Management of laryngomalacia in children with congenital syndrome: the role of supraglottoplasty

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Abstract: BACKGROUND/IMPORTANCE: Supraglottoplasty is the surgical procedure of choice for severe laryngomalacia and has shown to be successful in most cases; however, patients with medical comorbidities present a higher rate of failure. To date, the best management of laryngomalacia in children with congenital syndrome remains unclear. PURPOSE: To study the outcome of supraglottoplasty in children with severe laryngomalacia, and to analyze the management and outcome in infants with a congenital syndrome. METHODS: Retrospective medical records review from January 2003 to October 2012 of all patients who underwent laser supraglottoplasty for severe laryngomalacia at the University Children’s Hospital Zurich, Switzerland. RESULTS: Thirty-one patients were included; median age at time of surgery was 3.5 months. Three patients (10%) had a genetically proven congenital syndrome with associated neurologic anomalies. Overall success rate was 87%. Failures were observed in four (13%) of 31 cases; including all three patients presenting a congenital syndrome. CONCLUSIONS: Supraglottoplasty is an effective and safe treatment for laryngomalacia in otherwise healthy children. Signs of a possible underlying predominant neurologic origin and discrepancy between the clinical presentation and the endoscopic findings have to be taken into account, as in children with congenital syndrome with neurologic anomalies the risk of failure is higher.

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Management of laryngomalacia in children with congenital syndrome:
The role of supraglottoplasty

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**Manuscript text:**

**Introduction**

Laryngomalacia is the most common cause of stridor in infants, accounting for up to 75% of all congenital laryngeal anomalies [1]. It is characterized by a dynamic obstruction of the upper airway due to an inward collapse of supraglottic structures during inspiration. Although several theories have been postulated [2-7], the exact etiology of laryngomalacia is not fully understood and different factors may contribute to the disease [6,8], notably gastroesophageal reflux [9-10]. Laryngomalacia typically presents with a moderate to high-pitched fluttering inspiratory stridor being more marked during increased air demands. The symptoms usually begin within the first weeks of life, progress to a peak around the age of 6 to 9 months and resolve by 12 to 24 months [7,11]. While in most cases treatment consists of watchful waiting, 10-20% of children with laryngomalacia require further intervention [7,12]. Signs of severity and indications for surgical intervention are dyspnea with suprasternal/intercostal retractions, recurrent cyanosis, hypoxia, life-threatening apneas, feeding difficulties with failure to thrive, cor pulmonale, and right heart failure [7,13]. In these severe forms, an endoscopic examination of the entire upper airway has to be performed to confirm the clinical diagnosis, to characterize the endoscopic findings and to rule out other associated anomalies.

Endoscopic supraglottoplasty is the procedure of choice in case of severe laryngomalacia.

The aims of this study were to: 1) review our patients’ outcomes after supraglottoplasty; 2) analyze cases of supraglottoplasty failures in children with congenital syndrome and associated neurologic disease; 3) identify factors influencing the results.
Methods

This retrospective study was conducted at the University Children’s Hospital of Zurich, and includes 31 consecutive patients who underwent CO$_2$ laser supraglottoplasty for severe laryngomalacia from January 2003 to October 2012. Institutional review board approval was obtained for this study.

The diagnosis of laryngomalacia was based on clinical presentation. Severe laryngomalacia needing surgical treatment by supraglottoplasty was defined as severe stridor with dyspnea, usually with suprasternal retractions during inspiration. Other symptoms such as feeding difficulties, failure to thrive, and obstructive apnea or hypoxia were sought but not required for inclusion. These children were considered as requiring endoscopy under general anesthesia for precise upper airway evaluation and therefore no bedside fiberoptic endoscopy was attempted.

The diagnosis of laryngomalacia was confirmed by transnasal fiberoptic laryngoscopy during spontaneous respiration under general anesthesia allowing a dynamic view of the airways including the vocal cord function (Fig.1). Rigid laryngotracheobronchoscopy was then performed to complete the evaluation of the airways and to rule out synchronous lesions. All endoscopies were video-recorded.

All supraglottoplasties were conducted by the same surgeon under general anesthesia, the patient being ventilated through a small caliber endotracheal tube positioned to minimize interference with the exposure of the concerned supraglottic areas. The suspension laryngoscope was positioned to expose the structures to be resected, and the procedure was performed using the CO$_2$ laser (Lumenis 30C
(Sharplan), superpulse mode, 2.5-3 W) connected to a microscope micro-
manipulator. The precise surgical technique was adapted to the patient's area of
major obstruction (Fig. 2, 3): section of the shortened aryepiglottic folds and/ or
resection of the lateral edge of the epiglottis and/or vaporization of redundant
mucosa over the arytenoids or epiglottopexy consisting in erecting the epiglottis by
creating a raw surface on the base of the tongue and suturing the lingual surface of
the epiglottis to the base of the tongue. During the first 5 years of the inclusion period
the general attitude in our clinic was to admit the children post-operatively intubated
to the intensive care unit and to leave them intubated up to 24 hours. This attitude
evolved with growing experience of the different teams involved: extubation was
always attempted in the operating theatre and the child admitted to the intensive care
unit for overnight monitoring. The records of all patients were reviewed for
demographics, pre-operative signs and symptoms, comorbidities, endoscopic
findings (including evaluation of the video recordings), surgical techniques, post-
operative symptoms, complications and outcome. Retrospective analysis of the
recorded video-endoscopies was performed. The site of supraglottic obstruction was
classified according to Olney [14]: prolapse of the mucosa overlying the arytenoids'
cartilage (type 1); shortened aryepiglottic folds commonly associated with a long,
tubular, omega-shaped epiglottis that curls on itself (type 2); overhanging epiglottis
that collapses posteriorly (type 3). Furthermore, the severity of the obstruction was
graded according to visualization of the vocal cords during respiration: + vocal cords
visible during inspiration and expiration, ++ vocal cords visible solely during
expiration, +++ vocal cords non-visible during inspiration and expiration.

Success of supraglottoplasty was defined as resolution of the initial symptoms
without the need for further intervention. Cases with a residual stridor but without
labored breathing were also considered as successful. Failure was defined as insufficient improvement of the initial symptoms requiring further intervention such as revision surgery, oxygen therapy, non-invasive ventilation, tube feeding or tracheotomy.

Results
Thirty-one patients underwent supraglottoplasty for severe laryngomalacia between January 2003 and October 2012. There were 18 males (58%) and 13 females (42%). The median age at surgery was 3.5 months (1 to 53 months).

Five patients (16%) presented comorbidities: three (10%) had a genetically proven congenital syndrome with an associated neurologic condition. One child presented with an isolated retrognathia, and one patient had a congenital heart disease (Fallot tetralogy) that had been surgically corrected previously. The median age at surgery of the five children with comorbidities was 4.5 months and 1.5 months for the three children with a congenital syndrome.

Symptoms appeared in 26 cases (84%) during the first three weeks of life, and in 14 cases (45%) stridor was noted to be present at birth. At the time of diagnosis all children presented with stridor. In addition, 19 of 31 (61%) children presented feeding difficulties, 13 (42%) failure to thrive, and 5 (16%) hypoxia and desaturations. No children presented a pectus excavatus, cor pulmonale or pulmonary hypertension. All three children with a congenital syndrome had feeding difficulties, failure to thrive and severe desaturations. Symptoms suggestive of gastroesophageal reflux were present in 22 patients (71%).
Analysis of the videotaped endoscopic examination was possible in 25 cases (81%). Shortened aryepiglottic folds, corresponding to type 2 on Olney’s classification, was the most common finding. In three cases, endoscopy showed a combination of more than one type. There was no relation between endoscopic features, demographic and clinical findings. No synchronous airway lesions were found.

No relation was found between the endoscopic findings, the surgical technique used and the clinical presentation. There were no anesthesiologic complications. Twenty-nine patients (94%) were extubated within the first 24 hours after the operation; of these, 19 (61%) were extubated immediately at the end of supraglottoplasty. During the last five years of the study, all but two of the 17 children were extubated immediately after the procedure. The patient with the isolated retrognathia was extubated 72 hours after the procedure; one patient with a congenital syndrome had already a tracheotomy.

Success was achieved in 27 of 31 patients (87%) with resolution of symptoms. A well-tolerated intermittent stridor without labored breathing persisted in most of the cases (25/27; 93%). Neither post-operative nor long-term complications occurred.

Four patients (13%) were considered as failures and needed further intervention. One of them was a 3-month-old otherwise healthy boy. Stridor, feeding difficulties, and poor weight gain recurred four months after initial complete resolution of the symptoms. Persistence of shortened aryepiglottic folds and redundant mucosa over the arytenoids' region was successfully managed by revision supraglottoplasty. The postoperative course was then uneventful.
The other three failures occurred in patients with a congenital syndrome (Table 1). Patient 1 was a girl with dysmorphic features (micrognathia, retrognathia, and microtia), cardiac malformation, failure to thrive, psychomotor retardation and neurologic anomalies including hypotonia. Smith-Magenis syndrome was diagnosed genetically at a later date. She presented a stridor, feeding difficulties and obstructive apneas since birth. At 8 months of life, massive hypopneas with episodes of oxygen desaturation up to 40% were recorded. By the time of cardiac catheterization for valvuloplasty, an endoscopy of the upper airway showed a massively overhanging epiglottis with a posterior collapse of the supraglottis. Since extubation could not be achieved because of respiratory compromise, a tracheotomy had to be performed 2 weeks later. The breathing was then normal, but feeding difficulties persisted. At 8.5 months of life supraglottoplasty in form of epiglottopexy was performed. Further endoscopic controls showed a persistent collapse and mucosal swelling of the supraglottis. The situation improved slightly with time, so that the patient could be decannulated after 14 months. As obstructive sleep apneas persisted, C-PAP therapy had to be administered at night during one year, followed by nocturnal O₂ therapy for several years until the age of 9 years, when her polysomnography values were normal.

Patient 2 was a girl born at 36 weeks of gestational age and a birth weight over the 90th percentile, presenting since birth an inspiratory stridor, suprasternal retractions, and oxygen desaturations as low as 75%. Polysomnography was consistent with obstructive apneas. She was partially fed via a nasogastric tube because of feeding difficulties. Physical examination showed coarse facial features, retrognathia and deep implanted ears as well as loose, soft skin. Endoscopy showed swelling of the mucosa of the arytenoids’ region; there was no other associated anomaly of the
upper airway. A dis-coordinated respiration pattern was noted. High dose acid suppression therapy was introduced without any symptomatic improvement. Supraglottoplasty was performed at the age of 1.5 months, without significant improvement of respiratory and feeding symptomatology. Because of respiratory exhaustion with CO₂ retention intubation followed by tracheotomy was performed. Despite resolution of the breathing obstruction after tracheotomy, feeding difficulties with un-coordinated suck-swallow-breathe sequence and feeding was continued via a nasogastric tube. Neurological abnormalities (poor head control, sparse movements of the extremities, and hypotonia of the trunk) led to a genetic examination confirming the clinical suspicion of Costello syndrome. The genetic mutation did not correspond to the classic form, but to a milder variant. Further endoscopic controls of the upper airway showed a complete collapse of the pharyngeal and supraglottic structures with a posteriorly hanging epiglottis. At the age of 2 years, tracheotomy could be removed. After decannulation, breathing stayed uneventful.

Patient 3 was a boy with trisomy 21. Since birth, he presented feeding difficulties, poor gain weight and was partially fed through a nasogastric tube. Three weeks after birth, stridor appeared with increasing labored breathing and suprasternal retractions. The clinically massive gastroesophageal reflux was treated with a proton pump inhibitor, but no improvement of symptoms occurred. The endoscopic assessment at the age of 5 weeks of life showed a severe laryngomalacia with very short aryepiglottic folds. Supraglottoplasty consisting in transection of aryepiglottic folds was performed. Breathing improved significantly, but feeding was still difficult with uncoordinated swallow-breathe sequence, frequent oxygen desaturations as low as 75% and severe stridor. The patient was managed with home nasal oxygen therapy.
and monitoring allowing full oral feeding. Oxygen therapy could be stopped three months later.

Discussion
Laryngomalacia is a common cause of stridor in infancy, and in 10-20% upper airway obstruction is severe enough to warrant surgical intervention [7,12]. Over the last 20 years, endoscopic supraglottoplasty has become the procedure of choice for this condition. According to the literature, supraglottoplasty has a success rate of 70-100% [13,15,16]. Our overall success rate was 87%, the results in children without associated neurologic anomalies being better, with resolution in 96%. Nevertheless, children with comorbidities, particularly those with neurologic anomalies, seem to be at higher risk for treatment failure [17-21]. The literature regarding those patients is scarce, rendering their analysis difficult. In our series, supraglottoplasty for the three children with neurologic anomalies in the context of a genetic syndrome was not successful and other treatments were required. Better understanding of the reasons for supraglottoplasty failure and the etiology of laryngomalacia could help to improve the management of children with co-existing neurological symptoms.

To date, the pathophysiology of laryngomalacia is still not fully understood and several factors may contribute to the disease [6,8]. Several anatomic changes of the supraglottis are observed in laryngomalacia [2-4]. Immaturity of the laryngeal cartilage has been proposed to be a contributing factor [5,6]. Increasing evidence suggests a neurologic etiology: altered sensorimotor integrative function of the larynx
leads to neuromuscular hypotonia of the pharyngolaryngeal structures causing supraglottic collapse during inspiration [7].

The presence of neurologic anomalies including hypotonia seems to influence the outcome negatively and to be associated with a higher risk of supragлотtoplasty failure. In our study, generalized hypotonia was a common clinical feature in the three children with a congenital syndrome.

In Down syndrome laryngomalacia is the most common airway problem during the first two years of life [22]. These children are prone to have generalized hypotonia and anatomical abnormalities at different sites of the upper airway have been described [23,24]. Supragлотtoplasty seems to be less successful in cases of Down syndrome, although no outcome studies have been published. Smith–Magenis syndrome is a complex disorder characterized by variable mental retardation, craniofacial and skeletal anomalies, speech and motor delay. Hypotonia, feeding difficulties leading to failure to thrive, and marked oral sensory and motor dysfunction with poor suckling reflex complicate early infancy [25]. In our series, the patient with Smith–Magenis syndrome (patient 1) presented with a massively overhanging epiglottis. According to Landry et al. [16], this type of laryngomalacia is more often observed in infants with severe forms and this condition seems challenging to treat, epiglottopexy being of limited success [26].

Costello syndrome is characterized by failure to thrive in infancy as a result of severe feeding difficulties, mental retardation, as well as generalized hypotonia [27,28]. In our study, the initial endoscopic finding of the patient with Costello syndrome (patient 2) described swelling of the arytenoid mucosa as the main abnormality but supragлотtoplasty did not improve the respiratory situation. Follow-up endoscopies showed an overhanging epiglottis, as well as a complete collapse of the pharyngeal and supragлотttic region. These observations suggest discoordinate
pharyngolaryngomalacia, as described in 1997 by Froehlich et al. [29], characterized by inspiratory collapse of the pharynx and larynx without shortened aryepiglottic folds or redundant mucosa of the arytenoid region. This entity is suspected to be of neurologic origin and supraglottoplasty is typically not sufficient to cure the disease [30]. Furthermore, the observation of changing endoscopic findings in this case suggests that the natural course of the respiratory status depends on the underlying mechanism of upper airway obstruction. Della Marca et al. [31] found a high prevalence of upper airway obstruction in patients with Costello syndrome. They described a characteristic pattern of hypopharyngeal soft tissue hyperlaxity with concentric collapse during inspiration, supporting the hypothesis of a greater neuromuscular component to the disease in these cases. Two of the children with a congenital syndrome were managed with tracheotomy during 12 and 14 months. In the series of Schroeder et al. [32] 55% of the infants with a neurologic condition needed a tracheotomy, the other patients being managed with postoperative nonsurgical airway support and longer hospital stay. When analyzing our supraglottoplasty failures in syndromic children, we conclude that tracheotomy is not indicated as a first line treatment in all patients with neurological anomalies and that those syndromes should not preclude supraglottoplasty. However, the higher risk of supraglottoplasty failure and subsequent tracheotomy should be taken into account when managing such patients. Like Roger et al. [13], we found that symptoms are often difficult to analyze in these complex cases. Either hypotonia may be caused by laryngomalacia, or it can be the origin of a presumed laryngomalacia. Furthermore, the diagnosis of the underlying comorbidity or syndrome has often not yet been established by the time of laryngomalacia treatment. Thus, the possibility of a disease underlying laryngomalacia has to be kept in mind, particularly in cases with additional clinical signs and symptoms, when
discrepancy exists between the clinical presentation and the endoscopic findings, or in cases with supraglottic collapse due to a posteriorly overhanging epiglottis.

No relation was found between the endoscopic findings, the surgical techniques used and the clinical presentation and outcome.

The reported incidence of synchronous airway lesions in laryngomalacia varies from 8-58%. Although performing routinely rigid laryngotracheobronchoscopy before supraglottoplasty we had no synchronous airway lesions in our series. This may partly be explained by the method of evaluation of the subglottis, since we did not do systematically endotracheal tube sizing and could have underestimated the incidence of grade I subglottic stenosis. Even if controversy exists concerning the clinical significance of these synchronous lesions and despite the lack of synchronous airway lesions in our series, we support complete upper airway evaluation in children with severe laryngomalacia prior to supraglottoplasty.

**Conclusion**

Supraglottoplasty is an effective and safe treatment for laryngomalacia in otherwise healthy children. In children with associated disease, especially congenital syndrome with neurologic anomalies, the risk of failure is higher. As a result of the findings in the present study, we consider a posteriorly hanging epiglottis and discrepancy between the clinical presentation and the endoscopic findings as signs of possible underlying neurologic anomalies to be taken into account when managing these patients.
References


Legends for table

Table 1. Failures of supraglottoplasty in children with congenital syndrome: Symptoms, endoscopic features, surgical procedure and further treatment

+ vocal cords visible during inspiration and expiration, ++ vocal cords visible during expiration, +++ vocal cords non-visible during inspiration and expiration
<table>
<thead>
<tr>
<th>Patient</th>
<th>Congenital Syndrome</th>
<th>Symptoms</th>
<th>Associated anomalies</th>
<th>Preop endoscopic findings (Olney’s classification)</th>
<th>Severity of obstruction</th>
<th>Surgical procedure</th>
<th>Postop endoscopic findings</th>
<th>Further treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Smith-Magenis</td>
<td>Stridor, apneas, feeding difficulties</td>
<td>Generalized hypotonia, psychomotor retardation, failure to thrive, cardiac malformation, facial dysmorphism</td>
<td>Posteriorly hanging epiglottis (type 3)</td>
<td>+++</td>
<td>Epiglottopexy</td>
<td>Persistent collapse and mucosal swelling of the supraglottis</td>
<td>Tracheotomy during 14 months; after decannulation: C-PAP therapy during 1 year and nocturnal O₂ therapy during 6 years</td>
</tr>
<tr>
<td>2</td>
<td>Costello</td>
<td>Stridor, apneas, feeding difficulties</td>
<td>Hypotonia of the trunk, poor head control, loose skin, coarse facial features</td>
<td>Arytenoid swelling (type 1)</td>
<td>+</td>
<td>Vaporization of arytenoid mucosa</td>
<td>Complete collapse of the pharyngolarynx</td>
<td>Tracheotomy during 22 months</td>
</tr>
<tr>
<td>3</td>
<td>Down</td>
<td>Stridor, feeding difficulties</td>
<td>Hypotonia, facial dysmorphism</td>
<td>Shortened aryepiglottic folds with omega-shaped epiglottis (type 2)</td>
<td>+++</td>
<td>Section of the aryepiglottic folds</td>
<td>No postop endoscopy</td>
<td>Nasal oxygen therapy and home monitoring during 3 months</td>
</tr>
</tbody>
</table>
Legends for figures

Figure 1: Endoscopic photograph showing supraglottic airway collapse due to laryngomalacia.

Figure 2: Method of supraglottoplasty: the precise surgical technique is adapted to the area of major obstruction.

Figure 3: Endoscopic photograph of the larynx after Laser CO\textsubscript{2} Supraglottoplasty consisting in section of the shortened aryepiglottic folds, resection of the lateral edges of the epiglottis and vaporization of redundant mucosa over the arytenoids.

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