Colorado retinopathy of prematurity model: a multi-institutional validation study

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PURPOSE The Colorado retinopathy of prematurity (ROP) prediction model (CO-ROP), developed using a cohort of infants from Colorado, calls for ROP examination of infants meeting all of the following criteria: gestational age of ≤30 weeks, birth weight of ≤1500 g, and a net weight gain of ≤650 g between birth and 4 weeks of age. The purpose of this study was to perform an external validation to assess the sensitivity and specificity of the CO-ROP model in a larger cohort of babies screened for ROP from four academic institutions in the United States.

METHODS The medical records of neonates screened for ROP according current national guidelines was conducted at 4 US academic centers were retrospectively reviewed. Sensitivity, specificity, and respective 95% confidence intervals in detecting ROP using CO-ROP were calculated for type 1, type 2, and any grade of ROP.

RESULTS A total of 858 cases were included. The CO-ROP algorithm had a sensitivity of 98.1% (95% CI, 93.3%-99.8%) for type 1 ROP, 95.6% (95% CI 78.0-99.9%) for type 2 ROP, and 95.0% (95% CI, 93.1-97.4%) for all grades of ROP. The CO-ROP model would have reduced the total number of infants screened by 23.9% compared to current 2013 screening guidelines.

CONCLUSIONS CO-ROP demonstrated high sensitivity in predicting ROP and would have greatly reduced the number of infants needing examination. (J AAPOS 2016;20:220-225)

Retinopathy of prematurity (ROP) is an adverse complication of preterm birth that is characterized by abnormal vascularization of the immature retina.[1] It is the most common preventable cause of blindness in the developed world and the third leading cause of blindness in children.[2] The Multicenter Trial of Cryotherapy for Retinopathy of Prematurity (CRYO-ROP) and Early Treatment for Retinopathy of Prematurity (ETROP) studies demonstrated a reduction of unfavorable anatomical and visual outcomes through timely detection and treatment of infants with severe ROP.[3,4] Current (January 2013) United States screening guidelines recommend ROP examinations under the following conditions: "infants with a birth weight of ≤1500 g, infants with a gestational age 30 weeks or less (as defined by the attending neonatologist), and select infants with a birth weight between 1500 and 2000g or gestational age of >30 weeks with an unstable clinical course, including those requiring cardiorespiratory support and who are believed by their attending pediatrician or neonatologist to be at high risk for ROP."[5] While this screening algorithm is very sensitive, <10% of the total number of infants identified for examinations eventually require treatment for ROP.[6-8]

Several investigators have proposed alternative models for screening babies at risk for ROP, with the goal of improving efficiency and reducing the number of infants requiring stressful and costly ROP examinations.[6,8,9] The Colorado ROP model (CO-ROP)[10] is a novel ROP screening model designed to maintain high sensitivity for all cases of ROP while reducing the number of

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examinations performed for low-risk infants. The Colorado model calls for ROP examination in an infant meeting all of the following criteria: gestational age of ≤30 weeks, birth weight of ≤1500 g, and a net weight gain of ≤650 g between birth and 4 weeks of age.[10] Using these three simple objective criteria, CO-ROP aims to reduce the number of examinations. The purpose of the present study was to validate the model and to assess its sensitivity and specificity of CO-ROP in a larger and more demographically diverse population than that in which the model was first tested.

Subjects and Methods

The records of infants included in the analytic dataset were screened for ROP at the following 4 institutions: University of California–Los Angeles (institution A), University of California–San Diego (institution B), Baylor College of Medicine (institution C), and Vanderbilt University (institution D). This multicenter study was approved by the Colorado Multiple Institutional Review Board (COMIRB). Each contributing institution also obtained local institutional review board approval.

ROP was graded using the International Classification of ROP criteria.[11] For the purposes of this study, the maximum grade of ROP was defined as the highest stage and lowest zone of ROP noted in the worse eye during any ROP examination. Patients with type 1 ROP (stage 1 or 2 ROP in zone I with plus disease, stage 3 ROP zone I with or without plus disease, or stage 2 or 3 ROP in zone II with plus disease) were treated in accordance with recommendations from the Early Treatment of Retinopathy of Prematurity Randomized Trial (ETROP).[4] Type 2 ROP was also defined according to ETROP criteria: stage 1 or 2 ROP in zone I without plus, or stage 3 ROP in zone II.[4] For the purposes of this study, infants who develop type 1 or type 2 ROP were grouped as "high grade" ROP. All infants who developed ROP that did not meet type 1 or type 2 criteria were grouped as "low grade" ROP.

Data Collection

The medical records of neonates screened for ROP at each of the 4 institutions were reviewed retrospectively. Data collected included sex, gestational age, birth weight, ROP outcome (stage, zone, presence of plus disease), and weight at 1 month of age (defined as chronological 28th day of life). Gestational age was conservatively estimated by rounding down to the nearest week. For example, an infant born at 30 weeks and 6 days was counted as 30 weeks gestational age.

Eligible subjects included in the study were consecutive neonates screened for ROP at each individual institution using current (January 2013) national guidelines (all neonates with birth weight of ≤1500 g or gestational age of ≤30 weeks; or select infants with a birth weight of 1500–2000 g or gestational age of >30 weeks).[5] To be included, each infant had to meet 2013 screening guidelines, have a known weight on chronologic day of life 28, and have a known ROP outcome. Infants who did not meet all three criteria were excluded.

The records of this cohort of infants were reviewed with respect to CO-ROP criteria: gestational age of ≤30 weeks, birth weight of ≤1500 g, and a net weight gain of ≤650 g between birth and 4 weeks of age.[10]

Statistical Analysis

Demographic information across groups was compared using χ^2 tests for categorical variables and Kruskall-Wallis for continuous variables. CO-ROP was assessed by calculating sensitivities and specificities for detection of high grade ROP, low grade, and overall ROP.[12] Corresponding 95% confidence intervals were calculated using exact Clopper-Pearson confidence limits for binomial proportions. Statistical analysis was performed using SAS version 9.4 software (SAS Institute Inc, Cary, NC, 2013).

Results

A total of 858 infants were included in the analysis. Of these, 83 (9.7%) developed type 1 ROP, 23 (2.7%) developed type 2 ROP, 135 (15.7%) developed low-grade ROP, and 617 (71.9%) did not develop any ROP. The median net weight gain at 1 month of age across all institutions was 220 g (range, −70 to 860 g) for high-grade ROP (type 1 and 2), 265 g (range, −135 to 805 g) for low-grade ROP, and 416 g (range, −30 to 987 g) for infants who did not develop ROP ($P < 0.01$). Baseline demographics for each cohort appear in Table 1. There were no statistically significant differences in the birth weight and gestational age across the 4 institutions. There were differences in net weight gain at 1 month of age and distribution of ROP severity among the 4 institutions. Institution A had a higher rate of ROP, which could likely be explained by the lower net weight gain.

The CO-ROP model signaled an alarm in 653 (76.1%) infants who were otherwise screened using current national guidelines as being at risk for ROP (Table 2). The CO-ROP algorithm had a sensitivity of 98.8% (95% CI, 93.5%-100%) for type 1 ROP, 95.7% (95% CI, 78.1%-99.9%) for type 2 ROP, and 95.0% (95% CI, 91.5%-97.4%) for all grades of ROP (Table 3). Similar sensitivities were observed across all 4 institutions. The CO-ROP model would have reduced the total number of infants screened with no ROP by 31.3% compared to current 2013 screening guidelines.

The 23% of infants who were deemed low risk after applying the CO-ROP model had a mean birth weight of 1443 g, gestational age of 30.6 weeks, and net weight gain of 520 g between birth and 1 month of age. Using the CO-ROP model, 1 infant with type 1 ROP, 1 with type 2 ROP, and 10 infants with low-grade ROP were missed compared to current guidelines (Table 4). Applying the CO-ROP model would have reduced the overall number of infants being examined by 23.9% ROP screening examinations based on current ROP screening recommendations.