A Pulmonary Score for Assessing the Severity of Neonatal Chronic Lung Disease

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ABSTRACT. Background. Limited data are available to describe the spectrum of severity of neonatal chronic lung disease. In the multicenter Supplemental Therapeutic Oxygen for Prethreshold Retinopathy of Prematurity trial, all infants had some degree of pulmonary dysfunction, because eligibility required a median oxygen saturation of ≤94% with room air. Infants randomized to the supplemental oxygen group (oxygen saturation target of 96–99%) had more pulmonary morbidity than did those in the conventional group (oxygen saturation target of 88–94%). This prompted the retrospective development of a pulmonary severity score to compare the baseline status of the 2 groups.

Objectives. To describe a pulmonary score that reflects the severity of neonatal lung disease and to evaluate the association of the score and its components with subsequent pulmonary morbidity through 3 months of corrected age.

Design and Methods. A pulmonary score was developed empirically by a consensus panel of 3 neonatologists and was defined as the fraction of inspired oxygen ($F_{IO2}$) × (support) + (medications), where $F_{IO2}$ is the actual or “effective” (for nasal cannula) $F_{IO2}$ support is 2.5 for a ventilator, 1.5 for nasal continuous positive airway pressure, or 1.0 for nasal cannula or hood oxygen; and medications is 0.20 for systemic steroids for bronchopulmonary dysplasia, 0.10 each for regular diuretics or inhaled steroids, and 0.05 each for methylxanthines or intermittent diuretics. The scores could range from 0.21 to 2.95. Pulmonary morbidity was defined as any of the following occurring from randomization at a mean of 35.4 weeks’ postmenstrual age through 3 months of corrected age: death or rehospitalization with a pulmonary cause; an episode of pneumonia/sepsis/exacerbation of chronic lung disease; or continued hospitalization, supplemental oxygen therapy, diuretic treatment, or systemic steroid therapy at 3 months. Between-group differences were tested with the Kruskal-Wallis or χ² test.

Results. Data through death or the 3-month corrected age examination were available for 588 infants. Enrolled infants represented a wide spectrum of severity of chronic lung disease, with baseline pulmonary scores at randomization ranging from 0.21 to 2.6. The median pulmonary score at enrollment did not differ between the conventional and supplemental groups (0.42 and 0.45, respectively). However, higher baseline pulmonary scores were observed for infants who did versus did not develop subsequent pulmonary morbidity (0.48 vs 0.38). The pulmonary score was associated with subsequent pulmonary morbidity. Regression analyses adjusting for Supplemental Therapeutic Oxygen for Prethreshold Retinopathy of Prematurity group assignment, gestational age at birth, race, gender, and postmenstrual age at randomization revealed that the score was a significant independent predictor of subsequent pulmonary morbidity (odds ratio: 7.2; 95% confidence interval: 3.6-14.4).

Conclusions. The pulmonary score, calculated near term, reflects a wide spectrum of bronchopulmonary dysplasia severity and is associated with subsequent pulmonary morbidity through corrected age of 3 months. This simple score could prove useful in clinical and research settings. Validation of the score requires additional study.

ABBREVIATIONS. BPD, bronchopulmonary dysplasia; PMA, postmenstrual age; STOP-ROP, Supplemental Therapeutic Oxygen for Prethreshold Retinopathy of Prematurity; CPAP, continuous positive airway pressure; $F_{IO2}$, fraction of inspired oxygen; AIC, Akaike Information Criterion.

Bronchopulmonary dysplasia (BPD) or chronic lung disease is a common and important form of neonatal morbidity that is associated with adverse long-term pulmonary and developmental outcomes.1-3 Since its original description,4 various definitions of BPD have been used clinically and for purposes of research. Definitions include the continued need for oxygen at 28 (or 30) days of age5-8 and a need for supplemental oxygen at 36 weeks’ postmenstrual age (PMA),9 with or without the use of respiratory support and with or without characteristic radiographic changes at 36 weeks’ PMA.10 These “present or absent” definitions, however, do not account for the broad spectrum of BPD severity among infants who require supplemental oxygen at 28 days of life (or at 36 weeks’ PMA). Recently, Falta et al11,12 described a BPD severity score that included radiographic data and was predictive of 5-year pulmonary...
outcomes. We found no other published data that described the severity of BPD quantitatively and correlated the results with subsequent pulmonary morbidity. A description of BPD that reflects clinical severity could be useful for both clinical and research purposes.

Analysis of the data from the Supplemental Therapeutic Oxygen for Prethreshold Retinopathy of Prematurity (STOP-ROP) trial showed that infants randomized to the supplemental group (oxygen saturation targets of 96–99%) had more subsequent pulmonary morbidity than did those in the conventional group (oxygen saturation targets of 88–94%). This prompted the retrospective development of a pulmonary severity score to compare the baseline status of the 2 groups. The purpose of this report is to describe that score and to evaluate its association with subsequent pulmonary morbidity through 3 months of corrected age.

METHODS

Patient Population and Database
Entry criteria for the STOP-ROP study required the diagnosis of prethreshold ROP in at least 1 eye, a median pulse oximetry value of ≤94% breathing room air, and informed consent of the family/guardian. A total of 649 infants were enrolled in the STOP-ROP trial from 1994 through 1999 (324 in the supplemental group and 325 in the conventional group). The baseline characteristics (mean ± SD) of the 2 groups were similar in birth weight (726 ± 160 g), gestational age (25.4 ± 1.5 weeks), PMA (35.4 ± 2.5 weeks), weight at randomization (1547 ± 443 g), and race (55% white), although there were more male subjects in the supplemental group. Infants were examined weekly until either theirROP resolved or they progressed to threshold ROP disease. Surviving infants were evaluated again at 3 months after their due date (50–56 weeks' PMA). In addition to ophthalmic evaluations, interval medical histories were obtained from the caregivers. Data were collected on respiratory support (fraction of inspired oxygen [FiO2]), nasal cannula, continuous positive airway pressure (CPAP), and mechanical ventilation), medications, subsequent adverse pulmonary events, rehospitalizations, and death. Infants were included in the current analysis if complete data were available through the 3-month examination at ≤50 weeks or if they died before the 3-month examination.

Pulmonary Score
The pulmonary score was developed to evaluate the baseline pulmonary status of the 2 STOP-ROP study groups at the time of randomization (mean age: 35.7 weeks' PMA for all enrollees). It was developed by 3 neonatologists and was limited to the descriptors of respiratory support prospectively collected during the study (radiographic findings were not collected). These descriptors included the use of medications during the week preceding randomization (methylxanthines, systemic or inhaled steroids, or diuretics), the amount of supplemental oxygen, and the type of ventilatory support. These database items were selected because they were related to the severity of pulmonary disease. The relative weight (numeric value) for each item was decided through clinical consensus of the neonatologists. Greater weight was given to the therapeutic interventions that involved more nursing care and costs to administer and reflected a greater degree of respiratory disease. The pulmonary score was calculated as pulmonary score = \( \text{FiO}_2 \times \text{support} + \text{medications} \), where \( \text{FiO}_2 \) is expressed as the fraction (eg, room air: 0.21) if a ventilator, CPAP, or hood is used or as “effective \( \text{FiO}_2 \)” if a nasal cannula if used; support is 2.5 for ventilator, 1.5 for nasal or endotracheal CPAP, or 1.0 for nasal cannula flow (even if room air), hood oxygen, or no oxygen, and medications is a sum of weights, namely, 0.20 for systemic steroids given for treatment of BPD, 0.10 each for regular diuretics or inhaled steroids, and 0.05 each for methylxanthines or intermittent diuretics. Infants with a tracheostomy were scored as if using a ventilator. Use of medications was determined for the week preceding the calculation of the pulmonary score. If systemic steroids (or inhaled steroids) were used at any time during that week, the child was considered to be receiving the drug. If diuretics were given regularly each day or every other day, administration was ranked as regular. If they were given less often than every other day, they were considered intermittent; this included even a single dose of diuretics during the week period before the calculation of the score. Effective \( \text{FiO}_2 \) was calculated with a pair of tables developed from the equation described by Benaron and Benitz, which are presented in Appendix 1. Therefore, the continuous pulmonary score could have a range of values between 0.21 (no pulmonary support, no oxygen, and no medications) and 2.95. Examples are provided in Appendix 1. Other models/scores were also considered (available from the authors on request).

Pulmonary Morbidity
To judge the merit of the pulmonary score, its composite value was tested to determine whether it was associated systematically with subsequent pulmonary morbidity. Pulmonary morbidity was defined as any one of the following events from the time of randomization through the last follow-up visit at the 3-month examination: (1) death from a pulmonary cause, (2) pneumonia/sepsis with a positive blood culture or requiring antibiotics for >5 days, (3) probable/definite pneumonia or exacerbation of BPD, (4) rehospitalization for a pulmonary cause, (5) continued hospitalization at 3 months, or (6) continued use of oxygen, diuretics, or systemic steroids at the 3-month examination. Alternative definitions of pulmonary morbidity were not analyzed.

Data Analyses and Statistical Considerations
The differences in baseline pulmonary severity values between groups were tested with the Kruskal-Wallis test, whereas differences between groups with respect to the proportion of infants with any pulmonary morbidity were assessed with the \( \chi^2 \) test. The ability of the score and other STOP-ROP study variables to predict pulmonary morbidity was determined with logistic regression. The association of the score and its components with subsequent pulmonary morbidity was compared with 2 performance criteria, ie, area under the receiver operating characteristic curve (the c statistic) and the Akaike Information Criterion (AIC), as discussed below. All calculations were conducted with SAS software, version 8.2 (SAS Institute, Cary, NC).

RESULTS

Population
Five hundred eighty-eight of 649 infants enrolled in the STOP-ROP trial (90.6%) had complete data through death or the 3-month corrected age examination and were included in the current analysis. Data for the remaining 61 were excluded because of incomplete follow-up data (Fig 1). The included infants had a mean gestation of 25.9 weeks at birth and a mean birth weight of 727 g. At the time of enrollment and randomization, they had reached a mean PMA of 35.4 weeks (Table 1). Subsequently, 319 of 588 infants (54%) experienced at least 1 pulmonary morbidity. Table 1 also shows patient characteristics for infants who either did or did not experience subsequent pulmonary morbidity. Infants who had a subsequent pulmonary morbidity were slightly older at enrollment and were more often male and black. As might be anticipated, they were more likely to be using systemic steroids, diuretics, or a ventilator at enrollment and the baseline \( \text{FiO}_2 \) was higher among those who developed a new pulmonary morbidity subsequently.

Pulmonary Score
Baseline pulmonary scores were calculated for each of the 588 infants and ranged from 0.21 to 2.60,
with a median value of 0.43. Among the 61 excluded infants, the baseline pulmonary scores ranged from 0.21 to 1.98, with a median of 0.37. Figure 2 shows the distribution of pulmonary scores, which was skewed toward milder disease. The distributions are shown separately for those who did and did not develop a subsequent pulmonary morbidity. The values were higher (median: 0.48; range: 0.21–2.6) for those who did develop a morbidity, compared with those who did not (median: 0.38; range: 0.21–1.9; \( P < .0001 \), Kruskal-Wallis test).

We next examined the association of the score with individual pulmonary morbidities through 3 months of corrected age. Table 2 shows the median (and range) of baseline pulmonary scores for infants with or without each pulmonary morbidity. Baseline pulmonary scores were significantly higher for infants who experienced each subsequent pulmonary morbidity. The median baseline pulmonary score was highest for infants who at 3 months were receiving systemic steroid treatment (0.72) or remained hospitalized (0.67). However, infants who had been discharged from the hospital by 3 months of age and who were no longer receiving medications or supplemental oxygen had lower baseline scores (median: 0.38).

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**TABLE 1.** Enrollment Characteristics of the Population According to Subsequent Occurrence of Pulmonary Morbidity Through the 3-Month Examination

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Pulmonary Morbidity Through the 3-Month Examination</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No (n = 269)</td>
</tr>
<tr>
<td><strong>At birth</strong></td>
<td></td>
</tr>
<tr>
<td>Birth weight, g*</td>
<td>734 ± 153</td>
</tr>
<tr>
<td>Gestational age at birth, wk*</td>
<td>25.9 ± 1.6</td>
</tr>
<tr>
<td>Male, %</td>
<td>55</td>
</tr>
<tr>
<td>Black, %</td>
<td>29</td>
</tr>
<tr>
<td><strong>At enrollment</strong></td>
<td></td>
</tr>
<tr>
<td>PMA, wk*</td>
<td>34.6 ± 2.1</td>
</tr>
<tr>
<td>Ventilator, %</td>
<td>13</td>
</tr>
<tr>
<td>CPAP, %</td>
<td>12</td>
</tr>
<tr>
<td>Fio(_2) for ventilator/oxyhood/CPAP/tracheostomy*</td>
<td>0.49 ± 0.18 (n = 85)</td>
</tr>
<tr>
<td>Effective Fio(_2) for nasal cannula*</td>
<td>0.26 ± 0.08 (n = 170)</td>
</tr>
<tr>
<td>Steroids, %†</td>
<td>25 (n = 240)</td>
</tr>
<tr>
<td>Intermittent or regular diuretics, %</td>
<td>45</td>
</tr>
<tr>
<td>Methylxanthines, %</td>
<td>77</td>
</tr>
</tbody>
</table>

* Mean ± SD.
† Data on baseline steroid status were not available for 65 infants, because steroid use was not recorded during the early months of enrollment.
Pulmonary Scores in the STOP-ROP Study

Because the score proved to be related positively to subsequent pulmonary morbidity, we thought it had face value. We therefore used it to examine the possible differences in baseline pulmonary status for the STOP-ROP study groups. As reported previously, infants in the STOP-ROP study experienced different postrandomization rates of pulmonary morbidity depending on their treatment assignment. At enrollment, the median baseline pulmonary scores were similar for the conventional (0.42) and supplemental (0.45) groups (\( P = .12, \) Kruskal-Wallis test). We were also able to examine the baseline pulmonary scores for the study groups over time, and they did not change during the 5-year period of the STOP-ROP study enrollment (data not shown).

Despite the similarity in baseline scores, however, a higher incidence of pulmonary morbidity was seen for the supplemental group (\( P = .004, \chi^2 \) test). We were also able to examine the baseline pulmonary scores for the study groups over time, and they did not change during the 5-year period of the STOP-ROP study enrollment (data not shown).

Despite the similarity in baseline scores, however, a higher incidence of pulmonary morbidity was seen for the supplemental group (\( P < .0004, \chi^2 \) test). Table 3 examines the relationship between baseline pulmonary scores and the subsequent rates of pulmonary morbidity, according to assigned study group. With the exception of the lowest quartile of scores, the supplemental group had a greater proportion of infants who developed pulmonary morbidity in each quartile, compared with the conventional group. Figure 3 shows the cumulative rates of pulmonary morbidity according to the increasing severity of baseline pulmonary scores in both study groups. As the pulmonary severity score increased to \( \geq 0.50 \), the rates of pulmonary morbidity increased more steeply in the supplemental oxygen group.

Alternative Pulmonary Scores

An effective score should have predictive power for subsequent morbidity but should also be as simple as possible to use. In Table 4, we investigated whether the ability of the pulmonary score to predict pulmonary morbidity could be improved by using various combinations of the components of the score, i.e., \( \text{FiO}_2 \), support, and medications. We considered 2 criteria for judging the predictive power of these combinations. The \( c \) statistic is the area under the receiver operating curve and can range from 0.5 to 1.0, with large values being desirable. The AIC is a popular method for comparing models fitted through maximal likelihood; it penalizes the likelihood for the number of estimated parameters. Small values of AIC are desirable. As shown in Table 4, these performance criteria (\( c \) and AIC) agreed that the best of the models tested was the weighted combination of just \( \text{FiO}_2 \) and medications (without support). However, this model is only a minor improvement over the composite pulmonary score reported in the first line of Table 4. Perhaps the lack of additional predictive power of the ventilatory support component in this population is related to the small number of infants who were receiving mechanical ventilation at study enrollment (94 of 588 subjects, 16%). The total predictive power of the score was similar with or without the ventilatory component included.

We also used a multivariate logistic regression to determine how well the score would predict subsequent pulmonary morbidity. The regression model included the pulmonary score, STOP-ROP study treatment assignment, gestational age at birth, race, gender, and PMA at randomization. The pulmonary score predicted subsequent morbidity (odds ratio: 7.2; 95% confidence interval: 3.6–14.4; \( P < .0001 \)). Therefore, after controlling for the other covariates,

### Table 2: Relationship Between Pulmonary Score and Pulmonary Morbidities Occurring by the 3-Month Follow-Up Examination

<table>
<thead>
<tr>
<th>Individual Pulmonary Morbidities</th>
<th>Score for Infants Who Did Not Experience This Pulmonary Morbidity</th>
<th>Score for Infants Who Experienced This Pulmonary Morbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( N )</td>
<td>Median</td>
</tr>
<tr>
<td>Rehospitalized for pulmonary reasons after discharge*</td>
<td>501</td>
<td>0.42</td>
</tr>
<tr>
<td>BPD exacerbation from randomization to 3 mo†</td>
<td>523</td>
<td>0.42</td>
</tr>
<tr>
<td>At 3-mo examination</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Receiving systemic steroids‡</td>
<td>482</td>
<td>0.42</td>
</tr>
<tr>
<td>Remaining hospitalized‡</td>
<td>528</td>
<td>0.42</td>
</tr>
<tr>
<td>Receiving oxygen†</td>
<td>373</td>
<td>0.39</td>
</tr>
<tr>
<td>Receiving diuretics†</td>
<td>422</td>
<td>0.40</td>
</tr>
</tbody>
</table>

* \( P < .05 \).
† \( P < .0001 \).
‡ \( N = 539 \), i.e., less than 588, because information on steroid use was not collected during the early months of the study.
PM indicates pulmonary morbidity after randomization through the 3-month follow-up examination.

**TABLE 3.** Relationship Between Pulmonary Scores at Enrollment and Pulmonary Morbidity According to Assigned STOP-ROP Randomization Group

<table>
<thead>
<tr>
<th>Pulmonary Score</th>
<th>Conventional Oxygen Group, No. (% with PM)</th>
<th>Supplemental Oxygen Group, No. (% with PM)</th>
<th>All, No. (% with PM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st quartile (0.21–0.32)</td>
<td>79 (47)</td>
<td>63 (41)</td>
<td>142 (44)</td>
</tr>
<tr>
<td>2nd quartile (0.32–0.42)</td>
<td>73 (29)</td>
<td>71 (52)</td>
<td>144 (40)</td>
</tr>
<tr>
<td>3rd quartile (0.42–0.63)</td>
<td>67 (54)</td>
<td>81 (77)</td>
<td>148 (66)</td>
</tr>
<tr>
<td>4th quartile (0.64–2.6)</td>
<td>74 (59)</td>
<td>80 (70)</td>
<td>154 (65)</td>
</tr>
<tr>
<td>All</td>
<td>293 (47)</td>
<td>295 (61)</td>
<td>588 (54)</td>
</tr>
</tbody>
</table>

**TABLE 4.** Performance Characteristics of Some Predictors of Pulmonary Morbidity With Various Components of the Pulmonary Score

<table>
<thead>
<tr>
<th>Model</th>
<th>Performance Criterion</th>
<th>c</th>
<th>AIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha + \beta$ (pulmonary score)</td>
<td>0.62</td>
<td>786</td>
<td></td>
</tr>
<tr>
<td>$\alpha + \beta$ (support)</td>
<td>0.53</td>
<td>811</td>
<td></td>
</tr>
<tr>
<td>$\alpha + \beta$ ($\text{FiO}_2$)</td>
<td>0.60</td>
<td>791</td>
<td></td>
</tr>
<tr>
<td>$\alpha + \beta$ (medications)</td>
<td>0.63</td>
<td>786</td>
<td></td>
</tr>
<tr>
<td>$\alpha + \beta$ ($\text{FiO}_2$)(support)</td>
<td>0.58</td>
<td>797</td>
<td></td>
</tr>
<tr>
<td>$\alpha + \beta$ ($\text{FiO}_2$) + $\gamma$ (support)</td>
<td>0.60</td>
<td>793</td>
<td></td>
</tr>
<tr>
<td>$\alpha + \beta$ ($\text{FiO}_2$) + $\gamma$ (medications)</td>
<td>0.66</td>
<td>773</td>
<td></td>
</tr>
<tr>
<td>$\alpha + \beta$ (support) + $\gamma$ (medications)</td>
<td>0.63</td>
<td>787</td>
<td></td>
</tr>
<tr>
<td>$\alpha + \beta$ ($\text{FiO}_2$)(support) + $\gamma$ (medications)</td>
<td>0.65</td>
<td>778</td>
<td></td>
</tr>
</tbody>
</table>

The components of $\text{FiO}_2$, support, and medications continue to be converted to numbers as described in the text. The coefficients $\alpha$, $\beta$, and $\gamma$ are the coefficients calculated from the logistic regression analyses and weight the components as indicated. c is the area under the receiver operating characteristic curve that depicts the relationship between observed pulmonary morbidity and pulmonary morbidity predicted by the model; large values are desirable. The AIC is for comparisons of linear models and is proportional to the negative log-likelihood plus the number of independent parameters estimated. Small values are desirable. Both measures of performance support the alternate model $\alpha + \beta$ ($\text{FiO}_2$) + $\gamma$ (medications) as most favorable, but it is only marginally better than the first model, $\alpha + \beta$ (pulmonary score), described in this report.

**DISCUSSION**

This study describes a severity score for neonatal chronic lung disease in a cohort of infants who all had BPD by at least 1 definition. The pulmonary score had a strong association with subsequent pulmonary morbidity and proved useful for comparing the baseline severity of BPD in 2 groups of infants at randomization.

Although all infants in the STOP-ROP trial had BPD, infants with higher pulmonary scores who were randomized to the supplemental arm of the STOP-ROP study had a significantly higher rate of subsequent pulmonary morbidity than did those who were randomized to the control arm. The increase in risk for the supplemental group, compared with the conventional group, was not seen among infants with the lowest quartile of pulmonary scores, which suggests that administration of supplemental oxygen at a target of $96\%$ to $99\%$ saturation to infants with pulmonary scores above $-0.5$ was associated with increased pulmonary morbidity at least through 3 months of corrected age.

Other recent studies showed that more supplemental oxygen, administered both early and later in the neonatal course, is associated with more adverse pulmonary outcomes. The study by Askie et al., in which oxygen-dependent infants were randomized at 32 weeks’ PMA to a controlled trial of different supplemental oxygen targets, also demonstrated that infants randomized to the supplemental oxygen group (oxygen saturation of $95–98\%$, compared with $91–94\%$) had a greater incidence of subsequent adverse pulmonary sequelae, with no improvement in growth. Other smaller studies reported beneficial effects of oxygen supplementation on the growth and survival rates for infants with BPD, although none was a randomized trial. In the historical control cohort study by Tin et al., which differed because it involved exposure from birth, extremely low gestational age infants maintained at a lower oxygen saturation ($70–90\%$, in contrast to $88–98\%$) from early in the neonatal course required significantly shorter durations of both supplemental oxygen and artificial ventilation.

Evaluation of various combinations of the components of the reported pulmonary score showed that the simple combination of $\text{FiO}_2$ and medications (quantified with the numerical values used in the
score, as described above) was most highly predictive of subsequent pulmonary morbidity but was only marginally better than the composite pulmonary score developed originally. Other combinations, such as the numerical value for medications only or the ventilator score plus the medications score at the time of STOP-ROP study enrollment, were also reasonably predictive of pulmonary morbidity through 3 months of corrected age. Although the combination without the ventilator component was slightly more predictive than the full model, it is possible that, if the score was used for a cohort with a larger proportion of infants on ventilators, then the ventilator component would contribute more to the effectiveness of the total score. Additional or alternative combinations of the components of the score were not explored in these analyses.

There is growing interest in refining the description or classification of BPD for use as a predictor of pulmonary morbidity or as a pulmonary outcome. The need to differentiate among infants with BPD of varying degrees of severity is driven by concern that older definitions of BPD are less relevant in the current era of neonatal care and do not reflect the variable severity of BPD.8,9,21–28 The definition of BPD used by Shennan et al,9 ie, the need for supplemental oxygen via nasal cannula, but both infants who require ventilator support at 36 weeks’ PMA, is one of the most commonly used BPD definitions in neonatal studies, because of its ease of use and because it was shown to be predictive of subsequent pulmonary morbidity through 3 years of age. However, the relevance of this definition for predicting subsequent morbidity has been questioned for more recent neonatal populations.8,11,28 In addition, the definition of BPD based on the use of supplemental oxygen at 36 weeks’ PMA does not differentiate between infants with varying degrees of severity of BPD.29,30 An infant who requires ventilator support at 36 weeks’ PMA obviously has more severe respiratory disease than an infant who requires only a minimal amount of supplemental oxygen via nasal cannula, but both infants would be classified as having BPD. In a survey of participants in the Vermont Oxford Network, a wide variation was noted among participants with respect to the oxygen saturation criteria applied, as well as other clinical indicators used to initiate or continue use of supplemental oxygen at 36 weeks’ PMA.30 Some of the intercenter variability in BPD may be explained on the basis of the variation in criteria for oxygen supplementation. There is a need for refinement of the “oxygen dependence at 36 weeks” definition of BPD.31

The growing interest in the description or classification of BPD for use as an outcome variable led the National Institute of Child Health and Human Development to develop a severity-based definition of BPD that classifies infants with a continued need for supplemental oxygen at ≥28 days as having mild (no need for oxygen at 36 weeks’ PMA), moderate (treatment with <30% oxygen at 36 weeks’ PMA), or severe (treatment with >30% oxygen and/or positive-pressure ventilation at 36 weeks’ PMA) BPD.29 Infants with severe BPD according to this definition had more adverse pulmonary and neurodevelop-

mental outcomes, which illustrates again the importance of describing the severity of BPD.29 The score proposed by Palta et al11 is effective and validated but is complex to calculate and requires rating of chest radiographs, as does the score proposed by Toce et al.32 Research trials would require a central reading center to score radiographs, and the costs and complexity could preclude its use in many studies.11 Because we did not have radiographic results, we could not compare directly the present score and that developed by Palta et al.11

One limitation of this and other scoring systems is that no system is completely independent of variations in clinical practice (such as the criteria for use of inspired oxygen, CPAP, or medications).30,31 However, the pulmonary score described in this study is a composite score that uses an arithmetic sum of weighted clinical therapies, and it may reflect the spectrum of pulmonary illness in clinical practice better than a scoring system that uses oxygen alone. For example, increasing the use of diuretics or steroids to wean an infant from low-flow oxygen could artificially make the infant appear to have no BPD if the determination of BPD was limited solely to receiving oxygen. A pulmonary score that takes administration of medications into account thus gives a more comprehensive view of the treatments used. Incorporating the use of bronchodilators into the score might have been helpful but the dataset was limited to the medications actually recorded. We had access only to data on the use of methylxanthines. Calculation of the predictive value of the score without methylxanthines but with other medications was not performed.

Both methylxanthines and nasal cannula room air might have been used for apnea as well as for chronic lung disease. High-flow nasal cannula oxygen or room air was used rarely during the STOP-ROP trial; therefore, this score was developed without consideration of its potential use for CPAP. However, in view of the evidence that high-flow nasal cannulae provide effective continuous airway pressure, we anticipate scoring high-flow cannula therapy (≥1.5 L/min) as CPAP in the future.33

A pulmonary severity score is potentially useful in many ways, as a stratification variable, predictor, or outcome measure. It may be used as a stratification variable at the time of randomization or as a case-mixture adjustment or predictor variable for quality-assurance outcomes. The pulmonary severity score might also be used as a quantitative pulmonary outcome measure to describe the spectrum of resultant BPD severity in response to a prevention or treatment modality for BPD and to compare differences in pulmonary outcomes among centers. In this regard, it might be more informative as a quality-assurance outcome when significant differences are observed in BPD versus no-BPD rates. As noted in this study and other studies,11,12,32 a pulmonary score could be used to predict the risk of follow-up pulmonary morbidity. Because the pulmonary score reported here was developed with data for infants in the middle 1990s who had grown to near 35 weeks’ PMA, its use among younger infants as a tool for
stratification or as a predictor of pulmonary morbidity requires additional study.

CONCLUSIONS

The pulmonary score describes a spectrum of severity of neonatal chronic lung disease near term and is related to subsequent pulmonary morbidity through 3 months of corrected age. It is simple to calculate and could prove useful in several settings, such as research, quality assurance projects, and counseling of parents. Validation of this pulmonary score requires subsequent study.

APPENDIX 1

Effective FIO2 Conversion Tables for Infants Receiving Nasal Cannula Treatment

Effective FIO2 is calculated with tables that simplify the use of the equations described by Benaron and Benitz14 (Tables A1 and A2). The infant’s weight and nasal cannula flow are used to determine the conversion factor from Table A1, and then the factor and oxygen concentration are used with Table A2 to determine the effective FIO2. The tables should be reasonably accurate for most STOP-ROP study infants.

An example is a hypothetical neonate weighing 2.5 kg, with a nasal cannula flow of 0.25 L/min and FIO2 of 0.40. With Table A1, weight and flow are found on the 2 borders of the table; where they cross yields a factor of 10. With Table A2, the factor of 10 is crossed with the oxygen concentration of 40% to yield a predicted effective FIO2 of 0.23 (23% oxygen concentration).

Examples of Calculation of the Pulmonary Score

The pulmonary score = (FIO2)(support) + (medications), where FIO2 is expressed as a fraction (room air: 0.21) for ventilator, CPAP, or hood and as effective FIO2 for nasal cannula; support is 2.5 for ventilator or tracheostomy, 1.5 for CPAP (nasal or endotracheal), and 1.0 for nasal cannula, hood oxygen, or no oxygen; and the medications score is 0.20 for systemic steroids for chronic lung disease, 0.10 each for regular diuretics (daily or every other day) or...
inhaled steroids, and 0.05 each for methylxanthines or intermittent diuretics.

In example 1, infant A is a 1200-g infant who was delivered at 28 weeks of gestation, is now at 36 weeks’ PMA, has a diagnosis of BPD, and weighs 2.6 kg. She is currently receiving furosemide once per day, 0.25 L/min of 100% inspired oxygen via nasal cannula, and no other medications. Her effective FiO2 is 0.29 (see above). Her score is as follows: pulmonary score = (0.29)(1.0) + 0.1 = 0.39.

In example 2, infant B is a 1000-g infant who was delivered at 26 weeks of gestation, is now at 36 weeks’ PMA, has BPD, and weighs 1.8 kg. He is delivered at 25 weeks of gestation, is now at 36 weeks’ PMA, has BPD, and weighs 2.2 kg. He is receiving a flow of room air at 2.0 L/min via a nasal cannula and theophylline, and weighs 1.5 kg. He is being treated with a ventilator, receiving 60% oxygen (FiO2 = 0.60), furosemide once per day, and prednisone once per day. Her score is as follows: pulmonary score = (0.60)(2.5) + (0.20 + 0.10) = 1.8.

In example 3, infant C is a 860-g infant who was delivered at 25 weeks of gestation, is now at 36 weeks’ PMA, has BPD, and weighs 2.3 kg. She is currently receiving furosemide once per day. Her score is as follows: pulmonary score = (0.26)(1.0) + (0.05) = 0.26.

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