August 20, 2019

SCREENING FOR SICKLE CELL RETINOPATHY AT THE UNIVERSITY OF IOWA

1. SCREENING GUIDELINES

A. Children with Sickle Cell Disease (HbSS, HbSC, and HbSβ-thalassemia) who are visually asymptomatic should be screened by the Pediatric Ophthalmology or Retina Service starting at age 10 years.

B. Repeat Examinations will be arranged based on findings, but routine screening should occur yearly.

C. Visually symptomatic children or those who fail a vision screen can be referred to Pediatric Ophthalmology at any time.

D. Suggested testing at the time of screening:

i. Complete eye exam including dilated fundus exam
ii. Wide field fundus photography – Claris with montage or Optos
iii. Macular OCT (Spectralis)
iv. OCT-A
    1. *Cirrus SD-OCTA 3x3 and 6x6*
    2. *Plex Elite swept source OCT- 12x12 and 15x0 montage (needs to be done by Brice Critser)*

2. BACKGROUND

A. This screening program is designed to identify children with proliferative sickle cell retinopathy which may require treatment and to screen for early retinal changes that have unknown significance and no current treatment.

B. There is no consensus in the literature regarding timing of screening for sickle cell retinopathy.

C. New evidence with OCT shows that temporal retinal thinning occurs at ages younger than 10 years but the significance of this finding is not known.

D. If new evidence appears that may impact this policy, changes to the screening schedule should be implemented.

E. Review of recent studies related to pediatric screening since the NIH Expert Panel report in 2014:

i. **Fundus exam and SD-OCT in detecting sickle cell retinopathy among pediatric patients: Jin et al. J AAPOS 2018**

1. *Recent report of 61 children with sickle cell disease and 8 with sickle trait aged 5-20 years in Delaware*
2. *16% had fundus findings, none had proliferative retinopathy*
    a. *Hemorrhage*
    b. *Hypo- or hyperpigmentation*
3. *69% had inner retinal thinning on OCT*
    a. *Heidelberg Spectralis*
4. *Average age of OCT findings was younger than fundus abnormalities findings*
    a. *Age Funduscopy apparent disease present 15.5 years +/- 3.6 years*
    b. *Age OCT abnormalities present 13.7 years +/- 4.1 years*

ii. **Paramacular temporal atrophy in sickle cell disease occurs early in childhood. Martin et al. BJO 2018**

1. *81 children aged 5-18 years seen in a Paris hospital*
2. *Used Goldberg's severity staging, from 1 to 5: stage 1 (peripheral arterial occlusions), stage 2 (arteriovenous anastomoses: hairpin loop), stage 3 (neovascular and/or fibrous proliferations: sea fans), stage 4 (vitreous haemorrhage), or stage 5 (retinal detachment)*
3. *9 children had stage 1, 2 or 3; mean age 13.4 years +/- 2.75 years*
4. *2 children had stage 3; aged 17 and 17.5*
5. *HbSC genotype was associated with more severe stages*
6. *52% had temporal retinal thinning on OCT*
    a. *Heidelberg Spectralis*
    b. *Youngest patient with OCT changes was 5.5 years*

iii. **Sickle cell retinopathy in Children in Brazil. D Almeida Olivera et al. 2014**

1. *51 children in Northern Brazil mean age 11.7 years +/- 3.7 years*
2. *Non-proliferative retinal changes 39%*
    a. *4 (8%) were < 10 years*
3. *Proliferative retinopathy Stage 1 (16%) and stage 2 (23%), none less than 10 year.*

iv. **OCT-A in Sickle Cell Disease. Ian Han et al. Am J Ophthalmol 2017**

1. *OCT-A in adults with sickle cell disease shows temporal macula vascular abnormalities*

2. *Although this study did not include children it shows the power of OCT-A in detecting temporal retinal vascular abnormalities.*
3. *Using this technique in children may be helpful to understand the early retinal vascular changes that lead to retinal ischemia/atrophy*

v. **Correlation of OCTA and wide-field FA. Han et al. Ophth Ret 2018.**
   1. *Quantification of macular vascular density by OCT-A correlates with severity of peripheral non-perfusion as measured by ultra-wide-field FA in adults*
   2. *Patients 26 years old or younger had the strongest correlation between macular flow loss and peripheral nonperfusion*
   3. *The degree of peripheral nonperfusion is best predicted by deep plexus flow loss in the temporal subfield*

vi. Ultra-wide-field FA detects a higher stage of sickle retinopathy but does not change clinical decisions. Han et al. Retina 2018

vii. Peds Sickle Cell Patients have lower vascular density and larger FAZ compared to age-matched controls. Roemer et al. Retina 2018

viii. Adolescent sickle cell patients have high prevalence of sickle retinopathy by UWF-FA and flow loss on OCTA. Pahl DA et al. AJO 2017

ix. Chronic chelation and HgF are the most important systemic factors linked to sickle cell maculopathy Dell'Art L, et al. PLoS One. 2018

3. REFERENCES

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H. Roemer S. et al. *Assessment of Macular Vasculature of Children with Sickle Cell Disease compared to that of healthy controls using Optical Coherence Tomography Angiography.* Retina 2018 October 16.

I. Pahl DA, et al. *Optical Coherence Tomography Angiography and Ultra-widefield Fluorescein Angiography in Early Detection of Adolescent Sickle Retinopathy.* Am J Ophthalmolol. 2017 Nov;183:91-98

J. Dell'Arti L et al. *Sickle cell maculopathy : Identification of systemic factors, and microstructural analysis of individual retinal layers of the macula.* PLoS One. 2018 Mar 1;13(3):e0193582