Efficacy of wide-field digital retinal imaging for retinopathy of prematurity screening

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ABSTRACT

Background: To evaluate the efficacy of wide-field digital retinal imaging for retinopathy of prematurity screening.

Design: Retrospective study in a quaternary public neonatal intensive care unit.

Participants: A total of 108 premature infants screened for retinopathy of prematurity.

Methods: Retrospective chart and photo review were performed on participants screened by both serial wide-field digital retinal imaging and concurrent binocular indirect ophthalmoscopy. Review of captured digital photos was performed independently by a masked reader. Using the binocular indirect ophthalmoscopy findings as the gold standard, the efficacy of wide-field digital retinal imaging in detecting treatment-requiring retinopathy of prematurity, defined as type 1 prethreshold disease, was determined.

Main Outcome Measures: Sensitivity and specificity of wide-field digital retinal imaging in detecting treatment-requiring retinopathy of prematurity.

Results: Treatment-requiring retinopathy of prematurity was detected in 11 infants by both binocular indirect ophthalmoscopy examination and telemedicine images taken at the same visit. Wide-field digital retinal imaging has a sensitivity of 100% (95% CI: 76.2–100%) and a specificity of 97.9% (95% CI: 93.4–99.7%) in detecting infants with treatment-requiring retinopathy of prematurity. Positive and negative predictive values of wide-field digital retinal imaging were 84.6% (95% CI: 57.8–97.3%) and 100% (95% CI: 96.9–100%), respectively.

Conclusions: Wide-field digital retinal imaging is accurate, reliable and efficient in detecting treatment-requiring retinopathy of prematurity. Incorporating wide-field digital retinal imaging with telemedicine in standard retinopathy of prematurity management can potentially improve delivery, accessibility, quality and cost of retinopathy of prematurity care.

Key words: diagnostic imaging, mass screening, photography, retinopathy of prematurity.

INTRODUCTION

Retinopathy of prematurity (ROP) is a leading cause of preventable childhood blindness. In the USA, approximately 1500 infants annually develop severe ROP that threatens sight and requires treatment.1 As early detection and prompt treatment of severe ROP can significantly decrease the incidence of severe visual loss and adverse outcome, screening of at-risk infants has been the cornerstone of ROP management.2

The delivery of quality ROP care has faced several challenges in recent years. First, the current gold standard method for ROP screening, binocular indirect ophthalmoscopy (BIO), is not completely ideal. Scleral depression required in BIO can cause systemic complications such as bradycardia secondary to oculocardiac reflex,3 as well as potentially serious ophthalmic complications such as vitreous and subretinal haemorrhages.4,5 BIO is labour and time intensive for ophthalmologists, as well as...
potentially logistically difficult for neonatal intensive care unit staff, especially in hospitals where access to ophthalmologists experienced in ROP screening is not readily available. Documentation of BIO findings, which relies on drawing by the examining ophthalmologist, is somewhat subjective and therefore prone to controversy in ROP malpractice trials.6

Second, manpower issues exist in meeting the increasing demand for ROP screening. The rising demand is partly due to increasing survival rate of premature infants especially in the middle-income countries.7 Revisions made in 2006 for ROP screening recommendations also increased the proportion of premature infants eligible for screening.8 Regional shortages in the availability of ophthalmologists have been a problem worldwide.9,10 To compound this issue, a worrying trend has been observed worldwide where increasingly fewer ophthalmologists are willing to perform ROP screening. In a 2006 American Academy of Ophthalmology survey of its retinal and paediatric subspecialist members, 25% of respondents discarded ROP screening within the 10 years prior, leaving only 50% to carry out the needed examinations. Twenty-three per cent of the 10 years prior, leaving only 50% to carry out the needed examinations. Twenty-three per cent of the present screeners planned to discontinue the practice because of medicolegal liabilities, logistical difficulties and lack of financial incentive.11

The combination of wide-field digital retinal imaging (WFDRI) and telemedicine technology offer a potential solution for the aforementioned challenges in ROP care. A WFDRI-based ROP telemedicine screening strategy involves capturing retinal photos of at-risk infants using WFDRI, and transmitting the photos for remote evaluation by ophthalmologists. With a relatively low treatment yield (around 8%) of all screened infants,12 WFDRI can free ophthalmologists from examining the vast majority of infants who would never require treatment. The move from bedside examination to photo reading has been shown to reduce the ophthalmologist’s time by up to 10 times per infant screened.13 Screening by WFDRI may allow a more flexible screening schedule if imaging can be performed by trained nursing staff. In addition, WFDRI has been shown to cause less cardiorespiratory stress to the screened infants in comparison with BIO.14

Before WFDRI-based ROP telemedicine screening can be implemented, the safety and efficacy of WFDRI in detecting severe ROP disease that requires treatment need to be closely scrutinized. Previous studies either focused on the detection of all stages of ROP by photographic screening,15–17 had modest sample sizes18–20 or used the eye as the unit of analysis that influenced the statistical power of the study outcome.15–24 The aim of conducting this study was to retrospectively evaluate the longitudinal outcome of WFDRI in detecting treatment-requiring ROP.

**Methods**

**Patients**

Retrospective chart and photo reviews were performed on all infants who underwent ROP screening from 1 June 2006 to 31 December 2007, when hospitalized in the Auckland City Hospital Neonatal Intensive Care Unit (a quaternary NICU). The screening criteria followed the established NICU protocol that included infants with gestational age less than 30 weeks, birth weight less than 1250 g, as well as older and heavier infants with an unstable clinical course who were believed to be at high risk for ROP by their attending neonatologist. Infants were excluded from the study if they had structural ocular anomalies or systemic malformations, or if they had previously received laser photocoagulation or other ocular surgery. Data collected included patient gestational age, birth weight, findings of serial BIO examinations as well as age at each examination.

**Examination schedule**

The first ROP examination was generally performed at 4–6 weeks of postnatal age. Some infants were examined later than this, because of either an unstable condition or transfer from elsewhere into the study unit. Based on the BIO examination findings, the schedule for subsequent examinations followed the published Joint Statement recommendations for ROP screening by the American Academy of Paediatrics, the American Academy of Ophthalmology and the American Association for Paediatric Ophthalmology and Strabismus.8 Screening was continued until the retinal vasculature was mature, the infant required treatment, or the infant was discharged from NICU.

**Examination technique**

Each infant underwent two sequential examination procedures under topical anaesthesia with application of tetracaine 0.5% to both eyes immediate prior to insertion of an eyelid speculum at the NICU bedside. Pupillary dilation was achieved with 0.5% cyclopentolate and 2.5% phenylephrine 30 to 60 min prior to examination. All examinations were performed with close cardiac and respiratory monitoring. If the cardiorespiratory indices of the infant were deemed unacceptable at any stage of the examination, the procedure was halted until the infant was deemed stable to continue. Retinal photos
from each eye were taken by a paediatric ophthalmologist (SD) using a RetCam 2 Wide Field Digital Retina Camera (Clarity Medical Systems, Pleasanton, CA, USA) equipped with a 130-degree field ROP lens (Fig. 1). A minimum of three photos capturing the posterior pole, nasal and temporal retina were taken. The captured images were stored uncompressed in a digital video disc. Immediately after the completion of retinal photography, BIO examination was performed by the same ophthalmologist (SD) for each eye with a 28-D condensing lens and scleral depression. Infants were re-screened within 1 week if their captured images were of poor quality. The presence or absence of ROP, its location and extent, and the presence or absence of plus disease were documented according to the international classification of ROP.25

Review of digital photography

All digital retinal photos captured were initially stored in compact discs. The photos of infants included in this study were later retrieved and uploaded onto a MacBook Pro laptop (Apple Inc., Cupertino, CA, USA) for review using image-viewer software (Mac Preview, Cupertino, CA, USA). The photos were then interpreted independently by a paediatric ophthalmologist (AV) who was masked from the BIO findings.

The interpretation of the retinal photos was based on the established criteria from the Early Treatment for Retinopathy of Prematurity (ETROP) study.2 Each photo set was graded as:

- No ROP
- Type 2 prethreshold ROP (defined as zone 1, stage 1 or 2 ROP without plus disease; or zone 2, stage 3 ROP without plus disease)
- Type 1 prethreshold ROP (defined as zone 1, any stage ROP with plus disease; zone 1, stage 3 ROP without plus disease; zone 2, stage 2 or 3 ROP with plus disease) (Fig. 2)
- Indeterminable
  Treatment-requiring ROP was defined as ‘type 1 prethreshold ROP’ based on the criteria from ETROP study.2

Data analysis

The findings of WFDRI and BIO for each eye, as well as other data collected from chart review for study infants were tabulated in separate columns using statistical software (Microsoft Excel, Seattle, WA, USA). To reflect the impact of care at the patient level, the ‘infant’ was used as the unit of analysis. If a discrepancy of ROP grading existed between the two eyes of an infant during an examination, the infant was analysed as having the higher grade disease detected. For example, if a BIO or photographic examination diagnosed type 1 prethreshold ROP in one eye and type 2 prethreshold ROP in the opposite eye, the infant was considered to have type 1 prethreshold ROP disease for that examination. The sensitivity and specificity for WFDRI in detecting
treatment-requiring ROP was determined using the BIO findings as the gold standard. Positive predictive value and negative predictive value were calculated to assess the clinical usefulness of WFDRI. The calculation of confidence intervals for each measurement was performed using web-based open statistical software.26

RESULTS

A total of 109 infants were included in this study. One infant was excluded as the ROP had already been treated with laser photocoagulation, leaving 108 infants eligible for analysis. The baseline characteristics of these eligible infants are shown in Table 1. A total of 422 simultaneous photographic and BIO examinations were performed. No photographic or BIO examinations had to be aborted because of infant’s stress.

Of the 108 infants, treatment-requiring ROP was detected in 11 by BIO. All 11 infants with treatment-requiring ROPs were also detected by WFDRI at the same visit as the BIO detection. Two sets of digital retinal photos, from infants clinically classified as type 2 ROP, were classified as type 1 ROP by the masked observer (Table 2).

Wide-field digital retinal imaging has a sensitivity of 100% (95% CI: 76.2–100%) and a specificity of 97.9% (95% CI: 93.4–99.7%) in detecting infants with treatment-requiring ROP. The positive predictive value of treatment-requiring ROP detection by WFDRI was 84.6% (95% CI: 57.8–97.3%) and the negative predictive value was 100% (95% CI: 96.9–100%).

Table 1. Baseline characteristics of infants included in the study

<table>
<thead>
<tr>
<th>Total number of infants</th>
<th>108</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>57 (52%)</td>
</tr>
<tr>
<td>Female</td>
<td>49 (48%)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>NZ European</td>
<td>60 (56%)</td>
</tr>
<tr>
<td>Maori</td>
<td>30 (28%)</td>
</tr>
<tr>
<td>Pacific Island</td>
<td>12 (11%)</td>
</tr>
<tr>
<td>Others</td>
<td>6 (5%)</td>
</tr>
<tr>
<td>Gestational age</td>
<td></td>
</tr>
<tr>
<td>Mean (weeks)</td>
<td>27</td>
</tr>
<tr>
<td>Range (weeks)</td>
<td>23–32</td>
</tr>
<tr>
<td>&lt;27 weeks</td>
<td>49 (45%)</td>
</tr>
<tr>
<td>27–31 weeks</td>
<td>56 (52%)</td>
</tr>
<tr>
<td>&gt;31 weeks</td>
<td>3 (3%)</td>
</tr>
<tr>
<td>Birth weight</td>
<td></td>
</tr>
<tr>
<td>Mean (g)</td>
<td>966</td>
</tr>
<tr>
<td>Range (g)</td>
<td>450–1645</td>
</tr>
<tr>
<td>&lt;1000 g</td>
<td>61 (56%)</td>
</tr>
<tr>
<td>1000–1500 g</td>
<td>45 (42%)</td>
</tr>
<tr>
<td>&gt;1500 g</td>
<td>2 (2%)</td>
</tr>
</tbody>
</table>

Fifteen per cent of digital retinal photo sets obtained on the first ROP screening visits were deemed indeterminable by the observer secondary to poor photo quality, of which 72% were taken during the first few months of this study. For all infants with indeterminable photo sets, subsequent retinal photos taken in re-screening were adequate for photographic ROP interpretation.

DISCUSSION

The results of this study confirm the efficacy of WFDRI and therefore the feasibility of telemedicine photographic screening in detecting treatment-requiring ROP. The reported sensitivity of 100% demonstrates that all infants with ROP requiring treatment would be promptly detected and referred for treatment. The positive predictive value of 84.6% indicates that WFDRI tended to overestimate the severity of some ROP cases – important for the safety of screening. Nevertheless, the high specificity of 97.9% achieved means that only a small proportion of unnecessary referrals would result.

These results are comparable with previous studies focusing on the detection of severe ROP by WFDRI (Table 3). The suboptimal efficacy achieved in the PHOTO-ROP study,22 studies by Schwartz et al.18 and by Dhaliwal et al.,27 might be related to the retinal camera used (RetCam 120), an older camera model previously noted to pose several technical hindrances to adequate imaging15,16,27 when compared with newer retinal camera models.20,28 The reported technical hindrances of RetCam 120 included incompatibility between its camera head and lid speculum arms, and inability to adequately image retinal periphery.15,16 Similar results were achieved whether photography was performed by ophthalmic or non-ophthalmic personnel. The reported efficacy of WFDRI-based ROP screening is indeed more impressive than the only large-scale telemedicine screening strategy in ophthalmology, namely diabetic retinopathy screening (with reported sensitivities from 60% to 92%, and specificities from 83% to 95% for detection).

Table 2. Comparison of WFDRI and BIO findings in ROP screening

<table>
<thead>
<tr>
<th>BIO (no. of infants)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR-ROP† (no. of infants)</td>
<td>11</td>
</tr>
<tr>
<td>Other‡</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
</tr>
</tbody>
</table>

†Treatment-requiring ROP. ‡Other: ROP less severe than type 1 prethreshold disease. BIO, binocular indirect ophthalmoscopy; ROP, retinopathy of prematurity; WFDRI, wide-field digital retinal imaging.
Table 3. Reported efficacy of WFDRI in detecting severe ROP

<table>
<thead>
<tr>
<th>Study</th>
<th>Positive screening criteria</th>
<th>No. of infants</th>
<th>Photographer</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current study</td>
<td>Type 1 prethreshold ROP</td>
<td>108</td>
<td>Ophthalmologist</td>
<td>100</td>
<td>97.9</td>
</tr>
<tr>
<td>Schwartz et al. 2000</td>
<td>Prethreshold ROP or worse</td>
<td>19</td>
<td>Ophthalmologist</td>
<td>89</td>
<td>–</td>
</tr>
<tr>
<td>Els et al. 2003</td>
<td>Referral warranted ROP</td>
<td>44</td>
<td>Ophthalmologist</td>
<td>100</td>
<td>96</td>
</tr>
<tr>
<td>Wu et al. 2006</td>
<td>Prethreshold ROP or worse</td>
<td>43</td>
<td>Ophthalmologist or technician</td>
<td>100</td>
<td>97.5</td>
</tr>
<tr>
<td>Chiang et al. 2007</td>
<td>Type 2 prethreshold ROP or worse</td>
<td>67</td>
<td>Neonatal nurse</td>
<td>100</td>
<td>≥85</td>
</tr>
<tr>
<td>PHOTO-ROP 2008</td>
<td>Clinically significant ROP§</td>
<td>51</td>
<td>Ophthalmologist</td>
<td>92</td>
<td>37</td>
</tr>
<tr>
<td>SUNDROP 2009</td>
<td>Prethreshold ROP or worse</td>
<td>97</td>
<td>Neonatal nurse</td>
<td>100</td>
<td>98.9</td>
</tr>
<tr>
<td>Dhaliwal et al. 2009</td>
<td>Prethreshold ROP or worse</td>
<td>81</td>
<td>Ophthalmologist</td>
<td>80</td>
<td>98</td>
</tr>
<tr>
<td>Lorenz et al. 2009</td>
<td>Suspected treatment-requiring ROP§</td>
<td>1222</td>
<td>Ophthalmologist</td>
<td>100</td>
<td>–</td>
</tr>
</tbody>
</table>

†Referral warranted ROP was defined as the presence of zone 1 disease, plus disease or any stage 3 ROP. ‡Clinically significant ROP was defined as the presence of any ROP without vascular dilation or tortuosity in zone 1; stage 2 or 3 ROP with up to one quadrant of vascular dilation and tortuosity in zone 2; any vascular dilation or tortuosity noted in eyes for which disc features (plus disease) were not interpretable (not imaged or poor image quality); any ROP noted in eyes for which ridge characteristics were not interpretable (not imaged or poor image quality). §Suspected treatment-requiring ROP was defined as the presence of any ROP without vascular dilation or tortuosity in zone 1; stage 2 or 3 ROP with up to one quadrant of vascular dilation and tortuosity in zone 2, type 1 prethreshold disease or possibly treatment-requiring ROP that could not be reliably classified from the images. ROP, retinopathy of prematurity; WFDRI, wide-field digital retinal imaging; –, data not available.

...
three photos capturing views of the posterior pole, temporal and nasal retina were taken. Concentrating on the three retinal regions and excluding the periphery may bias against the reader detecting peripheral ROP. Currently no standard retinal imaging protocol for ROP has been established. When designing this study, it was felt that this pragmatic approach would allow for adequate imaging of treatment-requiring disease, which either involves zone 1 and zone 2 disease or plus disease (diagnosed in posterior pole).2

Wide-field digital retinal imaging-based ROP screening, when applied to telemedicine, can improve delivery, accessibility, quality and cost of ROP care, with potential to alleviate the manpower challenge in ROP care. WFDRI-based telemedicine screening can increase access to ROP screening in medically under-resourced hospitals and is perhaps more cost-effective than BIO.18 It can minimize harm to the screened infants’ well-being through a less stressful examination and a more flexible screening scheduling. More accurate documentation is produced by retinal photography in comparison with the sketches of even experienced BIO screeners. Such objective documentation may provide greater protection for ophthalmologists in ROP malpractice trials.8 The disadvantages of WFDRI-based telemedicine screening include high initial capital cost and limitation in imaging very peripheral retina.18,19,22

In conclusion, our study demonstrates that WFDRI is accurate and reliable in detecting severe ROP requiring treatment. The potential of WFDRI, when used in a telemedicine setting, in improving ROP care is certainly promising. Before WFDRI can be adopted in routine ROP screening, several issues must be addressed by professional bodies in this field. These include establishment of a universal photography protocol, standardization of training requirements for photographers, guidelines for selection and training of readers and recommendations for ROP severity cut-off for referral.

REFERENCES


