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Analysis of Complications in (Crico-) Tracheal Resection Anastomosis in Adults: A Multicenter Study

Ivana Fiz, MD; Marta Filauro, MD, PhD; Claudio Sampieri, MD; Alessandro Ioppi, MD; Alberto Vallin, MD; Francesco Fiz, MD, PhD; Jan Costantin Koelmel, MD; Davide Lancini, MD; Cesare Piazza, MD; Christian Sittel, MD, PhD; Giorgio Peretti, MD

Objectives: The gold standard treatments for advanced laryngotracheal stenosis (LTS) are represented by partial cricotracheal (PCTRA) or tracheal resection and anastomosis (TRA). These procedures are potentially burdened by high postoperative complication rates. We investigated the impact of the most common stenosis and patient-related characteristics on the onset of complications in a multicentric cohort.

Methods: We retrospectively analyzed patients who underwent PCTRA or TRA for LTS of different etiologies in three referral centers. We tested the effectiveness of these procedures, the impact of complications on the outcomes, and identified factors causing postoperative complications.

Results: A total of 267 patients were included in the study (130 females; mean age, 51.46 ± 17.64 years). The overall decannulation rate was 96.4%. Altogether, 102 (38.2%) patients presented at least one complication, whereas 12 (4.5%) had two or more. The only independent predictor of post-surgical complications was the presence of systemic comorbidities ($p = 0.043$). Patients experiencing complications needed additional surgery more frequently (70.1% vs. 29.9%, $p < 0.001$), and had a longer duration of hospitalization (20 ± 10.9 vs. 11.3 ± 4.1 days, $p < 0.001$). Six of 102 (5.9%) patients with complications had restenosis, although this event did not occur among patients without complications.

Conclusion: PCTRA and TRA have an excellent success rate even when performed for high-grade LTS. However, a significant percentage of patients may experience complications associated with a longer duration of hospitalization or the need for additional surgeries. The presence of medical comorbidities was independently related to an increased risk of complications.

Level of evidence: 4

Key Words: complications, cricotracheal resection, laryngeal stenosis, risk factors, surgery, tracheal resection, tracheal stenosis.

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From the Department of Otorhinolaryngology (I.F.), IRCCS Istituto Giannina Gaslini, Genoa, Italy; Unit of Otorhinolaryngology—Head and Neck Surgery (M.F., C.S., A.I., A.V., G.P.), IRCCS Ospedale Policlinico San Martino, Genoa, Italy; Department of Surgical Sciences and Integrated Diagnostics (DISC) (M.F., C.S., A.I., A.V., G.P.), University of Genoa, Genoa, Italy; Nuclear Medicine Department (F.F.), Ente Ospedaliero "Ospedali Galliera", Genoa, Italy; Department of Nuclear Medicine and Clinical Molecular Imaging (F.F.), University Hospital, Tübingen, Germany; Department of Otorhinolaryngology—Head and Neck Surgery (J.C.K., C.S.), Klinikum Stuttgart, Stuttgart, Germany; Unit of Otorhinolaryngology—Head and Neck Surgery (D.L., C.P.), ASST Spedali Civili of Brescia, Brescia, Italy; and the Department of Medical and Surgical Specialties, Radiological Sciences, and Public Health (D.L., C.P.), University of Brescia, Brescia, Italy.

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Send correspondence to Claudio Sampieri, Department of Surgical Sciences and Integrated Diagnostics (DISC), University of Genoa, IRCCS Ospedale Policlinico San Martino, University of Genoa, Unit of Otorhinolaryngology—Head and Neck Surgery, Largo Rosanna Benzi, 10, Genoa 16132, Italy. Email: claudio.sampieri@outlook.com

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INTRODUCTION

Laryngotracheal stenosis (LTS) represents a pathological narrowing of the upper airway, which significantly reduces the airflow during inspiration and phonation.[1] Its etiology is multifactorial and can include different benign and malignant causes; however, in up to 5% of cases, it cannot be classified and is therefore defined as idiopathic.[2,3]

LTS-related symptoms are also extremely variable, ranging from mild respiratory discomfort to life-threatening respiratory insufficiency, and seem to depend on disease-related (grade, extension), as well as patient-related (systemic and airway comorbidities) characteristics.[4] These features greatly impact preoperative surgical planning; in particular, it was demonstrated that intermediate-and high-grade LTS benefit from an open-neck approach, including partial crico-tracheal (PCTRA) or tracheal resection and anastomosis (TRA), because these procedures have lower recurrence rates than endoscopic ones (where they range from 40% up to 70%).[5] However, even these complex procedures are not free from failure in terms of recurrence of stenosis, as it may occur in up to 11% of patients.[6] Moreover, up to 40% of subjects undergoing PCTRA or TRA can experience a range of minor (laryngeal edema, hematoma, granulations, unilateral vocal fold palsy, infection) or major complications (anastomosis dehiscence, distal tracheal

stump necrosis, respiratory insufficiency, bilateral vocal fold palsy, major hemorrhage) that may require additional medical or surgical treatments, thus prolonging hospitalization or delaying decannulation.[7] Life-threatening events, such as anastomotic dehiscence, are reported to occur in around 10% of cases.[8,9]

In light of these considerations, it is pivotal to evaluate the risk of recurrence, as well as that of surgical complications, on a case-by-case basis. To do so, clinical tools such as risk scoring systems, built upon multicentric data, are key in allowing swift and reliable evaluation of patients requiring airway surgery. In recent years, the European Laryngological Society (ELS) grading score, which is able to predict the onset of complications, the need for additional treatment, and failure in achieving decannulation have been devised.[10] This system allows a multiperspective evaluation of LTS patients, as it summarizes the length and degree of airway stenosis, as well as the presence of comorbidities, in a single score.

In this study, we aimed to identify risk factors that increase the rate of complications following PCTRA and TRA, thus potentially leading to restenosis and failure of the procedure itself. To do so, we tested different patients and stenosis characteristics in a multicentric cohort. Furthermore, we investigated the impact of complications on the need for additional treatments, decannulation, hospitalization, and stenosis recurrence because we believe that all this information can help surgeons in the preoperative patients' counseling and reduce the number of complications, simultaneously mitigating their potentially devastating effects.

MATERIALS AND METHODS

Patient Population

The local databases were searched for patients affected by acquired or congenital LTS and treated by TRA or PCTRA at three Departments of Otorhinolaryngology–Head and Neck Surgery, between September 1996 and December 2020: University Hospital of Brescia and Genoa, Italy (159 and 28 patients, respectively), and Klinikum Stuttgart, Germany (80 patients). All procedures were performed by four different surgeons. Laryngoplasty, laryngotracheal reconstruction, and endoscopic procedures were excluded from the present study.

All patients signed a written informed consent form, which was reviewed and approved by the respective local ethics committees (11240, CER Liguria Register N. 63/2021), and included the use of anonymized data for research purposes.

Preoperative Workup

Detailed endoscopic evaluation of the upper airway was always performed as the mainstay of LTS clinical assessment, even though the preoperative workup adopted has evolved over the years. It included a transnasal fiberoptic laryngoscopy in the outpatient clinic, followed by laryngoscopy with 0° and 30° rigid telescopes, and direct microlaryngoscopy under general anesthesia, as described in previous studies.[11]

The grade of stenosis was determined according to the Myer-Cotton classification system, except in case of neoplastic LTS.[12] Since 2015, as suggested by the ELS consensus paper,[13] all benign stenoses were classified according to the ELS score as well, integrating information about the grade of stenosis (I–IV according to the Myer-Cotton grading system), the number of subsites involved ("a" to "d" for one to four airway subsites among supraglottis, glottis, subglottis, and trachea), and the presence ("+" sign) of relevant airway (e.g., obstructive sleep apnea/ malacia/ secondary LTS) or systemic comorbidities (lung insufficiency, symptomatic cardiac or vascular disease, neurologic sequelae or mental impairment, swallowing disorder or aspiration, symptomatic gastroesophageal reflux, eosinophilic esophagitis, syndromic/non syndromic anomalies, diabetes mellitus, obesity).[10] The term any comorbidity was used to indicate the presence of at least one type of comorbidity: airway or systemic. For cases treated before 2015, a retrospective staging according to the ELS proposal was performed using an electronic, prospectively maintained database, endoscopic images, and videos. An ELS score ≥ IIIb was used as a cutoff value to indicate high-grade LTS, as previously proposed.[14] The Charlson Comorbidity Index (CCI) was also calculated for each patient, as previously proposed in this setting.[15,16]

A morphological imaging evaluation (computed tomography or magnetic resonance) was performed for every patient with neoplastic stenosis.

Surgical Technique

All patients underwent one of the four types of TRA or PCTRA, as described by Piazza et al. (Fig. 1).[14,17] The three centers share a uniform policy regarding patient selection criteria. Exclusion criteria were represented by a bilateral vocal fold paralysis, high-grade tracheobronchomalacia, stenosis length more than 5.5 cm, obesity (BMI > 35 kg/m^2), high-grade malignancies, and advanced neurological or cardiovascular disease entailing an elevated anesthesiologic risk (scores 4–5 according to the American Society of Anesthesiologists).[18] The severity of complications was categorized according to the Clavien-Dindo classification.[19,20]

Endpoints

We detailed all medical and surgical complications following PCTRA and TRA, as well as their management. Furthermore, we calculated the complication rate as the percentage of patients with a postoperative event requiring additional treatment. Ultimately, three main endpoints were analyzed, as listed below:

1. Effectiveness of PCTRA and TRA in treating LTS, using patent airway rate for non-neoplastic LTS (percentage of patients that at their last follow-up had a tracheotomy-, and stent-free airway and were free of dyspnea during normal physical activity), and 5-year local control as a proxy of surgical success for neoplastic lesions;
2. Identification of factors causing postoperative complications and requiring additional treatments;
3. Impact of complications on decannulation rate, length of hospitalization, stenosis relapse, and the number of additional treatments.

Statistical Analysis

Patient age, gender, comorbidities, previous treatment, Myer-Cotton and ELS grading scores, preoperative tracheotomy, length of resection, and LTS etiology were correlated with the onset of complications. Furthermore, the presence of complications was correlated with decannulation, time to decannulation,

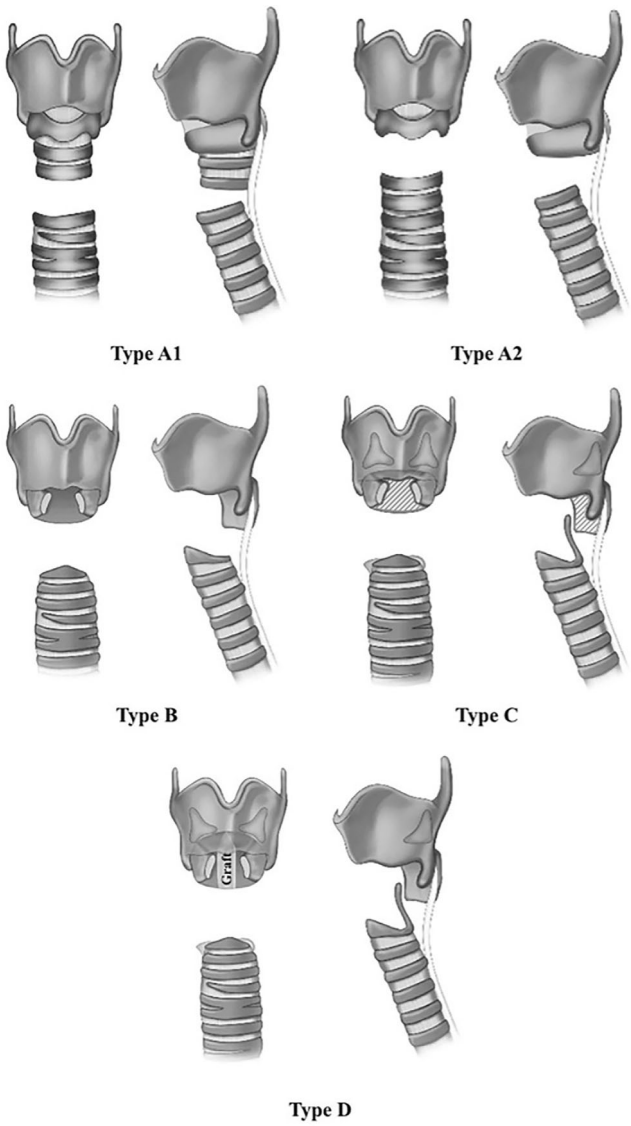

Fig. 1. Tracheal Resection and Anastomosis (TRA) and Partial Crico-tracheal Resection and Anastomosis (PCTRA) classification according to Piazza et al.[14,17] Type A refers to the removal of tracheal rings only, with subsequent tracheo-tracheal (Type A1) or crico-tracheal anastomosis (Type A2). Type B refers to the removal of the first tracheal rings with the cricoid arch and subsequent thyro-crico-tracheal anastomosis. Type C refers to the removal of the anterior cricoid arch, with circumferential mucosal removal at the cricoid level and reduction of the thickness of the cricoid plate (area indicated with lines) with the burr; this area will be then covered with mucosal flap from tracheal posterior wall, and subsequently the thyro-crico-tracheal anastomosis will be performed. Type D refers to the removal of the anterior cricoid arch with the posterior cricoid split up to its upper margin, with subsequent insertion of a costal graft and performance of a thyro-crico-tracheal anastomosis.

need for additional treatments, and restenosis. Differences in the distribution of categorical data between groups were tested by χ^2 or Fisher's exact test, as appropriate. Differences in continuous variables between groups were tested using Mann–Whitney U test. A multinomial binary logistic regression model was built to test the predictors of complications. A p-value <0.05 was considered significant. Data analysis was carried out using R software for statistical computing version 4.0.1 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

General Characteristics

A total of 267 patients were included in the study (130 females; mean age, 51.46 ± 17.64 years; range, 17–86). The data originated from the Universities of Genoa, Brescia, and the Klinikum Stuttgart in 28, 159, and 80 cases, respectively. The most frequently performed surgery (39%) was Type B procedure. Over half of the patients presented with high-grade and complex stenosis (52% with an ELS score ≥ IIIb). Preoperative tracheotomy was present in 54 (20%) of patients. One hundred twenty-four patients (47%) had at least one comorbidity and 138 patients (52%) underwent at least one endoscopic procedure before TRA/PCTRA.

LTS etiology was both acquired (iatrogenic, idiopathic, autoimmune, neoplastic) and congenital (4 patients, 1.5%). Iatrogenic etiology was the most frequently encountered (143 patients, 54%), followed by neoplastic (71 patients, 27%), idiopathic (42 patients, 16%), and autoimmune (5 patients, 1.9%; including 3 patients with granulomatosis with polyangiitis, 1 with relapsing polychondritis, and 1 with laryngeal amyloidosis). Neoplastic stenoses were due to thyroid cancers infiltrating the airway (n = 35), chondrosarcomas (n = 23), paratracheal lymph nodes metastases (n = 5), salivary gland tumors (n = 4), and squamous cell carcinomas of the trachea (n = 4). For the whole oncologic cohort, the 5-year local control rate was 83.1%, as 12 (16.9%) patients presented a local tumor recurrence. The median follow-up for all patients was 19 months (range 12–140). The longest follow-up was carried out for neoplastic patients (median 34 months, range 12–140). The median follow-up for both iatrogenic and congenital stenosis was 12 months (range 12–23, and 12–14 months, respectively).

Postoperative Complications Following PCTRA/TRA

Altogether, 102 (38.2%) patients experienced at least one postoperative complication, although 17 (6.4%) had two postoperative adverse events. The majority of patients in this subgroup (n = 77, 75.5%) suffered from a surgical complication, whereas 10 (9.8%) had a medical one. The most frequent surgical complication was laryngeal edema (29 events), which required tracheotomy in 4 and reintubation in 2 patients (Table I). The majority of these events (25 patients, 86.2%) occurred after a PCTRA procedure. The second most frequent complication was anastomotic dehiscence (24 events, 31.2%) which always required surgical revision (intubation with rigid telescope, open neck airway exploration, with anastomosis reinforcement in case of visible leakage and possible flap coverage, and drain positioning; immediate extubation, or postponed after 48 hours; tracheotomy in case of persistent mucosal inflammation on repeated endoscopy). Unilateral vocal fold palsy (18 events, 23.4%) was the third

TABLE I.
List of Surgical and Medical Complications and Their Treatment, When Needed.

Surgical Complication		Treatment
Laryngeal edema	29	Intubation 2;
Anastomosis dehiscence	24	Tracheotomy 4; Revision surgery 24;
Unilateral recurrence palsy	18	Tracheotomy 2 Wait and see
Granulation tissue	10	Endoscopic removal 5;
Hemorrhage	5	Steroids injection 6 Revision surgery 5
Endolaryngeal hematoma	3	Wait and see
Neck hematoma	1	Revision surgery
Bilateral vocal fold palsy	3	Tracheotomy 3
Fibrin deposition	2	Endoscopic removal
Pneumothorax	2	Pleural drainage
Cartilage necrosis	1	Wait and see
Delayed wound healing	2	Wait and see
Laryngospasm with cervical emphysema	1	Tracheotomy
Tracheomalacia	1	Revision surgery and stenting
Neck abscess	1	Surgical drainage
Type of Medical Complication	**N**	**Treatment**
Dysphagia	4	Swallowing rehabilitation 4;
Pneumonia	2	Tracheotomy due to aspiration 2; Antibiotics 2
Pulmonary edema	1	Intubation
Pulmonary insufficiency	4	Intubation 2;
Myocardial infarction	1	Positive pressure ventilation 2 Medical treatment
Cardiorespiratory arrest	2	Resuscitation with intubation 1;
Atrial fibrillation	1	Tracheotomy 1 Cardioversion

most common complication, where a wait and see approach was followed in all cases. The most frequent medical complication was dysphagia (4 events, 40%) which required swallowing rehabilitation in all cases and temporary tracheotomy in 2 patients. Most of the adverse events encountered in this series were classified as Clavien-Dindo Grade IIIb, thus requiring surgical management under general anesthesia (Table II).

Seventeen patients experienced more than one complication: 7 (41.2%) presented restenosis, which required endoscopic treatment in all cases. One was submitted to endoscopic removal of granulation tissue, although another underwent endoscopic reduction of bilateral arytenoid edema. One patient required open neck revision surgery due to postoperative bleeding, although another affected by neoplastic stenosis presented an esophageal fistula, which was repaired with a radial forearm free flap. The latter also had restenosis, which was treated successfully with endoscopic dilatations and injection of cortisone and Mitomycin C.

Impact of the Stenosis and Patients' Characteristics on Complications

According to univariate analysis, complications occurred more frequently in patients affected by at least one systemic comorbidity ($p = 0.016$), having an ELS score ≥ IIIb ($p = 0.004$), or bearing a stenosis involving more than one subsite ($p = 0.021$) (Table III). No single type of comorbidity influenced the complications rate; particularly, diabetes and obesity could not predict adverse surgical events ($p = 0.65$ and $p = 0.74$, respectively). Moreover, CCI could not tell apart those who would and would not experience complications ($p = 0.74$). The type of surgery performed also had an impact on the onset of complications. The sole resection of tracheal rings, followed by tracheo-tracheal (Type A1) or cricotracheal (Type A2) anastomosis, was associated with significantly fewer complications compared to other types of procedures (Type A, 25% vs. Type B, 46% [$p = 0.002$] vs. Type C, 45% [$p = 0.01$] vs. Type D, 75% [$p = 0.03$]). On the other hand, no statistically significant difference was noted across Types B-C-D procedures (Fig. 2). Patients submitted to infrahyoid release had more complications compared with those where such a maneuver was not required (48% vs. 34% respectively, $p = 0.024$) (Table III). The complication rates varied across LTS etiologies as well: it was highest in patients with autoimmune disease (60%), followed by those with an idiopathic etiology (52.4%) (Fig. 3).

At multivariate analysis, the main predictive factor of any type of complication was the presence of systemic comorbidities ($p = 0.043$) (Table IV).

Impact of Complications on Postoperative Course

Altogether, 26% of patients needed at least one additional treatment following PCTRA/TRA. Patients experiencing complications needed more frequently additional

TABLE II.
Distribution of the Severity of the First Surgical or Medical Complication Based on Clavien-Dindo Classification.[19,20]

	Severity of Complication						
Type of Complication	I	II	IIIa	IIIb	IV	V	Total Number (%)
Surgical only	21	3	4	45	4	/	77 (75.5)
Medical only	/	4	/	/	5	1	10 (9.8)
Surgical and medical	/	1	1	12	1	/	15 (14.7)
Total number (percent)	21 (20.6)	8 (7.8)	5 (4.9)	57 (55.9)	10 (9.8)	1 (1.0)	102 (100.0)

TABLE III.
Patient Characteristics and Univariate Analysis of the Determinants of Complications.

Variable	Overall: Number (%) $N = 267$	Complications: Number (%)		p-Value
		No = 165 (62)	Yes = 102 (38)	
Age				0.48
Mean (SD)	51.46 (17.64)	50.68 (18.49)	52.68 (16.25)	
Number of Previous Treatments				0.49
Mean (SD)	1.26 (2.14)	1.25 (2.32)	1.27 (1.80)	
Length of Resection (cm)				0.18
Mean (SD)	2.78 (1.16)	2.74 (1.30)	2.85 (0.90)	
Charlson Comorbidity Index				0.56
Mean (SD)	3.18 (2.04)	3.25 (2.10)	3.07 (1.94)	
Gender				0.27
Female	130 (100%)	76 (58%)	54 (42%)	
Male	137 (100%)	89 (65%)	48 (35%)	
Obesity				0.74
No	258 (100%)	160 (62%)	98 (38%)	
Yes	9 (100%)	5 (56%)	4 (44%)	
Diabetes				0.65
No	241 (100%)	150 (62%)	91 (38%)	
Yes	26 (100%)	15 (58%)	11 (42%)	
Etiology				0.15
Autoimmune	5 (100%)	2 (40%)	3 (60%)	
Congenital	4 (100%)	3 (75%)	1 (25%)	
Iatrogenic	143 (100%)	89 (62%)	54 (38%)	
Idiopathic	42 (100%)	20 (48%)	22 (52%)	
Neoplastic	71 (100%)	49 (69%)	22 (31%)	
Any Comorbidity				0.066
No	141 (100%)	94 (67%)	47 (33%)	
Yes	124 (100%)	69 (56%)	55 (44%)	
Systemic Comorbidity				**0.016**
No	184 (100%)	122 (66%)	62 (34%)	
Yes	81 (100%)	41 (51%)	40 (49%)	
Airway Comorbidity				0.51
No	200 (100%)	121 (60%)	79 (40%)	
Yes	63 (100%)	41 (65%)	22 (35%)	
Previous Treatment				0.45
No	125 (100%)	80 (64%)	45 (36%)	
Yes	138 (100%)	82 (59%)	56 (41%)	
Cotton-Meyer Grade				0.14
II	48 (100%)	33 (69%)	15 (31%)	
III	128 (100%)	69 (54%)	59 (46%)	
IV	16 (100%)	11 (69%)	5 (31%)	
ELS Score				**0.004**
<IIIb	92 (100%)	64 (70%)	28 (30%)	
≥IIIb	100 (100%)	49 (49%)	51 (51%)	
Number of Subsites Involved				**0.021**
1	78 (100%)	55 (71%)	23 (29%)	
2	114 (100%)	62 (54%)	52 (46%)	
3	9 (100%)	3 (33%)	6 (67%)	
Resection Type				**0.002**
A	97 (100%)	73 (75%)	24 (25%)	
B	103 (100%)	56 (54%)	47 (46%)	

(Continues)

TABLE III.
Continued

Variable	Overall: Number (%) $N = 267$	Complications: Number (%) No = 165 (62)	Complications: Number (%) Yes = 102 (38)	p-Value
C	60 (100%)	33 (55%)	27 (45%)	
D	4 (100%)	1 (25%)	3 (75%)	
Laryngeal Release				**0.024**
No	173 (100%)	115 (66%)	58 (34%)	
Yes	90 (100%)	47 (52%)	43 (48%)	
Preoperative Tracheotomy				0.28
No	211 (100%)	134 (64%)	77 (36%)	
Yes	54 (100%)	30 (56%)	24 (44%)	

Abbreviation: ELS, European Laryngological Society.
p values < 0.05 were reported in bold.

surgery than those without (70.1% vs. 29.9%, $p < 0.001$), and had longer hospitalization times (20 ± 10.9 vs. 11.3 ± 4.1 days, $p < 0.001$). Furthermore, 6 of 102 (5.9%) patients with complications had restenosis (whole population median follow-up: 19 months, range 12–140), although this event did not occur among patients without postoperative problems.

The overall decannulation rate was 96.4%, as 54 out of 56 patients with preoperative tracheotomy were decannulated. The occurrence of complications did not impact the decannulation rate ($p = 0.2$), time to decannulation ($p = 0.2$), or the number of additional treatments ($p = 0.7$) in our cohort of patients. The patent airway rate after PCTRA/TRA was 96.3%.

Finally, a single postoperative death occurred due to a myocardial infarction on the 5th postoperative day in a patient with preoperative systemic comorbidities who underwent a Type B PCTRA for an ELS IIIb+ LTS.

Sub-Cohort Analysis

Some differences in the distribution of the patients' characteristics, the distribution of the comorbidities, as well as the incidence of adverse events must be accounted for. When comparing the patients affected by neoplastic stenoses, we found that they were older ($p < 0.001$), were less likely to bear a tracheotomy pre-operatively ($p < 0.001$), had to undergo a relatively shorter resection ($p = 0.011$), had a greater prevalence of airway comorbidities ($p = 0.009$), and had less need for release ($p < 0.001$) than the non-cancer subjects (Table S1). Moreover, when we stratified the non-neoplastic population according to the degree of stenosis, we found that bearer of high-grade disease (≥IIIb according to the ELS scoring system) were more likely to have a pre-operative tracheotomy ($p = 0.003$), experienced more complications of any type ($p = 0.004$), and needed longer resection ($p < 0.001$), thus needed a laryngeal release more frequently

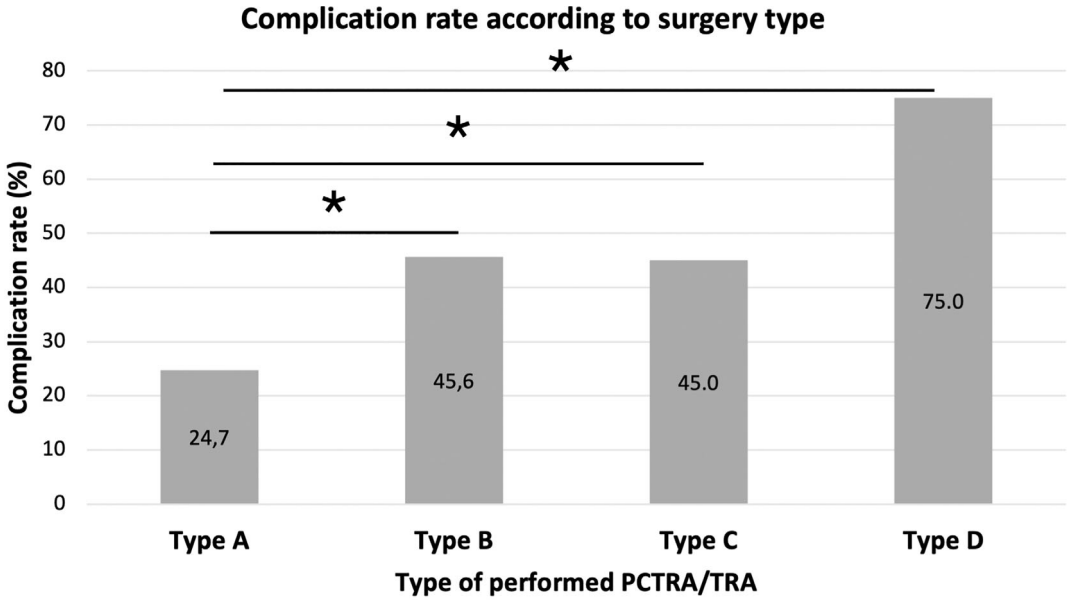

Fig. 2. Complication rate according to the type of surgery. PCTRA: partial crico-tracheal resection and anastomosis. TRA: tracheal resection and anastomosis. The symbol "*" refers to a $p < 0.05$.

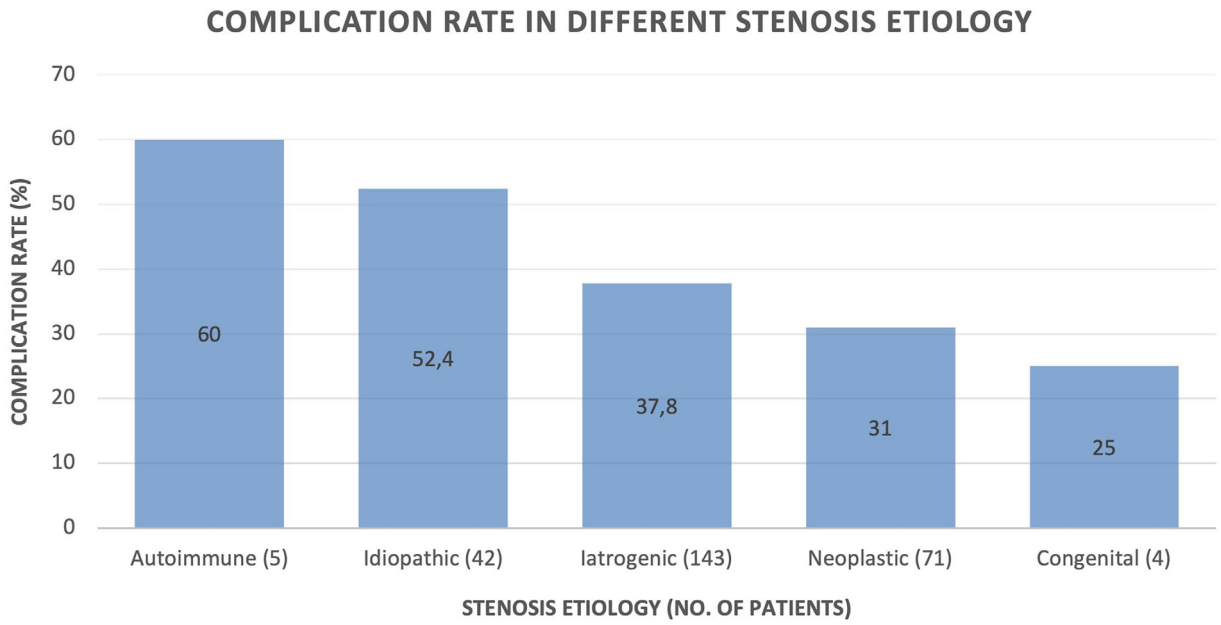

Fig. 3. Complication rate according to the etiology of the laryngotracheal stenosis. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

TABLE IV.
Multivariable Analysis of the Determinants of Complications.

Variables	OR	95% CI	p-value
Gender			
Female	—	—	0.17
Male	0.61	0.29, 1.25	
Etiology			
Autoimmune	—	—	0.62
Congenital	0.14	0.00, 2.95	
Iatrogenic	0.35	0.04, 2.70	
Idiopathic	0.42	0.04, 3.58	
Systemic Comorbidity			
No	—	—	**0.043**
Yes	2.07	1.02, 4.26	
ELS Classification			
<IIIb	—	—	0.17
≥IIIb	1.78	0.78, 4.18	
Hyoid Release			
No	—	—	0.34
Yes	1.46	0.67, 3.19	
Resection Type			
A	—	—	0.54
B	3.48	0.55, 33.8	
C	3.83	0.55, 39.1	
D	1.46	0.04, 78.6	
Number of Subsites Involved			
1	—	—	0.24
2	0.37	0.04, 2.30	
3	1.31	0.09, 20.7	

Abbreviation: ELS, European Laryngological Society.
p values < 0.05 were reported in bold.

($p = 0.018$) than those with low-grade stenosis. See Table S2 for details. Finally, when comparing the populations treated with TRA and PCTRA, we found that the latter subjects were more likely to be affected by idiopathic stenoses ($p < 0.001$) had a higher prevalence of higher-grade stenoses ($p < 0.001$), and comorbidities ($p = 0.018$), thus faced a higher complication rate ($p < 0.001$) than those with low-grade disease (Table S3).

DISCUSSION

High-and intermediate-grade complex LTS represent a significant surgical challenge. Our data show that both PCTRA and TRA are effective in treating these conditions, successfully curing nearly all patients, with a low rate of stenosis recurrence. When considering tumors of the crico-tracheal junction, these procedures definitively represent a viable surgical organ preservation strategy for low-and intermediate-grade malignancies.[14,21] Even though the wide variety of different histotypes treated in this series precludes further considerations at this level, the 5-year local control rate of 83.1% is in accordance with published data in other series.[21–24] On the other hand, complications were relatively frequent, affecting more than one-third of patients. In this regard, the present study allowed us to identify a specific risk profile, which includes both patient-and stenosis-related factors. In fact, our data highlighted that the presence of any systemic comorbidity as a broad umbrella category, such as respiratory, cardiovascular, neurological, and gastroenterological impairments, as well as diabetes mellitus, obesity, and syndromic/non syndromic anomalies led to greater complications. However, also in light of our selection criteria, we also found that no specific condition, such as hypertension, diabetes, or obesity, could single-

handedly predict the occurrence of surgical adverse events. Since the landscape of the possible concurring ailments was very varied, it is likely that targeted, prospective investigations are required to disclose the mechanisms underlying the interaction between the pre-existing conditions and the increased surgical risk. Even the inclusion of an omni-comprehensive comorbidity assessment could not tell the two patients' categories apart.[15] These findings appear to be at odds with the study led by Gelbard, which indicated how CCI was associated with a significant likelihood increase of tracheostomy dependence. However, our population includes a majority of patients who were treated many decades after the creation of this scoring system, which still places a heavy focus on now-manageable conditions, such as HIV infection or some types of Stage-IV cancers. An adapted version of this evaluation system might work, however, the development of such a tool was beyond the scope of the present study.

Furthermore, Tawfik et al identified patients with diabetes to be at higher risk for decannulation failure, although Fehervari et al associated higher patients' weight with higher number of additional endoscopic airway procedures following open airway surgery.[25,26]

Furthermore, patients with subglottic extension, and thus requiring PCTRA Types B, C, or D, are more prone to experience complications, independently of stenosis etiology. The type D resection-anastomosis is required when the subglottic stenosis extends to the glottis.[27] In that case, the incision on the cricoid plate and the insertion of the costal cartilage graft are performed in order to enlarge the posterior glottic space and assure the complete resolution of the stenosis. This surgical variant was associated with good decannulation rate (Cui et al reported 83%, whereas in our case series was 75%).[27] Furthermore, its complication rate was comparable with the ones reported for the PCTRA type B and C. However, our results are limited by the specimen size (only 4 patients underwent this type of surgery in our case series).

More in general, patients displaying higher-grade stenoses, both as longitudinal extension as well as in terms of the degree of airway narrowing (i.e., those with ELS grade IIIb or greater), showed a higher incidence of complications as well. This is in keeping with our previous findings, where the ELS score higher than IIIb+ was associated with the onset of complications, delayed decannulation and higher number of retreatments.[13]

Further factors that appear to come into play as determinants of complications and that should be taken into account when evaluating LTS patients are etiology, number of involved subsites, and need for laryngeal release.

In particular, the latter two are closely connected. It has been already suggested that both infra-and suprahyoid releases reduce the anastomotic tension and thus the risk of dehiscence, and that it should be carried out routinely in long-segment (crico-)tracheal resections, because these patients could be particularly prone to anastomotic dehiscence.[14] Accordingly, we reported a higher complication rate in these patients, compared with those who did not need any laryngeal release maneuver.

These findings were expected, because PCTRA and TRA are considered to be complex major surgeries, with a substantial risk for postoperative complications. The overall rate of complications described in the literature ranges from 15% to 39%, which is consistent with our findings.[7] These surgeries can result in life-threatening complications as well, caused first and foremost by anastomotic dehiscence, described in up to 10% of cases in the literature.[8,9] In our cohort, this complication occurred in 8.6% of patients, a proportion comparable to the vast majority of similar series.

However, most of the observed surgical complications in our cohort were minor and managed most frequently endoscopically. Even though medical complications were less frequent compared with surgical ones, their treatment often required some days in the intensive care unit or a temporary tracheotomy.

The occurrence of more than one complication was indeed a rare event, represented in the majority of cases by stenosis recurrence. These data mirror the results from one of the largest series of patients who underwent PCTRA and TRA ($n = 901$).[8] In fact, the recurrence of high-grade stenosis following these procedures still seems to be significantly lower than the recurrence rate observed after purely endoscopic approaches.[6] Furthermore, minor additional endoscopic procedures were sufficient to assure a patent airway in all cases of restenosis in our cohort of patients.

The present data show that the occurrence of complications is not only relevant *per se* but also because these untoward events carry a risk of prolonged hospitalization and are associated with the need for further surgical revision. Therefore, avoiding the onset of complications should be pivotal in reducing the overall procedure costs although significantly improving the patients' quality of life.

Altogether, these data highlight that preoperative assessment is key in ensuring procedural success. Among the tools that airway surgeons can use during patients' evaluation, scoring systems definitively play a relevant role. In fact, the predictive capacity of the ELS grading system on complications, decannulation, and the need for additional treatments has already been tested in two multicentric studies involving both adult and pediatric patients.[13,28] However, this method cannot be applied to oncological stenoses; in this context, the evaluation of subglottic involvement might serve as a proxy for this score.

When examining the possible difference across the various etiologies of LTS, we found that idiopathic and autoimmune stenoses showed a trend for higher recurrence, and complication rates compared with patients having other etiologies, such as iatrogenic and tumor-related ones. Actually, idiopathic stenosis arises from the subglottic area of the larynx, and thus requires a PCTRA surgical technique for the complete removal of the scar tissue, and this procedure was characterized by higher complication rate in our case series. Additionally, the presence of inflammation in the scar tissue of patients with idiopathic stenosis has already been described,[3] and it has been hypothesized that the persistent

inflammation, which can be exacerbated by surgical maneuvers, may foster the perpetuation of the mechanisms underlying the LTS. Furthermore, it has been suggested that hormonal pathways may also play a role, but this finding has not shown a translational impact yet.[29] Moreover, the granulomatosis with polyangiitis (GPA) represents the most common inflammatory diseases presenting with subglottic stenosis, followed by relapsing polychondritis, amyloidosis, sarcoidosis, pemphigoid, eosinophilic granulomatosis with polyangiitis and inflammatory bowel diseases.[30] Patients affected by GPA are eligible for airway resection-anastomotic procedures, even though a high complication rate (55%), and a need for additional treatments (in almost two-thirds of patients) may be expected, as the presence of chronic inflammation may cause the condition to relapse.[31] In fact, Herridge et al. proposed surgical intervention as a viable option in selected patients with GPA, whose component had been initially controlled with medical therapy.[32] Even though the best candidates would be patients in remission, who are not in treatment with immunosuppressive therapy, this is not always possible, and the decision-making is driven by the severity of symptoms and history of previous therapeutic attempts. In fact, Herridge et al. reported a successful resection and reconstruction of the airway without postoperative compromise of anastomotic integrity or wound healing despite concurrent use of prednisone, and cyclophosphamide during disease remission.[32]

Finally, patients with subglottic involvement faced complications more frequently compared with those requiring a pure tracheal resection (TRA Types A1 and A2 according to our classification system), as already suggested by Wright and colleagues.[8] In fact, the subglottic area represents a particular subsite of the larynx, and its different caliber, transient type of epithelium, proximity to vocal folds, and recurrent laryngeal nerves, make surgery in this region particularly challenging. Accordingly, the onset of complications was dependent on the type of performed surgery. Contrarily, the length of airway resection did not impact the onset of complications, even though patients that required the resection longer than 5.5 cm were excluded from this type of surgery. Indeed, pure tracheal resection had a lower complication rate compared with those involving the subglottis, independently of the overall length of resection.

This study is not without limitations. As with every retrospective multicentric study, it may be affected by a number of biases, even though these three referral centers share a common airway management strategy, and the constant communication among local investigators ensured that patients were analyzed and treated as homogeneously as possible. Another limitation is represented by the inclusion of patients treated over a prolonged period of time, during which PCTRA/TRA techniques, as well as the diagnostic workup and the scoring system itself, gradually evolved. Actually, the retrospective staging according to the ELS score was performed using archived endoscopic videos and images among other data, which quality had been evolving over the time with the technology improvement.

Finally, oncological stenoses could not be graded using the Myer-Cotton or the ELS scoring systems, thus limiting our understanding of such evaluations in this specific subgroup of patients.

CONCLUSIONS

PCTRA and TRA are highly effective in restoring airway patency in patients affected by LTS of diverse origins, even though they are burdened by a high rate of complications which can, in turn, be associated with longer hospital stays or the need for additional operations. Knowledge of predisposing risk factors could help surgeons during preoperative planning and counseling, in order to be prepared for every occurrence and adjust the patients' preoperative expectations.

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