Association between subglottic stenosis and endotracheal intubation in tracheostomized pediatric patients

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ABSTRACT

Objective. Considering that intubation time is the primary cause of subglottic stenosis, tracheostomy is suggested in adult patients following 10-15 days. The objective of this study was to analyze the association between intubation time and stenosis in pediatric patients, as well as to establish whether there is an adequate timing for tracheostomy in order to reduce the incidence of stenosis.

Materials and methods. A retrospective study (2014-2019) of tracheostomized newborns and children after an intubation period was carried out. Endoscopic findings at tracheostomy were analyzed.

Results. Tracheostomy was conducted in 189 patients, 72 of whom met inclusion criteria. Mean age was 40 months (1 month - 16 years). The incidence of stenosis was 21%, with a mean age of 23 months and a mean intubation time of 30 days vs. 19 days in the non-stenosis group (p= 0.02). The incidence of stenosis increased by 7% five days following intubation, reaching 20% after one month. Patients under 6 months old had greater tolerance to intubation periods without stenosis (incidence < 6% after 40 days, and median time to stenosis of 56 days vs. 24 days in patients over 6 months old).

Conclusions. In patients with long intubation periods, preventive measures should be taken in order to avoid laryngotracheal injuries, and early tracheostomy should be considered.

KEY WORDS: Tracheal stenosis; Tracheostomy; Laryngostenosis; Intubation.

ASOCIACIÓN ENTRE ESTENOSIS SUBGLÓTICA E INTUBACIÓN ENDOTRAQUEAL EN PACIENTES PEDIÁTRICOS TRAQUEOSTOMIZADOS

Objetivos. Considerando el tiempo de intubación la principal causa de estenosis subglótica, en adultos se sugiere realizar una traqueostomía a los 10-15 días. Se buscó determinar la asociación entre tiempo de intubación y estenosis en pediatría y establecer si existe, un momento en el que realizar una traqueostomía reduciría la incidencia de estenosis.

Material y métodos. Estudio retrospectivo (2014-2019) de neonatos y niños traqueostomizados luego de un período de intubación. Se analizaron los hallazgos endoscópicos al realizar la traqueostomía.

Resultados. Se traqueostomizaron 189 pacientes y 72 cumplieron criterios de inclusión. La edad media fue de 40 meses (1 mes a 16 años). La incidencia de estenosis fue de 21%, con edad media de 23 meses e intubación media de 30 días versus en el grupo sin estenosis fue de 19 días (p= 0 ,02). La incidencia de estenosis aumentó un 7% a los cinco días de intubación alcanzando el 20% al mes. Los menores de 6 meses presentaron mayor tolerancia a períodos de intubación sin estenosis (incidencia <6% luego de 40 días y mediana de tiempo hasta la estenosis de 56 días, versus 24 días en mayores de 6 meses).

Conclusiones. En pacientes con intubación prolongada, se deben tomar medidas preventivas para evitar el desarrollo de lesiones laringotraqueales incluyendo la consideración de una traqueostomía temprana.

PALABRAS CLAVE: Estenosis traqueal; Traqueostomía; Laringoestenosis; Intubación.

INTRODUCTION

Airway injuries following endotracheal intubation represent a severe problem in pediatrics. Subglottic stenosis has a reported incidence of 0.9-8.3%[1,2]. Even though laryngotracheal stenosis can be of congenital origin, it is acquired in more than 90% of cases, with endotracheal intubation being the primary etiological factor directly related to it[3].

The development of this pathology is impacted by multiple factors, such as traumatic intubation, tube size, presence of balloon, and intubation time, as well as other patient-related factors such as low weight at birth, prematurity, associated infections, immunosuppression, and gastroesophageal reflux[2-6].

Various publications have demonstrated that endotracheal intubation time is a key factor in the etiopathogenesis

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of airway stenosis in adult patients[7,8]. Therefore, early tracheostomy –less than 10-15 days following intubation– is regarded as beneficial to prevent laryngotracheal injuries in this population[7,8]. These injuries have also been described in the neonatal period, with newborns seemingly having greater tolerance to longer intubation periods than infants[5,6]. However, the evidence reported is scarce both for pediatric and newborn patients, which explains why there are no recommendations regarding the management of children requiring long intubation times[4,9].

Early tracheostomy has been demonstrated to be beneficial when it comes to reducing mechanical ventilation time, intensive therapy, sedation and analgesia, hospital stay, and healthcare costs, both in adults and in children[9-11]. However, since children have fewer airway injuries, the indication of routine early tracheostomy could be considered excessive[9].

The objective of this study was to analyze the impact of intubation time and other risk factors on the development of subglottic stenosis in pediatric patients, as well as to establish whether there is an adequate timing for prophylactic tracheostomy in order to reduce the risk of stenosis.

MATERIALS AND METHODS

A retrospective study of all patients under 18 years of age undergoing tracheostomy after an orotracheal intubation period from 2014 to 2019 was carried out. Exclusion criteria were surgery conducted at another institution and previous airway abnormalities –either congenital or acquired. Patients who did not undergo endoscopic airway assessment at tracheostomy were also excluded.

The study research protocol was approved by the hospital's Ethics Committee in August 2019 (identification number: 5226). Owing to the retrospective nature of the study, no informed consent was requested.

Demographic and clinical data was obtained from electronic clinical records. Intubation-related variables (duration, tube type and size) and endoscopic findings were assessed. In the analysis, patient comorbidities and history of previous intubations were taken into account. Confidentiality and personal data management were ensured at all times.

Endoscopies and tracheostomies were conducted by pediatric surgeons at the Pediatric and Neonatal Intensive Care Unit's operating room. Flexible 3.6 mm endoscopes (Ambu aScope) and 2.7 mm, 0-degree scope bronchoscopes (Storz Endoscopy) were used. Stenosis severity was categorized according to Myer-Cotton's classification[12].

Quantitative variables were expressed as mean and standard deviation or median and interquartile range, according to distribution. Qualitative variables were expressed as an absolute number and a percentage. Incidence was expressed as a percentage, with its confidence interval. The chi-squared test or Fisher's test was used for categorical variables, whereas the Student's t-test or Mann-Whitney U test were employed for continuous variables, according to distribution. To analyze the relationship between intubation time and stenosis grade, the Kruskal-Wallis test was used. Stenosis-free survival was compared by age groups using the log rank test. Time to stenosis was measured by means of Kaplan-Meier curves. Stenosis-free survival was calculated with a 95% confidence interval (CI).

A Cox regression model was created to assess other factors associated with stenosis, such as age and number of previous intubations. The data is presented with crude and adjusted hazard ratios (HR). Statistical significance was established at $p<0.05$. The Stata software, version 13, was used.

Table 1. Baseline patient characteristics.

		n (%)
Male patients		42 (58%)
Age	< 1 year	33 (46%)
	1-5 years	25 (34%)
	6-12 years	7 (10%)
	12-17 years	7 (10%)
Prematurity (< 1 year)		24 (67%)
Congenital cardiopathy		28 (39%)
Oncological disease		11 (15%)
Genetic/chromosomal syndromes		24 (33%)

RESULTS

A total of 189 patients were tracheostomized during the study period, 72 of whom (38%) met inclusion criteria (Fig. 1). 58% were male and 42% were female. 46% (n= 33) were under 1 year of age, and 34% (n= 25) were in their early childhood (Table 1).

Mean age at tracheostomy was 40 months (range: 1 month-16 years). The three main reasons for intubation were: need for mechanical ventilation for surgery (31%; n= 22), respiratory impairment (26%; n= 19), and neurological disorders (18%; n= 13). Failed extubation and dependence on long mechanical ventilation periods were the primary cause of tracheostomy (Fig. 2).

The incidence of stenosis was 21% (n= 15), with a similar frequency in both sexes. Mean age in this group was 23 months (SD= 23). Mean time of endotracheal intubation was 30 days (SD= 37) in the patients with subglottic stenosis vs. 19 days (SD= 24) in the non-stenosis group. However, stenotic patients following a 5-day intubation period and patients with long intubation periods –up to 119 days– were identified, without airway caliber reduction (p= 0.19).

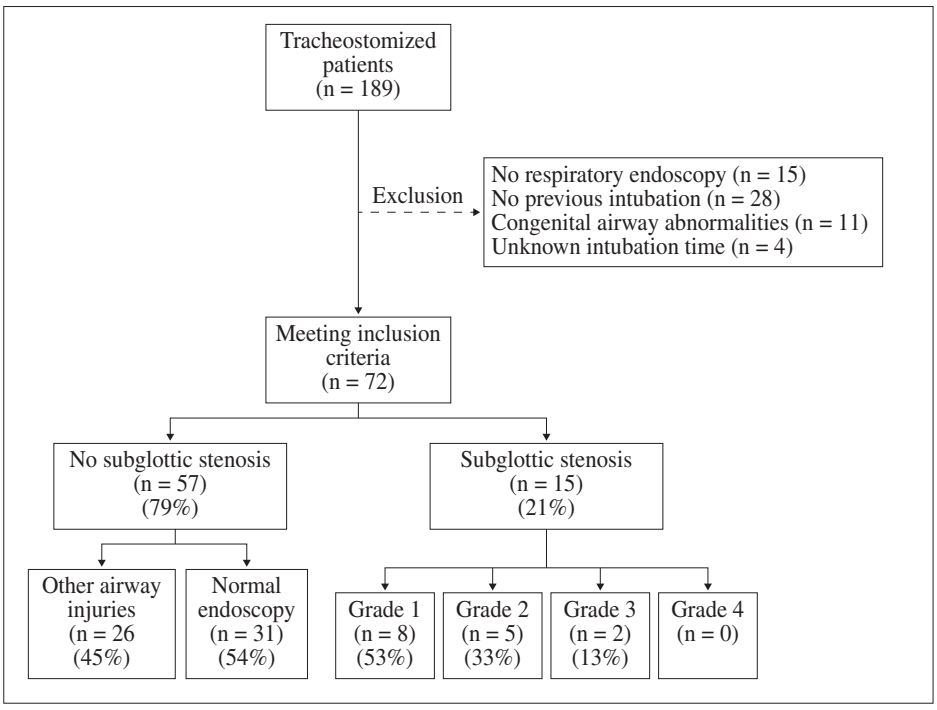

Figure 1. Patient flow diagram.

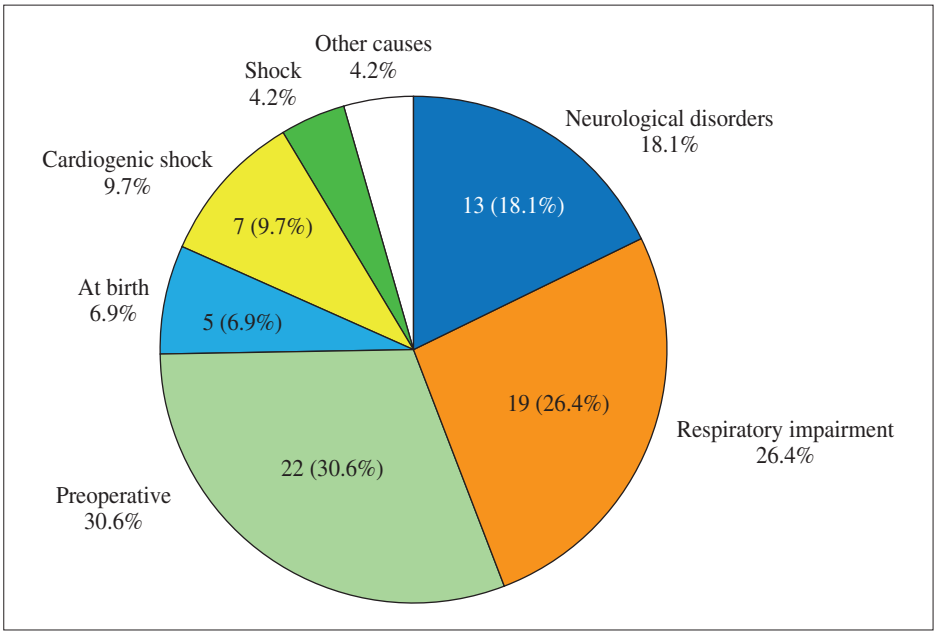

Figure 2. Intubation causes.

The characteristics related to stenosis pathogenesis –comorbidities, prematurity, tube size, and presence or absence of balloon– were described. No significant impact of any of these variables was demonstrated (Table 2).

Stenosis-free survival was 98% (CI: 90-99%) 5 days following intubation, 91% (CI: 81-96%) 10 days following intubation, 82% (CI: 61-92%) 30 days following intubation, 60% (CI: 25-82%) 60 and 90 days following intubation, and 40% (CI: 0.76-72%) 120 days following intubation (Fig. 3). Of the patients with subglottic stenosis, 53.3% (n= 8) had grade 1 stenosis with a median time of endotracheal intubation of 11 days (IQR: 7-32), 33.3% (n= 5) had grade 2 stenosis with a median time of 20 days (IQR: 20-21), and 13.3% (n= 2) had grade 3 stenosis with a median time of 56 days (IQR: 5-107) (p= 0.86). In this study, no cases of grade 4 stenosis (Fig. 4A and 4B) were

Table 2. Stenotic and non-stenotic patient characteristics.

		Global n= 72	*Non-stenotic n= 57*	*Stenotic n= 15*
			Mean (SD)	
Weight (kg)		15 (17)	16 (19)	10 (7)
Age (months)		40 (55)	44 (61)	23 (23)
Intubation days		21 (23)	19 (24)	30 (37)
No. of previous intubations		2 (2,6)	2 (3)	2 (3)
			N (%)	
Tube with balloon		63 (87%)	48 (84%)	15 (100%)
Male patients		42 (58%)	33(58%)	9 (60%)
Congenital cardiopathies		28 (39%)	25 (44%)	3 (20%)
Prematurity (< 1 year)		11/33 (33%)	10/31 (32%)	1/2 (50%)
Tube size	2.5		0	3 (100%)
	3		5 (100%)	0 (0%)
	3.5		22 (88%)	3 (12%)
	4		11 (68%)	5 (31%)
	4.5		7 (87.5%)	1 (12.5%)
	5		1 (50%)	1 (50%)
	5.5		3 (60%)	2 (40%)
	6		1 (100%)	0
	6.5		1 (100%)	0
	7		4 (100%)	0
	7.5		2 (100%)	0
Genetical/chromosomal syndrome		24 (33%)	19 (33%)	5 (33%)
Oncological disease		11 (15%)	8 (14%)	9 (20%)
Emergency intubation		44 (61%)	36 (63%)	8 (53%)
Scheduled intubation (immediately pre-surgery)		28 (39%)	21 (37%)	7 (47%)

SD= standard deviation

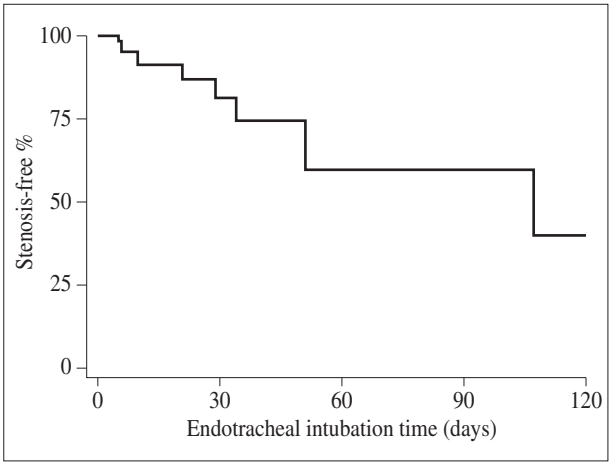

Figure 3. Stenosis-free survival; Kaplan-Meier curve.

identified. No statistically significant differences were noted when analyzing these groups (p= 0.76).

Of the 57 non-stenotic patients, 46% (n= 26) had other airway injuries at tracheostomy: ulcers in 21% (n= 12), edema in 12.3% (n= 7), and granuloma in 8.8% (n= 5). Mean intubation time in this group was 20 days (SD= 23 days), with injuries being noted from intubation day 3 (range: 3-119 days).

When classifying patients according to the age group, the incidence of stenosis was 15% (3/20) in patients under 6 months old. In this group, mean intubation time in stenotic patients was 56 days (SD= 49) and 31 days (SD= 26) in non-stenotic patients. In the group of patients over 6 months old, the incidence was higher, with 23% (12/52). Mean intubation time in stenotic patients was 24 days (SD= 32) and 14 days (SD= 8) in non-stenotic patients (p= 0.2) (Fig. 5).

When using a Cox regression model to assess the factors associated with stenosis time, such as age and number of previous intubations, no significant relationship was found between them and the development of stenosis (Table 3).

During follow-up, 19 (33.3%) patients died as a result of the underlying disease, and follow-up was lost in 3

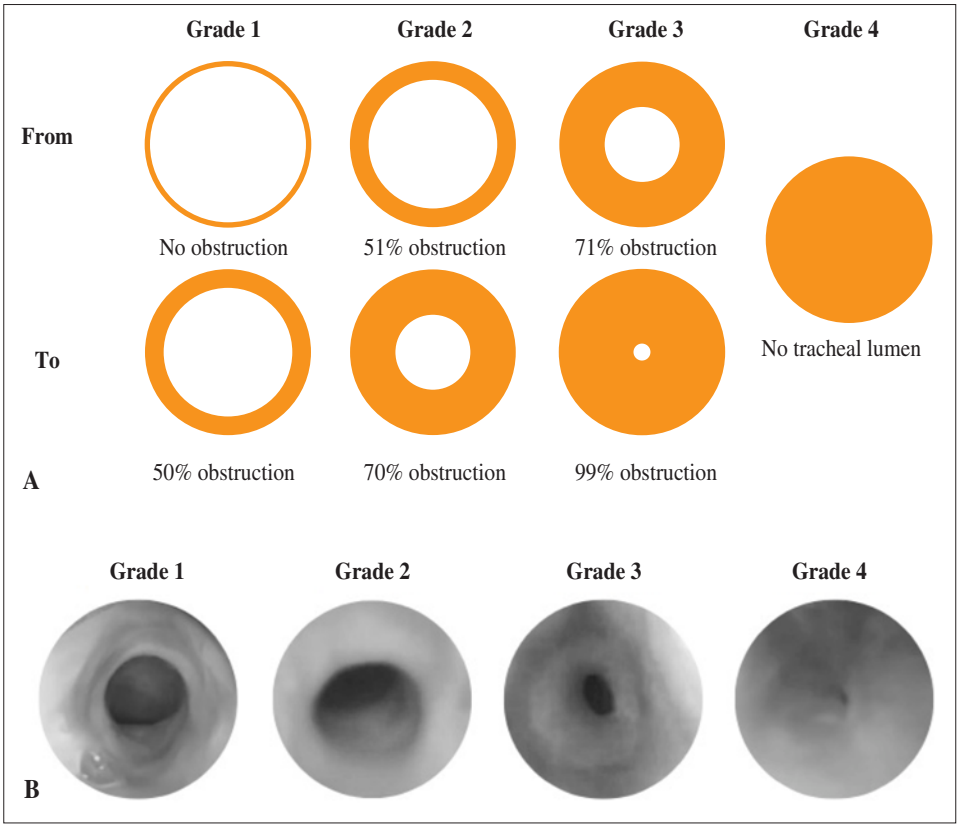

Figure 4. A) Myer-Cotton classification[12]. B) Endoscopies conducted in our patients. NB: The patient with grade 4 stenosis was not included in this study because inclusion criteria were not met.

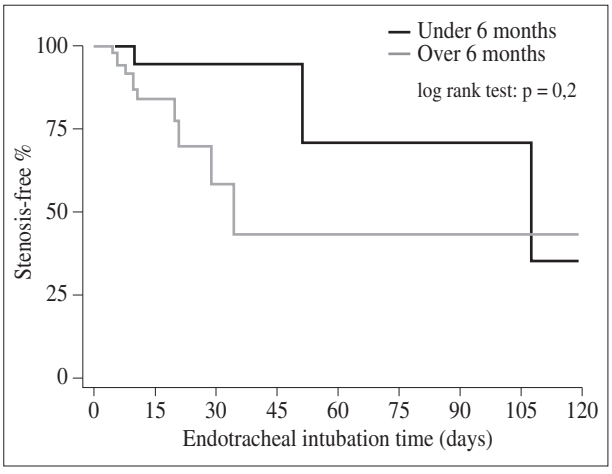

Figure 5. Stenosis-free survival according to age; Kaplan-Meier curve.

cases. Of the remaining patients, 70% (28/40) of the non-stenotic patients were decannulated. Of the stenotic patients, 5/10 (50%) achieved decannulation, with two of them requiring previous surgeries.

DISCUSSION

The incidence of subglottic stenosis in our population was higher than that reported in the literature. These findings may be due to the fact the population analyzed was exclusively made up of patients undergoing tracheostomy following an intubation period, contrarily to most studies published up until now, which assess extubated patients[1,2,4,5].

Table 3. Stenosis-associated factors.

	cHR	*95% CI*	*p*	*aHR*	*95% CI*	*p*
Age	0.99	0.98-1.01	0.88	1	0.99-1.01	0.92
No. of previous intubations	1.04	0.86-1.26	0.68	1.04	0.86-1.26	0.7

cHR= crude hazard ratio; aHR= adjusted hazard ratio; CI= confidence interval.

Even though there was a relationship between intubation times and the development of stenosis and other injuries (such as ulcers, edemas, and granulomas), the latter were noted from intubation day 3. Meanwhile, injury-free endoscopies were found in patients with up to 55 intubation days. This may stem from the multi-factor origin of airway injuries, which includes both patient-related and intubation-related factors[1,3-6,13,14].

Two studies conducted in pediatric patients estimated that every 5 intubation days, the risk of developing subglottic stenosis increases by 50.3%[4,14]. In addition, according to their findings, the incidence of laryngotracheal injuries seems to grow by 7.3% per day[14]. In our study, a 7% increase in the incidence of stenosis after five intubation days was observed, and a 9% rise was noted following 10 days. When comparing the results with the evidence available in the adult population, greater tolerance to endotracheal intubation was detected in pediatric patients[15], which could be explained by the anatomical differences of the airway and the fact children's cartilages are more elastic[2,16].

When analyzing the patients according to their age, greater tolerance to long intubation periods was noted in patients under 6 months of age, with a time to stenosis of 56 days. This doubles tolerance in the older group (24 days), where incidence progressively increases from day 5.

Even though greater predisposition to stenosis was observed in intubations with balloon, this association was not significant. Our study found no differences in other factors such as sex, underlying disease, or reason for intubation. This lack of statistical significance could be explained by the fact events were not numerous in each group, which means a larger patient cohort is required for such purpose.

Similarly to other studies[17,18], decannulation was feasible in 62% of the patients, including patients with subglottic stenosis. Therefore, tracheostomy could be regarded as a reversible procedure allowing for better tolerance to mechanical ventilation with earlier weaning and less need for sedation and hospitalization, which means early tracheostomy can be considered a valid therapeutic alternative in critical patients.

The limitations of this study are associated with its retrospective nature and reduced sample size, since this was a single-center study. This means not all tracheostomized patients were endoscopically assessed at the time, so excluding these patients can also create a bias. The lack of association between risk factors and the development of stenosis may be due to the reduced sample size. In addition, the incidence of subglottic stenosis was estimated based on intubated patients undergoing tracheostomy, with extubated patients not being considered. A prospective study with a larger sample size including these patients could help establish recommendations to guide the decision-making process in clinical practice.

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