Major Article

A national telemedicine network for retinopathy of prematurity screening

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PURPOSE	To report the results of retinopathy of prematurity (ROP) screening by a telemedicine system in Chile and evaluate its usefulness for referring patients who require treatment.
METHODS	Premature infants at risk of developing ROP from 11 neonatal intensive care units were included. Screening was performed on all infants born at a gestational age of <32 weeks and/or birth weight of <1500 g. A trained nonphysician operator used an imaging system to capture retinal images, which were reviewed by two independent ROP experts. All infants that required treatment were referred for further evaluation.
RESULTS	The study included 2,048 eyes of 1,024 premature infants. Mean gestational age was 28.8 ± 2.2 weeks, and mean birth weight was 1128 ± 279 g. A total of 5,263 telemedicine examinations were performed and reported. The average number of image sets per patient was 2.6 ± 2.5. Of the 5,263 images, 4,903 (93%) were recorded to at least the end of zone II; 5,172 (98%) were graded as having good quality, allowing for staging of ROP disease. Forty-two infants (4%) were referred for treatment. Discharged patients with ROP type 2 that regressed did not present with any complications or adverse effects during 6 months' follow-up.
CONCLUSIONS	Our study demonstrates the utility of telemedicine screening for ROP with ophthalmologist readers in a developing country. Telemedicine screening was able to detect treatment-requiring ROP. Most of the images had good quality and showed the end of zone II, two variables sufficient to discharge patients. (J AAPOS 2018;■:1-4)

A major obstacle to screening for retinopathy of prematurity (ROP) is the lack of ophthalmologists trained in performing dilated fundus examinations in premature infants. The problem is especially acute in underdeveloped countries that attempt to follow the screening guidelines of more developed countries.[1-4] ROP treatment success is based on regular screening and timely delivery of treatment.[5,6] Without treatment, 50% of eyes reaching the ROP threshold level will be permanently affected.[7] ROP screening by telemedicine provides one mechanism for addressing a shortage of examiners. This is particularly the case for sites that have advanced neonatology care units but not local ROP specialists that can perform regular eye screening.[8] Previous studies reported that digital photographs may be useful for the detection of advanced ROP disease requiring further evaluation and treatment.[9,10] This study aimed to report the results of ROP screening enabled by a telemedicine system in Chile.

Subjects and Methods

This study was approved by the Ethics Committee of Hospital Roberto del Río and conformed to all local laws and was compliant with the principles of the Declaration of Helsinki. Premature infants at risk of developing ROP from 11 neonatal intensive care units in Chilean territory were incorporated sequentially from January 2012 to April 2015. Screening for ROP according to Chilean regulations is performed in premature infants born at a gestational age of <32 weeks and/or with a birth weight of <1,500 g.[11] Infants with any ocular diseases other than ROP or those with ocular media opacities limiting the ability to perform imaging were excluded.

Testing was performed by a trained neonatology nurse, midwife, or ophthalmic technician. Screening began 4 weeks after delivery or when the premature infant reached a gestational age of 31 weeks. Subsequent examinations were scheduled according to ROP screening guidelines.[3,12,13] Examinations continued until both eyes reached full retinal vascularization or zone III immature vascularization at gestational age of ≥37 weeks or until ROP treatment was required. The RetCam Shuttle

imaging system (Natus Medical Incorporated, Pleasanton, CA) was used to capture retinal images. Before the examination, both pupils were dilated using 2.5% phenylephrine and 1% tropicamide, applied three times, 20 minutes apart. Immediately before examination, 1 drop of 0.5% proparacaine was applied to each eye followed by the insertion of a sterile wire lid speculum. At least 5 images were captured in each eye (one image demonstrating the posterior pole and the other four of each of the fundus quadrants). Indented images were not captured, because complete zone II was regularly reached without need for scleral depression. Images were saved in live script file format (.mlx) and transmitted via a secured inter-hospital virtual private network to a central reading center, where they were analyzed using the RetCam review station software by two independent masked ophthalmologists who were ROP experts (DO, RS). Results were sent by secured email to the clinician on the same day.

Severity of ROP disease was determined using the International Classification of ROP,[14] which is based upon the zone and stage of ROP and the presence of plus disease. Following review of the images, each independent reviewer classified the images as showing: no ROP, mild ROP, ROP type 1, ROP type 2, aggressive posterior ROP, threshold ROP, or stage 4a-4 b ROP. Image quality was also recorded according to the following definitions: *excellent*, good clarity/focus (an image that allows for detection of form and extension of blood vessels, and which has sufficient resolution to detect the stage) and vascularization into zone III; *good*, good clarity/focus and complete view of zone II; *sufficient*, good clarity/focus, and good, but not complete, view of zone II; *fair*, sufficient clarity/focus and/or adequate, but not completely clear, view of zone II; *poor*, insufficient clarity/focus, and/or zone I view or unclear zone II view; and *noninterpretable*, insufficient clarity or focus to interpret the zone or stage. Patients with noninterpretable images had a new set of images within 72 hours and, if the quality remained deficient, an ophthalmologist examined the patient.

Patients who met the treatment criteria according to currently accepted recommendations (type 1 ROP or threshold ROP) or in whom there was a question regarding possible treatment were referred for further evaluation by a pediatric ophthalmologist or retina specialist.

Results

This study included 2,048 eyes of 1,024 premature infants. Mean gestational age was 28.8 ± 2.2 (standard deviation) weeks; mean birth weight was 1128 ± 279 g. All imaging examinations were initiated 4-6 weeks after delivery. The average number of examinations per patient was 2.6 ± 2.5. In total, 5,263 telemedicine examinations were recorded (Table 1). Of these, 4903/5263 (93%) were graded as good or excellent quality, covering at least zone II completely. Evaluation of ROP disease was possible in 5,172 images (98%). The classification of ROP and clinical characteristics of patients are presented in Table 2.

Of the 1,024 infants screened, 42 (4%) were referred for ROP treatment following analysis of the ROP disease

Table 1. ROP imaging quality classification

Classification	Examinations, no. (%)
Excellent	1038 (19.7)
Good	3865 (73.4)
Sufficient	269 (5.1)
Fair	46 (0.9)
Poor	6 (0.1)
Noninterpretable	39 (0.7)

severity in the reviewed images. Almost all of these patients were treated, except for one infant whose disease was recorded as ROP type 1 based on images but was classified as ROP type 2 on clinical examination. This infant was followed with imaging, and no further treatment was required. All patients with regressed ROP type 2 were followed with telemedicine until complete regression; afterward they were followed by local ophthalmologists. To our knowledge, none of these patients presented with any complications or adverse effects during the 6 months' follow-up.

Discussion

This study demonstrates that telemedicine can be used for ROP screening and guiding treatment when needed, providing eye care for premature infants in areas where local eye examinations are not feasible.[15-20] The Stanford University Network for Diagnosis of Retinopathy of Prematurity (SUNDROP) study reported that 3.6% of examined premature infants required treatment,[16] which is similar to our treatment rate of 4%. Our study included 11 centers across Chile, which represents 39% of all nationwide neonatal intensive care units. The Chilean government supported and funded the program to enhance ROP screening and achieve universal and stable coverage.

Our telemedicine approach differs from other networks using referral-warranted ROP criteria. In our system, all screening and evaluations were performed by telemedicine, whereas in referral-warranted ROP-based networks, a combination of imaging and regular examination of children with more advanced disease is implemented. For example, in our system, an infant with ROP stage 3 in zone II and no plus disease would continue to be followed by imaging every week rather than being sent for a regular eye examination thereafter. We only examined children by indirect ophthalmoscopy before providing treatment to confirm that treatment is required based on the ROP classification. Our agreement rate of 98% between imaging and clinical judgment of treatment requirement is remarkable. In addition, it was determined that in the 1 child who was not treated, the clinical evaluation determined that the ROP disease was less severe than initially considered based on the image review.

To our knowledge this technology has not been used previously to guide ROP screening and treatment in a national system.[21] This methodology using digital retinal images