Original Article

Improving the Outcome of Management of Pediatric Laryngotracheal Stenosis: The Experience of a Tertiary Care Center

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ABSTRACT

Introduction:
Pediatric laryngotracheal stenosis (LTS) is a challenging problem that imposes a significant burden on patients, their families, and the health care systems. Every effort should be made to optimize the perioperative factors that influence the surgical outcome. The aim of this study is to review the experience of a tertiary care university hospital in management of LTS and to propose recommendation to improve the outcome of pediatric LTS at the study institution.

Methods:
A retrospective review was conducted on pediatric patients with acquired LTS managed in our tertiary care university hospital between 2016 and 2021. Demographic data, relevant medical and surgical history, preoperative, operative, and postoperative data were collected and analyzed, with a focus on the decannulation rate and the total number of procedures.

Results:
The records of 46 pediatric patients were reviewed. Prolonged intubation was the main cause of LTS. The outcome of endoscopic management using rigid bronchoscopic dilatation was not different from endoscopic balloon dilatation EBD). Early lesions with soft granulation tissue responded better to endoscopic management and had a better outcome than chronic fibrotic scar. The total number of procedures increased when open surgery was performed.

Conclusion:
LTS is still a challenging disease entity that requires every effort to optimize the patient's outcome. Early treatment in the soft incipient stenosis stage has a more favorable outcome. Establishing patient's care in a tertiary multidisciplinary center, preoperative microbial screening, and proper management of comorbidities are among the recommended measures to improve the outcome of these patients.

Key Words: Laryngeal; Laryngotracheal stenosis; pediatric; subglottic stenosis..

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INTRODUCTION

Paediatric laryngotracheal stenosis (LTS) is a challenging problem that imposes a significant burden on patients and their families as well as the health care systems[1,2].

Acquired LTS is by far more common than congenital stenosis and is most related to intubation[3,4]. Nearly 10% of intubated patients will subsequently develop LTS[5]. Intubation can cause a wide variety of lesions such as ulcers, granulations, and subglottic. These acute laryngeal intubation-related injuries are usually clinically manifest within 24 hours after extubation, and if not adequately addressed can lead to established laryngotracheal stenosis[6].

Post-intubation LTS mostly affects the subglottic region in the pediatric age group. Less commonly, the glottic region can be affected[6]. Affection of the trachea by post-intubation stenosis in paediatric patients is rare, representing less than 1% of cases in some reports[7]. Multilevel stenosis does occur and can complicate the surgical management of LTS.

Although post-intubation LTS results from prolonged intubation, stenosis has been reported even with shorter periods of intubation[8,9]. In addition, other comorbidities have been known to be associated with LTS, such as Down syndrome and gastroesophageal reflux disease (GERD)[1,10-12].

Paediatric patients with laryngotracheal stenosis have a risk of life-threatening acute severe airway obstruction that carries considerable morbidity and significant mortality. In addition, emergency airway intervention may be required at any time during the course of the disease, which has its inherent risks in paediatric patients especially in the setting of airway stenosis. Consequently, early and adequate management of these patients in dedicated airway centers is necessary for the prevention of the detrimental consequences of such airway crises[13].

Management of LTS can be achieved through endoscopic intervention or open reconstruction. Although open reconstruction has been considered the gold standard in treating LTS, endoscopic interventions have been revolutionized and open surgery or tracheostomy can be avoided in a substantial number of patients[14].

Because every incision in the airway represents a new trauma which may lead to new stenosis, it is generally agreed that the first operation is the patient's best chance of success. Consequently, every effort should be made to optimize the perioperative factors that influence the surgical outcome[15].

Despite the advances in the management of these complex lesions, there are still some limitations. First, complications related to poor wound healing can occur, which can manifest in the early postoperative period or late after surgery by recurrence of respiratory distress. The early complications related to wound healing range from mild abnormalities to severe complications. Early postoperative granulations, thin fibrous bands, and mild restenosis usually need prompt, multiple endoscopic interventions to prevent progression into frank stenosis and failure. Severe complications such as wound dehiscence and graft necrosis can occur and may necessitate tracheostomy placement or reoperation[15-18]. Secondly, late postoperative suboptimal healing can lead to delayed scarring and airway deformity (e.g., webbing at anastomotic site and A-frame deformity[15]. Thirdly, a category of patients, mostly with severe grades of stenosis, undergo multiple open surgical procedures and complementary endoscopic interventions and fail to achieve decannulation. These patients usually end up with permanent tracheostomy and irreversibly scarred airway. Lastly, being directly exposed to the external environment, microbial exposure and the relatively slow turn-over of the airway epithelium, the airway has a tendency to heal by granulation tissue formation and fibrosis after surgery or trauma, contributing to restenosis[19-21]. There is a 10% to 20% risk of procedure failure and restenosis despite the best clinical judgement. This depends, at least partly, on the process of wound healing following airway surgery[22-25].

The process of wound healing is known to be influenced by the differential concentrations of different growth factors at the site of tissue injury. Although very few studies have investigated the effect of different growth factors on the development of subglottic scar, it has been found that transforming growth factor $\beta 1$ may contribute to the formation of subglottic scar. Also, some growth factors may be associated with adequate postoperative wound healing while others may increase in patients with poor wound healing[25,26].

Many agents have been used to improve healing and decrease granulation and scarring after airway surgery. Examples include topical and systemic steroids and/or antibiotics, in addition to topical application of mitomycin and other antimetabolites. However, there are conflicting data regarding their efficacy in preventing and treating subglottic stenosis[27].

The present study was conducted to describe the experience of a tertiary care center in the management of paediatric patients with acquired LTS and to suggest further recommendations to improve the outcome of these patients.

AIM OF THE WORK

This study was conducted to review the outcome of the current management of paediatric laryngotracheal stenosis in our tertiary care center regarding the decannulation rate, the number of procedures required to achieve decannulation, and the postoperative complications and restenosis.

METHODS

The local Institutional Review Board (IRB number: 00012098) approved this study. A retrospective review was conducted on all patients younger than 18 years old with LTS managed in our tertiary care university hospital between 2016 and 2021. Patients with the diagnosis of acquired LTS were included. The collected data included demographic data and relevant medical and surgical history, including a history of endotracheal intubation and the presence of tracheostomy at initial presentation. Preoperative assessment findings, including the site, degree of stenosis (according to Myer-Cotton grading)[28], and the nature of the stenotic segment at the presentation, were analyzed. The nature of the stenotic segment was defined as soft if it was mainly granulation tissue with no fibrous tissue scars or cartilage damage present. A firm stenotic segment was formed mainly of firm fibrous tissue with or without cartilage damage (Figure 1). The descriptions of the stenotic segment were documented in the patients' records at the time of airway assessment. These descriptions were verified by the first author (E. I.) and the senior surgeons (A. G. and A. T.) by reviewing the video recordings of the patients' airway assessments. If airway video recordings were not available, patients were excluded from the study. Other exclusion criteria include patients with congenital LTS and incomplete medical records.

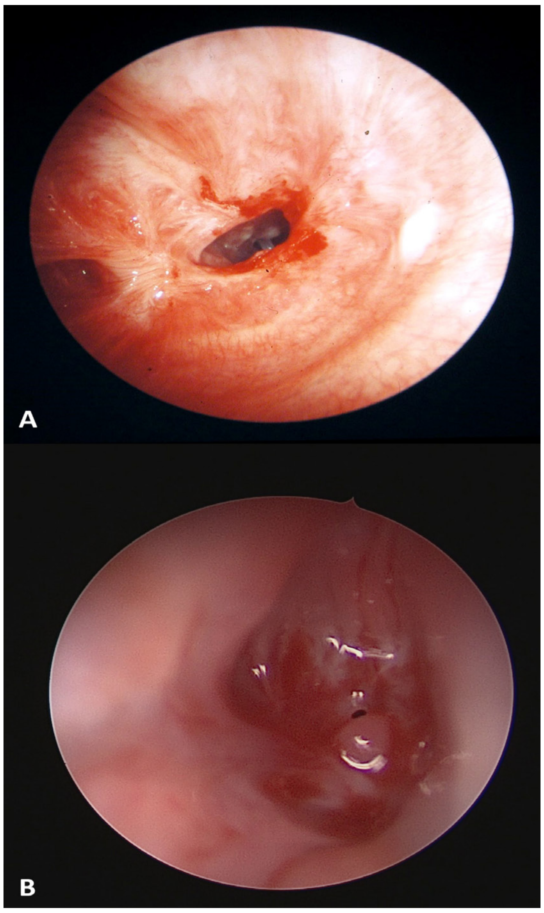

Fig. 1: Endoscopic view of the stenotic segment of two patients showing the nature of the stenotic segment. (a) a 12-year-old patient with grade 3 firm tracheal stenosis with deformed cartilage. (b) a 6-month-old child with soft subglottic grade 3 stenosis.

Operative data, including the number, the operative details of endoscopic and open surgical procedures, and the decannulation rate, was collected. All patients were managed by the senior surgeons in the study. Operative details, including initial management, total number of procedures, method of endoscopic dilatation (endoscopic balloon dilatation or rigid bronchoscopic dilatation), the need for open surgical procedures, and details of the surgical reconstruction techniques, were identified. During assessment under general anesthesia, trial endoscopic dilatation was attempted whenever applicable. The success of the endoscopic intervention was defined as the relief of airway obstruction symptoms, the prevention of tracheostomy, the avoidance of open surgery, and/or the decannulation of previously tracheostomized patients.

Endoscopic dilatation was done either by rigid bronchoscopic dilatation or by endoscopic balloon dilatation (EBD). Before dilatation, radial incisions of the stenotic segment were done using a CO_2 laser for thin fibrotic stenoses (Figure 2). These incisions were not performed for soft stenosis or long stenotic segments involving multiple subsites of the airway. Rigid balloon dilatation was the primary method of dilatation during the period when this study was performed. It was performed using serial dilatations starting from the smallest rigid bronchoscope (KARL STORZ SE & Co. KG – Tuttlingen, Germany) that can be admitted through the stenotic segment, then larger sizes were used systematically till reaching the size expected for age. EBD was performed sporadically, especially when the stenotic segment was thin and soft. EBD was done using angioplasty catheters. The size of the balloon used for airway dilatation was determined to be equal to the diameter of the age-appropriate endotracheal tube plus 1mm for subglottic stenosis or 2mm for tracheal stenosis[29]. Balloon dilatation was done under direct visualization by rigid Hopkin rod endoscope while the patient was under general anesthesia but spontaneously breathing. The duration of balloon inflation is about 1 minute, or until the oxygen saturation falls to 90% - 92% (Figure 3). Following endoscopic dilatation, all patients received inhaled steroids in the immediate postoperative period, systemic prednisolone (1mg/kg) for 5 days, and a proton pump inhibitor for 2 weeks. Topical application of mitomycin-C or steroids in the dilated airway was not a routine measure in our protocol.

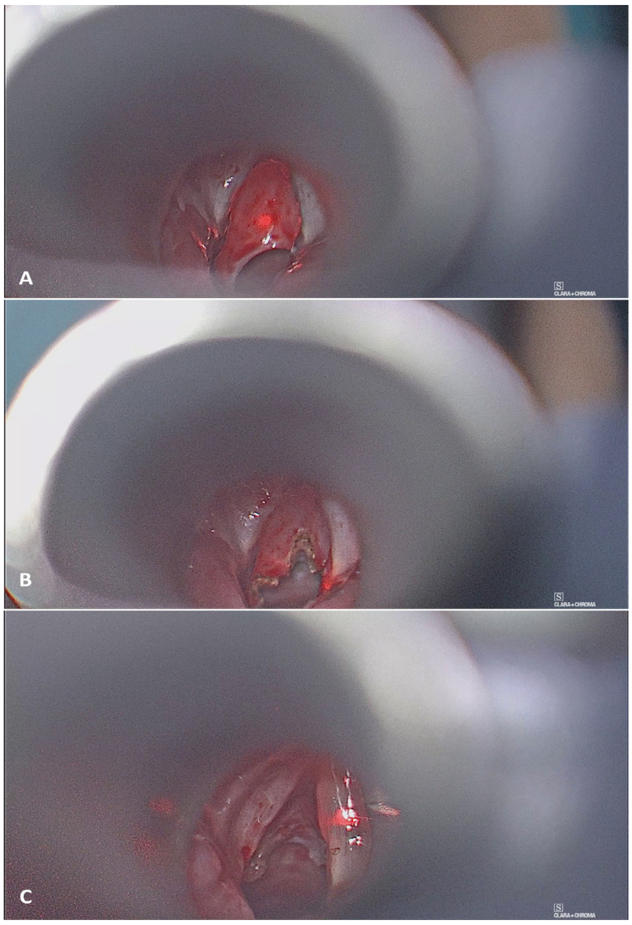

Fig. 2: Endoscopic rigid dilatation after radial incisions of a fibrotic stenotic segment. (a) endoscopic view of a grade III subglottic fibrotic stenosis. (b) radial incisions of the stenotic segment in a Mercedes-Benz fashion using CO_2 laser. (c) dilatation of the stenotic segment using rigid bronchoscopic dilatation.

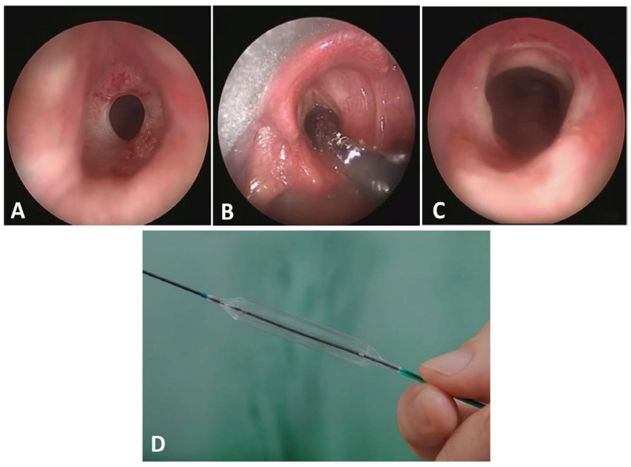

Fig. 3: EBD of grade 2 subglottic soft stenosis. (a) endoscopic view of subglottic grade 2 soft stenosis before dilatation. (b) endoscopic balloon dilatation using angioplasty balloon. (c) endoscopic view of the subglottic region post dilatation showing complete resolution of the subglottic stenosis. (d) angioplasty balloon used for dilatation.

Tracheostomy was indicated if the patient presented with severe airway compromise, if dilatation failed to widen and stabilize the airway, when endoscopic management resulted in decompensation of airway stenosis, or when the patient had severe associated comorbidity or significant aspiration that preclude definitive airway management. When endoscopic management failed or was not applicable, open surgical reconstruction was planned. Details of the open surgical technique were recorded. Laryngotracheal reconstruction was routinely performed as a double stage procedure in our department[30, 31] (Figure 4). All patients received systemic and inhaled steroids (1mg per kg for 5 days), prophylactic antibiotics (ceftazidime 50mg per kg for 5 days), and a proton pump inhibitor in the early postoperative period.

Postoperative data include the number of postoperative endoscopic interventions before achieving decannulation and the rate of postoperative complications. The follow-up period was defined as the period from the first assessment of the patient to the last clinical assessment. Follow-up evaluation visits were scheduled at 1-2 weeks postoperatively. If the patient had no symptoms at the follow-up visit, evaluation included only clinical assessment and flexible nasopharyngolaryngoscopy in the outpatient clinic. If a patient presented with airway obstruction symptoms, endoscopic examination under general anesthesia was added. The success of the endoscopic intervention was defined as the relief of airway obstruction symptoms, the prevention of tracheostomy, the avoidance of open surgery, and/or the decannulation of previously tracheostomized patients.

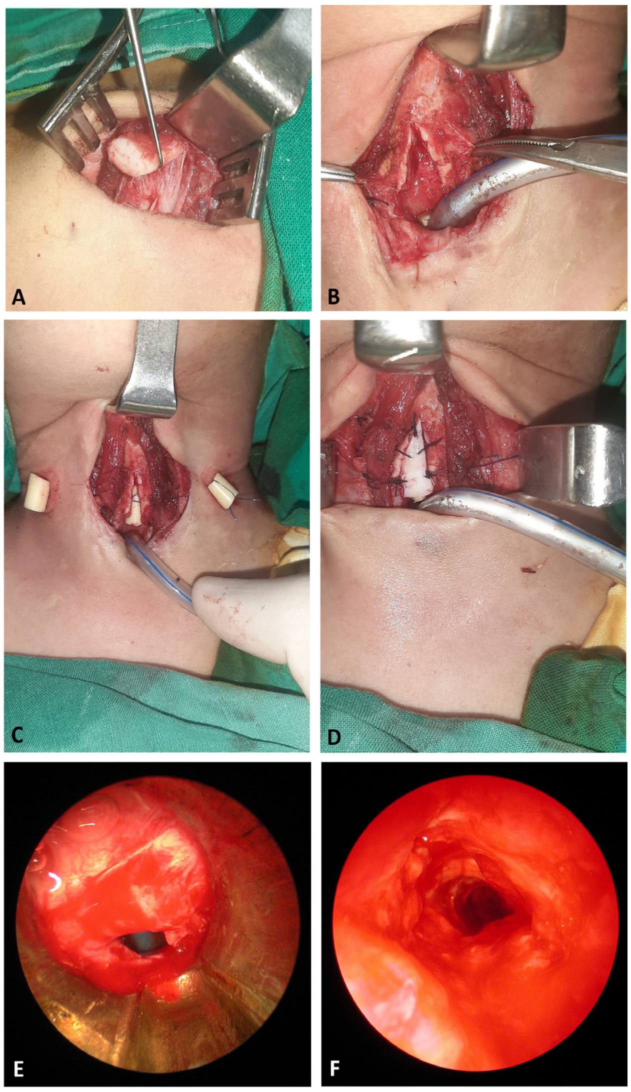

Fig. 4: Intraoperative photos of laryngotracheoplasty with anterior costal cartilage graft. (a) harvesting costal cartilage graft. (b) laryngofissure through the stenotic segment. (c) securing and insertion of the stent. (d) suturing the costal cartilage graft into the laryngofissure incision. (e) endoscopic view of the stenotic segment preoperatively showing severe grade III subglottic stenosis. (f) endoscopic view of the stenotic segment after endoscopic debridement of granulation tissue two weeks postoperatively.

Statistical analysis of the data was performed using IBM SPSS software package version 20.0 (Armonk, NY: IBM Corp.). The Shapiro-Wilk test was used to verify the normality of the distribution. The level of significance of the obtained results was judged at the 5% level. A chi-square test was used when comparing categorical variables. Fisher's Exact or Monte Carlo Correction for chi-square when more than 20% of the cells have an expected count less than 5. Mann-Whitney test for abnormally distributed quantitative variables to compare between two studied groups.

RESULTS

The records of 56 patients with the diagnosis of acquired LTS were managed at our institution during the specified period of the study. The records of these patients were analyzed. Ten patients were excluded from the analysis (due to failure to retrieve the video recordings of the patient's airway in 5 patients, and incomplete data in 5 patients). The remaining 46 patients were included in the study. Among the included patients, 37% (*n*= 17) were females and 63% (*n*= 29) were males. The mean age was 71.91±68.02 months (range from 1 to 204). All patients in our series have a history of intubation (mean= 18.78 days, range from 3 to 60 days), but prolonged intubation was the cause of LTS in 44 patients. Other causes were identified in the remaining two patients (blunt neck trauma in one patient and caustic ingestion in the other). Twenty-five patients were tracheostomized at the initial assessment. Tracheostomy was done either electively after prolonged intubation for equal or more than 15 days (*n*= 10), or after failed endoscopic dilatation (*n*= 11). The remaining 4 patients had tracheostomy without attempt endoscopic dilatation and described below.

According to the regions of the airway involved by LTS, 28 patients had isolated subglottic involvement, 4 patients had isolated tracheal stenosis, and 14 patients had more than one level involved (10 patients had subglottic and upper tracheal involvement, 3 patients had glottic and subglottic involvement, and 1 patient had multilevel stenosis (subglottic, glottic, and supraglottic). Fifty percent (*n*= 23) of patients had firm fibrotic stenotic segments, and 23 had soft stenosis in the form of granulation tissue. No grade 1 or grade 4 stenosis was found in the present series. The characteristics and degree of stenoses are summarized in Table (1). The average follow-up period was 28.35 months (ranging from 4 to 108 months).

Table 1: The characteristics and degree of stenoses:

Total number of patients	46
1. Site of stenosis	
Subglottic	28
Tracheal	4
Multilevel	14
• Subglottic + tracheal	10
• Subglottic + glottic	3
• Subglottic + glottic + supraglottic	1
2. Degree of stenosis*	
Grade 2	18
Grade 3	28
3. Nature of stenosis	
Soft	23
Fibrotic	23

According to Myer-Cotton grading[28].

Table 2: Comparison between EBD and Rigid Bronchoscopic dilatation according to different parameters (*n*= 41):

	Method of dilatation				Test of sig.	*P*
	EBD (*n*= 8)		Rigid (*n*= 33)			
	No.	%	*No.*	%		
Type of stenotic segment						
Fibrotic	2	25.0	16	48.5	c^2=1.442	FEp=0.429
Soft	6	75.0	17	51.5		
Tracheostomized Cases						
No	6	75.0	14	42.2	c^2=2.735	FEp=0.130
Yes	2	25.0	19	57.6		
Decannulation						
NA	6	75.0	14	42.4		
No	1	12.5	10	30.3	c^2=2.263	MCp=0.386
Yes	1	12.5	9	27.3		
Success of endoscopic intervention	7	87.5	17	51.5	3.435	FEp=0.110
Open surgery required						
No	8	100.0	23	69.7	c^2=3.206	FEp=0.165
Yes	0	0.0	10	30.3		
Total number of procedures						
Mean±SD.	1.88±0.83		2.55±1.86		*U*= 116.50	0.617

χ^2: Chi square test; FE: Fisher Exact; *U*: Mann Whitney test; *p*: *p* value for comparing between EBD and Rigid bronchoscopic dilatation.

EUGA and trial of endoscopic dilatation was the initial procedure in 41 patients. Rigid bronchoscopic dilatation was done in 33 patients, while EBD was performed in 8 patients. The remaining patients (*n*= 5) were initially managed as follows: two patients had anterior cricoid split as the initial procedure (of them, one was initially tracheostomized), one patient was managed primarily by tracheostomy due to near total obstruction of the airway, two patients required tracheostomy due to blunt neck trauma in one patient and severe associated comorbidity (viral encephalitis) in the other.

Among the patients treated initially by rigid bronchoscopic dilatation (*n*= 33), 11 required tracheostomies due to failed dilatation and 8 were tracheostomized before. Among these cases who required tracheostomy, 4 cases had unplanned emergency tracheostomy due to decompensated airway after failed endoscopic dilatation. Failure of decannulation after rigid bronchoscopic dilatation was present in 10 of 19 tracheostomized patients (10/19, 57.89%). In the patients treated by EBD (*n*= 8), no unplanned airway interventions were required. Two patients were tracheostomized before the procedure, one decannulated successfully after treatment, and one failed to be decannulated and planned for further endoscopic treatment (Table 2).

Fourteen patients in the present series required open surgical reconstruction: cricoid split in 2 patients, tracheal RA in 3 patients, LTP in 6 patients, and pCTR in 3 patients. Among these patients (*n*= 14), significant restenosis, which resulted in recurrence of symptoms of airway obstruction or failed decannulation, occurred in 4 patients (28.57%). Three of whom had LTP as the main surgical reconstruction technique and one patient underwent pCTR. Decannulation succeeded in 5 patients, failed in 6, and the remaining 2 patients were not tracheostomized before the procedure (Figure 5).

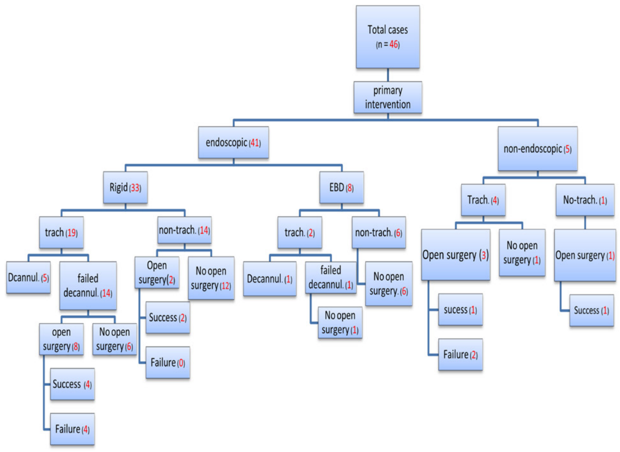

Fig. 5: A flow chart demonstrating the management approach to the patients included in the present series. Decann.: decannulation, trach.: tracheostomized, EBD: endoscopic balloon dilatation

Twenty-three cases presented with soft stenosis in the form of granulation tissue. Six cases underwent endoscopic balloon dilatation (EBD), and 17 cases underwent rigid bronchoscopic dilatation. Nine patients were tracheostomized (8 before and 1 patient after treatment), and six were successfully decannulated (decannulation rate= 66.6%). Overall, twenty patients avoided open surgery or were decannulated with stable airways (success rate= 87%), and three patients failed decannulation (one of them died due to an airway-unrelated cause; the remaining two patients were scheduled for further endoscopic intervention). The average number of procedures was 1.48±0.59 (min. – max.= 1.0 – 3.0).

Twenty-three cases presented with firm fibrotic stenosis. Sixteen were treated initially with rigid bronchoscopic dilatation; 2 cases were treated initially with EBD; 5 cases were treated initially with other procedures (1 case was treated with anterior cricoid split, 1 case with anterior cricoid split and tracheostomy, and 3 cases were managed by tracheostomy). Fourteen patients failed endoscopic intervention and either required tracheostomy and/or open surgery or failed to be decannulated. Among patients who required tracheostomies, four were unplanned and performed as emergency procedures due to airway decompensation. Fourteen cases required an open surgical procedure to stabilize the airway and/or to be decannulated. The average number of procedures in the patients presented with fibrotic stenosis was 3.39±1.85 (min. - max.= 1.0 – 7.0). The total number of tracheostomized patients was 16. Eleven of them failed to be decannulated (68.75%) (Table 3). Among the patients who required open surgery (*n*= 14), 11 were tracheostomized and 3 were non-tracheostomized. One patient was not tracheostomized before open surgery (tracheal resection-anastomosis) but required postoperative tracheostomy due to anastomotic dehiscence.

The average number of procedures per patient was 2.43±1.67. Univariate linear regression analysis revealed that the total number of procedures was significantly affected by fibrotic stenosis, the need for open surgical reconstruction, and the presence of tracheostomy. No significant relationship with the age, the level of stenosis or the method of dilatation was detected, although multivariate regression revealed a significant association only between the total number of procedures and the need for open surgical reconstruction (Table 4).

Overall, successful decannulation was achieved in 44% (11/25). Five patients achieved decannulation after open surgical reconstruction and 6 after endoscopic intervention. The mortality observed in the present series was 3/46 (6.5%); 2 of them were tracheostomized. One patient died due to airway obstruction outside the hospital (blocked tracheostomy) and another due to a comorbidity unrelated to the airway. After the exclusion of the deceased patients, 12 patients failed to be decannulated in the present series

(12/23, 52.17%). Wound complications were the cause of restenosis and failed decannulation in two patients (wound infection and graft loss after LTP in one patient and anastomotic dehiscence after pCTR in one patient). Nine patients had grade 3 stenosis and 10 patients had fibrotic stenotic segment. The characteristics of patients who failed to be decannulated are summarized in (Table 5, Figure 6). In addition to these patients, there was one patient who underwent RA for an isolated tracheal fibrotic stenosis. The patient was not tracheostomized before surgery (so was not described with the patients with failed decannulation), however; he suffered anastomotic leak and surgical emphysema 1 day after surgery. Revision surgery and reanastomosis was performed. After 5 days, the patient developed wound infection and surgical emphysema. Examination under general anaesthesia revealed infection and dehiscence at the anastomotic site. Consequently, tracheostomy was performed, and culture-based antibiotics were prescribed, and reassessment revealed severe grade 3 stenosis at the previous anastomosis site.

Table 3: Comparison between patients with soft and fibrotic stenosis:

Variable	Soft stenosis	Fibrotic stenosis	Test of significance	*p* value
Number	23	23		
Age (mean ±SD)	62.83±64.13	81.0 ± 71.96	*U*=221.50	0.344
Sex			χ^2= 2.333	0.127
Male	12	17		
Female	11	6		
Number of days on ETT	17.65 ±7.85	19.91 ± 13.0	*U*= 248.50	0.723
Grade of stenosis				
G 2	13	5	χ^2=5.841*	0.016*
G 3	10	18		
Level of stenosis				
Subglottic	16	12	χ^2=1.798	0.490
Tracheal	1	3		
Multilevel	6	8		
Primary intervention				
EBD	6	2	χ^2=6.799*	0.027*
Rigid dilatation	17	16		
Other	0	5		
Endoscopic intervention	23	18	χ^2=23.197*	<0.001*
Success	20	4		
Failed	3	14		
Total number of procedures	34	77		
(Mean ± SD)	1.48 ± 0.59	3.39 ± 1.85	*U*=85.0*	0.001<*
1	13	3	χ^2=9.583*	0.002*
>1	10	20		
Required open reconstructive surgery				
Yes	0	14	χ^2=20.125*	0.001<*
No	23	9		
Rate of decannulation	6/9	5/16	χ^2= 6.996*	0.030*

SD: standard deviation; ETT: endotracheal tube. G2; 3: grade 2, 3; GT: granulation tissue; EBD: endoscopic balloon dilatation; U: Mann Whitney test; χ^2: Chi square test; * Statistically significant (*p* value <0.05).

Table 4: Univariate and multivariate linear regression analysis for the parameters affecting total number of procedures (*n*= 46):

Total number of procedures	Univariate		#Multivariate	
	P	B (LL – UL 95%C.I)	*P*	B (LL – UL 95%C.I)
Fibrotic stenotic segment	<0.001*	1.913 (1.096 – 2.730)	0.205	0.604 (-0.342 – 1.550)
Age (months)	0.168	0.005 (-0.002 – 0.012)		
Level of stenosis on admission				
Tracheal	0.099	1.440 (-0.285 – 3.165)		
Subglottic	0.065	-0.929 (-1.917 – 0.059)		
Multilevel	0.351	0.504 (-0.575 – 1.583)		
Degree of stenosis [3]	0.388	0.440 (-0.578 – 1.459)		
Method of dilatation				
EBD	0.302	-0.678 (-1.984 – 0.629)		
Rigid	0.480	0.392 (-0.716 – 1.499)		
Other	0.818	0.185 (-1.425 – 1.795)		
Required open surgery	<0.001*	2.558 (1.794 – 3.322)	<0.001*	2.062 (1.029 – 3.096)
Tracheostomized	0.047*	0.975 (0.013 – 1.937)	0.637	0.177 (-0.575 – 0.929)
Number of ETT days	0.932	0.002 (-0.045 – 0.049)		

B: Unstandardized Coefficients; C.I: Confidence interval; LL: Lower limit; UL: Upper Limit; #: All variables with *p*<0.05 was included in the multivariate; *: Statistically significant at *p* ≤0.05; EBD: endoscopic balloon dilatation; ETT: endotracheal tube.

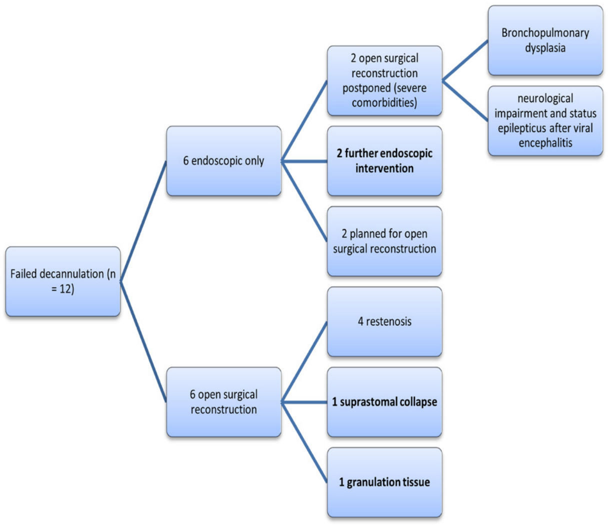

Fig. 6: A diagram summarizing the characteristics of patients who failed decannulation.

DISCUSSION

Post-intubation LTS remains a challenging health care problem that is notorious for repeated recurrence and the need for multiple procedures before achieving a safe airway. It was reported that about one third of patients would require additional surgery at one year, and about half of patients would require additional surgery after two years. [32] This results in a significant healthcare burden, accounting for healthcare costs comparable to other chronic diseases such as diabetes and COPD. [33] Multiple factors affect the outcome of its management and interact with each other to increase the complexity of this disease. Pediatric patients represent a special, added challenge due to the associated morbidity and mortality as well as the impact of this disease on child functional and psychological well-being.

Table 5: Clinical characteristics of the patients who failed decannulation.

age (m*)	Sex	LBW	Comorbidities/ congenital anomalies	ETT	Stenosis level(s)	Type of stenotic segment	Stenosis degree	Method of endoscopic dilatation	Open surgery	Total number of procedures
12	Male			30	subglottic	fibrotic	3	Rigid		2
7	Male	+	PFO	35	subglottic	fibrotic	3	Rigid		1
13	Male		viral encephalitis, status epilepticus	15	subglottic + tracheal	fibrotic	3	(Tracheostomy)		2
204	Male		SLE	15	Subglottic + tracheal	fibrotic	3	Rigid	pCTR	4
144	Female			30	subglottic	soft	2	EBD		2
60	Male			3	subglottic + glottic + supraglottic	fibrotic	3	(Tracheostomy)	LTP	5
18	Male			12	subglottic	fibrotic	3	-	cricoid split	2
84	Male		FT	15	subglottic	fibrotic	2	Rigid	LTP	3
60	Male			30	subglottic + suprastomal collapse	fibrotic	3	Rigid	pCTR	7
204	Male			25	subglottic + tracheal	Soft	3	Rigid		2
108	Male			14	subglottic	fibrotic	2	Rigid	LTP	6
2	Male		Bronchopulmonary dysplasia, ASD, mild TR	15	subglottic	fibrotic	3	Rigid		4

*Age in months; LBW: Low birth weight; PFO: Patent foramen ovale; SLE: systemic lupus erythematosus; FT: Fallot's tetralogy; ASD: atrial septal defect; TR: tricuspid regurgitation; ETT: days on endotracheal tube; pCTR: partial cricotracheal resection; LTP: Laryngotracheoplasty; EBD: endoscopic balloon dilatation.

Prolonged endotracheal intubation remains the most common cause of LTS. In the present series, prolonged intubation was the direct cause of LTS in 95.7% of cases (*n*= 44). Neck trauma and caustic ingestion represent rare causes, and in the current series, they were associated with more severe and multilevel stenosis. The most common site of stenosis in pediatrics is the subglottic region, which is the narrowest region and even minimal stenosis can produce significant symptoms.

In the present series about half of the tracheostomized patients failed to be decannulated. The decannulation rates described in the literature are quite variable, reaching more than 86% in large studies from specialized pediatric airway centers[34-36]. Although 5 of the 12 patients who failed decannulation in the present series are candidates for further definitive surgical intervention, this difference in the decannulation rate necessitates deeper analysis to identify areas in their management that may require further improvement. This was the reason for conducting the present study.

5.1 Preoperative assessment

5.1.1. Establishing patient's care in specialized pediatric aerodigestive center

A key prerequisite for a successful outcome is an accurate preoperative assessment that addresses all the factors that may affect this outcome. Given the complexity of laryngotracheal stenosis and its relationship to swallowing, phonation and respiration, multidisciplinary team approach is necessary for adequate perioperative planning of these patients, to optimize the surgical outcome and to minimize health care costs[37,38]. Moreover, it has been established that care of paediatric airway patients in integrated multidisciplinary paediatric aerodigestive units would decrease the morbidity and mortality of patients that result from inadequate care in non-specialized centres[37]. In addition, establishing patients care in these centers results in less examination under anesthesia procedures and less costs[37]. Consequently, integrated specialized pediatric aerodigestive centers have emerged worldwide. These centers have common structural elements: (1) Interdisciplinary medical and surgical team which includes at least pediatric otolaryngologist, gastroenterologist, pulmonologist, anesthetist, and speech and swallowing specialist, (2) coordination of care among different specialties, (3) Team meeting to discuss the clinical data of each patient and formulate individualized integrated treatment plan, and (4) Combined preoperative endoscopic assessment (triple endoscopy)[38]. In our department, pediatric patients with LTS were assessed and managed surgically, then patients were transferred to pediatric ICU in the University Children's Hospital. This may lead to interruption of care, inadequate postoperative follow-up, and absence of coordinated multidisciplinary care for these patients.

5.1.2. Preoperative microbial screen:

Patients undergoing airway surgery are often colonized by resistant bacteria (e.g. MRSA and Pseudomonas aeruginosa). Failure to detect and adequately eradicate these bacteria can be associated with poor outcomes after LTR[39]. This is attributed to the unique characteristics of this category of patients. Patients requiring open airway reconstruction usually have a history of repeated hospitalizations, prolonged and repeated antibiotic treatment, the presence of tracheostomy tubes for variable durations, and the presence of significant comorbidities[39]. The morbidity associated with postoperative infections caused by MRSA and other resistant micro-organisms is associated with longer hospital stays and increased healthcare costs. Consequently, most centers apply preoperative bacterial screening protocol to address this problem[39,40]. In a retrospective study conducted at Cincinnati Children's Hospital airway center, the prevalence of MRSA colonization in patients undergoing open airway surgery was more than 32%, higher than the colonization rates in patients undergoing other surgeries. The senior authors of this study have established MRSA colonization screening and treatment protocol after an observed increase in catastrophic postoperative events due to MRSA infections. After implementing this protocol, the rates of postoperative wound infections in MRSA-colonized and MRSA-non-colonized patients were not statistically significant[41]. In our institution, antimicrobial swabs from tracheostomy secretions are only implied when clear signs of infection are present (e.g. offensive odor, mucopurulent discharge, etc.). However, this may miss the asymptomatic colonization. In the present series, 3 patients failed open surgery due to postoperative severe wound infection, MRSA was the causative micro-organism in one of these three patients.

5.1.3. Preoperative upper GI endoscopic assessment

The presence of GERD or eosinophilic esophagitis is associated with decreased likelihood of success of LTR[34,42,43]. Therefore, upper GI endoscopy is included in the preoperative assessment checklist before LTR[39,40]. This includes observation of the gross appearance of the esophageal mucosa and the biopsy from abnormally-looking mucosa[39]. Wertz *et al*., found that performing upper GI endoscopy and PH probe testing as well as normal esophageal gross and microscopic upper GI findings were associated with increased overall success[43]. In our institution, upper GI endoscopy is not routinely performed. Instead, all patients receive postoperative anti-reflux treatment. This policy may miss the diagnosis and management of eosinophilic esophagitis and may not adequately address GERD before LTR.

5.2. Operative management:

5.2.1. The impact of the nature of the stenotic segment on pediatric LTS management outcome

In acute subglottic intubation-related trauma, patients can present with airway compromise after extubation or with failed decannulation if tracheostomized. Examination at this acute phase can reveal airway edema, granulations, ulcers, or rarely cysts according to the extent of trauma. Classification systems have been proposed to describe these early lesions and predict the risk of the development of subglottic stenosis[44]. The presence of soft granulation tissue stenosis represents a high-risk lesion that can develop into a mature firm fibrotic scar. Consequently, early detection and management of these lesions cannot be overemphasized, especially in patients with a history of prolonged intubation[44,45].

In the present series, half of the cases presented with soft stenosis in the form of granulation tissue, and the other half presented with firm fibrotic stenosis. Moreover, it was observed in our series that 10 (83%) patients who failed decannulation had fibrotic rather and the remaining 2 patients had soft stenosis. Although both lesions represent a continuum of the same disease, the outcome of management of these patients in our series is found to be significantly different. Patients with soft stenosis responded more efficiently to endoscopic management. In the present study, 3 of 23 failed endoscopic dilatation. On the other hand, patients presented with firm fibrotic stenosis were more likely to fail endoscopic treatment (n= 14, p<0.001). Consequently, these patients required tracheostomy to stabilize the airway before definitive airway reconstruction. Most importantly, 4 of them required emergency tracheostomy after suffering acute decompensation of the previously stable airway after failed endoscopic rigid dilatation. Furthermore, patients in this group were more likely to require open surgical intervention (p<0.001). As a result, the total number of procedures per patient was statistically different (p<0.001). The decannulation rate among patients of the two groups was also different, with more cases achieved decannulation in the soft stenosis group as compared to the firm stenosis group (p= 0.030). No statistically significant difference was observed between the two groups regarding the age, sex, level of stenosis, number of days on ETT, or the method of dilatation (EBD vs rigid dilatation) (Table 3).

Simpson et al. reported that circumferential firm stenosis is a poor predictive factor in endoscopic management of LTS[46]. Similarly, Avelino *et al*., reported 100% success rate of EBD in treating acute acquired subglottic stenosis, as compared with 39% in chronic stenosis[47]. Similar findings were reported by Lee *et al*., and they emphasized on the importance of early diagnosis of acute soft LTS due to the excellent outcome of EBD when performed on these lesions[48]. These studies are in accordance with our results, despite the fact that the present series shows that both rigid dilatation and EBD showed high efficacy in treating acute or soft stenotic segments. Chen *et al*., observed that acute segment even if severe grade will more likely respond to EBD, while chronic stenosis with mature scar is more likely to fail. In this situation, they suggested that adding other ancillary endoscopic procedures to EBD such as endoscopic anterior cricoid split, or radial laser incisions followed by EBD improve the success rate in managing severe stenosis. Therefore, they suggested that combining these ancillary procedures to EBD can be tried first in chronic stenosis before embarking on open surgery[49].

In a case series published by Önder *et al*., they described the stenotic segment as acute or chronic, and subdivided each type into thin and thick segments according to the length of the stenotic segment[50]. They found that EBD was 100% successful in all patients with thin stenotic segments regardless it was acute or chronic. Due to the use of EBD as the only dilatation method in their study, Avelino *et al*., reported minimal complications of endoscopic dilatation even in chronic firm stenoses[47]. On the other hand, as rigid bronchoscopic dilatation is still performed in our institution, we report that significant complications can occur if performed in severe firm stenoses as 4 patients required urgent tracheostomy due to acute airway decompensation. In the UK's largest multi-center study of EBD in LTS, complications of EBD were seen in 7 patients. Five developed symptoms of airway obstruction after the procedure, and one developed severe airway obstruction and needed an emergency tracheostomy. However, it was not mentioned whether these complications happened in patients with soft or firm stenosis[51]. Di Felice *et al*., published a case series of 63 patients with LTS, who have undergone endoscopic dilatation[52]. They divided the patients into two groups according to the method of dilatation (EBD vs. rigid bronchoscopic dilatation) and found out that there was no significant difference between both groups regarding the mean stenosis degree at follow-up. There were no complications observed in their series in either group, although most of their patients had grade 3, complex stenosis (>1cm in length, involving the subglottic region and trachea, or with associated malacia). However, they did not categorize their patients according to the nature of the stenotic segment. Lanye Hu *et al*., have studied the outcome of EBD in 33 patients with acquired subglottic stenosis[53]. They found that patients with firm stenosis (a firm scar with a duration of more than 60 days) needed a significantly greater number of dilatations than acute soft stenosis. However, in contrast to our findings, there was no significant difference between the two groups in procedural success, although the success rate was higher in acute soft stenosis (86.7% vs. 61.1%). They concluded that early intervention has a better outcome regarding the number of dilatations[53]. However, the small sample size in their study, which is similarly an important limitation in ours, may underestimate the difference between the two success rates.

These results confirm the importance of adding the nature of stenosis to the preoperative assessment checklist in patients with LTS and considering this factor in deciding the management plan of patients with LTS. If the stenosis is soft, endoscopic intervention can be the initial step as it is more likely to succeed even in severe stenosis. On the other hand, in severe firm fibrotic stenosis, endoscopic dilatation may have a lower success rate, although it can still have a significant role as an alternative, at least temporarily, to open airway surgical reconstruction. However, the surgeon may refrain from using the rigid dilatation method in cases of severe stenosis to avoid the catastrophic accident of acute airway decompensation.

The results of the present series should be viewed cautiously, as more patients in the soft stenosis group had grade 2 stenosis compared to the firm stenosis group, which included more patients with grade 3 ($p= 0.016$). It is well established that more severe stenosis is associated with a lower success rate of the endoscopic management of LTS[14,54]. However, 90% of patients with grade 3 soft stenosis ($n= 10$) were treated successfully with endoscopic intervention (9 patients had successful endoscopic treatment and 1 patient failed to be decannulated). Prospective comparative studies between the outcomes of management of soft and firm stenoses of the same degree are necessary to confirm the findings in the present study.

5.2.2. Rigid bronchoscopic dilatation Vs Endoscopic Balloon Dilatation

Mild stenosis can be treated endoscopically, while open surgical reconstruction is the gold standard in severe grades of stenosis. Endoscopic balloon dilatation has replaced rigid bronchoscopic dilatation as the preferred method of endolaryngeal dilatation due to the theoretical advantage of applying radial force on the stenotic segment, which produce less shear forces and less trauma to the airway. Consequently, rates of restenosis and reoperation after balloon dilatation were reported to be lower than rigid bronchoscopic dilatation[55]. In our department, rigid bronchoscopic dilatation is still used as a main dilatation method. As demonstrated in Table (2), among the 41 patients who underwent endoscopic intervention as the primary procedure for treatment of LTS, 8 patients underwent EBD, while the remaining 33 patients underwent rigid bronchoscopic dilatation. When both groups were collectively compared, no statistically significant difference was identified in terms of decannulation rates, the need for open airway reconstruction surgery, the success of endoscopic treatment, or the mean total procedures number ($p= 0.386$, $p= 0.165$, $p= 0.110$, $p= 0.617$, respectively).

In a systematic review exploring different methods of primary dilatation as a treatment modality for LTS, 8 rigid bronchoscopic dilatation sessions were needed per patient before achieving a final successful outcome, compared to 2 to 3 sessions of dilatations per patient were needed using other methods (balloon dilatation alone and balloon dilatation or rigid dilatation plus adjunctive treatments like radial incisions using CO_2 laser before dilatation). However, in the same review, no conclusion could be achieved regarding the superiority of one dilatation method over the other in achieving a successful outcome (extubation/decannulation, or achieving a secured patent airway without tracheostomy)[56]. Again, in a retrospective case series, the results of rigid bronchoscopic dilatation were comparable to balloon dilatation in regard to achieving a patent safe airway without tracheostomy or reconstructive surgery[57]. Although no prospective studies have been published comparing the two methods as regards the restenosis rate, efficacy, cost and complications; EBD has been widely accepted as theoretically less traumatic and more appealing method of dilatation. It is observed in the present series that 4 patients, for whom rigid bronchoscopic dilatation was performed, required unplanned emergency tracheostomy after the procedure due to airway decompensation. This serious complication did not occur in the patients who underwent EBD, although documented in previous studies after EBD[58].

5.2.3. Number of procedures

In the present series, the mean number of procedures was 2.43. Univariate linear regression analysis revealed that the number of procedures was dependent on the nature of the stenotic segment, and the need for open surgical reconstruction, and the presence of tracheostomy ($p<0.001$, $p<0.001$, $p= 0.047$ respectively). Fibrotic stenotic segments required more procedures than acute soft segments. This finding was in concordance with reported findings in the literature[47,49,59] Sinacori *et al.,* reported that patients with multilevel tracheal stenosis required a greater number of procedures as compared to patients with other subsite involvement[60]. In the same study, patients who required open surgical reconstruction required 7.2 procedures. However, we could not detect the level of stenosis as a significant factor for the need of multiple procedures. Furthermore, although reports from large retrospective studies confirmed the association of the degree of stenosis and the need for multiple procedures, this could not be demonstrated in the univariate regression analysis in the present study (Table 4)[61]. One explanation is that there were no cases with grade 1 or grade 4 stenosis in the present series. This may distort the relation between the grade of stenosis and the number of procedures, as cases with grade 4 stenosis would most likely require a higher number of procedures and cases with grade 1 stenosis would rarely need more than one procedure, if any.

5.3. Postoperative outcome

5.3.1. Failed decannulation

Analysis of the failed decannulation cases in our series revealed that 6 of the 12 patients underwent open reconstruction surgery. Three patients failed decannulation after LTR, 2 patients after pCTR, and one patient after open anterior cricoid split. Since all LTR cases in our series were performed as a double-stage procedure, it was reported that ds-LTR has less success rates that ss-LTR[16,62]. This may be related to the fact that patients who require double-staged procedure usually have adverse preoperative factors while patients who undergo single staged procedure usually have a more preferred profile. However, more recent reports revealed no significant differences between the two types of procedures regarding the decannulation rates[63]. On the other hand, pCTR is reported to have a high success rate, exceeding 90%. In a case series of 93 cases, overall decannulation rate was 94% and operation specific decannulation rate was 71%. In the same study, it was reported that postoperative vocal cord paralysis (unilateral or bilateral) was associated with failed decannulation [64]. The degree of stenosis, the presence of comorbidities, and the multilevel involvement of the airway were also associated with less decannulation rates[62,65,66]. In addition, Gustafson *et al*.,[67] reported that preoperative malacia, severe grades of stenosis, anterior and posterior costal cartilage graft LTR, the need for prolonged sedation especially if younger than 4 years old, were associated with postoperative airway compromise after ss-LTR. As summarized in Table (5), 9 of the 12 patients who failed decannulation in our series had grade 3 stenosis and only 3 patients had grade 2 stenosis. Furthermore, 4 patients had severe comorbidities (bronchopulmonary dysplasia, Systemic lupus erythematosus, Fallot's tetralogy, and severe neurological disease), and half of them had multilevel stenosis.

Despite the best management of patients with acquired LTS, restenosis after surgery can still occur. This is because every incision in the airway mucosa represents a new injury. Furthermore, as the airway has a limited regenerative capacity and a tendency to heal by scarring rather than regeneration, restenosis is a possibility after any airway reconstructive surgery[19-21]. As a result, it was estimated in some reports that there is a 10-20% risk of restenosis after seemingly optimal airway surgery[22-25]. This tendency of the airway for fibrosis and restenosis, in addition to the need for multiple procedures before achieving surgical success, elicited the need for innovative therapeutic options to optimize the airway healing process. This is the rationale for using adjunct treatments to reduce the incidence of postoperative granulation and fibrosis.

CONCLUSION

Acquired pediatric LTS still represents a significant challenge to the pediatric otolaryngologist. Optimizing the perioperative conditions in addition to adopting the best surgical techniques are imperative to a favorable outcome. Even though, a risk of restenosis is always present and innovative technologies are needed to change the postoperative healing process towards regeneration rather than fibrosis.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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REFERENCES

1. Arianpour K, Forman SN, Karabon P, Thottam PJ. Pediatric acquired subglottic stenosis: Associated costs and comorbidities of 7,981 hospitalizations. Int J Pediatr Otorhinolaryngol. 2019; 117:51-56. https://doi.org/10.1016/j.ijporl.2018.11.016.

2. Monnier P. The Compromised Paediatric Airway: Challenges Facing Families and Physicians. In: Monnier P (ed). Pediatric Airway Surgery: Management of Laryngotracheal Stenosis in Infants and Children. Berlin, Heidelberg: Springer Berlin Heidelberg; 2011. 3-6.

3. Clark CM, Kugler K, Carr MM. Common causes of congenital stridor in infants. JAAPA. 2018; 31(11):36-40. https://doi.org/10.1097/01.JAA.0000546480.64441.af.

4. Monnier P, Bernath MA, Chollet-Rivier M, Cotting J, George M, Perez M-H. Pediatric airway surgery: Management of laryngotracheal stenosis in infants and children. Egypt J Otolaryngol. 2014; 30:188-190. https://doi.org/10.1007/978-3-642-13535-4.

5. Stauffer JL, Olson DE, Petty TL. Complications and consequences of endotracheal intubation and tracheotomy. A prospective study of 150 critically ill adult patients. Am J Med. 1981; 70(1):65-76. https://doi.org/10.1016/0002-9343(81)90413-7.

6. Lambercy K, Pincet L, Sandu K. Intubation Related Laryngeal Injuries in Pediatric Population. Front Pediatr. 2021; 9:594832. https://doi.org/10.3389/fped.2021.594832.

7. Ho AS, Koltai PJ. Pediatric tracheal stenosis. Otolaryngol Clin North Am. 2008; 41(5):999-1021. https://doi.org/10.1016/j.otc.2008.04.006.

8. Schweiger C, Manica D, Pereira DRR, *et al.* Undersedation is a risk factor for the development of subglottic stenosis in intubated children. J Pediatr (Rio J). 2017; 93(4):351-355. https://doi.org/10.1016/j.jped.2016.10.006.

9. Manica D, Schweiger C, Marostica PJ, Kuhl G, Carvalho PR. Association between length of intubation and subglottic stenosis

in children. Laryngoscope. 2013; 123(4):1049-1054. https://doi.org/10.1002/lary.23771.

10. Karkos PD, Leong SC, Apostolidou MT, Apostolidis T. Laryngeal manifestations and pediatric laryngopharyngeal reflux. Am J Otolaryngol. 2006; 27(3):200-203. https://doi.org/10.1016/j.amjoto.2005.09.004.

11. May JG, Shah P, Lemonnier L, Bhatti G, Koscica J, Coticchia JM. Systematic review of endoscopic airway findings in children with gastroesophageal reflux disease. Ann Otol Rhinol Laryngol. 2011; 120(2):116-122. https://doi.org/10.1177/000348941112000208.

12. Venkatesan NN, Pine HS, Underbrink M. Laryngopharyngeal reflux disease in children. Pediatr Clin North Am. 2013; 60(4):865-878. https://doi.org/10.1016/j.pcl.2013.04.011.

13. Roberts J, Powell J, Begbie J, *et al*. Pediatric tracheostomy: A large single-center experience. Laryngoscope. 2020; 130(5):E375-380. https://doi.org/10.1002/lary.28160.

14. Quesnel AM, Lee GS, Nuss RC, Volk MS, Jones DT, Rahbar R. Minimally invasive endoscopic management of subglottic stenosis in children: success and failure. Int J Pediatr Otorhinolaryngol. 2011; 75(5):652-656. https://doi.org/10.1016/j.ijporl.2011.02.002.

15. de Alarcon A, Rutter MJ. Revision pediatric laryngotracheal reconstruction. Otolaryngol Clin North Am. 2008; 41(5):959-980. https://doi.org/10.1016/j.otc.2008.04.004.

16. Hartnick CJ, Hartley BE, Lacy PD, *et al*. Surgery for pediatric subglottic stenosis: disease-specific outcomes. Ann Otol Rhinol Laryngol. 2001; 110(12):1109-1113. https://doi.org/10.1177/000348940111001204.

17. Alvarez-Neri H, Penchyna-Grub J, Porras-Hernandez JD, Blanco-Rodriguez G, Gonzalez R, Rutter MJ. Primary cricotracheal resection with thyrotracheal anastomosis for the treatment of severe subglottic stenosis in children and adolescents. Ann Otol Rhinol Laryngol. 2005; 114(1 Pt 1):2-6. https://doi.org/10.1177/000348940511400102.

18. Triglia JM, Nicollas R, Roman S. Primary cricotracheal resection in children: indications, technique and outcome. Int J Pediatr Otorhinolaryngol. 2001; 58(1):17-25. https://doi.org/10.1016/s0165-5876(00)00452-3.

19. Roomans GM. Tissue engineering and the use of stem/progenitor cells for airway epithelium repair. Eur Cell Mater. 2010; 19:284-299. https://doi.org/10.22203/ecm.v019a27.

20. Rawlins EL, Okubo T, Que J, *et al*. Epithelial stem/progenitor cells in lung postnatal growth, maintenance, and repair. Cold Spring Harb Symp Quant Biol. 2008; 73:291-295. https://doi.org/10.1101/sqb.2008.73.037.

21. Snyder JC, Teisanu RM, Stripp BR. Endogenous lung stem cells and contribution to disease. J Pathol. 2009; 217(2):254-264. https://doi.org/10.1002/path.2473.

22. Herrington HC, Weber SM, Andersen PE. Modern management of laryngotracheal stenosis. Laryngoscope. 2006; 116(9):1553-1557. https://doi.org/10.1097/01.mlg.0000228006.21941.12.

23. Giudice M, Piazza C, Foccoli P, Toninelli C, Cavaliere S, Peretti G. Idiopathic subglottic stenosis: management by endoscopic and open-neck surgery in a series of 30 patients. Eur Arch Otorhinolaryngol. 2003; 260(5):235-238. https://doi.org/10.1007/s00405-002-0554-y.

24. Lano CF, Jr., Duncavage JA, Reinisch L, Ossoff RH, Courey MS, Netterville JL. Laryngotracheal reconstruction in the adult: a ten year experience. Ann Otol Rhinol Laryngol. 1998; 107(2):92-97. https://doi.org/10.1177/000348949810700202.

25. Walner DL, Heffelfinger SC, Stern Y, Abrams MJ, Miller MA, Cotton RT. Potential role of growth factors and extracellular matrix in wound healing after laryngotracheal reconstruction. Otolaryngol Head Neck Surg. 2000; 122(3):363-366. https://doi.org/10.1067/mhn.2000.102121.

26. Macauley SP, Schultz GS, Bruckner BA, Krawetz SA, Yang TP. Effects of transforming growth factor-beta1 on extracellular matrix gene expression by human fibroblasts from a laryngeal stenotic lesion. Wound Repair Regen. 1996; 4(2):269-277. https://doi.org/10.1046/j.1524-475X.1996.40216.x.

27. Hirshoren N, Eliashar R. Wound-healing modulation in upper airway stenosis-Myths and facts. Head Neck. 2009; 31(1):111-126. https://doi.org/10.1002/hed.20925.

28. Myer CM, 3rd, O'Connor DM, Cotton RT. Proposed grading system for subglottic stenosis based on endotracheal tube sizes. Ann Otol Rhinol Laryngol. 1994; 103(4 Pt 1):319-323. https://doi.org/10.1177/000348949410300410.

29. Sharma SD, Gupta SL, Wyatt M, Albert D, Hartley B. Safe balloon sizing for endoscopic dilatation of subglottic stenosis in children. J Laryngol Otol. 2017; 131(3):268-272. https://doi.org/10.1017/s0022215117000081.

30. Zalzal GH, Cotton RT. A new way of carving cartilage grafts to avoid prolapse into the tracheal lumen when used in subglottic reconstruction. Laryngoscope. 1986; 96(9 Pt 1):1039. https://doi.org/10.1288/00005537-198609000-00019.

31. Cotton R. Management of subglottic stenosis in infancy and childhood. Review of a consecutive series of cases managed by

surgical reconstruction. Ann Otol Rhinol Laryngol. 1978; 87(5 Pt 1):649-657. https://doi.org/10.1177/000348947808700509.

32. Hseu AF, Benninger MS, Haffey TM, Lorenz R. Subglottic stenosis: a ten-year review of treatment outcomes. Laryngoscope. 2014; 124(3):736-741. https://doi.org/10.1002/lary.24410.

33. Erlandsson A, Werner M, Holm A, Schindele A, Olofsson K. Balloon dilatation versus CO(2) laser surgery in subglottic stenosis, a retrospective analysis of therapeutic approaches. Acta Otolaryngol. 2023; 143(6):528-535. https://doi.org/10.1080/00016489.2023.2222756.

34. Jacobs IN, Giordano T, Soaper A, *et al.* A multicenter study analyzing the impact of pre-existing comorbidities on laryngotracheal reconstruction (LTR) outcomes. Int J Pediatr Otorhinolaryngol. 2023; 172:111631. https://doi.org/10.1016/j.ijporl.2023.111631.

35. Rutter MJ, Hartley BE, Cotton RT. Cricotracheal resection in children. Arch Otolaryngol Head Neck Surg. 2001; 127(3):289-292. https://doi.org/10.1001/archotol.127.3.289.

36. Agrawal N, Black M, Morrison G. Ten-year review of laryngotracheal reconstruction for paediatric airway stenosis. Int J Pediatr Otorhinolaryngol. 2007; 71(5):699-703. https://doi.org/10.1016/j.ijporl.2007.01.005.

37. Collaco JM, Aherrera AD, Au Yeung KJ, Lefton-Greif MA, Hoch J, Skinner ML. Interdisciplinary pediatric aerodigestive care and reduction in health care costs and burden. JAMA Otolaryngol Head Neck Surg. 2015; 141(2):101-105. https://doi.org/10.1001/jamaoto.2014.3057.

38. Piccione J, Boesch RP. The Multidisciplinary Approach to Pediatric Aerodigestive Disorders. Curr Probl Pediatr Adolesc Health Care. 2018; 48(3):66-70. https://doi.org/10.1016/j.cppeds.2018.01.002.

39. Monnier P, Dikkers FG, Eckel H, *et al.* Preoperative assessment and classification of benign laryngotracheal stenosis: a consensus paper of the European Laryngological Society. Eur Arch Otorhinolaryngol. 2015; 272(10):2885-2896. https://doi.org/10.1007/s00405-015-3635-4.

40. Filauro M, Mazzola F, Missale F, Canevari FR, Peretti G. Endoscopic Preoperative Assessment, Classification of Stenosis, Decision-Making. Front Pediatr. 2019; 7:532. https://doi.org/10.3389/fped.2019.00532.

41. Statham MM, de Alarcon A, Germann JN, Tabangin ME, Cohen AP, Rutter MJ. Screening and treatment of methicillin-resistant Staphylococcus aureus in children undergoing open airway surgery. Arch Otolaryngol Head Neck Surg. 2012; 138(2):153-157. https://doi.org/10.1001/archoto.2011.1171.

42. Tawfik KO, Houlton JJ, Compton W, Ying J, Khosla SM. Laryngotracheal reconstruction: A ten-year review of risk factors for decannulation failure. Laryngoscope. 2015; 125(3):674-679. https://doi.org/https://doi.org/10.1002/lary.24963.

43. Wertz A, Ryan M, Jacobs I, Piccione J. Impact of Pre-operative Multidisciplinary Evaluation on Laryngotracheal Reconstruction Outcomes. Laryngoscope. 2021; 131(7):E2356-E2362. https://doi.org/https://doi.org/10.1002/lary.29338.

44. Schweiger C, Manica D, Kuhl G, Sekine L, Marostica PJ. Post-intubation acute laryngeal injuries in infants and children: A new classification system. Int J Pediatr Otorhinolaryngol. 2016; 86:177-182. https://doi.org/10.1016/j.ijporl.2016.04.032.

45. Cakir E, Atabek AA, Calim OF, *et al*. Post-intubation subglottic stenosis in children: Analysis of clinical features and risk factors. Pediatr Int. 2020; 62(3):386-389. https://doi.org/10.1111/ped.14122.

46. Simpson GT, Strong MS, Healy GB, Shapshay SM, Vaughan CW. Predictive Factors of Success or Failure in the Endoscopic Management of Laryngeal and Tracheal Stenosis. Ann Otol Rhinol Laryngol. 1982; 91(4):384-388. https://doi.org/10.1177/000348948209100412.

47. Avelino M, Maunsell R, Jubé Wastowski I. Predicting outcomes of balloon laryngoplasty in children with subglottic stenosis. Int J Pediatr Otorhinolaryngol. 2015; 79(4):532-536. https://doi.org/https://doi.org/10.1016/j.ijporl.2015.01.022.

48. Lee J-C, Kim M-S, Kim D-J, *et al*. Subglottic stenosis in children: Our experience at a pediatric tertiary center for 8 years in South Korea. Int J Pediatr Otorhinolaryngol. 2019; 121:64-67. https://doi.org/https://doi.org/10.1016/j.ijporl.2019.02.044.

49. Chen C, Ni WH, Tian TL, Xu ZM. The outcomes of endoscopic management in young children with subglottic stenosis. Int J Pediatr Otorhinolaryngol. 2017; 99:141-145. https://doi.org/10.1016/j.ijporl.2017.06.012.

50. Önder Şahin S, Şahin Yılmaz A, Gergin Ö, Yılmaz B. Balloon Laryngoplasty for Pediatric Subglottic Stenosis: A 5-year Experience. Turk Arch Otorhinolaryngol. 2020; 58(4):208-213. https://doi.org/10.5152/tao.2020.5795.

51. Powell S, Keltie K, Burn J, *et al*. Balloon dilatation for paediatric airway stenosis: Evidence from the UK Airway Intervention Registry. Clin Otolaryngol. 2020; 45(3):334-341. https://doi.org/10.1111/coa.13492.

52. Di Felice C, Alraiyes AH, Gillespie C, *et al*. Short-term Endoscopic Outcomes of Balloon and Rigid Bronchoplasty in the Management of Benign Subglottic and Tracheal Stenosis. J Bronchol Interv Pulmonol. 2023; 30(1):54-59. https://doi.org/10.1097/lbr.0000000000000852.

53. Hu L, He N, He S, Jiao Y. Endoscopic balloon dilatation in the management of paediatric-acquired subglottic stenosis in children. Auris Nasus Larynx. https://doi.org/10.1016/j.anl.2023.07.004.

54. Bakthavachalam S, McClay JE. Endoscopic management of subglottic stenosis. Otolaryngol Head Neck Surg. 2008; 139(4):551-559. https://doi.org/10.1016/j.otohns.2008.07.024.

55. Günaydın R, Süslü N, Bajin MD, *et al*. Endolaryngeal dilatation versus laryngotracheal reconstruction in the primary management of subglottic stenosis. Int J Pediatr Otorhinolaryngol. 2014; 78(8):1332-1336. https://doi.org/10.1016/j.ijporl.2014.05.022.

56. Chueng K, Chadha NK. Primary dilatation as a treatment for pediatric laryngotracheal stenosis: a systematic review. Int J Pediatr Otorhinolaryngol. 2013; 77(5):623-628. https://doi.org/10.1016/j.ijporl.2013.02.003.

57. Yafit D, Cavel O, Ungar OJ, *et al*. Rigid dilatation of pediatric laryngotracheal stenosis as an adequate alternative to balloon dilatation. Eur Arch Otorhinolaryngol. 2018; 275(10):2529-2533. https://doi.org/10.1007/s00405-018-5087-0.

58. Maresh A, Preciado DA, O'Connell AP, Zalzal GH. A Comparative Analysis of Open Surgery vs Endoscopic Balloon Dilation for Pediatric Subglottic Stenosis. JAMA Otolaryngol Head Neck Surg. 2014; 140(10):901-905. https://doi.org/10.1001/jamaoto.2014.1742.

59. Wenzel AM, Schweiger C, Manica D, *et al*. Impact of balloon laryngoplasty on management of acute subglottic stenosis. Eur Arch Otorhinolaryngol. 2018; 275(9):2325-2331. https://doi.org/10.1007/s00405-018-5064-7.

60. Sinacori JT, Taliercio SJ, Duong E, Benson C. Modalities of treatment for laryngotracheal stenosis: the EVMS experience. Laryngoscope. 2013; 123(12):3131-3136. https://doi.org/10.1002/lary.24237.

61. Ochi JW, Evans JNG, Bailey CM. Pediatric Airway Reconstruction at Great Ormond Street: A Ten-Year Review:I. Laryngotracheoplasty and Laryngotracheal Reconstruction. Ann Otol Rhinol Laryngol. 1992; 101(6):465-468. https://doi.org/10.1177/000348949210100602.

62. Monnier P. Laryngotracheoplasty and Laryngotracheal Reconstruction. In: Monnier P (ed). Pediatric Airway Surgery: Management of Laryngotracheal Stenosis in Infants and Children. Berlin, Heidelberg: Springer Berlin Heidelberg; 2011. 257-277.

63. Smith LP, Zur KB, Jacobs IN. Single- vs double-stage laryngotracheal reconstruction. Arch Otolaryngol Head Neck Surg. 2010; 136(1):60-65. https://doi.org/10.1001/archoto.2009.201.

64. White DR, Cotton RT, Bean JA, Rutter MJ. Pediatric cricotracheal resection: surgical outcomes and risk factor analysis. Arch Otolaryngol Head Neck Surg. 2005; 131(10):896-899. https://doi.org/10.1001/archotol.131.10.896.

65. Monnier P, Ikonomidis C, Jaquet Y, George M. Proposal of a new classification for optimising outcome assessment following partial cricotracheal resections in severe pediatric subglottic stenosis. Int J Pediatr Otorhinolaryngol. 2009; 73(9):1217-1221. https://doi.org/10.1016/j.ijporl.2009.05.008.

66. Fiz I, Monnier P, Koelmel JC, *et al*. Implementation of the European Laryngological Society classification for pediatric benign laryngotracheal stenosis: a multicentric study. Eur Arch Otorhinolaryngol. 2019; 276(3):785-792. https://doi.org/10.1007/s00405-019-05353-4.

67. Gustafson LM, Hartley BE, Liu JH, *et al*. Single-stage laryngotracheal reconstruction in children: a review of 200 cases. Otolaryngol Head Neck Surg. 2000; 123(4):430-434. https://doi.org/10.1067/mhn.2000.109007.