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COVID-19

Post-COVID-19 airway stenosis treated by tracheal resection and anastomosis: a bicentric experience

Stenosi tracheali post-COVID-19 trattate con resezione e anastomosi tracheale: l'esperienza di due centri

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SUMMARY

Objective. The COVID-19 pandemic was an extraordinary challenge for the global healthcare system not only for the number of patients affected by pulmonary disease, but also for the incidence of long-term sequalae. In this regard, laryngo-tracheal stenosis (LTS) represents one of the most common complications of invasive ventilation.

Methods. A case series of patients who underwent tracheal resection and anastomosis (TRA) for post-COVID-19 LTS was collected from June 2020 to September 2021.

Results. Among 14 patients included, 50% had diabetes and 64.3% were obese. During intensive care unit stay, mean duration of orotracheal intubation (OTI) was 15.2 days and 10 patients (71.4%) underwent tracheostomy, which was maintained in 7 for an average of 31 days. According to the European Laryngological Society classification, 13 patients (92.9%) had a grade IIIa LTS and one a grade IIIa+. All patients underwent Type A TRA, according to the authors' classification. No major perioperative complications were reported and at the last follow-up all patients were asymptomatic.

Conclusions. With the appropriate indications, TRA represents an effective treatment in post-COVID-19 LTS patients. Short OTI times and careful tracheostomy are required in order to reduce the incidence of airway injury.

KEY WORDS: airway stenosis, COVID-19, tracheal resection, tracheal intubation, tracheostomy

RIASSUNTO

Obiettivo. *La pandemia da COVID-19 ha rappresentato una sfida straordinaria, sia per il numero di pazienti colpiti, che per l'incidenza di sequele. Tra queste, la stenosi laringo-tracheale (LTS) è tra le complicanze più comuni dopo ventilazione invasiva.*

Metodi. *È stata raccolta una casistica di pazienti sottoposti a resezione-anastomosi tracheale (TRA) per LTS post-COVID-19 dal Giugno 2020 al Settembre 2021.*

Risultati. *Tra i 14 pazienti inclusi, il 50% era affetto da diabete ed il 64,3% da obesità. Durante la degenza in terapia intensiva, la durata media di intubazione orotracheale (OTI) è stata di 15,2 giorni e 10 pazienti (71,4%) sono stati sottoposti a tracheotomia, mantenuta in 7 di loro per una media di 31 giorni. Secondo la classificazione della Società Europea di Laringologia, 13 pazienti avevano una LTS di grado IIIa ed uno di grado IIIa+. Tutti i pazienti sono stati sottoposti a TRA di Tipo A secondo la classificazione proposta dagli autori. Non ci sono state complicanze perioperatorie e all'ultimo follow-up tutti i pazienti sono asintomatici.*

Conclusioni. *Con le giuste indicazioni, la TRA è un trattamento efficace in pazienti affetti da LTS post-COVID-19. Un'OTI breve ed un'attenta tecnica tracheotomica sono necessarie per ridurre l'incidenza di lesioni tracheali.*

PAROLE CHIAVE: *stenosi tracheale, COVID-19, resezione tracheale, intubazione tracheale, tracheotomia*

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Introduction

Clinical management of patients affected by symptomatic SARS-CoV-2 infection has proven to be complicated and shaded by an unpredictable viral infection course. The cornerstone of treatment of COVID-19 is represented by respiratory support, which can be administered either through face/nose masks or via oral/nasal and tracheal intubation [1]. This latter invasive treatment, as reported by Grasselli and colleagues [2], is administered in nearly all (88%) patients admitted to the intensive care unit (ICU), with an absolute number of hospitalised patients who were intubated during the pandemic reaching a remarkable rate, as high as 33.1% from data collected in New York [3]. Notably, of those patients, the vast majority (72.5%) required prolonged endotracheal intubation (>7 days) [3], while it was needed in nearly 12% of all patients who were affected by COVID-19 [4,5].

As reported in the literature [6], prolonged endotracheal intubation may lead to mucosal damage and inflammation, granulation tissue formation, perichondritis, chondritis and subsequent cicatricial stenotic tissue formation. In addition, tracheostomy can add further damage to the already compromised tracheal lumen (tracheal rings fracture, collapse, necrosis, malacia, and superinfection) [7], while a number of authors [8,9] reported that the use of a large calibre endotracheal tube can increase the risk of airway mucosal damage. Moreover, the absence of accurate monitoring of the cuff pressure or the need to maintain it above 50 mmHg for clinical reasons (such as performance of high positive pressures ventilation in COVID-19 associated pneumonia) are related to mucosal ischaemia and necrosis, which play a fundamental role in establishing the above-mentioned complications [10]. Hence, use of the appropriate intubation technique minimising trauma related to arytenoid luxation or mucosal tearing, a precise tube calibre selection and the meticulous control of cuff pressure are of paramount importance to minimise the risk of ensuing laryngo-tracheal stenosis (LTS). The estimated rate of LTS due to endotracheal intubation ranges from 10% to 22% [11] if all the aforementioned technical issues are carefully followed. Moreover, only 1-2% of patients affected by this complication will possibly complain of severe dyspnoea, making post-intubation/post-tracheotomic critical LTS a rather rare event, with an estimated incidence of 4.9 patients/1,000,000 people per year [6].

In this respect, all due attentions have been commonly recommended and observed during the intubation protocol and management in the pre-pandemic era, while during COVID-19 this was often not achieved for a number of reasons. Indeed, especially at the beginning of the pandemic, the unpredictable course of the infection did not allow to foresee the patients' time of recovery. Moreover, the fear of contamination of health care workers during invasive and aerosol generating manoeuvers such as tracheostomy often led to the use of larger than normal tubes, maintenance of excessively high cuff pressure and delay in tracheotomy performance [7]. As a consequence, in post-COVID-19 patients, we expected an increased incidence of LTS and recommended that patients presenting with breathing difficulties within 6 months after ICU discharge receive a targeted evaluation aimed at ruling out the possibility of a iatrogenic LTS.

Following the European Laryngological Society (ELS) warning concerning the possible increased incidence of LTS in post-COVID-19 patients [7], we prospectively collected data regarding patients diagnosed with critical airway after a prolonged intubation due to SARS-CoV-2 infection and therefore treated in two tertiary referral academic centres by tracheal resection and anastomosis (TRA) as the index surgical procedure. The present study reports our experience in this clinical scenario and outlines critical issues that increase the patient's risk of developing post-intubation/post-tracheotomic LTS.

Materials and methods

Patient selection and data collection

Patients who underwent TRA for LTS as a consequence of invasive ventilation therapy for COVID-19 were selected at the Units of Otorhinolaryngology – Head and Neck Surgery of the Universities of Brescia and Genoa from June 2020 to September 2021. After approval by the local ethic committees (11240, CER Liguria Register N. 63/2021), data concerning patients demographics, comorbidities, COVID-19 ventilatory treatment, type of LTS and details of management were collected, and a dedicated database completed.

Demographics included patients age, gender and comorbidities, with particular attention to metabolic diseases. Data regarding COVID-19 respiratory support consisted of duration of ICU hospitalisation, time and duration of orotracheal intubation (OTI), presence and type of tracheostomy (i.e., surgical *vs* percutaneous), duration of tracheal intubation through the tracheostomy, time of ventilation weaning/tracheostomy tube removal, and eventual subsequent re-intubation. Time elapsed between ICU discharge and LTS diagnosis was also registered. Data regarding LTS features was collected using a standardised diagnostic work-up, and included length, anatomical subsite and grade of stenosis, according to the ELS classification [12]. Data concerning treatments encompassed the number and

type of endoscopic therapeutic procedures, extension and type of TRA according to the University of Brescia classification system [13] (Fig. 1), surgical complications, further interventions and postoperative medical therapy. Finally, data concerning surgical outcomes and clinical follow-up duration were collected.

Diagnostic work-up and surgery

All patients included in the present study referred to our centres complaining of dyspnoea at rest or progressive exertional dyspnoea, or the impossibility to be properly decannulated. In case of critical LTS at the first counselling, rigid bronchoscopic dilatation was first performed to allow proper symptom relief before adequate diagnostic work-up. If the procedure was not possible, or if it was insufficient in obtaining an adequate airway, a trans-stenotic tracheostomy was performed under local anaesthesia.

A standardised diagnostic protocol was then applied to each patient, as described by Monnier et al. [12]. Namely, each patient underwent awake nasal flexible fibreoptic laryngoscopy to assess vocal fold mobility and exclude other potential airway anomalies. If present, laryngoscopy was carried out also through the tracheostoma in order to evaluate the distal trachea and subglottic area from below. When an alteration of the laryngo-tracheal framework was suspected, radiologic examination by neck and chest CT was performed. Moreover, a direct laryngoscopy with rigid instrumentation under general anaesthesia was performed to assess the length and grade of LTS, and to remove by transoral carbon dioxide laser and gentle dilatation possible scar or synechiae, which could interfere with the final TRA procedure.

After collection of all this information, LTS was classified according to the ELS proposal [12] and the adequate surgical treatment planned. In detail, TRA was indicated in case of high grade mature stenoses (grade III-IV), with cranio-caudal extension > 1 cm (and < 5.5 cm), and/or laryngo-tracheal framework impairment, or in case of absence of response to multiple endoscopic procedures. TRA were then categorised according to the University of Brescia classification as previously described by Piazza et al. [13].

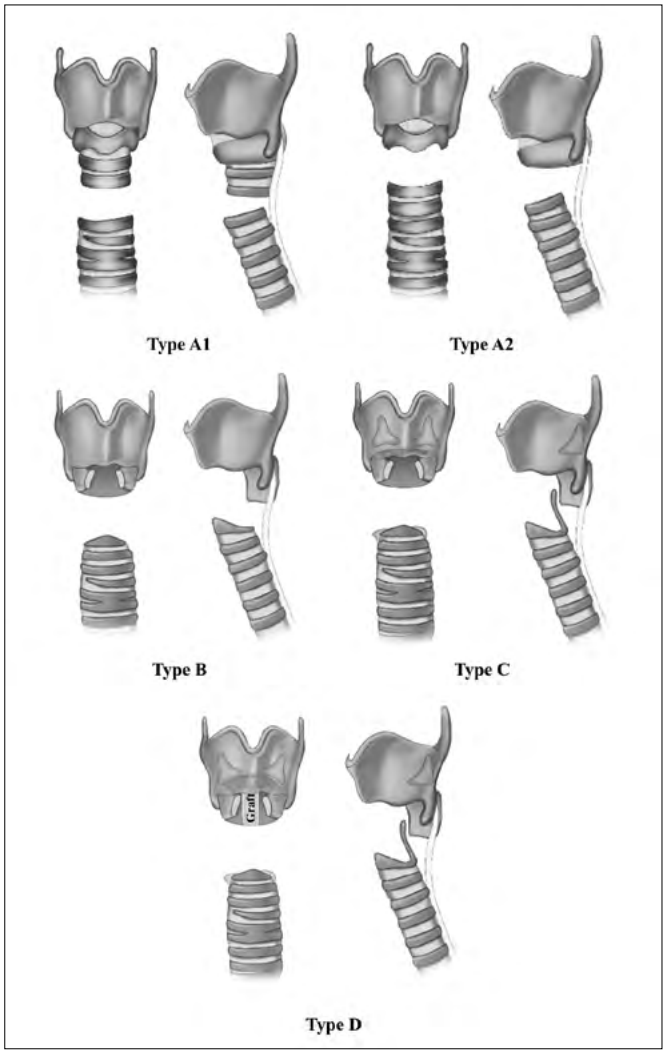

Figure 1. University of Brescia (C)TRA classification [13]. Type A1 refers to tracheal rings resection with tracheo-tracheal anastomosis; Type A2 is characterised by tracheal rings resection with crico-tracheal anastomosis; Type B includes tracheal rings resection with anterior cricoid arch removal and subsequent thyro-crico-tracheal anastomosis; Type C encompasses tracheal rings removal with anterior cricoid arch resection and posterior cricoid plate reshaping/partial removal up to the crico-arytenoid joints and subsequent thyro-crico-tracheal anastomosis and cricoid plate covering by a mucosal flap of pars membranacea; Type D is the same of Type C with posterior midline cricoid split and cartilaginous graft insertion for massive posterior glottic stenosis.

Results

Fourteen patients were treated by TRA for COVID-19 related LTS at our centres between June 2020 and September 2021. In particular, 9 (64.3%) patients were treated at the Unit of Otorhinolaryngology – Head and Neck Surgery of the University of Brescia, and 5 (35.7%) in the Unit of Otorhinolaryngology – Head and Neck Surgery of the University of Genoa. They represented 43.8% of the overall number of patients managed in the same time frame by (crico)-tracheal resection and anastomosis [(C)TRA] for all causes of LTS at both Institutions.

The male to female ratio was 11:3, and mean age was 54 years (range, 34-67). Twelve (85.7%) patients had at least one comorbidity; in detail, 7 (50%) reported diabetes mellitus and 9 (64.3%) obesity. One (7.1%) patient underwent tracheostomy in childhood for respiratory insufficiency due to viral infection and one (7.1%) presented with tracheo-

oesophageal fistula associated with airway stenosis. Additional details on comorbidities are listed in Table I.

All patients were hospitalised in the ICU for COVID-19: mean OTI duration was 15.2 days (range, 4-24) and 10 (71.4%) underwent tracheostomy during ICU stay. In detail, among patients who received tracheostomy, the mean OTI duration was 15.8 days (range, 4-24). Tracheostomy had been surgically performed in 6 (60%) patients and by a percutaneous technique in 4 (40%). Among those who underwent tracheostomy, 7 (70%) had the cannula removed at the end of the hospitalisation, and the average time of tracheostomy maintenance was 31 days (range, 16-49). In 3 cases, tracheostomy closure was not possible, and the cannula remained in place until TRA.

After the first ICU hospitalisation, 2 (14.3%) patients required further ICU admission for sudden clinical worsening. In detail, one patient, who already had the tracheostomy closed, was ventilated via OTI for one more day, while the second, who already received mechanical ventilation for 13 days, required 5 additional days of OTI support before surgical tracheostomy placement, which was maintained for 17 more days.

After ICU discharge and LTS diagnosis, 8 (57.1%) patients underwent rigid bronchoscopy dilatation before TRA and, among these, in 4 cases multiple endoscopic procedures were performed, with tracheal stent placement in one patient.

At preoperative assessment, all patients were affected by purely tracheal stenoses, being the cervical trachea the most common involved site (13 [92.9%] patients), while a central tracheal stenosis was reported in one patient (7.1%). Overall, 13 (92.9%) cases were classified as grade IIIa stenosis and one (7.1%) as IIIa+ (for the presence of associated tracheo-oesophageal fistula) according to the ELS classification system [12].

All patients arrived at the planned TRA surgical procedure without major respiratory distress, while in one case an emergency trans-stenotic tracheostomy was required for acute dyspnoea. Two (14.3%) patients underwent glottic synechia resection with carbon dioxide laser during microlaryngoscopy under general anaesthesia before TRA.

All patients underwent Type A TRA [15] (5 with tracheo-tracheal anastomosis or Type A1, and 9 with crico-tracheal anastomosis or Type A2) and were extubated immediately after surgery without the need to perform tracheostomy. Average extension of the resected stenotic tract was 5.5 tracheal rings (range, 4-7). The immediate postoperative course was uneventful for all patients, except for minimal subcutaneous emphysema in one (7.1%) patient that resolved spontaneously within 48 hours, and mean hospitalisation time was 12.1 days (range, 8-28). After hospital discharge, one (7.1%) patient developed a late circumferential re-stenosis at the anastomotic site, which required 3 further bronchoscopic dilatations and prolonged steroid therapy. At the last endoscopic evaluation, this patient had asymptomatic grade I stenosis. At follow-up, all the remaining patients remained asymptomatic and showed

Table I. Patient comorbidities, type of TRA performed, complications, and adjunctive procedures needed to obtain a patent airway.

Patient no.	Comorbidities	Type of TRA	Complications	Adjunctive procedures for obtaining a normal airway
1	Type II diabetes mellitus, hypothyroidism, hypertension, tracheostomy during childhood	A2	Tracheal stenosis at the anastomotic site	3 bronchoscopic dilatations and prolonged steroid therapy
2	Type II diabetes mellitus, critical illness neuropathy, obesity, tracheo-oesophageal fistula	A1	None	-
3	Grade A oesophagitis, chronic renal failure	A2	Subcutaneous emphysema	-
4	Hypertension, obesity, adrenal adenoma	A1	None	-
5	Hypertension, obesity	A1	None	-
6	None	A2	None	-
7	Type II diabetes mellitus, hypertension, obesity	A2	None	-
8	Type II diabetes mellitus, hypertension, bilateral carotid stenosis, hiatal hernia	A1	None	-
9	Hypertension, obesity, massive pulmonary thromboembolism during SARS-CoV-2 hospitalisation	A1	None	-
10	Type II diabetes mellitus, obesity, hypertension	A2	None	-
11	Type II diabetes mellitus, obesity, hypertension	A2	None	-
12	Obesity	A2	None	-
13	Type II diabetes mellitus, obesity, hypertension	A2	None	-
14	None	A2	None	-

Table II. Summary of main results.

ICU stay	
Mean OTI duration	15.2 days (4-24)
Tracheostomy	10 patients (71.4%)
	Surgical tracheostomy 6 (60%)
	Percutaneous tracheostomy 4 (40%)
Mean tracheostomy maintenance	31 days (16-49)
Preoperative treatment	
Endoscopic dilatation	8 patients (57.1%)
	Single procedure 4 (50%)
	Multiple procedures 4 (50%)
Emergency tracheostomy	1 (7.1%)
Glottic synechiae transoral CO2-laser resection	2 (14.3%)
LTS characteristics	
Tracheostomy presence	4 patients (28.6%)
LTS ELS grade	IIIa
	IIIa+13 (92.9%)

ICU: Intensive care unit, OTI: Oro-tracheal intubation, LTS: Laryngo-tracheal stenosis, ELS: European Laryngological Society.

no residual airway stenosis. A summary of main results is reported in Table II.

Discussion

As predicted during the first phase of the pandemic by the Laryngotracheal Stenosis Committee of the ELS [7], the wide application of invasive ventilatory support in a considerable number of COVID-19 patients led to an absolute increase of the number and severity of airway injuries. To the best of our knowledge, this paper describes one of the largest multicentric case series of patients surgically treated for LTS after prolonged invasive ventilation for SARS-CoV-2 infection [15-17]. Such a large number of patients was probably encountered because Northern Italy was one of the most affected European areas in the first pandemic wave and our hospitals are both referral centres for airway diseases.

All patients except one were hospitalised in the ICU for COVID-19 during the first wave of the pandemic. In fact, in the initial phase of SARS-CoV-2 spread, the airway management of affected patients and proper ventilation support strategy in the ICUs was debated, due to the lack of knowledge of the clinical behaviour of this new virus, consequent fear for health care worker contagion, and the huge and unexpected number of patients requiring rapid treatment. Looking at our case series, these problems find an exact reflection in the heterogeneity of OTI duration (range, 4-24 days) and consequent tracheostomy timing. Prolonged mechanical ventilation via OTI, using high ventilatory pressures, and consequent high tube cuff pressure, is the main factor leading to LTS and airway injuries [18]. Moreover, the need for repeated pronation cycles used in intubated patients with COVID-19 could have caused an increase in airway lesions, due to the possible increase in tube pressure at the anterior/posterior glottic level.

Furthermore, among the 14 patients, only 2 had no comorbidities, with obesity and diabetes being among the most common (5 [35.7%] patients had both diabetes and obesity, 4 [28.6%] only obesity, and 2 [14.2%] only diabetes). In particular, type 2 diabetes mellitus is a well-known predisposing factor for LTS, being probably related to different metabolism and fibroblast populations [19]. On the other hand, in overweight patients, the required ventilatory pressure is set to higher levels due to their lower thoracic compliance, and this can therefore contribute to the ischemic mechanism leading to post-intubation LTS formation.

What remains a major concern and doubt, even in the literature, is the timing of tracheostomy, which, among patients in the present case series, was after 15 days of OTI. Dealing with post-intubation LTS, Li and coworkers [20] described a significant 3.3 times higher probability of late tracheostomy (defined as > 10 days) among patients with post-tracheostomy tracheal stenosis. Beyond LTS outcomes, a recent meta-analysis[21] showed that early tracheostomy (< 10 days) performed in ICU patients was associated with better clinical outcomes, shorter ICU stays and lower long-term mortality. The same result, in terms of reduced duration of ICU stay, was also demonstrated in COVID-19 patients who received an early tracheostomy [22].

On the other hand, the literature is concordant in finding no major differences in outcomes between surgical and percutaneous tracheostomy when performed in COVID-19 patients, as also confirmed by our series [23]. Naturally, as a rule of thumb, the major concern in tracheostomy preparation should always be to allow a safe tracheal opening, without damaging the surrounding laryngotracheal framework. The issues of tracheal tube change, correct positioning and possibility of proper toilette in relation to the type of tracheostomy performed and canula applied have been so far scarcely considered, but definitely play a major role in airway stenosis formation.

Concerning treatment outcomes, the present series showed that (C)TRA still represents a sound, definitive and effective surgical technique, if applied with the right criteria and indications, even in post-COVID-19 patients, who may be affected by long-term airway and systemic sequelae. Moreover, the ELS classification of benign LTS [12] showed a high reliability in treatment selection also in the present population, proving high decannulation and low complications

rates for patients categorised as having airway stenosis graded as < IIIb [24,25]. This classification, in fact, showed a sound result in predicting outcomes of (C)TRA for benign LTS, both in adult and paediatric populations [24,25].

The most notable limitations of our work are the low number of included patients, which did not allow to perform adequate statistical analysis and comparison with other clinical conditions such as non-COVID-19 LTS treated by similar approaches, and the heterogeneity of ICU management, which was due both to the lack of guidelines in the first pandemic phase and to the difference in therapeutic attitudes among various ICU departments, covering a large part of the national territory. In this respect, a multicentric national or international wider study is more than needed.

Conclusions

The SARS-CoV-2 pandemic represented an extraordinary challenge both for the high number of patients who required an ICU treatment with ventilatory support, as well as for its late consequences, among which there is a non-negligible rate of post-intubation LTS. The present report describes one of the largest case series of patients managed by TRA for post-COVID-19 airway stenosis published in the literature.

Of note, a short OTI (< 10 days) is recommendable to provide better clinical outcomes and lower risk of LTS development. Surgical and percutaneous tracheostomy techniques showed comparable sequelae: their meticulous execution and proper maintenance/toilette therefore seem more important than the background philosophy in order to avoid major laryngo-tracheal framework injuries. Finally, TRA is confirmed to be an effective and resolutive surgical procedure, when applied to the appropriate patients and with proper expertise. Analogously, the ELS grading system of benign LTS [12] proved to be an excellent tool of outcome prediction even in the post-COVID-19 clinical scenario.

Conflict of interest statement

The authors declare no conflict of interest.

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Authors' contributions

Concept: CP, DL, MF, AD, GP. Data collection: CS, PB, GZ, AI, AV. Writing – original draf: DL, MF, PB, CS. Writing – review and editing: CP, AD, GP DL, PB.

Ethical consideration

This study was approved by the Institutional Ethics Committee (CER Liguria). Number of protocol: 63/2021.

The research was conducted ethically, with all study procedures being performed in accordance with the requirements of the World Medical Association's Declaration of Helsinki.

Written informed consent was obtained from each participant/patient for study participation and data publication.

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