Bronchiolitis

Clinical Characteristics Associated With Hospitalization and Length of Stay

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Objectives: Bronchiolitis is a leading cause of infant hospitalization in the United States; the mean length of stay (LOS) is 3.3 days. We sought to identify the initial clinical characteristics of bronchiolitis associated with admission and with longer LOS in a large multicenter clinical trial.

Methods: This study was a secondary analysis of a randomized trial conducted in 20 emergency departments in the Pediatric Emergency Care Applied Research Network. We examined age, sex, days of illness, Respiratory Distress Assessment Instrument score, vital signs, and oxygen saturation by pulse oximetry (SpO_2) at presentation in 598 infants aged 2 to 12 months with moderate to severe bronchiolitis. We used classification and regression tree and logistic regression analyses to identify associations with admission and longer LOS (defined as LOS > 1 night).

Results: Of the 598 infants, 240 (40%) were hospitalized; two thirds underwent longer LOS. The best predictor of hospitalization was initial SpO_2 value of less than 94%, followed by Respiratory Distress Assessment Instrument score of greater than 11 and respiratory rate of greater than 60. For this model, the sensitivity was 56% (95% confidence interval, 50%–62%) and the specificity was 74% (95% confidence interval, 70%–79%). Among admitted patients, the only decision point for prediction of longer LOS was initial SpO_2 value of 97% or less.

Conclusions: A model using objective findings had limited accuracy for predicting hospitalization after emergency department evaluation for bronchiolitis. In these infants with moderate to severe bronchiolitis, however, initial SpO_2 was the best predictor of hospital admission and of longer LOS. Efforts to better define and manage hypoxemia in bronchiolitis may be helpful.

Key Words: bronchiolitis, hospitalization, length of stay, projections and predictions, hypoxia

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Bronchiolitis is the leading cause of infant hospitalization in the United States,[1] with nearly 150,000 admissions annually.[2] Hospitalization rates for bronchiolitis among infants more than doubled between 1980 and 1996, and the proportion of hospitalizations due to bronchiolitis more than tripled, from 5% to 16%.[3]

Hospitalization for bronchiolitis is expensive, with US hospital charges alone exceeding $1 billion in 2006.[4] These charges in part reflect length of stay (LOS) in the hospital. The mean LOS for bronchiolitis in the United States is 3.3 days.[2,4] Hospitalization might decrease if infants with bronchiolitis could be treated in short-stay or 24-hour observation units, but patients with bronchiolitis often fail in such settings.[5,6] Many therapies are provided to infants hospitalized with bronchiolitis, but evidence in general does not demonstrate an effect on LOS.[7–11]

Of the many possible indications for hospitalization in infants with bronchiolitis, most are subjective. Identifying objective factors that predict hospitalization and especially longer hospitalization could help focus research on safe and effective measures to prevent some hospitalizations and shorten others, thus reducing the burden on parents, hospitals, and society. Understanding factors predicting LOS could also help select patients more likely to succeed in short-stay observation care. The goal of this study was to identify objective variables noted during initial emergency department (ED) evaluation that best predicted hospital admission and longer LOS.

METHODS

The data for this study were collected as part of a randomized controlled trial of dexamethasone for bronchiolitis[12] (ClinicalTrials.gov no. NCT00119002) conducted in 20 EDs of the Pediatric Emergency Care Applied Research Network during 3 bronchiolitis seasons (November through April) from January 2004 through April 2006. Infants were eligible if they were aged 2 to 12 months with first-time bronchiolitis, defined as wheezing with no history of any similar condition, and if their disease was moderate to severe, defined as a Respiratory Distress Assessment Instrument (RDAI)[13] score of 6 or greater. The components of the RDAI score used here are shown in Table 1.

The original study excluded infants with a previous adverse reaction to dexamethasone, known heart disease or lung disease (eg, cystic fibrosis), premature birth with less than 36 weeks of gestation, immune suppression or immune deficiency, treatment with corticosteroids within the previous 14 days, active varicella, known exposure to varicella within 21 days, or inability of the parents to speak English or Spanish. Patients with life-threatening complications of bronchiolitis, including apnea, respiratory failure, or the clinical appearance of sepsis or shock, were also excluded. The institutional review boards at all sites approved the

TABLE 1. The RDAI score*

	Points					
	0	**1**	**2**	**3**	**4**	**Maximum**
Wheezing						
Expiration	None	End	1/2	3/4	All	4
Inspiration	None	Part	ALL	—	—	2
Lung fields	None	≤2 of 4	≥3 of 4	—	—	2
Retractions						
Supraclavicular	None	Mild	Moderate	Marked	—	3
Intercostal	None	Mild	Moderate	Marked	—	3
Subcostaal	None	Mild	Moderate	Marked	—	3
Total						17

*Both wheezing and retractions are scored. The RDAI score is the sum of the row scores, with total range 0 to 17; higher scores indicate more severe disease.

study. Written informed consent was obtained from the parents of all subjects.

At enrollment, trained study clinicians confirmed clinical bronchiolitis, recorded the duration of symptoms, and determined an RDAI score. A nurse recorded clinical variables including respiratory and heart rates, temperature, and oxygen saturation by pulse oximetry (SpO_2) while breathing ambient air.

In the original trial, the patients were randomized to receive either oral dexamethasone or placebo. All other bronchiolitis treatments during study evaluation were administered according to clinician preference and local standards. We found no difference in the number of such treatments between the dexamethasone and placebo groups. Although no treatment effect was demonstrated in that study, treatment group assignment was included as a potential variable in the current analyses.

The outcomes of our study were (1) hospital admission and (2) longer admission. We defined longer admission as LOS of more than 1 night to exclude the patients who would have succeeded in 24-hour observation care and those whose admission might not have been necessary in retrospect. Study personnel calculated LOS from the date and time of hospitalization (not ED admission) until discharge. Because patients in the hospital are seldom sent home between midnight and 8 A.M., a stay through midnight was considered a night in the hospital.

The initial clinical variables including SpO_2 while breathing ambient air, heart rate, RDAI score, respiratory rate, and temperature were taken from the patient's assessment before study drug administration. Other variables considered were age, sex, days of illness, and assigned treatment group (ie, dexamethasone or placebo in the original study).

All infants in the clinical trial underwent 4 hours of ED observation before a disposition decision was reached. Admission to observation or inpatient care was counted as hospitalization. Because such decisions are typically made before 4 hours, we did not include the 4-hour data in the analysis of hospitalization per se. Ongoing assessment is available for patients in observation care, however, so the model examining longer LOS among admitted patients also included the 4-hour variables of SpO_2, RDAI score, and respiratory rate. To avoid possible artifacts due to treatment, the 4-hour variables of heart rate and temperature were excluded a priori from analysis.

To identify the most important predictors of the studied outcomes, we performed binary recursive partitioning using classification and regression tree (CART) software (Salford Systems, San Diego, Calif). In identifying predictors of hospitalization, the statistical costs of incorrectly predicting discharge were set at twice those for incorrectly predicting admission. Such models would tend to be sensitive to the need for admission. In the models examining LOS, costs of incorrectly predicting longer LOS were set to be half the costs of incorrectly predicting short LOS. Such models would tend to favor prediction of short LOS. All models were built using a 10-fold cross-validation.

To quantify the relative strength of association of the variables found in the CART analysis, we used multivariate logistic regression to calculate odds ratios for the variables and cut points identified in that analysis.

The 22 patients, or 3.7%, subsequently hospitalized during the 7 days after ED discharge were not treated as admissions in these analyses. To avoid artifact, the SpO_2 values from a single study center located at an altitude of approximately 1500 m were excluded from analysis a priori. Because CART can use surrogates for missing values, all other variables from that center were retained in the data set. When parallel sensitivity analyses were

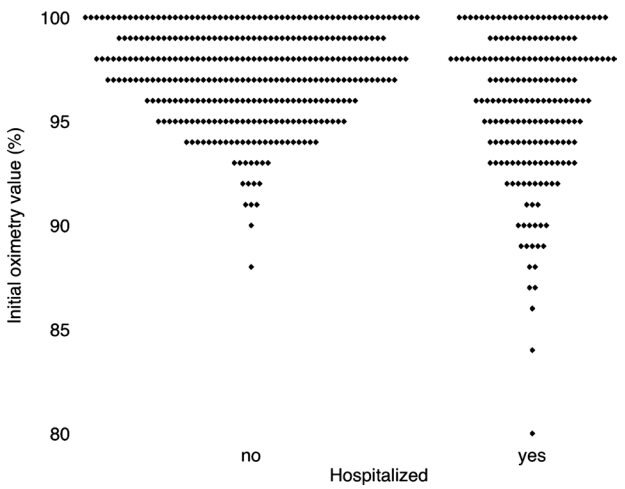

FIGURE 1. The distribution of initial oximetry values measured while breathing ambient air among patients discharged home and among patients admitted to the hospital. Each point represents 1 patient.

TABLE 2. Mean Values of Study Variables at ED Presentation by ED Disposition, With Mean Difference and 95% CI

Variable	Discharged	Admitted	Mean Difference (95% CI)	*P*
Age, mo	5.3	4.8	0.5 (0.03 to 0.9)	0.03
Day of illness	3.58	3.64	−0.06 (−0.5 to 0.3)	0.76
Heart rate, beats per min	154.4	161.8	−7.3 (−10.7 to −4.0)	<0.001
SpO_2, %	97.2	95.7	1.6 (1.1 to 2.1)	<0.001
RDAI score	8.7	9.6	−0.9 (−1.2 to −0.5)	<0.001
Respiratory rate, breaths per min	51.5	55.8	−4.2 (−6.4 to −2.1)	<0.001
Temperature, °C	37.6	37.8	−0.1 (−0.3 to 0.01)	0.06

run excluding all patients from that center, the resulting models did not alter the structure of the decision trees presented here.

RESULTS

Data were available for 598 patients. Their mean age was 5 months; 368 (62%) were boys. Among the 269 patients who underwent virological testing, 166 (62%) were positive for respiratory syncytial virus. The mean RDAI score at enrollment was 9. (The minimum score for enrollment was set at 6, and the maximum possible RDAI score was 17.) After excluding the center at high altitude, SpO_2 data were available for 519 patients. The median SpO_2 was 97% (interquartile range, 95%–99%). The distribution of SpO_2 values in admitted and discharged patients is shown in Figure 1.

Overall, 240 (40%) of 598 patients were hospitalized at the time of their study visit. Table 2 compares initial observations in those hospitalized and those discharged. Although several variables achieved statistical significance, no difference appears large enough to be of clinical importance.

Longer LOS occurred in 159 (66%) of the 240 admissions. The mean LOS among hospitalized patients was 2.4 days, with a median of 2 days.

For the model predicting hospitalization, the decision tree is shown in Figure 2. The best predictor of admission was SpO_2 value of less than 94%. Among the remaining patients with SpO_2 value of 94% or greater, RDAI score greater than 11 and then respiratory rate of greater than 60 also predicted admission. The results of logistic regression analysis for hospitalization are shown in Table 3.

Although we considered 4-hour variables for the model predicting longer LOS among hospitalized patients, this model (tree not shown) retained just 1 variable, predicting that patients with an initial SpO_2 value of 97% or less would have a longer admission. This model for longer LOS predicted that 165 such patients would be admitted; 127 (77%) actually were. Logistic regression using the single variable SpO_2 value of 97% or less yielded an odds ratio of 2.9 (95% confidence interval [95 % CI], 1.8–4.5) for longer admission.

All the models had limited predictive performance. For the 3-variable model predicting admission, the sensitivity was 56% (134/240; 95% CI, 50%–62%) and the specificity was 74% (266/358; 95% CI, 70%–79%). For the single-variable model predicting longer admission among hospitalized patients, the sensitivity was 77% (127/165; 95% CI, 70%–83%) and the specificity was 57% (43/75l; 95% CI, 46%–68%).

DISCUSSION

In this analysis of nearly 600 infants evaluated in an ED for moderate to severe bronchiolitis, the initial measurement of SpO_2 was the most important predictor of hospitalization and the only predictor of longer hospitalization.

It is not surprising that hypoxia is associated with hospital admission. Hypoxia may be taken as a mandatory indication for hospitalization.[14,15] More striking is the observation that initial oximetry results were the only variable associated with longer hospitalization. As noted, 4-hour variables were evaluated in the model examining longer LOS among hospitalized patients. No 4-hour variables, however, proved significant, and therefore, none appeared in the resulting decision model.

The hospitalization rate of 40% in this study is consistent with previously published rates for infants with moderate to severe bronchiolitis.[16,17] Other researchers have noted that hypoxia is a

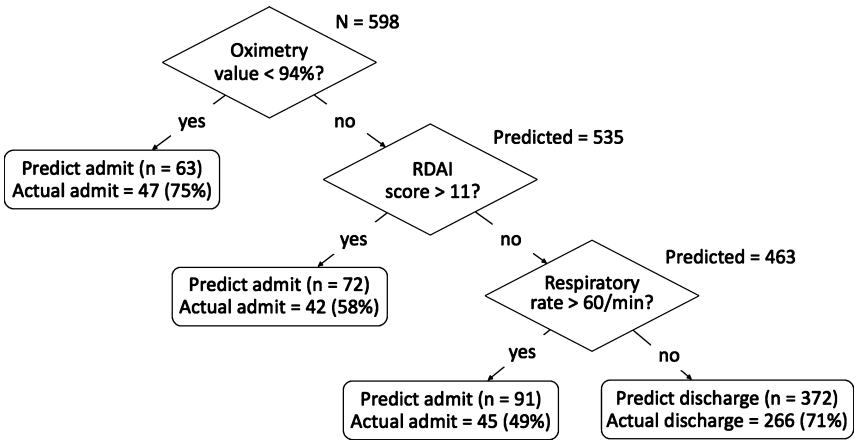

FIGURE 2. The CART tree predicting hospital admission or discharge home from the ED; each node shows the number of patients predicted. Decision nodes are shown as diamonds. Terminal nodes (rectangles) also show the actual dispositions within each prediction group.

TABLE 3. Results of Logistic Regression for Hospitalization

Variable	Adjusted Odds Ratio	95% CI	*P*
Initial oximetry value <94%	5.5	2.9 to 10.2	<0.0001
Respiratory rate >60/min	2.6	1.7 to 4.1	<0.0001
RDAI score >11	2.5	1.5 to 4.3	0.001

predictor of admission in bronchiolitis.[16,18,19] The increasing use of oximetry has been suggested as one cause for the increase in hospital admissions for bronchiolitis between 1980 and 1996.[3,20] Mallory et al[20] noted in a survey research study that describing an initial SpO_2 value of 92% instead of 94% in a bronchiolitis scenario increased the admission rate in survey responses from 43% to 83%. This is consistent with our finding that an SpO_2 value less than 94% predicted hospitalization.

Although hypoxia is naturally associated with admission, initial oximetry is not the only factor driving hospitalization. Excluding the center at high altitude, 75% of hospitalized patients had an initial Spo_2 value of 94% or greater, and there was a large degree of overlap in initial oximetry between discharged and admitted patients (Fig. 1).

The level of hypoxia that incurs patient risk in bronchiolitis has been debated.[8,21–24] Although marked hypoxia is a clear indication for admission, our data suggest that the hypoxia in many admitted patients may not be severe. Among the 25% of admitted patients with an initial SpO_2 value of less than 94%, most had oximetry values between 90% and 93% and almost all the rest had SpO_2 levels between 86% and 89%, so that only 2 patients had oximetry values of less than 85% (Fig. 1). Although hypoxia was likely not the only indication for many admissions, these findings suggest that the provision of home oxygen as reported by Bajaj et al[25] might help reduce admission in a meaningful number of cases. If, for example, half of the 18% of our patients with mild hypoxia had proven stable and eligible for home oxygen, the resulting 9% absolute reduction in admissions would have important benefits to society.

Our results are the first findings of which we are aware that initial oximetry is a predictor of LOS. Shaw et al[16] found that SpO_2 in the ED was the single best objective predictor of more severe disease. Ongoing hypoxia in the hospital has been noted to alter LOS. Schroeder et al[26] reported that, among 62 infants hospitalized with bronchiolitis, 26% had their LOS prolonged owing to hypoxia alone. Another study[27] suggested that the need for oxygen supplementation was the chief factor determining LOS for infants with bronchiolitis.

Successful observation unit care would decrease inpatient hospitalization for bronchiolitis. Bronchiolitis, although a common cause of admission to observation units, is also associated with a high rate of short-stay failure and continued inpatient care.[5,6] We found that only 34% of our admitted patients with moderate to severe bronchiolitis achieved hospital stays of 1 night or less.

Hypoxia and the need for supplemental oxygen are strongly associated with the failure of observation care.[5,6] This suggests that observation care may have limited success unless some means is found to facilitate early discharges. Bajaj et al[25] noted that the provision of home oxygen enabled discharge after 8 hours of observation in 70% of studied bronchiolitis patients with hypoxia.

We used CART analysis because it ranks predictor variables in order of their ability to discriminate between outcomes, resulting in simple hierarchical trees that are readily understood. In addition, it accounts for interactions between predictive variables, considers both discrete and continuous variables, and selects an optimal cut point for continuous variables.

This study was conducted to examine the associations between hospitalization and the initial findings in infants with bronchiolitis. We do not suggest that initial vital signs and SpO_2, taken in isolation, should be used to make decisions about hospitalization. Decisions regarding hospitalization are multifactorial. The difficulty of forecasting the course in bronchiolitis is well known, reflecting the complex nature of this condition. The limited predictive performance of our models emphasizes the importance of clinician judgment in bronchiolitis.

Clinicians may be surprised that heart rate and, especially, days of illness were not predictive of either hospitalization or LOS. The data regarding days of illness, however, may have been imprecise if parents confused a preceding upper respiratory tract infection and bronchiolitis per se.

Our study has potential limitations. The data collected for a clinical trial do not include all possible variables. Factors such as overall appearance, the presence and degree of dehydration, parental anxiety, the distance a child lived from the hospital, or the response to bronchodilator therapy were not recorded in our data set. We note, however, that most of these factors tend to be subjective, incapable of modification, or both. CART decision trees cannot model a generalizable hospital-level effect. We did not use specific institutions as predictors because this would not help decision makers at other hospitals.

As regards the ability to generalize these findings, our study excluded infants with mild bronchiolitis, those younger than 2 months, those with premature birth before 36 weeks, those critically ill, and those with other major comorbidities. The results, however, do address the patients of most interest with regard to hospitalization, that is, patients with moderate to severe bronchiolitis who lack other obvious indications for admission. This was a study of infants 2 to 12 months of age with first-time wheezing. As discussed in the report of the original trial,[12] among 8686 infants screened for eligibility, 7352 did not meet inclusion criteria. Two thirds of these had either previous wheezing (41%) or mild disease with an RDAI score of less than 6 (25%). We do not know if our current results pertain to older infants or those with recurrent wheezing.

This study examined clinical decision making, not physiology. For example, the finding that an initial SpO_2 value of less than 94% was associated with admission does not mean that such admissions are all necessary or that this cutoff is the best value. We suggest, however, that to understand hospitalization and LOS in this disease, we will need to study not only disease behavior but also the behavior of health care providers.

Our findings suggest some directions for future investigations and practices to decrease the admission rate and LOS for infants with bronchiolitis. Although specific therapies may not alter the course of bronchiolitis, the adoption of clinical guidelines can alter pertinent outcomes.[28] If data were available to suggest best practices, the appropriate use of oximetry and home oxygen supplementation could be incorporated into clinical guidelines. The role of home oxygen[25] deserves further research not only for use at discharge from observation care but also to shorten inpatient stays.

In summary, in this multicenter study of 598 infants evaluated in EDs for moderate to severe bronchiolitis, initial SpO_2 had the strongest association with hospitalization and with LOS among admitted patients. These findings draw attention to the role of hypoxia in driving and prolonging hospitalization for this condition. Although simple decision tools are not likely to perform

well in predicting outcomes for this complex clinical syndrome, efforts to reduce or shorten hospitalizations remain important.

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