Role of Direct Laryngoscopy and Bronchoscopy in Recurrent Croup

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Abstract

Objective. To determine risk factors in children with recurrent croup that predict moderate/severe findings on direct laryngoscopy and bronchoscopy and need for further operative interventions.

Study Design. Retrospective chart review cohort.


Subjects and Methods. Retrospective chart review of 103 patients diagnosed with recurrent croup who underwent diagnostic laryngoscopy and bronchoscopy from January 2004 to August 2013. Statistical analysis determined risk factors significantly associated with moderate/severe operative findings. A probability tree was formulated.

Results. Of 103 patients, 30.1% had history of intubation, 6.8% had a history of subglottic stenosis, 6.8% had a history of previous airway procedure, 11.7% consultations were inpatient, 64.1% had asthma, 47.6% had seasonal allergies, 60.2% had gastroesophageal reflux disease, 15.5% were aged ≤12 months, and 51.5% were ≤36 months. Statistically significant risk factors in predicting moderately/severely abnormal operative findings included consultation location (P = .010), history of intubation (P = .003), age younger than 36 months (P = .013), and seasonal allergies (P = .035). When using location of consultation, history of intubation, and age in a statistical model, diagnostic accuracy equaled 93.5%. Of children without history of intubation but who underwent inpatient otolaryngology consultation, 28.6% had moderate/severe findings. Likewise, 41.2% of children with a history of intubation who were younger than 36 months of age had moderate/severe findings.

Conclusion. Moderate to severe operative findings are encountered in only 8.7% of children with recurrent croup. Using statistical modeling, 2 high-risk groups are (1) patients without a history of intubation but inpatient consultation and (2) patients with a history of intubation and age younger than 36 months.

Keywords
laryngoscopy, bronchoscopy, croup, pediatric

Croup is a clinical syndrome characterized by acute-onset stridor, barking cough, and hoarseness secondary to inflammatory changes in the larynx and upper trachea. It is common to the pediatric population, affecting approximately 15% of children aged 0 to 8 years at some point in childhood.1

Recurrent croup is variably defined in the literature, often as 2 or more episodes of croup. Approximately 6.4% of children will experience multiple episodes of croup in the first 4 years of life.2 Recurrent croup can be either infectious or spasmodic (croup-like symptoms in the absence of fever or viral prodrome).3 When recurrent, croup frequently arouses suspicion for underlying nonviral disease.4 The workup commonly includes investigation for asthma, allergy, gastroesophageal reflux, and anatomic airway abnormalities, which may be congenital or iatrogenic.1,5,6 Otolaryngology consultation is frequently obtained.

Diagnostic workup is variable. Often, diagnostic laryngoscopy and bronchoscopy (DLB) are warranted to rule out conditions that require medical management or that mandate surgical repair. A number of studies have been published with the hope of clearly associating risk factors at the time of consultation with the likelihood of finding abnormalities on DLB, but these studies have suffered from smaller sample sizes, wide variability in reporting of abnormalities, and emphasis on reflux changes.7-10

The goal of this study is to systematically delineate which risk factors are associated with abnormal findings on DLB requiring further operative interventions. It is our hypothesis that DLB for recurrent croup seldom identifies operative findings that require a second operative intervention. Determining these factors could reduce unnecessary operative airway endoscopies, thereby avoiding the risks of anesthesia and promoting more efficient health care utilization. Using the classification

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paradigm of Jabbour and colleagues\textsuperscript{8} as a model, we present the largest series to date of children with recurrent croup who underwent operative endoscopy and propose a clinically useful diagnostic tree.

**Methods**

Nemours Institutional Review Board (IRB) approval was obtained. The databases of the Nemours/Alfred I. duPont Hospital for Children were queried to identify all patients who had the diagnosis of croup based on *International Classification of Diseases, Ninth Revision (ICD-9)* coding and also had undergone a DLB between January 2004 and August 2013. To be included in this study, patients had to be diagnosed with recurrent croup (2 or more episodes of croup symptoms confirmed medically or reported by the patient) by our otolaryngologists during a consultation and have had at least 1 DLB by an otolaryngologist at our institution.

The data recorded for each patient from his or her electronic medical record included date of birth, age at diagnosis, sex, whether initial consultation was outpatient or inpatient, history of intubation, prior airway procedures, history of subglottic stenosis prior to recurrent croup, history of gastroesophageal reflux disease (GERD), history of asthma, history of seasonal allergies, number of DLBs, findings on DLB, medical management, and surgical management. A history of GERD, asthma, or seasonal allergies was defined as having been diagnosed with or treated for these conditions by an otolaryngologist or other provider. Medical management was defined by actively taking medication for GERD, asthma, or seasonal allergies. Surgical management was defined by either surveillance endoscopy or surgical treatment of subglottic stenosis or other airway pathology. Degree of subglottic stenosis was graded according to the Myer-Cotton grading system.\textsuperscript{11} The DLB findings were categorized using Jabbour and associates’ classification scheme\textsuperscript{8}:

- **Normal**—no abnormalities noted
- **Mildly abnormal**—grade I subglottic stenosis or other minor abnormality not requiring surgical intervention or further monitoring with operative endoscopy
- **Moderately abnormal**—grade II subglottic stenosis or other non–life-threatening abnormality requiring surgical intervention or further operative endoscopy for monitoring
- **Severely abnormal**—grade III or IV subglottic stenosis or other life-threatening abnormality requiring surgical intervention and repeat operative endoscopy for monitoring

Normal and mildly abnormal findings were grouped together for statistical analysis because they do not necessitate additional surgical management. Likewise, moderately and severely abnormal findings were grouped together as both required further surgical intervention. Findings of only airway erythema or tracheal/bronchial cobblestoning were categorized as normal to decrease presumed interobserver variance in reporting.

Summary statistics, including means with respective standard errors and proportions, were calculated for the appropriate variable types. Two-sample unpaired Student *t* test, Fisher exact test, and Pearson $\chi^2$ test of independence were used to test the distributional difference between the clinical characteristics of children who had normal or mildly abnormal findings and of children with moderately to severely abnormal findings. Two-sided *P* values and associated 95% confidence intervals (CIs) were presented. The risk factors that were statistically significantly different at the 5% level in the hypothesis tests were selected to be potential factors for a chi-squared automatic interaction detector (CHAID) decision tree. The CHAID decision tree is a nonparametric technique that was chosen for its robustness against any potential violations for normality. Multiple algorithms were attempted, and the final decision tree was selected for the highest classification accuracy in combination with the highest clinical utility. Multivariable logistic regressions were run in parallel to all candidate decision trees to evaluate the cumulative performance of the factors in each decision tree. Adjusted odds ratios with corresponding 95% CIs, as well as the area under the receiver operating characteristic (ROC) curve, were reported for the multivariable logistic regression associated with the final decision tree. The statistical software R version 2.15.1 (R Foundation for Statistical Computing, Vienna, Austria) was used to perform the analyses.

**Results**

In total, 247 charts were reviewed and 103 patients were identified who had recurrent croup and underwent DLB in evaluation for the diagnosis of recurrent croup. Twenty-two (21.4%) patients were female and 81 (78.6%) were male. The average age at diagnosis by our otolaryngology team (at the time of either inpatient or outpatient consultation) was 41.2 months. The incidences of the possible risk factors (variables) studied were the following: 11.7% (n = 12) consultations were in the inpatient setting and 88.3% (n = 91) were in the outpatient setting, 30.1% (n = 31) had a history of intubation, 6.8% (n = 7) had a history of previously diagnosed subglottic stenosis, 6.8% (n = 7) had a history of a previous airway procedure, 64.1% (n = 66) had a history of asthma prior to diagnosis, 47.6% (n = 49) had a history of seasonal allergies prior to diagnosis, 60.2% (n = 62) had a history of GERD prior to diagnosis, 15.5% (n = 16) were younger than 12 months of age, and 51.5% (n = 53) were younger than 36 months of age.

Normal findings occurred in 65.0% (n = 67) of patients, mildly abnormal findings in 26.2% (n = 27), moderately abnormal findings in 7.8% (n = 8), and severely abnormal in 0.97% (n = 1). Therefore, 91.3% (n = 94) did not require further operative intervention. The association of risk factors with normal/mild vs moderate/severe findings and the *P* values are presented in Supplemental Table S1 (available at otojournal.org). Four risk factors met the criteria for
statistical significance in determining whether further operative intervention would be required (moderate or severe operative findings). These factors include age younger than 36 months ($P = .013$), inpatient consultation ($P = .010$), a history of intubation ($P = .003$), and a history of seasonal allergies ($P = .035$). The following variables did not meet criteria for statistical significance: prior diagnosis of subglottic stenosis, history of airway procedures prior to diagnosis of recurrent croup, history of asthma, history of GERD, age 12 months or younger, and age 36 months or older.

The operative findings and incidence of medical and surgical intervention are listed in Table 1. Each operative finding is listed separately. Most patients with recurrent croup, regardless of operative findings, were treated with a medical intervention (ie, asthma, seasonal allergy, GERD management). Two patients with grade 1 subglottic stenosis were in the moderately abnormal findings group and underwent operative intervention: one of these patients had the additional finding of a vocal cord nodule and was surveilled operatively, and the other had a subglottic cyst that was treated with balloon dilation and then was later surveilled operatively. One patient with grade 2 subglottic stenosis was lost to follow-up, and no further surgical intervention was performed after the diagnostic endoscopy.

Using the model with the covariables of history of prior intubation (yes or no), age younger than 36 months and age 36 months or older, and location of consultation (inpatient vs outpatient) resulted in the greatest classification accuracy at 93.5% (receiver operating characteristic/area under the curve analysis). The probability tree itself gives clinicians a sequential and hierarchical way to use these covariables but is not equivalent to the area under the curve analysis (Figure 1). The tree demonstrates that, if there was no history of intubation and the consultation occurred as an outpatient (65 patients), the rate of moderate/severe operative findings was 0.0%. If there was a history of intubation and the patient was 36 months or older (14 patients), the rate of moderate/severe operative findings was also 0.0%. For patients without a history of intubation and for whom an inpatient consultation was obtained (7 patients), moderate/severe operative findings were encountered 28.6% (2 of 7 patients) of the time. Patients with an intubation history but who were younger than 36 months of age (17 patients) had moderate/severe operative findings 41.2% (7 of 17 patients) of the time (Figure 1).

### Discussion

The present study is the largest series to date (103 patients) to evaluate the operative findings from DLB for children with a diagnosis of recurrent croup. The purpose of the study was to decide which patients should be considered for operative endoscopy to look for underlying anatomic causes for recurrent croup, since some may be treatable and/or pose risk to the child. This study is not intended to propose a strict formula to guide this decision. Our results show a considerable incidence, 35.0%, of abnormalities on operative endoscopy. However, only 8.7% of patients will have airway findings that merit surgical follow-up. This is not to
say that operative endoscopy in croup is not valuable when erythema, cobblestoning, or mild findings (such as grade 1 subglottic stenosis) are encountered because these may support medical diagnoses, such as GERD or aspiration, and thus guide medical management. We must stress, though, that findings such as airway edema and erythema are not diagnostic of any specific condition. For the purposes of our study, we did not consider airway erythema or cobblestoning to be a mild finding because of the assumed large interobserver variability among our 8 surgeons. Reportable findings were defined as stenosis or a mass lesion.

We analyzed various risk factors and determined that age younger than 36 months, a history of intubation, a history of inpatient consultation, and seasonal allergies were significant risk factors for predicting moderate or severe findings on DLB. These risk factors, except for seasonal allergies, were then combined in various models to assess the diagnostic accuracy of predicting moderate to severe findings. Presence of seasonal allergies was omitted from the modeling because of the reporting variability of this risk factor. This diagnostic method is admittedly limited, but not all patients had allergy testing to establish the diagnosis. The result of this modeling is that using the age, history of intubation, and location of consultation results in a diagnostic accuracy of 93.5%. Furthermore, a clinically relevant probability tree was created to assist clinicians in predicting which patients may have moderate to severe operative findings. In evaluating the decision tree, it may not seem intuitive to make history of intubation a first branching point, as opposed to an algorithm that equally considers 3 significant risk factors (history of intubation, location of consultation, and age 36 months or younger). However, this modeling technique gives the highest classification accuracy for predicting risk, so it was used instead of more common algorithm techniques. The tree shows that in patients who had no history of intubation and underwent an outpatient otolaryngology consultation, none had moderate or severe operative findings. Likewise, for patients with a history of intubation who were age 36 months or older at the time of otolaryngology consultation, none had moderate or severe operative findings. These results are valuable not only to otolaryngologists but also to pediatricians and other pediatric subspecialists in understanding which patients are at risk for significant operative findings and in counseling patients and families about the utility of operative intervention.

This project builds on the prior work by Jabbour et al, who presented an excellent study in 2011 that succinctly clarified stratifying the risk for significant airway findings in children with recurrent croup. Jabbour and colleagues subdivided the nonspecific “normal” vs “abnormal” findings designation that has been used in most prior studies into 2 groups: normal or mild findings vs moderate or severe findings. This is helpful in determining which patients can be managed by observation and/or medical intervention, and subsequently followed clinically, and which patients need further surgical intervention. This methodology helps prioritize the broad range of disease that can coexist with recurrent croup. Perhaps, due in part to the practice of grouping airway findings simply into “normal” and “abnormal,” there is quite a large variability in reported positive findings on operative endoscopy from 33% to 100%. One institution reports abnormal findings in 98% and 100% of patients. The goal of our work was to separate which findings would require intervention beyond medical management alone, which limits possibly unnecessary surgery and surgical risk. Indeed, our results use a different statistical approach, which provides further support for the findings of Jabbour et al—specifically, that intubation history and inpatient consultation are associated with significant operative findings. Unlike in the Jabbour et al study, we did not find age 12 months or younger to be statistically significant but did find age 36 months or younger to be a significant risk factor for recurrent croup. This is similar to the findings of Chun and colleagues.

In considering the risk factors that were deemed clinically significant, 3 of the 4 are intuitively and anecdotally “red flag” risk factors to many otolaryngologists. Specifically, age younger than 36 months at diagnosis and inpatient consultation imply clinical significance of a medical problem. Intubation history is a known risk factor for developing subglottic stenosis. The presence of seasonal allergies was significantly associated with moderate to severe operative findings. We thought that GERD, asthma, or seasonal allergies may be associated
with airway edema, hyperreactivity, and possibly grade 1 subglottic stenosis but were not expecting an association with moderate to severe findings. All 3 factors can be associated with airway hyperreactivity and the spasmodic, or atypical, variant of croup. 

Contrary to “conventional wisdom,” a history of subglottic stenosis, an implicit risk factor for croup, did not reach statistical significance, whether due to resolution of subglottic stenosis or our incomplete understanding of the risk factors for recurrent croup.

The size of our study group is the largest reported to date for analyzing this clinical scenario. This strength is enhanced by using the framework proposed by Jabbour and colleagues because of its clinical relevance and applicability. In combining the data from these 2 studies where possible, more statistical power is available: normal or mild findings in 90.8% (167/184) and moderate to severe findings in 9.2% (17/184). Both of our studies found that patients with a history of an inpatient otolaryngology consultation and a history of intubation were significantly more likely to have moderate to severe operative findings: 28.6% (8/28) for inpatient consult and 32.0% (16/50) for history of intubation. Jabbour et al report this as relative risk: inpatient consultation relative risk is 5.3 (our relative risk is 6.1), and history of intubation relative risk is 9.8 (our relative risk is 8.1).

The weakness of our study is primarily in its retrospective analysis. Inherent selection bias for operative intervention is largely based on perceived risk of finding an airway anomaly. Due to the scope of our data mining methods, we did not determine how many patients were specifically evaluated by our otolaryngology division for recurrent croup and did not undergo operative evaluation. We would assume that the incidence of moderate and severe operative findings would be less than what we reported had all of these patients been surgically evaluated. In addition, there is the potential for inter-observer variability due to the 8 attending otolaryngologists in our division who may have performed the operative DLBs. Reliance on clinical rather than objective laboratory criteria for the diagnoses of seasonal allergies, GERD, and asthma may be another shortcoming. Prospective data management and evaluation of children with recurrent croup could support the conclusions of Jabbour et al and the present study. Alternatively, adopting a policy of when to operate based on the proposed risk factors and, subsequently, auditing the records to determine the rate of positive findings and the rate of need for later operative evaluation of patients initially deemed low risk could validate the risk stratification.

Although this effort represents the largest series to date in determining the rate of airway findings in recurrent croup in children, the number of children we identified with significant risk factors is low, and our findings certainly should not be extrapolated to larger populations of children other than the intended study group.

The use of statistical analysis and modeling has identified a history of intubation, a history of inpatient consultation, and age younger than 36 months as risk factors for identifying moderate to severe operative findings on DLB for recurrent croup. Our modeling will help us determine which patients can avoid the health care expense of operative endoscopy and its inherent risk, albeit low. Furthermore, our findings allow us to inform referring physicians and counsel parents regarding risk factors and operative utility.

In conclusion, operative airway endoscopy in the evaluation for recurrent croup can be selectively performed in children with certain risk factors. Inpatient consultation, history of intubation, and age younger than 36 months are statistically more likely to be associated with significant operative findings. The vast majority (91.3%) of children with recurrent croup will have normal or mild findings on DLB. In children without a history of intubation, with outpatient consultation, or who underwent consultative evaluation at age 36 months or older, significant operative findings are rarely encountered. Seasonal allergies likely contribute to recurrent croup and may be associated with more significant operative findings.

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Author Contributions

Dennis R. Delany, substantial contribution to concept and analysis and interpretation of data, drafting and revising and final approval of manuscript, accountable for content; Douglas R. Johnston, substantial contribution to concept and analysis and interpretation of data, drafting and revising and final approval of manuscript, accountable for content.

Disclosures

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Supplemental Material

Additional supporting information may be found at http://otojournal.org/supplemental.

References


