A Comparative Analysis of Open Surgery vs Endoscopic Balloon Dilation for Pediatric Subglottic Stenosis

Alison Maresh, MD; Diego A. Preciado, MD, PhD; Ashley P. O’Connell, BA, BS; George H. Zalzal, MD

IMPORTANCE Minimally invasive endoscopic techniques are an appealing alternative to open surgical management of pediatric subglottic stenosis (SGS), but more information is needed to understand the comparative risks, benefits, and limitations of such interventions.

OBJECTIVE To compare the effectiveness of endoscopic balloon dilation (EBD) and laryngotracheoplasty (LTP) in pediatric patients with SGS and to identify patient and disease factors that are associated with successful EBD.


MAIN OUTCOMES AND MEASURES Success was defined as decannulation or tracheotomy avoidance. Additional outcomes were total number of procedures and number of unplanned procedures. Univariate χ² analyses and multivariate regression analyses were performed to identify patient and disease factors statistically associated with success within treatment groups.

RESULTS Overall, 86 of 90 patients (96%) successfully avoided tracheotomy or were decannulated. Fourteen patients were successfully treated with EBD, but for 13 patients, EBD failed, and they underwent LTP. A total of 76 patients underwent LTP. In univariate analyses, patients for whom EBD was successful were more likely to have mild (grade 1 or 2; n = 10) than severe (grade 3 or 4; n = 4) SGS compared with patients for whom EBD failed (grade 1 or 2, n = 0 vs grade 3 or 4, n = 13) (P < .001). Three patients who underwent initial EBD had worsening stenosis. Patients initially treated with EBD were more likely to require unplanned surgical intervention during their treatment (6 of 27; 22%) than patients initially treated with LTP (3 of 63; 5%) (P = .01). Patients initially treated with EBD had a lower number of airway interventions and/or evaluations under anesthesia (mean, 6.7) during their course of treatment than patients initially treated with LTP (mean, 9.2) (P = .003). In multivariate analyses, only severe SGS was significantly associated with failure of initial EBD (13 of 13 [100%] with type 3 or 4 vs 4 of 14 with type 1 or 2 [29%]) (P = .002).

CONCLUSIONS AND RELEVANCE For severe SGS, EBD has limited application compared with LTP, and in some cases failed EBD is even detrimental, increasing the risk of unplanned urgent interventions compared with LTP.

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As an emerging tool in the endoscopic management of pediatric subglottic stenosis (SGS), the role of endoscopic balloon dilation (EBD) remains poorly defined. It was first described in 1984 by Cohen et al, and case series data over the past few years have begun to document the success of EBD. However, there is still much to be learned about the patient and disease characteristics for which this procedure is both safe and effective.

Airway stenosis can be congenital, but most cases are acquired, usually the result of intubation injury. Despite a heightened awareness of this pathologic process, intubation-related stenosis constitutes the majority of cases requiring evaluation and management. While the subglottis is the most commonly affected subite, glottic and tracheal stenosis is also frequently identified, and some patients have multilevel narrowing.

Open airway surgery with laryngotracheoplasty (LTP) or cricotracheal resection have served as gold standard techniques for treatment of patients with SGS. These procedures have well-documented outcomes that have been well-defined for different stages of disease severity. Outcomes have been successful decannulation or prevention of tracheotomy in 81% to 100% of patients, even for those with the most severe stenosis. However, this surgery is invasive, involving long operative times, surgical site and graft donor site morbidity, and prolonged hospitalizations. In addition, further endoscopic and/or open procedures are often needed to achieve successful outcomes.

Less invasive techniques such as endoscopic dilation are an attractive alternative to open surgery. Before balloon technology, dilations were performed with metal dilators or endotracheal tubes, both of which deliver significant shearing forces across the stenotic segment that can cause subepithelial injury, fibrosis, and worsening disease. High-pressure noncompliant airway balloons have now gained approval from the US Food and Drug Administration and have the advantage of delivering radial pressures that can be measured and controlled.

Our goal was to review comparative outcomes of both EBD and LTP from our institution, compare success rates for these interventions, and identify patient and disease characteristics that should be considered when planning treatments. Through similar studies and additional continued assessments of associated clinical variables, this research may lead to the development of a management algorithm for pediatric patients with SGS.

Methods

This was a retrospective medical record review approved by the Children's National Medical Center institutional review board, which waived written informed consent. Medical records for all patients undergoing EBD or LTP at our tertiary pediatric hospital were reviewed starting April 2006, the date of the first EBD, through July 2013. Patients were excluded if they were older than 21 years, if they did not have SGS, or if they did not have follow-up records. Information obtained included demographic data, disease-specific details including Cotton-Myer grade of stenosis, and whether there were other airway abnormalities or medical comorbidities. Grade of stenosis was determined objectively by sizing the airway with endotracheal tubes and assessing for a leak; in premature and/or early infants where the small size limited endotracheal tube sizing, subjective assessment was made by the surgeon. We also documented procedural details, number of procedures, and complications.

Univariate analysis was used to identify differences in outcomes between treatment groups, including overall success as well as number of interventions and number of unplanned interventions. Unplanned interventions were defined as unscheduled, urgent surgical airway interventions to address severe symptoms of obstruction within a day of evaluation of these symptoms. Multivariate regression was performed to identify patient and disease factors that were statistically associated with outcomes in successful and unsuccessful EBDs. Specifically, we looked at age at first intervention, prematurity status, type of stenosis (congenital vs acquired), presence of a syndrome, presence of medical comorbidities, presence of multilevel airway disease, and severity of stenosis.

Results

There were a total of 90 patients with SGS who underwent EBD and/or LTP included in our review. Patient demographics and comorbidities are summarized in Table 1. Our patient group included 49 male and 41 female patients. There were no differences in distribution of sex or ethnicity among treatment groups. The ages at first intervention ranged from 4 weeks to 19 years, with a median age of 1.4 years. There was no difference in the mean age between treatment groups.

Seventy-six patients underwent a total of 86 LTP procedures. Sixty-three patients underwent LTP as initial treatment, 17 of whom also underwent EBD as part of their fol-

<table>
<thead>
<tr>
<th>Table 1. Patient Demographics and Comorbidities by Treatment Group</th>
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<tr>
<td>Treatment Group</td>
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<tr>
<td>Successful EBD</td>
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<tr>
<td>Failed EBD requiring LTP</td>
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<td>Initial LTP</td>
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Abbreviations: EBD, endoscopic balloon dilation; LTP, laryngotracheoplasty.
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Patients who underwent successful EBD were more likely to have mild grade 1 or 2 SGS (n = 10) as opposed to severe grade 3 or 4 (n = 4) (P < .001). Similarly, for patients treated initially with LTP, successful treatment without rescue EBD was more likely in patients with mild stenosis (n = 16 for mild stenosis; n = 27 for severe stenosis) compared with patients who required EBD treatments after LTP (n = 3 for mild stenosis; n = 14 for severe stenosis) (P = .02).

Table 3 summarizes treatment outcomes. Patients initially treated with EBD were more likely to require unplanned surgical intervention at some point during their treatment (6 of 27; 22%) compared with patients initially treated with LTP (3 of 63; 5%) (P = .01). However, patients initially treated with EBD had a lower number of airway interventions and/or evaluations under anesthesia during their course of treatment (mean, 6.7) compared with patients initially treated with LTP (mean, 9.2) (P = .003).

When comparing the patients who were successfully treated with EBD with patients for whom EBD failed, we identified several trends (Tables 1 and 2). No patients with congenital stenosis (n = 2), syndromes (n = 2), or multilevel airway disease (n = 3) were successfully treated with initial EBD. There was a higher rate of prematurity in patients who underwent failed EBD (8 of 13; 62% vs 6 of 14; 43%), and there was a higher rate of medical comorbidities in patients who underwent failed EBD (11 of 13; 85% vs 6 of 14; 43%). Finally there was a higher rate of severe grade 3 or 4 stenosis in patients who underwent failed EBD (13 of 13; 100% vs 4 of 14; 29%). However, when all of these factors were analyzed using multivariate regression, the only statistically significant variable was the presence of severe stenosis (P = .002). Congenital stenosis, syndromes, multilevel stenosis, prematurity, and comorbidities were not significant.

No posttreatment complications occurred after EBD. After LTP, there were 3 patients with wound infections, 4 patients treated for pneumonia, 1 patient with pneumomedias tinum that was managed conservatively, and 1 patient with chronic aspiration. One patient died of a nonairway cause 3 days after LTP with no preceding airway and/or respiratory events.

Discussion

The overall success rate in preventing tracheotomy or decannulation in our total patient group was 96% (86 of 90). Our success rate in patients undergoing LTP was 95% (72 of 76); this compares favorably with other studies of open surgical management of SGS in pediatric patients, with numbers ranging from 81% to 100%. A for our patients initially undergoing EBD,

Table 2. Disease Factors by Treatment Group*

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Total Patients</th>
<th>Successful Treatment, a No. (%)</th>
<th>Procedures, Mean No.</th>
<th>Unplanned Procedures, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful EBD</td>
<td>14</td>
<td>14 (100)</td>
<td>7.3</td>
<td>6 (22)</td>
</tr>
<tr>
<td>Failed EBD requiring LTP</td>
<td>13</td>
<td>0</td>
<td>13 (100)</td>
<td>0</td>
</tr>
<tr>
<td>Initial LTP b</td>
<td>63</td>
<td>3 (5)</td>
<td>9.2</td>
<td>3 (5)</td>
</tr>
</tbody>
</table>

Abbreviations: EBD, endoscopic balloon dilation; LTP, laryngotracheoplasty.

* Successful treatment is defined as decannulation or tracheotomy avoidance.

Table 3. Outcomes by Initial Treatment

<table>
<thead>
<tr>
<th>Initial Treatment</th>
<th>Total Patients</th>
<th>Successful Treatment, a No. (%)</th>
<th>Procedures, Mean No.</th>
<th>Unplanned Procedures, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EBD</td>
<td>27</td>
<td>27 (100)</td>
<td>7.3</td>
<td>6 (22)</td>
</tr>
<tr>
<td>LTP</td>
<td>63</td>
<td>59 (94)</td>
<td>9.2^</td>
<td>3 (5)^</td>
</tr>
</tbody>
</table>

Abbreviations: EBD, endoscopic balloon dilation; LTP, laryngotracheoplasty.

^ P = .003.

* unless otherwise noted, data are reported as number (percentage) of patients.

b Stenosis grade was unknown in 3 patients.

low-up airway management. Forty-four patients underwent a total of 94 EBD procedures, of whom 27 underwent primary treatment with 47 EBD procedures. There were 14 patients successfully treated with EBD only, while 13 patients initially treated with EBD required an LTP after EBD failed to adequately improve their symptoms.

There was an overall success rate of 96% (86 of 90) in decannulation or avoiding tracheotomy; at last follow-up, 3 patients were still tracheotomy dependent, and 1 patient died after LTP. The overall success rate of EBD in avoiding LTP was 52% (14 of 27). Of the 14 patients successfully treated with EBD, the number of interventions ranged from 1 to 5, with a mean of 1.9 dilations per patient. Of the 13 patients for whom EBD failed, 1 already had a tracheotomy and was successfully decannulated, and 3 required a temporary tracheotomy prior to decannulation.

Table 2 summarizes disease characteristics in our treatment groups. In the group of patients successfully treated with EBD, there were 10 with Cotton-Myer grade 2 SGS, and 4 with grade 3 stenosis. All 13 patients for whom EBD failed had grade 3 stenosis. For the patients treated initially with LTP, 3 had grade 1 stenosis; 16, grade 2 stenosis; 38, grade 3 stenosis; and 3, grade 4 stenosis; in 3 of these patients, the grade of stenosis prior to intervention could not be identified from the medical record.

Patients who underwent successful EBD were more likely to have mild grade 1 or 2 SGS (n = 10) as opposed to severe grade 3 or 4 (n = 4) (P < .001). Similarly, for patients treated initially with LTP, successful treatment without rescue EBD was more likely in patients with mild stenosis (n = 16 for mild stenosis; n = 27 for severe stenosis) compared with patients who required EBD treatments after LTP (n = 3 for mild stenosis; n = 14 for severe stenosis) (P = .02).
100% were successfully treated without a tracheotomy (27 of 27), but only 52% successfully avoided LTP (14 of 27). Previous case series have reported success rates from 54% to 70% for EBD to avoid open procedures.11-14

Our assessment of patient and disease factors associated with successful EBD outcomes showed that only severity of stenosis was significant. Lang and Brietzke15 found a similar association in a pooled data study of 7 published series of EBD cases. Another series identified multilevel airway disease as a significant factor in the success of EBD.14 While no patients with multilevel disease in our case series were successfully treated with only EBD—all required LTP—this trend did not achieve statistical significance in multivariate analysis.

There were several trends of note in successful EBD vs failed EBD comparisons. No patients with syndromes, multilevel disease, or congenital stenosis were successfully treated with EBD, and there was a trend toward failure in premature infants and patients with comorbidities. However, none of these trends were statistically significant. Many of these morbidities were concurrent with severe stenosis, which was significant, and they were found only in low numbers in our series, thereby limiting our ability to identify significance.

There was no difference in overall success rate between patients initially treated with EBD compared with patients initially treated with LTP. However, successful outcomes were seen for patients in our LTP treatment group for all grades of stenosis, while severe stenosis was a significant predictor of failure in patients initially undergoing EBD. While more procedures were needed overall for patients undergoing LTP compared to EBD, this likely reflects a greater severity of disease for these patients and likely reflects the treatment bias of our retrospective review. The mean number of surgical procedures (6.7 for patients initially treated with EBD and 9.2 for patients initially treated with LTP) is quite large and reflects all occurrences in which the airway was evaluated, even if there was no intervention. It is partially skewed by several patients with complex cases who underwent many procedures, and it also likely underestimates the actual mean because several patients in our series were still following up through our clinic at the close of the study period, and these may yet undergo further airway examinations and/or interventions.

Of note, most of the initial procedures after first treatment (LTP or EBD) are scheduled surveillance procedures. Our collective practice pattern is aggressive, such that after LTP or EBD, patients are routinely scheduled to undergo direct laryngoscopy and bronchoscopy 1 to 2 weeks later. This approach to airway monitoring partially accounts for the relatively high number of procedures per patient. At the same time, the observed increased rate of unplanned admissions and/or interventions after initial EBD occurred despite this aggressive surveillance approach and, in our opinion, is not explained by a more relaxed follow-up approach to the EBD-treated subjects.

Because EBD is a minimally invasive technique, it may seem rational to propose initial EBD trials for patients with SGS prior to committing to open reconstruction. However, EBD is not a technique without morbidity, and limitations should be carefully considered. Three patients in our series initially treated with EBD had worsening stenosis after the procedure (11%). While it is inappropriate to assume a direct cause-and-effect relationship between EBD and worsening stenosis for these patients, the intentional airway injury caused by the EBD procedure is a likely cause. Radial forces in EBD theoretically decrease subepithelial injury and fibrosis compared with shearing-type rigid dilations. However, there have been only a few studies of the histologic changes that occur with EBD, and these have assessed only the immediate changes in animal models rather than long-term histologic changes, which are key to clinical outcomes.16,17 Very little is therefore known about whether there are long-term advantages to EBD compared with traditional rigid dilations, and studies have yet to prove a clinical outcome advantage.18 So in addition to potentially worsening the airway status in a number of patients who undergo EBD, the fact that tissue integrity is being compromised should be considered because this compromised tissue might affect both the technical difficulty of subsequent open surgery and the healing process after such a procedure.

Patients in our study initially treated with EBD were more likely to require unplanned airway evaluation and intervention at some point during their treatment compared with patients undergoing LTP. All 6 patients requiring urgent intervention had grade 3 stenosis, and 5 of these 6 patients ended up needing LTP. While urgent airway compromise is not a direct complication EBD, the risk does appear to increase in patients with severe stenosis, and its occurrence in many cases delays definitive airway management. Finally, while there were no direct postoperative surgical complications in our study population, other series have demonstrated that EBD can have risks, and cases of tracheitis, pneumomediastinum, tracheal laceration, and death have been reported.11

There are several significant limitations when comparing outcomes of treatment groups for a retrospective review. Without randomization, there already exist patient and disease factors that bias clinicians to a type of intervention. This inherent bias limits our ability to objectively assess what role certain disease conditions play in affecting the outcomes of EBD. In the present study, EBD was successful in the treatment of patients with low-grade stenosis and should therefore be used as a first-line treatment for these patients. However, there were 19 patients with grade 1 or 2 stenosis who were treated initially and successfully with LTP, many of whom had confounding factors such as multilevel disease or additional airway abnormalities. For these more complex cases, we were unable to demonstrate significant negative impact on EBD outcome, largely owing to retrospective treatment bias: these patients with complex cases were in the LTP arm of our study. To create an effective treatment algorithm, further work is needed to better identify which factors limit EBD success.

Another study limitation is related to our assessment of success in the EBD treatment group. Appropriate surgical decision making involves identifying a surgical procedure for a specific disease in which the benefits outweigh the risks. Given the minimally invasive nature of EBD compared with open surgery of a pediatric airway, it follows that the threshold for intervention should be different for these procedures. All patients with mild grade 1 or 2 stenosis initially treated with EBD in our study avoided open reconstruction. However, it is likely...
that the severity of clinical disease in some of these patients warrants a surgical risk profile for EBD but not for LTP. Therefore, their success, as defined in our study as avoiding LTP, did not necessarily involve clinical improvement. This same limitation has been seen in other series, and its effect may be an overestimate of the benefits of EBD.

Conclusions

Despite an overall lower success rate, EBD treatment of SGS is an attractive option, given the lesser morbidity compared with open surgical procedures. However, it is clear that there are limitations in its ability to successfully treat this disease, especially in cases of more severe stenosis. In addition, the safety profile for EBD is poorly defined. The procedure carries risks that include worsening stenosis, compromised airway tissue integrity, increased incidence of urgent airway intervention, and delayed definitive management, and all these factors must be carefully considered when developing treatment plans for these patients. While severe SGS is the only significant factor associated with failure of EBD in our series, further work may identify additional considerations that will allow for a pediatric SGS management algorithm.