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Posterior pole vascular changes before treatment of retinopathy of prematurity

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Abstract

Importance: Some proponents of telemedicine screening for retinopathy of prematurity (ROP) believe a screening system based on posterior pole vessel characteristics is sufficient for identifying infants needing treatment.

Objective: To evaluate the vascular characteristics present when it was determined treatment was needed, and the number of days between examinations from when the vessels of both eyes were last noted to be normal until a decision was made to treat.

Design: Retrospective study; June 2013-May 2017

Setting: Neonatal intensive care unit; academic medical center

Participants: All infants treated for ROP who were longitudinally examined at our institution

Main Outcomes and Measures: Vascular characteristics present on clinical examination when it was determined an infant needed treatment and the number of days between examinations from when the vessels of both eyes were last noted to be normal until a decision was made to treat.

Results: 55 infants met eligibility criteria, with mean birthweight 733g (range: 420–1060), gestational age 25.1 weeks (range: 22.9–27.7), and post menstrual age at the time a decision was made to treat 36.7 weeks (range: 31.4–43.0). When it was determined an infant needed treatment, 51 (92.7%) had plus disease, 3 (5.5%) pre-plus, and one (1.8%) neither. The number of days between examinations from when an infant was noted to have normal vessels bilaterally until a decision was made to treat was 0 to 49 days. The interval was at least 14 days for 42 infants (76%) and at least 7 days for all but one infant (98%). The exception was one infant with the rare

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scenario of neither pre-plus nor plus with zone I, stage 3 ROP (type 1 ROP) at the time the examiner decided to treat.

Conclusions and Relevance: At the time it was determined an infant needed treatment for ROP, all but one infant had pre-plus or plus disease. These results suggest that narrow-field imaging for ROP screening should include all of zone I, to identify the rare treatment-requiring ROP with normal posterior pole vessels. If confirmed, with sufficient image quality, weekly photographic screening of zone I likely should capture changes indicative of impending treatment-requiring ROP.

INTRODUCTION

Retinopathy of prematurity (ROP) requires proper screening and treatment to reduce the risk of progression to retinal detachment and blindness. Because of the sequential progression of ROP, at-risk infants need to be evaluated longitudinally. Currently, published screening guidelines suggest a follow-up examination schedule based on retinal findings noted at each examination, based on the international classification system.^{1,2} As the use of digital photographs for ROP screening expands, it will be important to establish an appropriate imaging interval to ensure treatable ROP is not missed. While some proponents of telemedicine screening for ROP believe that the periphery must be captured in acquired images,^{3,4} others propose that a screening system based solely on vessel characteristics in the posterior pole is sufficient.^{5–7} We would like to determine if the vessel characteristics seen in the posterior pole are sufficient for identifying infants who need treatment for ROP and a maximal imaging interval to ensure treatment-requiring ROP is not missed. Thus, the purpose of this study was to evaluate the vascular characteristics present at the time it was determined an infant needed treatment for ROP, and the number of days between examinations from when the vessels were last noted to be normal bilaterally until a decision was made to treat.

METHODS

This retrospective study was approved by the Duke University Health System Institutional Review Board and conformed to the requirements of the United States Health Insurance Portability and Privacy Act.

All infants treated for ROP who were longitudinally examined in the Neonatal Intensive Care Unit (NICU) at Duke University Hospital from June 22, 2013 to May 2, 2017 were included in this study. In our NICU, infants are screened using indirect ophthalmoscopy by one of two fellowship-trained pediatric ophthalmologists (SFF or DW), each with over 20 years of experience screening for ROP. Screening is performed according to current ROP screening guidelines in the United States² and treatment is performed when infants reach criteria for type 1 ROP, defined as zone I ROP with plus disease, zone I with stage 3, or zone II with stage 2 or 3 and plus disease.⁸

We calculated the number of days between examinations from when the vessels in the posterior poles of both eyes were last noted to be normal until a decision was made to treat for ROP in one or both eyes.

RESULTS:

Between June 22, 2013 and May 2, 2017, 55 infants were treated for ROP after being longitudinally examined in our NICU. None of the infants had abnormal posterior pole vessels on their first clinical examination. Of the 55 infants included, mean birthweight was 733g (range: 420–1060), gestational age (GA) 25.1 weeks (range: 22.9–27.7), and post menstrual age (PMA) at the time a decision was made to treat 36.7 weeks (range: 31.4–43.0). All infants met criteria for type 1 ROP when a decision was made to treat (Table 1). Of all infants treated for ROP, 51/55 (92.7%) had plus disease. Four of 55 (7.3%) infants had zone I, stage 3 ROP without plus disease (3 with pre-plus, and one with neither pre-plus nor plus).

The number of days between examinations from when the vessels were noted to be normal bilaterally until a decision was made to treat ROP was 0 to 49 days (Table 2). For 13 infants (24%), the interval was less than 14 days. Of these infants, 10 had ROP in zone I and 3 in zone II. For all but one infant (98%), the interval was at least 7 days. The one infant with neither pre-plus nor plus disease in either eye at the time the examiner decided to treat for type 1 ROP was born at 730g and 24.4 weeks. On the first ROP examination at a PMA of 30.1 weeks, the infant had immature vessels in zone I and normal posterior pole vessels bilaterally. The infant was examined weekly and always had ROP in zone I with neither pre-plus or plus disease. In both eyes, stage 1 was noted at PMA=31.1 weeks, stage 2 at PMA=32.1 weeks, and stage 3 at PMA=34.1 weeks, at which time a decision was made to treat the infant for ROP as it had reached criteria for type 1 ROP (6 clock hours of stage 3 ROP in zone I bilaterally). On the day the decision was made to treat, the examiner noted in both eyes that there was no vascular dilation or tortuosity, but that the “number of and branching of vessels is prominent” bilaterally.

DISCUSSION:

We found that on the clinical examination when it was determined an infant needed treatment for ROP, most infants had pre-plus or plus disease and at least 7 days had passed from when they were noted to have normal vessels in both eyes. The exception was one infant with neither pre-plus nor plus at the time a decision was made to treat. This infant had ROP in zone I and a prominent number of, and branching of vessels bilaterally. While one study found that “normal posterior pole vessels are a reliable marker for the absence of stage 3 ROP” among 132 consecutive patients screened for ROP,⁹ we suspect the single exception we found in this study may be due to either the low GA (24.4 weeks) (the range of GAs of infants in the study conducted over 25 years ago was not published) and/or the rarity of this clinical scenario. Both examiners, each with over 20 years of ROP screening experience, have never seen a similar case. It is important that ophthalmologists screening for ROP are aware that while rare, it is possible to have zone I, stage 3 ROP with neither pre-plus nor plus disease. One limitation of this study is that we did not have photographic documentation of this “exception” case. Thus, we cannot say for certain whether or not any vascular abnormalities (i.e. slight vascular tortuosity or dilation that did not qualify as pre-plus disease) were present.

As the use of digital photographs for ROP screening increases, it will be important to establish the minimum field of view and imaging interval needed to ensure that infants are appropriately screened and that treat-requiring disease is not missed. While narrow-field imaging devices can be used to screen for ROP with high sensitivity,⁵⁻⁷ we suspect that as long as the field of view includes all of zone I, no treatable ROP will be missed with images of acceptable quality. In this study, the one case where neither pre-plus nor plus disease was present when a decision was made to treat, it is likely that narrow-field imaging including zone I would have demonstrated the stage 3 ROP and/or the abnormal vessel branching seen in zone I, to prompt referral for ophthalmic examination. Our findings also showed that imaging with a narrow-field device at 2 week intervals could miss up to 24% of infants needing treatment, while imaging at intervals of 7 days should identify infants needing treatment.

CONCLUSIONS:

Our results suggest that narrow field imaging for ROP screening should include all of zone I, to identify the rare treatment-requiring ROP with normal posterior pole vessels. If confirmed, with sufficient image quality, weekly photographic screening of zone I should capture changes indicative of impending treatment-requiring ROP.

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Key Points

Question:

When it was determined an infant needed treatment for retinopathy of prematurity (ROP), what vascular characteristics were present and how many days passed from the last examination when the vessels were normal bilaterally?

Findings:

In this retrospective study of 55 infants, when a decision was made to treat, all but one had pre-plus or plus and at least 7 days passed from when the vessels were noted normal.

Meaning:

When imaging to screen for ROP, as long as the field of view includes all of zone I and imaging is performed weekly, it is unlikely to miss treatment-requiring ROP.

Table 1.

Classification of retinopathy of prematurity (ROP) at time a decision was made to treat

Classification of ROP at the time a decision was made to treat*	Number of infants
Zone I ROP with plus disease	24
Zone I, stage 3 ROP (no plus disease)	4
Zone II, stage 2 or 3 ROP with plus disease	27

* for asymmetric disease, the first eye treated or the eye with the lower zone with worst posterior pole disease was selected for classification

Table 2.

Number of days between examinations from when the vessels of both eyes were last noted to be normal on clinical examination until a decision was made to treat *

Number of days	Number of infants
0	1
7	5
8	1
9	4
10	1
13	1
14	10
15	1
16	7
21	9
22	1
23	3
27	1
28	2
29	1
30	1
31	1
36	3
37	1
49	1

* If disease was asymmetric and the eyes were not treated at the same time or only one eye was treated, then we used the time when a decision was made to treat the first eye