Comparison between weight gain and Fenton preterm growth z scores in assessing the risk of retinopathy of prematurity

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Several studies have shown that postnatal weight gain is a significant predictor for retinopathy of prematurity (ROP) in preterm infants. Using a cohort of 1,301 infants from a single-center ROP registry, we investigated whether incorporation of changes in Fenton preterm growth curve *z* scores (ie, deviation from the population average) provides improved predictive ability for developing ROP compared to weight gain alone. Three logistic regressions were fit to severe ROP: (1) baseline model that included gestational age and birth weight, (2) the baseline model adding weight gain, and (3) the baseline model adding change in *z* score. The area under the receiver operating characteristic curve (C index) was used to compare models. Both weight gain and change in *z* scores were significant predictors after adjusting for birth weight ($P = 0.01$) and gestational age ($P < 0.01$). The C indices were not significantly improved by including weight gain or *z* score to the baseline model; however, for a subset of subjects, change in weight *z* score may be a more useful measure compared to simple weight gain with regards to assessing risk for severe ROP.

Retinopathy of prematurity (ROP) is a leading cause of preventable childhood blindness. Risk factors for the development of ROP include early gestational age, very low birth weight, and fluctuating or high levels of oxygen concentrations in the neonatal period.[1] Several investigators have recently included postnatal weight gain into predictive models for ROP.[2-6] However, this additional criterion may vary for infants with different birth weights; an infant with a lower birth weight may not need to gain as much weight to reduce risk of ROP compared to an infant with a higher birth weight. Clinically, the inability to maintain growth velocity, or failure to thrive, is defined using growth charts and is a valuable marker of the health of an infant in the first weeks of life. *Z* scores calculated from growth charts are the number of standard deviations from the population average; a *z* score of 0 indicates an infant's weight is average for their gestational age and sex. A consistently negative *z* score over time would indicate a smaller-than-average infant who is maintaining their anticipated growth velocity, whereas an infant with a decreasing *z* score over time would indicate an inability to maintain growth velocity. The Fenton Preterm Growth Chart provides *z* score estimates that serve as a useful measure of a preterm infant's growth trajectory based on gestational age and birth weight.[7] In this study we examine whether incorporation of changes in growth curve *z* scores provides improved predictive ability for developing severe ROP (type 1 or type 2 ROP) compared to weight gain alone.

Subjects and Methods

This study was approved by the Colorado Multiple Institutional Review Board. The medical records of patients in an ROP registry (January 2006 through December 2017) developed by the Department of Ophthalmology at the University of Colorado School of Medicine and described in detail elsewhere[8,9] were reviewed retrospectively. The registry includes infants who fulfilled the 2013 screening criteria for ROP[1] and survived to the time of the first ROP examination. Weight information was collected on all infants at birth and at 4 weeks. *Z* scores were calculated based on gestational age and birth weight using the Fenton Preterm Growth Chart.[7] The main outcome of the study was the development of severe ROP defined as type 1 or type 2 ROP.[10]

Statistical Analysis

Pearson correlations were used to assess associations. Shape of the associations between the continuous predictors and the ROP outcome were examined graphically with LOESS curves. Three logistic regression models were fit: (1) baseline model that included gestational age and weight, (2) the baseline model adding weight gain, and (3) the baseline model adding change in *z* score. Based on the graphical inspection of the associations, piecewise linear associations were included, with breakpoints at 30 weeks for gestational age, 1000 g for birth weight, 400g for weight gain and −0.05 for change in *z* score (eSupplement 1, available at jaapos.org). Area under the receiver operating characteristic curve (C index) and predicted probabilities were used to compare models. All analyses were performed using SAS software (version 9.4, SAS Institute Inc, Cary, NC).

Results

A cohort of 1,301 infants was used for the analysis (Table 1). Weight gain was significantly lower in those who developed ROP (mean with standard deviation,

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Table 1. Patient characteristics of ROP cohort

Risk factors N (%) or mean (SD)	Results[a] (N = 1,301 infants)
GA at birth, weeks	28.7 ± 2.4
BW, g	1119 ± 348
BW *z* score	−0.22 ± 0.95
Male sex	670 (52)
Baby Race	
White	893 (69)
African American	160 (12)
Other	248 (19)
Hispanic	447 (34)
Singleton	963 (74)
Severe ROP	132 (10)

BW, birth weight; *GA*, gestational age; *ROP*, retinopathy of prematurity; *SD*, standard deviation.
[a]Mean ± SD or result (%).

237 ± 104 g) versus those without ROP (448 ± 178 g). See eSupplement 2, available at jaapos.org). The majority of infants had a decreasing weight *z* score (96% [n = 1,249]) ranging between −2.8 and −0.01. Weight gain was positively correlated with both birth weight ($r = 0.63$; $P < 0.01$) and gestational age at birth ($r = 0.68$; $P < 0.01$). Infants with higher birth weights tended to have larger drops in z-scores ($r = -0.20$; $P < 0.01$) See eSupplement 3, available at jaapos.org.

Both weight gain and change in *z* score were significant after adjusting for birth weight ($P = 0.01$) and gestational age ($P < 0.01$). The C index was highest in the model with change in *z* score (C index: 0.920; $P = 0.09$ compared to baseline model), the model including weight gain also had improved predictive ability (C index of 0.919; $P = 0.14$). See Figure 1. Neither the addition of weight gain or change in *z* score significantly improved the overall predictive ability from the baseline model.

Improvement in prediction at the subject level is defined as a higher probability for ROP cases and a lower probability for subjects without ROP. Compared to the baseline model, improvement was observed in 64% of infants after adding weight gain and in 68% by adding change in *z* score. For infants with low birthweight (<550 g) and high birthweight (>1,000 g), the model with change in *z* scores provided higher predicted probabilities for infants who developed ROP compared to the other two models (see eSupplement 4, available at jaapos.org).

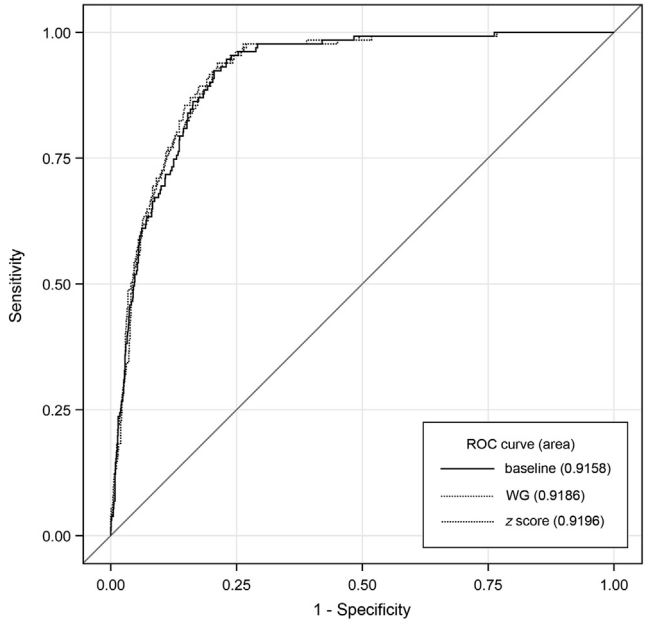

FIG 1. ROC curves for each of the three logistic regression models for severe retinopathy of prematurity (ROP). The three models included are (1) baseline model that included gestational age and weight, (2) a model including weight gain and (3) a model including change in z-score. The area under the ROC curve (c-index) is compared across the three models. The model that included change in *z* score has the highest c-index but all three models have very similar and overlapping curves.

Discussion

Several studies have evaluated postnatal weight gain as a predictor for ROP.[2-6] This is the first to evaluate changes in *z* scores using the Fenton preterm growth curve to predict ROP. We found that for the majority of infants, the baseline model (including gestational age and birth weight) provided predictions that were not significantly improved by adding weight gain or change in *z* scores. For the subset of infants who developed ROP, the predicted probabilities from the model that included *z* scores were higher than the probabilities from the other two models when birth weight was <550 g or >1000 g. The high correlation between weight gain with birth weight and gestational age makes the inclusion of weight gain less likely to contribute independent information toward predicting ROP. The *z* score calculation, however, is adjusted for gestational age and birth weight and therefore contains information that is independent from the baseline risk factors.

Change in weight *z* score may be a more useful measure of growth failure compared to simple weight gain with regard to assessing risk for ROP. We believe understanding inadequate growth during the neonatal period facilitated by a clinically relevant growth chart may improve classification for developing ROP and can eventually help create better intervention strategies.

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Older age and larger cyst size in children with spontaneous rupture of periorbital dermoid cysts

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We analyzed clinical and histopathologic data of 97 pediatric patients who underwent excision of dermoid cysts. On review, 16.5% of the sample population demonstrated localized chronic inflammatory changes, including the presence of giant cells and epithelial disruption. These features were considered indicative of prior cyst rupture. Age at time of initial presentation was significantly older and cyst size was significantly larger in patients with histopathologic signs of previous rupture. Longer time to presentation and time to excision were associated with increased odds of spontaneous rupture.

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Periorbital dermoid cysts are lesions commonly seen in pediatric ophthalmology. The congenital lesions are typically benign, grow slowly, and are asymptomatic. The cysts possess a keratinizing, stratified squamous epithelial lining with dermal structures in their wall. Frequently they are located in the supratemporal quadrant along the orbital rim.[1] There is no universally accepted algorithm for management of these lesions, which are often either observed or surgically removed for cosmetic reasons. Surgery is also performed to avoid the potential for persistent inflammation that can be associated with spontaneous cyst rupture.[2] Spontaneous cyst rupture can be thought of as clinically evident, histopathologically evident, or both. Generally, clinically evident rupture is found in older patients with deep, complex cysts and associated with pain; histologically evident cyst rupture, however, may be clinically silent, but evidence of localized inflammation may be seen on histopathologic review. Previous studies have demonstrated the relationship between chronic granulomatous inflammation and epithelial disruption on histology with cyst rupture.[3] The aim of the current study was to find relationships between patient and dermoid characteristics and histopathologic signs of prior cyst rupture.

Subjects and Methods

This study was approved by the Boston Children's HospitalInstitutional Review Board and complies with the requirements of the US Health Insurance Portability and Accountability Act of 1996. The medical records of consecutive patients with pathologically confirmed periorbital dermoid cysts who underwent excisional surgery between 2005 and 2015 at Boston Children's Hospital were reviewed retrospectively. Cysts that were ruptured during excision, as noted in the operative report, were excluded. The cysts evaluated in our study were all periorbital and did not have extension into the orbit or orbital bones. Patients with with incomplete data were also excluded. Our primary dependent variable of interest was histopathologic evidence of prior cyst rupture, including disruption of the epithelial cell layer and presence of chronic inflammatory changes in the cyst wall from a single representative pathologic slide section. Independent variables included patient age at presentation, patient age at the time of surgical removal, sex and race, size (calculated as the square area from the pathology gross specimen report) and location of the dermoid, history of dermoid size fluctuation, history of trauma, and presence of pain. For data analysis, we dichotomized the self-reported race variable into patients who self-reported their race as white versus all others; we dichotomized the