SLIDE LARYNGOTRACHEOPLASTY: A NEW SOLUTION FOR CONGENITAL SUBGLOTTIC STENOSIS IN NEONATES AND INFANTS

PhD Thesis

Eszter Erdélyi M.D.

Department of Oto-Rhino-Laryngology, Head and Neck Surgery

University of Szeged

University of Szeged,

Clinical Medical Sciences Doctoral School

PhD Program:

Clinical and Experimental Research for Reconstructive and Organ-sparing Surgery

Program director: Prof. Lajos Kemény M.D.

Supervisor: Ádám Bach M.D.

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1. INTRODUCTION

The adequate treatment of subglottic stenosis (SGS) is a major challenge of laryngology even nowadays. After laryngomalacia and vocal fold palsy, SGS is the third most common congenital laryngeal malformation. However, it is the laryngeal anomaly most commonly necessitating tracheostomy in newborns and infants. Low-grade congenital subglottic stenosis (CSGS) may improve with growth, but in severe cases, no spontaneous airway improvement is expected over time; thus, selecting the optimal surgical treatment strategy is paramount.

The ultimate goal of management is to ensure an adequate airway with the preservation of voicing and swallowing. Despite the well-defined endpoints (e.g., avoidance of a tracheotomy, definitive decannulation, socially acceptable voice quality, safe swallowing without aspiration), the surgical treatment of CSGS remains heterogeneous and depends almost as much on the experience of the airway team as on the child's condition. Definitive airway surgery is usually preceded by tracheostomy despite its many well-known physical and psychosocial adverse effects.

In consideration of the special anatomy and vulnerable tissues of the pediatric airway, the potentially hidden comorbidities, and the associated congenital malformations, choosing the appropriate surgical method is crucial at this early age. In cases of high-grade SGS, endoscopic procedures are not suggested. Laryngotracheal reconstruction (LTR), cricotracheal resection (CTR), and extended cricotracheal resection (ECTR) have been used for decades, and they have proven to be favorable solutions with good long-term results. These complex open neck surgeries require major tissue resection, stent implantation, or airway expansion by rib cartilage grafts. To reduce the possible complications and maintain airway stability extended resection of the cartilaginous framework should be limited to allow tension-free anastomosis, and if graft implantation is necessary, well vascularized, easily available, regional tissue is

desirable. Moreover, a definitive (one-step) surgical solution is preferable to perform as soon as possible in carefully selected patients.

Over the past three decades, the Department of Oto-Rhino-Laryngology, Head and Neck Surgery, University of Szeged has become a regional center for patients with upper airway stenosis. The intensive and exceptional relationship with the partner institutions made it possible to routinely apply and improve the well-known airway reconstruction techniques not only in adults but in pediatric patients too. The culmination of this cooperation is obviously the introduction of different innovative surgical techniques in the most fragile subpopulations of newborns and infants.

I have been working in the Department of Oto-Rhino-Laryngology, Head and Neck Surgery, University of Szeged since 2015. In the first year of my residency, I joined the upper airway stenosis workgroup under the supervision of Professor Dr. László Rovó. Over the past 6 years, I took part in several operations of different types of airway stenoses in adult and pediatric patients too. I have also presented our related results at several Hungarian and international conferences as well. During my daily work, one of my main tasks is the evaluation of the preoperative and postoperative status of children with upper airway stenosis. I am also responsible for liaising with the parents and our colleagues in the Pediatric department. Soon, I would like to continue my career as a pediatric otolaryngologist.

2. CONGENITAL SUBGLOTTIC STENOSIS

2.1. Pathogenesis

In a full-term neonate, SGS is defined as a lumen ≤4 mm in diameter at the level of the cricoid, whereas it is defined as a lumen <3 mm in diameter in preterm infants. Congenital SGS

is attributed to the incomplete recanalization of the laryngeal lumen during the 10^{th} week of gestation. Failures at different stages of recanalization of the epithelial lamina lead to various degrees of SGS. This entity is closely related to laryngeal webs and atresia, which also result from a laryngeal recanalization failure. This accounts for the frequent cartilaginous subglottic component seen in extensive glottic webs and the complete obliteration of the atretic larynx. The most frequent forms of cartilaginous CSGS are composed of a thick anterior lamina and a generalized thickening of the cricoid ring or an elliptical cricoid. CSGS amounts to 5% of all subglottic stenoses, but its true incidence is difficult to assess as many cases are aggravated by an emergency endotracheal intubation leading to the so-called acquired on congenital or mixed SGS.

2.2. Symptoms

Airflow resistance is inversely proportional to the radius to the fourth power (r^4). Accordingly, a 50% reduction of the radius causes a 16-fold increase in airflow resistance. This significantly increased resistance imposes a huge physical burden on newborns and infants equally. A cartilaginous CSGS causes biphasic stridor with a more prominent inspiratory phase. Depending on the degree of the CSGS, typical signs of respiratory distress, such as severe obstructive dyspnea with suprasternal or chest retractions appear right after delivery. Nevertheless, even a 50% - 70% luminal diameter restriction can often remain asymptomatic for weeks. However, infants with this airway status may experience recurrent episodes of croup with a barking cough, primarily when the infection is associated with mucosal edema.

2.3. Diagnostics and classification

The prenatal diagnosis of subglottic stenosis is not routinely possible. The perinatal events largely determine the diagnostic and subsequent therapeutic interventions. Indisputably, endoscopic assessment is the golden standard for the evaluation of the compromised airway in infants and children. During laryngo-tracheoscopy, the exact location, craniocaudal extension, grade, and histological nature (cartilaginous/soft tissue) of a SGS can be appropriately assessed. However, the endoscopic appearance of SGS may be disproportionate concerning the clinical presentation as infants are remarkably tolerant to airway compromise. During the endoscopic examination, other congenital disorders of the laryngotracheal airway can be explored as well. Imaging procedures are not required in terms of CSGS but might be useful in cases of suspected hidden comorbidities and associated congenital malformations.

Since the symptoms and the applicable treatment modalities are mostly determined by the severity of stenosis, precise evaluation of the airway obstruction is crucial. The Cotton-Myer classification is a simple, effective, and internationally applied grading system. Originally it was used to predict lumen surface reduction in case of endotracheal tube application, it was then extended to describe both pediatric and adult subglottic and/or tracheal stenosis. The classification consists of IV grades: Grade I: 0 to 50% decrease in lumen surface; Grade II: 51 to 70% decrease; Grade III: 71 to 99% decrease, and Grade IV: no evidence of detectable lumen. In order to describe the complex anatomy of this particular area, laryngotracheal stenosis classifications have proliferated in the literature in the last few decades. McCaffrey et al. and Lano et al. proposed classifications to describe the extension of the stenosis among the most commonly involved subsites: glottis, subglottis and trachea. Meanwhile, the classic Cotton-Myer grading system was also extended, incorporating three additional parameters: comorbidities, glottic involvement and the association of both.

2.4. Treatment

2.4.1. Perinatal care

Depending on the degree of the CSGS, signs of respiratory distress at delivery warrant prompt and proper airway management to ensure adequate ventilation and oxygenation of the newborn. Routine oropharyngeal/nasopharyngeal suctioning at birth has been the standard of care for newborns for decades. In the mildest cases, an oxygen hood might be a sufficient solution. In severe cases nasal high flow or nasal continuous positive airway pressure (CPAP) or biphasic positive airway pressure (BiPAP) is necessary. When non-invasive positive pressure ventilation fails, urgent endotracheal intubation or tracheotomy cannot be avoided.

2.4.2. Definitive treatment of congenital subglottic stenosis

Generally, children with low-grade (grade I or grade II) CSGS do not require surgical intervention. As affected children grow, spontaneous airway improvement can typically be expected. Even mild grade III stenosis can often remain asymptomatic for weeks. However, infants with this airway status may experience recurrent airway symptoms, primarily when the infection is associated with mucosal edema. Physiological development and growth are significantly impaired in cases of high-grade CSGS; thus, a ‘watch and wait’ policy is not endorsed. When definitive extubation repeatedly fails, airway widening surgical intervention is necessary. For this purpose, tracheostomy is the most commonly performed primary intervention. As a life-saving procedure, the merits of tracheostomy are indisputable, however, it can negatively affect voicing, swallowing, and the quality of life (QOL). Bacterial colonization and dynamic collapse of the trachea are also real threats. A definitive surgical solution that can be performed in one step could prevent many consequential problems such as accidental decannulation or airway obstruction, chronic airway infection, poor voice quality,

negative effects on speech development, tracheomalacia, need for multiple procedures, and high medical and nursing costs.

The number of surgical options has significantly increased over the past 50 years. Still, the proper management of CSGS remains both challenging and complex. Endoscopic, minimally invasive solutions (e.g., balloon dilatation, excision or incision of scar tissue with cold steel or CO_2 laser, intralesional or topical adjuvant therapy such as mitomycin-C application or steroid injection) are optimal for patients with isolated low-grade (grade I–II) SGS without a history of previous treatment failure. However, these techniques can also increase the incidence of urgent/unplanned airway interventions and potentially delay a definitive solution. Moreover, the chance of success with endoscopic, minimally invasive techniques decreases with the worsening of the initial grade of subglottic stenosis.

Patients with grade III–IV SGS or multilevel airway stenosis mostly require open surgical procedures. Although these interventions carry a higher risk of morbidity, this is balanced by the fact that these treatments provide a definitive solution. In addition, we cannot ignore the fact that the first operation provides the best chance for a successful airway intervention. Therefore, the avoidance of multiple, inappropriately selected, potentially futile (endoscopic) airway surgeries is essential. Laryngotracheal reconstruction (LTR) and cricotracheal resection (CTR) are the prevailing procedures globally. In pediatric patients, CTR provides an overall decannulation rate exceeding 80% with a highly variable reoperation rate of 4%–41% (depending on the patient's comorbidities and grade of stenosis). Meanwhile, 22%–45% of patients require reoperation after LTR. Significant manipulation of the laryngotracheal framework is i1 using these techniques. However, by reducing the amount of resected tissue and minimizing potential graft problems, the success rate could be theoretically increased.

3. AIMS OF THE THESIS

1. Introducing a novel single-stage procedure without tracheostomy and stenting for high-grade congenital subglottic stenosis in neonates and infants to provide an adequate airway with the preservation of voicing and swallowing.
2. Evaluation of the functional results of the surgery by objective and subjective tests.
3. Evaluation of the physical development of the patients.
4. Assessing long-term reliability of the procedure performed in this age of rapid development of the laryngeal structures.

4. MATERIALS AND METHODS

4.1. Patients

Between January 2012 and May 2018 slide laryngotracheoplasty was performed in seven consecutive patients on the 10^{th}, 14^{th}, 68^{th}, 105^{th}, 92^{nd}, 130^{th}, and 120^{th} days of life, respectively. Two patients (patients #1 and #2) had been admitted to the perinatal intensive care unit (PICU) immediately after birth, and two patients (patients #2 and #5) had been intubated due to severe stridor and inspiratory dyspnea. One infant (patient #3) required temporarily continuous positive airway pressure (CPAP) ventilation. One infant (patient #7) required tracheostomy and gastrotube in the fifth week after birth. In three infants (patients #3, #4, and #5) the severe inspiratory stridor occurred after an upper airway infection. Discontinuance of oxygen support (patients #3 and #4) and definitive extubation (patient #5) was not possible in these cases. Endoscopic evaluation of the airway and reconstructive airway surgery was performed on the fifth day of intubation in patient #5 and 3 days after the onset of the dyspnea in patients #3 and #4. Preoperative high resolution computed tomography (CT) or magnetic resonance imaging (MRI) scan was performed in all cases. The preoperative investigations included dynamic and rigid airway endoscopy along with neonatological and neurological

evaluations. Concentric cartilaginous, Cotton-Myer grade III CSGS was detected with a direct endoscopic examination in six of seven patients (patients #2–7), and patient #1 had Cotton-Myer grade II SGS. In one case (patient #4), CSGS was associated with Cohen grade III laryngeal web.

4.2. Surgical technique

4.2.1. Endoscopic evaluation

The procedure began with the direct endoscopic examination of the upper and lower airways to assess the craniocaudal extension of the stenosis and determine its (cartilaginous/soft tissue) nature. Laryngo-tracheoscopy with a rigid 0° and 30° endoscope was performed under general anesthesia via total intravenous anesthesia (TIVA) and supraglottic jet ventilation with readiness for possible intubation. Jet ventilation was performed by using the Moonsune III device (Acutronic Medical Systems, Hirzel, Switzerland) with the following parameters: inhalation time = 20%, frequency = 130/min, pause pressure = 10 cmH_2O, and peak inspiratory pressure (PIP) 12 cmH_2O. The patient with tracheostomy was induced through the cannula and an additional age-appropriate endotracheal tube (ETT) was passed orally and left in the laryngeal inlet.

4.2.2. Resection of the stenotic airway

After the diagnostic laryngomicroscopy orotracheal intubation was performed. The surgery began with a horizontal collar incision made at the level of the cricoid cartilage. The strap muscles were divided and the laryngotracheal complex was bluntly explored from the upper edge of the thyroid cartilage to the superior mediastinum, protecting the recurrent

laryngeal nerves and the great vessels. The thyroid isthmus was divided in the midline and the cricothyroid muscles were left untouched. The cricotracheal ligament was dissected and a partial midline anterior laryngofissure was performed dividing the cricoid and the thyroid cartilage until the level of the anterior commissure. The cricotracheal junction was dissected circumferentially and divided carefully avoiding injury to the esophagus. Cross-field ventilation was carried out using a second set of sterile anesthesia tubings. After visualization of the laryngeal lumen a posterior cricoid incision was performed with preservation of the posterior perichondrium, the posterior cricoarytenoid, and pharyngeal constrictor muscles integrity. The distal trachea was mobilized until the anterior cartilage rings could be easily pulled up to the level of the anterior commissure. The membranous part was resected till the level of the second tracheal cartilage.

4.2.3. Surgical variation in case of laryngeal web

The membranous component of an associated grade III laryngeal web was divided in the midline using Ultra Dream Pulse (UDP) CO_2 laser (DS-40U, Daeshin Enterprise, Seoul, Korea) with 20 ms repeat time, 90 μs pulse duration, 315 W peak power, 0,16 mm spot diameter. The cartilaginous subglottic stenosis was untouched by the laser.

4.2.4. Laryngotracheal anastomosis

An anastomosis was created between the trachea, the anterior cricoid and the midline incised thyroid cartilage using 2.0 or 3.0 PDS suture. The anastomosis started in the posterior midline. Two double-armed continuous locked sutures were placed clockwise and counter-clockwise. After the posterior wall was reconstructed the previously passed ETT was descended into the trachea, then the sutures of the lateral and the anterior wall were completed. Finally,

the threads arriving from the opposite directions were knotted in the anterior midline - with the knots lying outside the airway. Thus, a continuous suture ring was created. The pre-laryngeal muscles and the skin were sutured in two layers, and a 10 Ch drain (Redax - Redon) was inserted for 2 to 3 days.

4.2.5. Postoperative care

The patient was transferred to a pediatric/neonatal intensive care unit. Parenteral antibiotic (amoxicillin-clavulanic acid 25 mg/5 mg/kg for 8 hours or depending on the bacteriologic aspirate) was administered for 7 days. On the day of extubation (3^{rd} through 10^{th} day), the patient was given a steroid (methylprednisolone, 4 mg/kg) bolus. Nasogastric tube feeding was continued for a few days after extubation and oral feeding started progressively.

4.3. Functional evaluation and follow-up

The functional results of the intervention were evaluated with the efficacious help of the parents. Length growth, body weight gain, breathing or swallowing problems were systematically recorded. Breathing, swallowing, voice, and overall satisfaction was assessed using a quality of life (QOL) questionnaire. Voice analysis was performed 36 months after SLTP according to our previously published protocol based on the guidelines elaborated by the Committee on Phoniatrics of the European Laryngological Society. Shimmer (%), jitter (%), fundamental frequency, and the harmonics-to-noise ratio were analyzed. Endoscopic examinations under general anesthesia were strongly recommended in the first postoperative year. Follow-up intervals were 125, 118, 88, 68, 66, 50, and 48 months for the patients, respectively.

5. RESULTS

There were no major peri- and postoperative complications. Extubation was considered safe on the 7th, 5th, 10th, 4th, 3rd, 7th, and 5th postoperative days, for each of the seven patients, respectively. All patients were able to tolerate a progressive oral diet without the use of any thickener within 2 to 3 days post-extubation except one child, who was fed through nasogastric tube from the fifth week after birth (patient #7). In the case of patients #3 and #6, postoperative reintubation was necessary because of their RSV infection, for 4 and 2 days respectively. Repeated endoscopic airway surgery (UltraPulse CO_2 laser vaporization) was required in patients #1 and #3 in the second postoperative month because of the excessive formation of granulation tissue. In the other patients, only planned control endoscopies were performed (two or three times in the first postoperative year). No patient required open revision surgery. All children had stable and adequate airway during follow-up. Significant restenosis was not observed in any of the patients, moreover, the subglottic airway has become wider than the physiological one after SLTP. According to the parents' judgment, breathing was normal in all patients. The children did not require an exemption from physical education.

Patient #4 experiences learning difficulties and delayed speech development. The remaining children had a social life in line with their biological age. In case of patient 4, weak voice was detected because of a 2-mm blunting at the anterior commissure.

6. DISCUSSION

After SLTP, the reconstructed subglottic area is wider than the physiological one, even without extended resection or rib cartilage grafting. This 'reserve capacity' ensures a patent airway even in the event of mild restenosis. The cricothyroid complex together with the

interposed trachea flap provides a well-vascularized stable ring. The cartilages in these young children are flexible and are well stabilized with a double-armed continuous knotted suture. Sacrifice of the segmental tracheoesophageal arteries is necessary at the site of resection because of mobilization of the trachea and cropping of its membranous wall. However, the lateral longitudinal anastomoses and transverse intercartilaginous arteries can be preserved, potentially allowing a complication-free, quick recovery. Therefore, resorption of the local tracheal graft is modest, and the late postoperative result becomes easier to predict. In the absence of rib cartilage grafting, donor site complications can also be excluded. Furthermore, the trachea is covered by respiratory mucosa, which prevents granulations, subsequent restenosis, and adhesion of airway secretions through physiological mucociliary clearance. By reducing the extent of tissue resection and omitting the dissection of the cricod cartilage, the cricothyroid muscle, the chance of recurrent laryngeal nerve injury is lower, which leads to optimal voicing and swallowing function. During the surgery, the anterior commissure remains untouched, which has an obvious positive impact on the postoperative voice quality. However, decent voice analysis is cumbersome for infants, the objective voice parameters supported the parents' satisfied opinion on voice quality. The children's voices were more than socially acceptable. The assessed objective voice parameters were in the physiological ranges in all patients.

Since the integrity and the innervation of the posterior commissure remains intact, the possibility of aspiration is significantly lower. The patients' bodyweight gain and length growth were satisfactory according to growth charts, and the parents were pleased with the children's postoperative QOL in general. One child (patient #4) with Di George syndrome has experienced learning difficulties and delayed speech development. During at least 3 years of observation, the anastomosis was stable and growing dynamically with the patient.

If the general health status is appropriate and no critical comorbidity is present, SLTP is an addition to the surgical armamentarium for treating selected cases of CSGS. Adequate patient selection is crucial. The decision concerning whether to perform SLTP must be based on the overall health conditions of the infant in contrast to the severity of SGS itself. In children with certain craniofacial anomalies, neuromuscular disorder, high risk for aspiration, or low pulmonary function, decannulation may be counterproductive.

The drawbacks of this study include its small sample size and single-center nature. Therefore, further studies are required to explore the potential and limitations of this novel surgical technique.

7. CONCLUSION AND NEW RESULTS

Slide laryngotracheoplasty is an excellent single-stage procedure without tracheostomy and stenting for the reconstruction of high-grade congenital subglottic stenosis in neonates and infants to provide an adequate airway.

Swallowing function and voice production are not disrupted by the procedure, which ensure the possibility of physiological development despite the severe congenital airway anomaly.

Despite the rapid development, the newly formed laryngotracheal structure remains stable over the course of time.

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