinning Using Spectral-domain Optical Coherence Tomography Imaging of Sickle Cell Retinopathy Eyes Compared to Age- and Race-Matched Control Eyes. Am J Ophthalmol. 2018;192:229-238.

Purpose

- To identify risk factors associated with macular thinning in sickle cell versus control eyes using spectral domain optical coherence tomography (SDOCT) in a prospective cohort study

Methods

- Prospective observational study of sickle cell and age and race-matched controls enrolled at University of Illinois at Chicago
  - Clinical evaluation (visual acuity, slit lamp biomicroscopy, dilated ophthalmoscopy) yearly
  - SDOCT imaging yearly
- Analysis of SDOCT data from eyes with $\geq$ 1 year of follow-up

Methods

- Rates of change of SDOCT ETDRS subfield measurements per year calculated and compared
  - Between sickle and control eyes
  - Across Hgb subtypes
- Associations between rates of retinal thinning and ocular and systemic conditions determined

Results: Demographics

	Sickle Cell Group					Control Group	
	Patients	Eyes	SS eyes	SC eyes	S Thal eyes	Patients	Eyes
Total Number Enrolled	310	606	377	163	66	60	105
Number with follow-up $\geq$ 1 year	175	344 (57%)	219	92	33	31	46 (44%)
Mean follow-up interval (months)	54	54	51	59	54	55	57

Results: Change in Clinical Parameters

- Sickle cell retinopathy stage progression was low for most eyes:
  - 2.7% progression by year 1
  - 14.3% progression by year 5
- Visual acuity was unchanged:
  - decreased 0.07 lines (0.10) per year ($p < 0.001$) for sickle
  - increased 0.02 lines (0.03) per year for control

Retinal Thickness Change Over Time

- Sickle cell eyes thinned over time in all inner quadrants, outer nasal, temporal and inferior quadrants ($P<0.0001$)
- Control eyes thinned over time in inner inferior ($p=0.03$), outer nasal ($p=0.02$), outer inferior ($p<0.001$) quadrants

Comparison of Rates of Change: Sickle vs. Control Eyes

- Rates of thinning for sickle eyes (all subtypes) > controls

ETDRS Subfield	Rate of Retinal Thinning per Year (u/yr)		
	Sickle Cell Eyes	Control Eyes	P Value
CST	-0.18 (0.09)	0.23 (0.38)	0.105
Inner nasal	-0.92 (0.09)	0.26 (0.35)	**< 0.001**
Inner superior	- 1.38 (0.12)	-0.29 (0.51)	**0.006**
Inner temporal	- 0.93 (0.11)	-0.31 (0.25)	**0.028**
Inner inferior	- 0.87 (0.09)	-0.47 (0.22)	0.097
Outer nasal	- 0.82 (0.08)	-0.41 (0.18)	**0.036**
Outer superior	-0.24 (0.22)	0.10 (0.30)	0.536
Outer temporal	-0.99 (0.18)	-0.51 (0.34)	0.267
Outer inferior	-0.97 (0.10)	-0.89 (0.28)	0.754

Comparison of Retinal Thinning by Hgb Subtype

- Rates of thinning were greatest for Hgb SC or SThal

Subtype	CST	Inner nasal	Inner temporal	Inner superior
SS	-0.04 (0.12)	-0.79 (0.12)	-0.71 (0.13)	-1.16 (0.13)
SC	**-0.20 (0.15)**	**-0.97 (0.12)**	**-1.11 (0.19)**	-1.66 (0.23)
SThal	**-1.04 (0.34)**	**-1.64 (0.43)**	**-1.67 (0.51)**	-1.88 (0.47)
P Value	**0.012**	**0.027**	**0.023**	0.073

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Rates of Change for Sickle Cell Eyes: Systemic Risk Factors

- Rates of thinning increased with hypertension (all subfields), acute chest syndrome (all inner; outer nasal & inferior subfields)
- Rates of thinning affected by DM (outer inferior) and CVA (inner temporal)

ETDRS Subfield	HTN			ACS			DM			CVA		
	Thinning rate difference	se	p-value	Thinning rate difference	se	p-value	Thinning rate difference	se	p-value	Thinning rate difference	se	p-value
Central	1.52	0.27	**<0.001**	0.47	0.25	0.06	0.48	0.37	0.192	1.71	1.19	0.150
Inner Nasal	1.59	0.25	**<0.001**	0.76	0.24	**0.001**	0.05	0.34	0.874	1.39	1.11	0.210
Inner Superior	1.73	0.33	**<0.001**	1.13	0.32	**<0.001**	0.33	0.46	0.469	1.88	1.49	0.209
Inner Temporal	1.68	0.31	**<0.001**	0.75	0.29	**0.01**	0.77	0.41	0.061	4.27	1.38	**0.002**
Inner Inferior	1.25	0.26	**<0.001**	1.00	0.25	**<0.001**	0.39	0.35	0.277	0.61	1.16	0.600
Outer Nasal	1.30	0.22	**<0.001**	1.10	0.21	**<0.001**	0.40	0.30	0.184	1.54	1.58	0.116
Outer Superior	1.67	0.67	**0.013**	0.77	0.650	0.235	0.71	0.89	0.427	0.90	2.92	0.758
Outer Temporal	1.11	0.52	**0.030**	0.36	0.490	0.459	0.83	0.70	0.235	2.68	2.29	0.242
Outer Inferior	1.07	0.31	**<0.001**	1.07	0.300	**<0.001**	1.11	0.40	**0.005**	1.89	1.28	0.140

Comparison of Rates of Change: Hydroxyurea Usage was Protective

- Slower rate of thinning associated with hydroxyurea usage for CST, inner superior, temporal & inferior and outer nasal subfields

ETDRS Subfield	Hydroxyurea Status (Current vs. None)		
	Thinning rate difference	se	p-value
Central	-0.91	0.35	**0.009**
Inner Nasal	-0.60	0.33	0.067
Inner Superior	-0.91	0.44	**0.037**
Inner Temporal	-1.22	0.41	**0.003**
Inner Inferior	-0.74	0.34	**0.030**
Outer Nasal	-0.58	0.29	**0.047**
Outer Superior	-0.35	0.86	0.688
Outer Temporal	-0.44	0.67	0.510
Outer Inferior	-0.43	0.39	0.277

Comparison of Rates of Change: Stage Progression

- Increased rates of thinning associated with sickle cell stage progression for inner nasal & superior, outer nasal & inferior subfields

ETDRS Subfield	Stage Progression vs. None		
	Thinning rate difference	se	p-value
Central	0.42	0.28	0.137
Inner Nasal	0.79	0.26	**0.003**
Inner Superior	0.89	0.36	**0.013**
Inner Temporal	0.17	0.32	0.601
Inner Inferior	0.44	0.28	0.112
Outer Nasal	1.28	0.23	**<0.001**
Outer Superior	0.54	0.74	0.465
Outer Temporal	0.30	0.55	0.582
Outer Inferior	1.30	0.34	**<0.001**

Comparison of Rates of Change: Baseline Thickness

- Increased rates of thinning associated with thicker baseline ETDRS measurements

Baseline CST Quartile	Coefficient	SE	P value
1	0.471	0.169	0.005
2	0.328	0.188	0.082
3	-0.484	0.154	0.002
4	-0.941	0.209	0.000

Conclusions

- Sickle cell stage remained stable for most eyes although SDOCT thinning occurred over time
- Rates of thinning were greater for sickle than control eyes
- Risk factors for retinal thinning included age, HgbSC and SThal, thicker baseline retina, sickle cell stage progression, history of hypertension, acute chest syndrome, diabetes, stroke
- Hydroxyurea usage was a protective risk factor

Thank you!