Original Article

Tracheal stenosis as a complication of prolonged intubation in coronavirus disease 2019 (COVID-19) patients: a Peruvian cohort

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Background: Tracheal stenosis (TS) is associated with prolonged intubation and inflammation due to coronavirus disease 2019 (COVID-19) infection. Because of the COVID-19 pandemic, longer times of mechanical ventilation have been required, and different tracheostomies beyond 10 to 12 days have been made. All of these have increased the number of cases and complexity of tracheal pathology in patients with severe COVID-19 infection.

Methods: A retrospective, chart review, from patients who were managed in the Service of Thoracic Surgery of Guillermo Almenara Irigoyen National Hospital, Lima, Peru, with a diagnosis of TS, tracheo-esophageal fistula and tracheomalacia between June 2020 until May 2021.

Results: Sixty-three patients were diagnosed with TS because of prolonged intubation due to COVID-19 infection. Mean hospitalization time in the intensive care unit (ICU) was 30 days. Mean mechanical ventilation time was 25 days. The most frequent anatomical localization of TS was upper and middle third (55.6%), upper third (44.4%). Fifty-three patients (84.1%) had TS between 1–4 cm, and ten patients (15.9%) had TS longer than 4 cm. Most patients with TS were classified with Cotton-Myer grade III (88.9%).

Conclusions: We report a retrospective study of 63 patients with a diagnosis of TS, in whom corrective surgery was performed: cervical tracheoplasty, Montgomery T tube, or tracheostomy.

Keywords: Tracheal stenosis (TS); coronavirus disease 2019 (COVID-19); tracheo-esophageal fistula; tracheomalacia

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Introduction

In December of 2019, a new coronavirus [coronavirus disease 2019 (COVID-19)] caused acute severe respiratory disease in China. World Health Organization (WHO) declared the novel coronavirus outbreak a public health emergency of international concern at the end of January 2020 (1). The most common and severe complication of patients with COVID-19 infection is a severe acute respiratory syndrome (SARS) requiring oxygen and ventilation therapies (2). According to some studies published until June 2020, the proportion of patients in intensive care unit (ICU) that required invasive mechanical ventilation (IMV) range between 29.1–64% among China population (3). In one study made in Wuhan, China, 26.1% of hospitalized patients were admitted to ICU because of complications that included SARS (61.1%), shock, and arrhythmias; and 47.2% of patients admitted to ICU required IMV (4). It has been demonstrated that COVID-19 patients had mean mechanical ventilation duration of 17 days and a high rate of reintubation (5,6).

Mortality among patients with IMV and treatment in the ICU has always been high. This rate increases if we add comorbidities and COVID-19 infection. In the UK, 65% of patients with COVID-19 in IMV died; and in the USA the number could go as high as 88% (3,7).

Tracheal stenosis (TS) is a complication that appears after prolonged intubation or performing a tracheostomy. The pathologic pathway of TS is due to prolonged ischemia that produces fibrotic tracheal scarring (8). For COVID-19 patients, where last up to as a mean of 17 days and many times requiring reintubation, TS after tracheostomy is around 1.5–2.6%, and 1–2% for cases with orotracheal intubation (9). Usually, these complications appear in patients with intubation or tracheostomy of more than 10 days (10). Factors that increase the risk of developing concentric TS are obesity, size of the endotracheal tube, the material of the endotracheal tube, and use of corticosteroids. The main symptoms are dyspnea, inspiratory stridor, and non-productive cough (11).

Peru is one of the most affected countries due to COVID-19 in all Latin America, with an incidence of 23.57 newly diagnosed cases per 1,000 population during the month September 2020 (12). It has; also, the highest mortality rate worldwide, 601.6 deaths per million population (13). This scenario is aggravated by the lack of healthcare providers and ICU providers, noting that Peru has the lowest indexes of ICU providers, ICU beds, and mechanical ventilators per 10,000 patients in South America (14).

So far, there have not been studies published that show the association between TS and COVID-19 infection. We present our case series and a revision of the literature of COVID-19 patients who developed TS after prolonged IMV and were managed in our hospital. We present the following article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-21-1721/rc).

Methods

Design, population, and sample size

The Service of Thoracic Surgery of Guillermo Almenara Irigoyen National Hospital is a national referral center for the surgical management of tracheal pathology. We developed a retrospective study of all the patients referred to our center with a diagnosis of TS, tracheoesophageal fistula (TEF), and tracheomalacia (TM) who were previously intubated due to COVID-19 infection and they underwent surgery between the months from June 2020 until May 2021.

Data collection and study variables

A total of 63 patients with TS, or other complications such as TEF and TM, were surgically managed. We obtained demographic data like age, sex, body mass index (BMI), previous pathologic history (arterial hypertension, diabetes mellitus, asthma), time of endotracheal intubation, time of hospitalization in ICU, functional class. Additionally, we obtained data of the TS: TS percentage, number of damaged rings, location of damaged rings, maturity of the mucosa from the TS, presence of subglottic involvement.

The maturity criteria of TS were established through bronchofibroscopy. Immature TS: erythema, granulomas, friability, ulcer, bleeding mucosa and mature TS: pale mucosa, established scar.

To define functional class, we have used the WHO scale "Classification of Functional State of the World Health Organization":

WHO I: asymptomatic: ordinary physical activity does not cause symptoms.

WHO II: symptomatic on exertion: there is no discomfort at rest, but normal physical activity, causes increased symptoms.

WHO III: symptomatic with daily activity: there is no

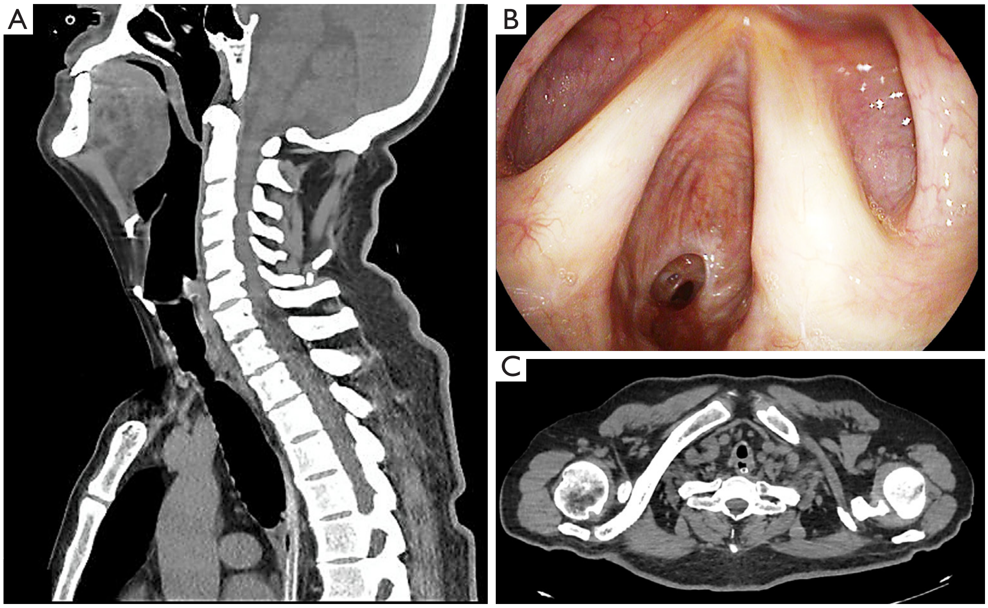

Figure 1 Severe subglottic and TS showed by thoracic CT-scan and fiberoptic bronchoscopy. (A) Sagittal thoracic CT-scan showing severe subglottic and TS; (B) fiberoptic bronchoscopy showing severe subglottic and TS; (C) axial thoracic CT-scan showing severe subglottic and TS. TS, tracheal stenosis.

discomfort at rest, but less than ordinary activity causes increased symptoms.

WHO IV: symptomatic at rest: symptoms may be present at rest and are increased by almost any physical activity.

In respect of the presence of TEF, we obtained: the size of TEF, anatomic ubication, maturity. In respect of TM, localization and severity were obtained. Each patient was evaluated pre-surgically with a physical exam, lab analysis, antigenic test for COVID-19, cervicothoracic tomography with trachea-bronchial reconstruction, and fiberoptic bronchoscopy for evaluation of the mobility of vocal cords and characteristics of the TS such as severity, maturity, localization, size (*Figure 1*), and associated lesions like TEF and TM. When TEF was suspected, an upper endoscopic was made. We defined severe TS as the one occluding more than 50% of the tracheal lumen, or if it produced symptoms like dyspnea, laryngeal stridor. TEF was defined as the epithelized pathological communication between the trachea and esophagus, that was seen in the tomography, fiberoptic bronchoscopy, and confirmed with an upper endoscopy (*Figure 2*).

Ethical aspects

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Institutional Ethics Committee of NIT (No. 1141-2021-123), and individual consent for this retrospective analysis was waived.

Surgical technique

After pre-surgical evaluation, surgical options were tracheoplasty, Montgomery T tube placement (with or without tracheal resection), tracheostomy cannula placement (with or without tracheal resection) and TEF closure.

The choice was made considering the extent of injury (number of damaged rings), involvement of the subglottic region, the elasticity of the trachea, presence of associated lesions (TEF or TM), previous procedures in stenotic areas (dilatation, tracheostomy, laser) and the overall status of the patient.

The criteria for tracheal resection were extension of the stenosis <50% of the tracheal length, that the location of the stenosis does not cover the subglottic region, the elasticity of the trachea and functional class of the patient I–II according to WHO scale, however, the final decision was made intraoperatively.

The specific criteria for each type of surgical technique

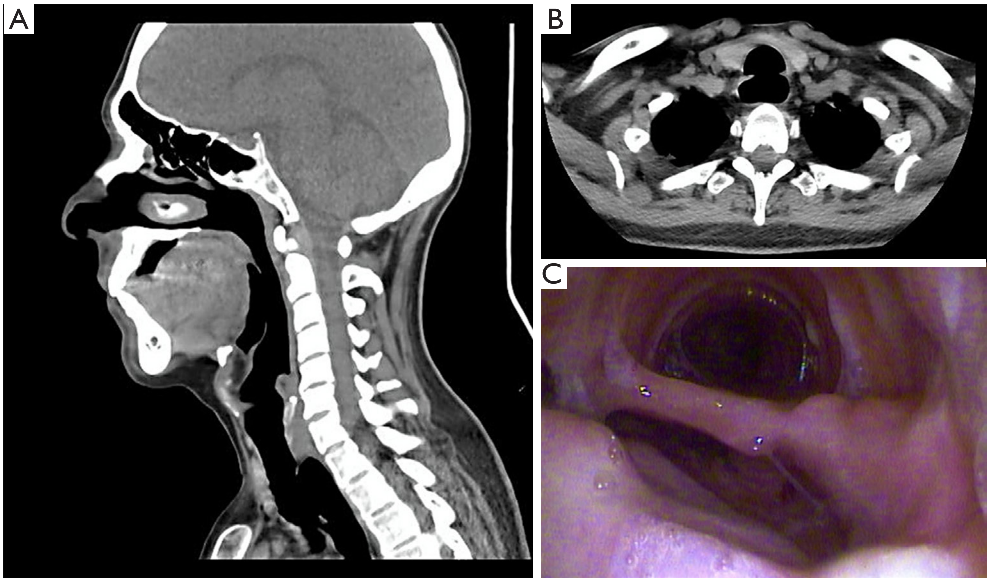

Figure 2 Tracheo-esophageal fistula showed by thoracic CT-scan and fiberoptic bronchoscopy. (A) Sagittal thoracic CT-scan showing tracheo-esophageal fistula; (B) axial thoracic CT-scan showing tracheo-esophageal fistula; (C) fiberoptic bronchoscopy showing tracheo-esophageal fistula.

were the following:

Tracheostomy: patients admitted in poor general condition or functional class III–IV according to WHO scale.

T-tube placement: patients without criteria for tracheal resection, extensive and subglottic lesions.

Tracheal resection + tracheostomy: patients with ET + TEF with TS and poor general condition.

Tracheal resection + T-tube: patients with risk anastomosis, extension of lesion >50% of length.

Tracheoplasty: patients in good general condition, lesions <50% in length.

A T-shaped cervical incision was made. Infrahyoid muscles were separated from the midline. The anterior, posterior, and lateral part of the trachea is mobilized with blunt dissection and dissection with a scalpel for a better exposure and with care not to damage the recurrent laryngeal nerves.

Damaged tracheal rings are removed. Tracheal anastomosis was made with polyglycolic acid suture, stitches began in the lateral part of the cartilaginous trachea with 3/0 polyglycolic acid suture that allowed us proper tension. After that, stitches of 4/0 polyglycolic acid suture were placed on the opposite site of the surgeon with an interval of 3 mm.

A nasogastric tube was introduced through the proximal trachea, and we asked the anesthesiologist to pass the endotracheal ringed tube for placement under direct vision below the anastomosis. Separate stitches were placed with 3/0 polyglycolic acid suture. Hemostasia was revisited, and a Jackson Pratt drainage was left on the pre-tracheal plane. (*Figure 3*).

In those patients where after tracheal ring resection, it was noticed inflammatory immature tissue, extensive damage, disease at the level of cricoid or subglottic, extensive damage of more than 50% of the trachea, we opted for the placement of a Montgomery T tube, verifying proper positioning in its proximal end and distal one, with intraoperative flexible fiberoptic bronchoscopy.

All TEF were managed through cervical T incision, the trachea was dissected circumferentially, the fistula was identified, separation of the trachea from the esophagus (*Figure 4A*) then two-layer planes are sutured: separate stitches by 3 mm with 4/0 polyglycolic acid suture in mucosae layer and then for the muscular layer invaginating stitches with 3/0 polyglycolic acid suture (*Figure 4B*), then muscle (sternocleidomastoid and/or prethyroid muscles) is placed between trachea and esophagus being sutured over the esophageal defect, later on the treatment of the tracheal defect is continued (*Figure 4C*).

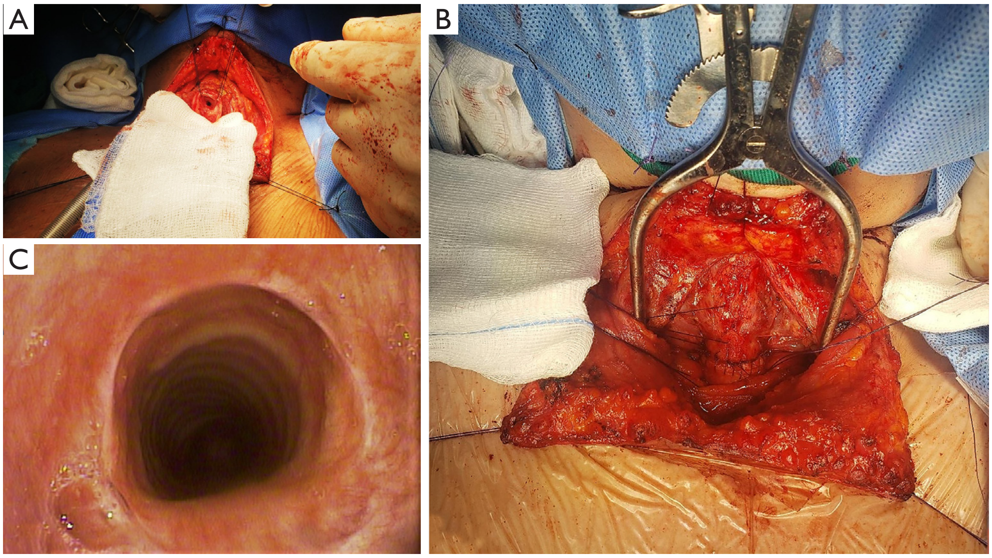

Figure 3 Intraoperative image showing TS and the tracheal anastomosis made. Finally, fiberoptic bronchoscopy was made showing an anastomotic suture line. (A) Intraoperative image showing TS; (B) tracheal anastomosis was made with polyglycolic acid suture. Separate stitches were placed with an interval space of 4 mm between them with 3/0 polyglycolic acid suture; (C) fiberoptic bronchoscopy showing anastomotic suture line. TS, tracheal stenosis.

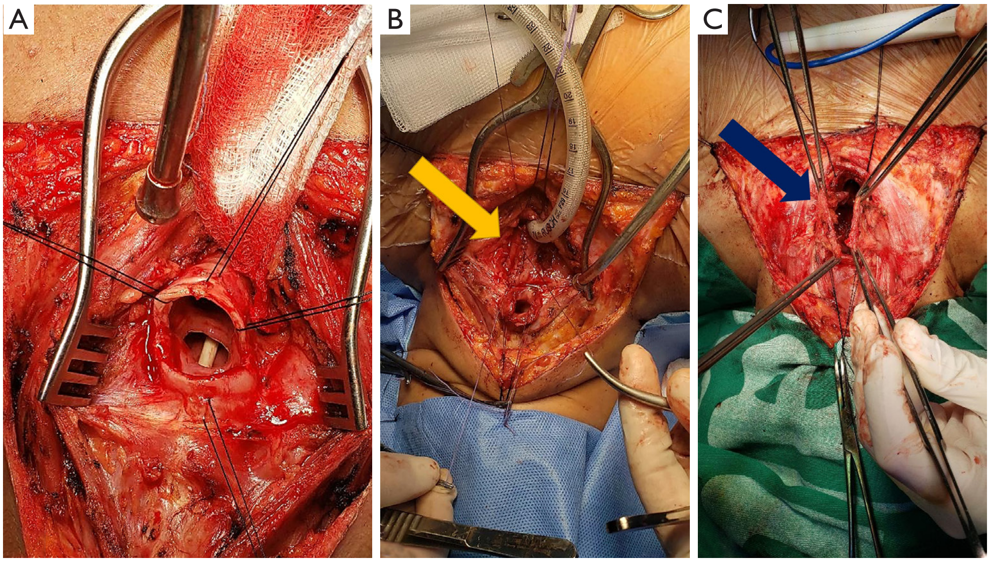

Figure 4 Intraoperative image showing the separation of the trachea from the esophagus where two-layer planes are sutured. Besides, prethyroid muscles were placed between trachea and esophagus. (A) Cervical T incision and the separation of the trachea from the esophagus; (B) two-layer planes are sutured; (C) prethyroid muscles placed between trachea and esophagus.

Table 1 Pre-operative characteristics of COVID-19 patients with TS (N=63)

Variables	N	Percentage (%)
Age (years)	49.8	(±10.4)
30–39	10	(15.9)
40–49	22	(34.9)
50–59	19	(30.2)
60–69	10	(15.9)
>70	2	(3.2)
Gender		
Male	47	(74.6)
Female	16	(25.4)
Comorbidities		
Arterial hypertension	11	(17.5)
Diabetes mellitus	9	(14.3)
Asthma	2	(3.2)
BMI (kg/m^2)		
Normal (18.5–24.9)	7	(11.1)
Overweight (25–29.9)	23	(36.5)
Obesity I (30–34.9)	25	(39.7)
Obesity II (35–39.9)	4	(6.3)
Obesity III (>40)	4	(6.3)
Time in ICU (days)	35.9	(±22.3)
Intubation time (days)	27.8	(±15.8)
Time from hospital discharge to tracheal surgery	3.4	(±1.7)
WHO functional class		
I	20	(31.7)
II	32	(50.8)
III	8	(12.7)
IV	3	(4.8)
Admission diagnosis		
TS	42	(66.7)
TS + TEF	15	(23.8)
TS + TM	1	(1.6)
TEF + TS + TM	5	(7.9)

Table 1 (*continued*)

Table 1 (*continued*)

Variables	N	Percentage (%)
Vocal cord paralysis (diminished mobility)		
Unilateral	5	7.9
Bilateral	2	3.2
Previous procedures		
Dilatation	1	1.6
TCT	21	33.3
None	41	65.1

COVID-19, coronavirus disease 2019; TS, tracheal stenosis; BMI, body mass index; ICU, intensive care unit; WHO, World Health Organization; TEF, tracheoesophageal fistula; TM, tracheomalacia; TCT, tracheostomy.

Statistical analysis

A descriptive analysis was made. Continuous variables were shown as median and interquartile range, categoric variables were shown as percentages. Statistical analysis was made with Microsoft Excel 2016, STATA MP, and SPSS v25.

Results

Data from 63 patients diagnosed with TS due to prolonged intubation associated with COVID-19 infection were reviewed. The mean age was 49.8 (±10.4) years old, most diagnosed in men (74.6%). Mean BMI was 30.4 kg/m^2, being grade I obesity the most frequent (39.7%). The main comorbidities were arterial hypertension (17.5%), diabetes mellitus (14.3%), asthma (3.2%). The meantime of hospitalization in the ICU was 30 days. The average orotracheal intubation time was 25 days. Most patients were classified as functional class II (50.8%) and functional class I (31.7%). Admission diagnoses were TS (42 patients), TS + TEF (15 patients), TS + TM (1 patients), TS + TEF + TM (5 patients) (*Table 1*).

Regarding patients with TS, the most frequent anatomical localization was upper and middle third (55.6%), upper third (44.4%) (*Figure 5*). Fifty-three patients (84.1%) had a TS with a length of 1–4 cm, and ten patients (15.9%) had a TS with a length >4 cm. Most patients with TS were classified as Cotton-Myer grade III (88.9%). Mature stenosis was seen in 73% of patients with TS. Diminished

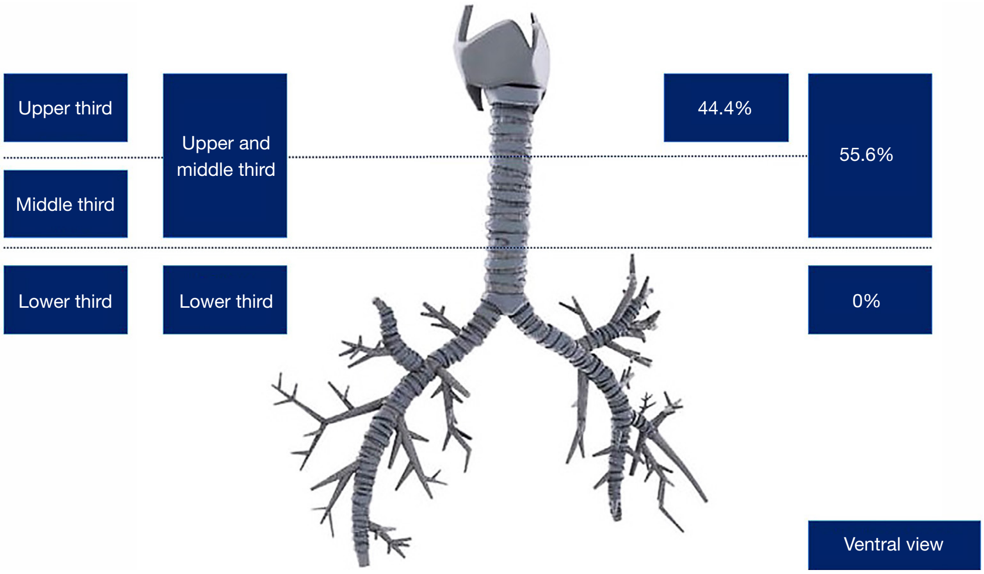

Figure 5 Frequency of TS cases according to their anatomical distribution and affected tracheal third. We can see the most frequently affected tracheal third was the upper + middle third. TS, tracheal stenosis.

unilateral mobility of the vocal cords was seen in 5 patients (7.9%), and it was bilateral in 2 patients (3.2%) (*Table 2*).

Regarding patients with TEF, the mean size was 3.2± 1.5 cm, most of them were localized in the upper third (85%), with 75% of them being mature. Nutrition in these patients was made through a nasojejunal tube (19%). Regarding patients with TM, localization was in the upper third (66.7%), and 50% were mild.

Primary tracheoplasty was made in 30 patients (47.6%), ring resection plus insertion of Montgomery T tube in 25 patients (39.7%), ring resection plus insertion of tracheostomy cannula in 4 patients (6.3%), insertion of Montgomery T tube alone in 1 patient (1.6%) and insertion of tracheostomy cannula in 3 patients (4.8%). The average amount of tracheal rings removed was 6.9±1.6. In patients with TEF, full direct closure was made in all patients, in 14 of them (70%) direct closure plus muscular flap interposition, being the sternothyroid muscle the most frequently used. Additionally, repair of tracheomalacia was made in 3 patients.

Regarding immediate post-operative complications, 17 patients (27%) had superficial surgical site infection (SSI) and only 1 patient (1.6%) had a deep SSI. Two patients (3.2%) had partial dehiscence of the tracheoplasty suture, while 2 patients also (3.2%) had partial dehiscence of the suture that closed the TEF. We had 2 patients with non-severe anterior wall tracheal anastomosis dehiscence who were managed conservatively with observation and antibiotic therapy in both cases, and spontaneous closure was achieved.

Besides, there was two tracheoesophageal fistula closure dehiscence; one was mild that was managed with observation, antibiotic therapy, enteral nutrition, and spontaneous closure was achieved; and the second presented significant fistula dehiscence, a tracheostomy tube was placed and currently is awaiting corrective surgery.

Six patients (9.5%) had restenosis and seven patients (11.1%) presented T tube obstruction. Concerning the patients who presented restenosis, two patients underwent grade I Cotton-Myer restenosis in whom the management was conservative, three patients underwent grade II Cotton-Myer restenosis in which a T-tube was changed in one patient and a T-tube was placed in the other two patients; finally, one patient presented grade III Cotton-Myer restenosis in whom a T-tube was placed.

Of the 7 patients in whom T-tube obstruction was presented, fiberoptic bronchoscopy was performed in 5 patients, T-tube replacement in 1 patient, and placement of a tracheostomy cannula in 1 patient. Among other complications, 2 patients had hospital-acquired pneumonia (3.2%), 2 patients had bleeding (3.2%) and from all patients, only 1 patient (1.6%) died in the postoperative (*Table 3*). The deceased patient was a 61-year-old male, overweight, who had severe COVID-19 infection in March 2020, a

Table 2 Clinical and surgical characteristics of COVID-19 patients with TS (N=63)

Variable	N	Percentage (%)
TS	63	
Localization (thirds)	63	100.0
Upper	28	44.4
Upper and middle	35	55.6
Vertical length (cm)		
1–4	53	84.1
>4	10	15.9
Cotton-Myer		
I	3	4.8
II	3	4.8
III	56	88.9
IV	1	1.6
Mature	46	73.0
Immature	17	27.3
Subglottic	7	11.1
TEF	20	
Size (cm)	3.2±1.5	
Localization to the trachea	20	100.0
Upper	17	85.0
Middle	2	10.0
Upper middle	1	5.0
Mature	15	75.0
Immature	5	25.0
Nutrition		
Gastrostomy	4	6.3
Jejunostomy	5	7.9
NJT	12	19.0
TM	6	
Localization to the trachea	6	100.0
Upper	4	66.7
Middle	1	16.7
Upper middle	1	16.7
Severity	6	100.0
Mild	3	50.0
Moderate	1	16.7
Severe	2	33.3
Surgical management		
TS	63	100.0
Primary surgery	30	47.6
Ring resection + T tube	25	39.7
Ring resection + TCT	4	6.3
T tube insertion	1	1.6
TCT canula insertion	3	4.8
Resected tracheal rings	6.9	±1.6
TEF	20	100.0
Muscle interposition	14	70.0
Sternocleidomastoid	1	5.0
Sternothyroid	6	30.0
Sternohyoid	2	10.0
Omohyoid	5	25.0
Tracheomalacia	6	100.0
Plication	3	50.0

COVID-19, coronavirus disease 2019; TS, tracheal stenosis; TEF, tracheoesophageal fistula; NJT, nasojejunal tube; TM, tracheomalacia; TCT, tracheostomy.

patient referred from a less capacity hospital with diagnoses of TS and tracheoesophageal fistula.

He came emergency with stridor and in poor general condition and underwent emergency surgery resection of tracheal rings + closure of tracheoesophageal fistula and tracheostomy, awaiting definitive corrective surgery, after improving his clinical condition, he died of an acute myocardial infarction 2 months after.

Discussion

TS is a disease caused by ischemic necrosis associated with airway pressure. The main factor that causes TS is the pressure of the cuff in the tracheal mucosa; where a cuff pressure of more than 30 mmHg results in a decrease in capillary perfusion on the tracheal mucosa, which produces

Table 3 Post-operative characteristics of COVID-19 patients and TS

Complications	N	Percentage (%)
Infection		
Superficial	17	27.0
Deep	1	1.6
TS dehiscence	2	3.2
TEF dehiscence	2	3.2
Re-stenosis	6	9.5
Severity		
Cotton-Myer		
I	2	3.2
II	3	4.8
III	1	1.6
IV	0	0
Treatment		
Observation	2	
T tube insertion	3	
T tube change	1	
T tube obstruction	7	11.1
Treatment		
Fibro bronchoscopy	5	
T tube rechange	1	
TCT canula	1	
Other complications		
Pneumonia	2	3.2
Bleeding	2	3.2
Death	1	1.6

COVID-19, coronavirus disease 2019; TS, tracheal stenosis; TEF, tracheoesophageal fistula; TCT, tracheostomy.

ischemia of the mucosa, inflammation of the tracheal cartilages; furthermore, more inflammation and fibrosis of several grades of circumferential distribution causes TS (15).

Before the COVID-19 pandemic it had been established that ischemic lesion on the tracheal mucosa could happen even in the next minutes after cuff insufflation with fibrotic changes around the 3–6 upcoming weeks. The incidence of TS after endotracheal intubation in the ICU is 6–21%, although only 1–2% of them are symptomatic (16). The time where symptoms initiated after TS goes from 28 days to 6 months according to previous cases (17-19). It should be suspected the risk of development of TS especially in patients that have been under mechanical ventilation for more than 10 days (7). Likewise, many risk factors associated with TS after endotracheal intubation have been studied like the size of the endotracheal tube, traumatic intubation, concomitant infection, female gender, estrogenic effect, obesity, and smoking (20,21).

Besides, various investigations were published evaluating patients with TS associated with prolonged intubation, which developed over more than 10 years, while our series presented a similar number of cases in 1 year (*Table 4*), which shows a significant increase in TS cases, highlighting the impact of COVID-19 infection on prolonged intubation time and the incidence of tracheal injuries (22-26).

With the COVID-19 pandemic, where longer times of mechanical ventilation have been required, the use of prone position in a systematic way for the management of this kind of patients (27,28), and differed tracheostomies to more than 10–12 days (29), there has been a significant rise in the number of cases and complexity of tracheal pathology in patients with severe COVID-19 infection.

Recommendations regarding the time to perform either surgical or percutaneous tracheostomy in patients with COVID-19 infection varied widely. Many sources lacked a clear recommendation regarding time. When tracheostomy timing was established, it ranged from 3–4 to 21–28 days. Most protocols recommended a minimum of 14 days of MV for consideration of performing a tracheostomy. Likewise, some contraindications were considered, such as cardiac or respiratory instability, positive COVID-19 test, poor prognosis, and lack of clinical improvement (30). Subsequently, a study was performed where they proposed to delay the tracheostomy until the maximum of day 10 of MV, and it is considered only when patients show signs of clinical improvement (31).

In our study, we have evaluated clinical characteristics, anatomical distribution, and surgical management done in patients who developed TS after prolonged intubation. Some isolated case reports have been published, but to this date, there is not enough data or a big series that shows the association between TS and COVID-19 infection (9-11,32-35). Regarding TS findings, we had a mean age of 49 years old, being more frequently diagnosed in males (74.6%). Mean BMI was 30.4 kg/m^2, being grade I obesity the most frequent (39.7%). The meantime of hospitalization in the ICU was 30 days. The mean time of orotracheal

Table 4 Literature review of tracheal stenosis series

Author*	Paris *et al.*	Rea *et al.*	Sarper *et al.*	Weindenbecher *et al.*	Andrilli *et al.*	Palacios *et al.* (our study)
Research	Retrospective cohort	Retrospective cohort	Retrospective cohort	Retrospective cohort	Retrospective cohort	Retrospective cohort
Year of publication	1990	2002	2005	2007	2008	2022
Range of years	1973–1989	1991–2001	1985–2004	1985–2002	1991–2006	2020–2021
Number of years	16 years	10 years	19 years	17 years	16 years	1 year
Number of patients	112	65	45	101	35	63
Male	44	39	34	55	19	47
Female	68	26	11	46	16	16
Ratio M/F	0.65/1	1.5/1	3.1/1	1.2/1	1.2/1	2.93/1
Age mean	41	33	38	NR	43	49
Age range (years)	9–81	14–74	2–72	7–77	14–71	30–77
IMV (days)	NR	NR	8–11	NR	NR	25
Tracheal lesions associated, n (%)						
Tracheomalacia	7 (6.3)	NR	NR	NR	NR	6 (9.5)
Tracheoesophageal fistula	3 (2.7)	NR	NR	NR	NR	20 (31.7)
Vocal cord paralysis	NR	NR	NR	12 (11.8)	NR	7 (11.1)
Surgery technique						
Resected tracheal length (cm)	2.7 (1.5–7)	2.5 (1.5–4)	1.5–4	2–6	1.5–6	3.5 (2–5)
Previous treatment, n (%)						
Tracheal dilatation	NR	NR	NR	NR	NR	1 (1.6)
Tracheostomy	28 (25.0)	38 (38.5)	NR	NR	13 (37.1)	21 (33.3)
Tracheal complications, n (%)						
Infection	NR	5 (8.0)	2 (6.0)	NR	NR	3 (8.4)
Dehiscence	NR	4 (6.0)	NR	NR	NR	NR
Granuloma	NR	2 (3.0)	3 (9.0)	NR	NR	NR
Death	NR	1 (1.5)	1 (3.0)	NR	NR	1 (1.6)

*, all the authors mentioned in the table have been cited in the article references. M, male; F, female; IMV, invasive mechanical ventilation; NR, no reported.

intubation was 25 days.

Our results show patients with TS developed more complex lesions, with longer stenosis percentages, more time hospitalized in the ICU, and more time with endotracheal intubation.

Comparing the incidence by gender, we found a male/female ratio of 2.93/1, which is higher than reported by D'Andrilli *et al.* (1.2/1) (22) and by Rea *et al.* (1.5/1) (25). This information could be due to the higher prevalence of severe COVID-19 in male patients. Paris *et al.* (26) conducted a retrospective cohort of patients with TS before the COVID-19 pandemic, where most patients were female (60.8%). The mean age found in our cohort was 49 years, which is consistent with the most frequent age range affected by COVID-19 infection (adult: 30–59 years).

TS associated with COVID-19 implies a longer IMV time; Sarper *et al.* published a series of cases with 45 patients with ST where the IMV interval was 8 to 11 days (24), which is shorter compared to our IMV range which was 27±15.8 days. This could also be due to the delayed tracheostomy time in patients with endotracheal intubation at the onset of the pandemic for up to >14 days.

París *et al.* reported 7 cases (6.3%) of tracheomalacia and 3 cases (2.7%) of tracheoesophageal fistula (26), unlike our cohort where we found 6 cases (9.5%) of associated tracheomalacia and 20 cases (31.7%) of associated tracheoesophageal fistula. We can observe more severe lesions in cases of post-intubation TS due to COVID-19, probably due to a longer intubation time, inflammatory process due to COVID-19 in the airway, poor care of the intubated patient, prone position, hypoxic mucosal damage, poor medical condition, excessive use of corticosteroids, history of diabetes and obesity. Knowing these findings, we propose to reinforce preventive measures for associated injuries such as proper care of the endotracheal tube, cuff pressure measurement (<30 mmHg), use of a soft silicone tube, chronic avoidance of systemic steroids, and early tracheostomy.

We present 7 cases (11.1%) of unilateral or bilateral vocal cord paralysis (decreased mobility), like that reported by Weidenbecher *et al.* (23). However, six patients presented FTE as an associated aggregate. The resected length in our cohort was 3.5 cm on average, greater than that reported by Rea *et al.* and París *et al.*, with a length of 2.7 and 2.5 cm respectively (25,26); confirming the greater severity concerning the extension of the tracheal compromise, which leads to a lower probability of tracheal resection in patients with a history of COVID-19 infection. This is probably due to the inflammatory component of the tracheal mucosa exerted by viral invasion, as well as increased inflammation and fibrosis at the level of the tracheal cartilages.

In our cohort, a tracheostomy was performed as a treatment before tracheal reconstruction surgery in 21 patients (33.3%), like a pre-pandemic series report. D'Andrilli *et al.* and París *et al.* (22,26). Tracheostomies were performed in patients in poor general condition (WHO functional class III–IV), those with TEF to ensure airway, and some patients were referred to our center with tracheostomy for reconstructive surgery. Procedures before definitive surgery (CO_2 laser, tracheal dilation, tracheostomy, stent placement) could decrease the probability of successful airway reconstruction.

Among the post-surgical complications, we found 18 cases (28.6%) of SSI, higher than that reported in other series with a range of 6–8% (22,24,25). However, of this group, 17 patients had superficial access which was resolved with antibiotic coverage and local cure. We only had one case of deep operative site infection that required surgical cleaning in the operating room. This high incidence of infection at the surgical site may be because they were patients with prolonged stay in the ICU, with bacterial colonization, and malnourished. Half of these cases occurred in patients with associated TEF.

The dehiscence rate in our study was 6.4%, like the pre-pandemic study by Rea *et al.* (6%) (25). These patients also had SSIs, which probably contributed to the development of dehiscence. This complication increases morbidity and hospital stay.

Regarding restenosis, it had a rate of 9.5%, probably due to a tension anastomosis, wide dissection due to an inflammatory process that caused devascularization of the anastomosis area, as well as the extension of the resected tracheal segment (3–4 cm).

In our study, natural ventilation, digestive tract restoration, and voice recovery were restored in 59 patients (93.7%) compared with other series published in the literature (good results reported between 87% and 100%) (22,24,25). Confirming the role of surgery as the treatment of choice in tracheal pathology. Furthermore, we only reported one patient who died (1.6%) due to a cause unrelated to the surgery.

TEF is pathologic communications between the esophagus and trachea, these can be congenital or acquired; the latter is the most frequent and is more commonly reported in patients with esophagus or lung cancer complications (36). Acquired TEF can also be formed due to prolonged intubations. In this setting, they are usually reported between 0.3% to 3% of patients (37). Is because of that, TEF can be developed in patients with COVID-19 and SARS who need mechanical ventilation (38). Symptoms are frequent cough after eating, bronchitis or purulent pneumonia, and recurrent aspiration; in COVID-19 patients with FET, gastric distention and sudden desaturation after extubating can be the first sign of suspicion (36,37).

TS, TEF, and other complications after endotracheal intubation are more frequent in COVID-19 patients probably because of prolonged intubation times, delay in performing a tracheostomy, lack of trained staff in ICU, prolonged prone position, and physiopathologic mechanisms of COVID-19 infection such as prothrombotic and antifibrinolytic status, high viral replication in the trachea epithelium that weakens its mucosa and high doses of systemic steroids that lead to mucosa atrophy (11,36).

Regarding patients that developed TEF, from 63 patients with TS, 20 patients develop TEF. The average size was 3.2±1.5 cm, the most common localization was upper third (85%) and most of them were mature TEF (75%). The nutrition of patients was possible through a nasojejunal tube (19%). Management was made by direct closure in all 20 patients, while in 14 patients (70%) a direct closure plus muscular flap interposition (with sternothyroid muscle). Two patients (3.2%) developed dehiscence of the surgery site.

Tracheal injuries due to endotracheal intubation in COVID-19 have different characteristics compared to patients with tracheal injuries due to intubation in the pre-COVID-19 era, such as an increase in the number of cases of tracheal injuries due to prolonged intubation in patients COVID-19, the highest prevalence in males, probably related to the greater distribution of severe COVID-19 in males. The average age of patients ranges between 30–51 years, which coincides with the age with the highest prevalence of severe COVID-19 infection. The lesions are more severe, with a higher prevalence of associated lesions such as TEF, tracheomalacia, and vocal cord paralysis. The extent of the lesion is on average greater than that reported in previous studies (3.5 cm).

For primary repair of the trachea, favorable prognostic factors are age, sex, size of the tracheal damage, trachea elasticity, presence of associated lesions (TEF, TM); general status of the patient and presence of diminished unilateral or bilateral mobility of vocal cords. It seems reasonable to predict that ventilation with positive pressure required in COVID-19 patients with the consequent prolonged intubation and late tracheostomy, in conditions of a COVID-ICU, along with airway inflammation by vasculitis phenomena, associated with the collapse of the health system all around Latin America and in our country, plus lack of ICU-trained staff are factors that increases the incidence of tracheal damage, not only in number but in complexity also with several associated lesions.

Limitations

The main limitations were the retrospective nature of our cohort, the absence of a control group of patients with tracheal pathology without COVID-19 infection, and the relatively short follow-up time after surgery.

Conclusions

TS is an airway pathology associated with both mechanical damages due to prolonged intubation and inflammatory damage due to COVID-19 infection. This condition can be associated with tracheoesophageal fistula, tracheomalacia, among others. We present a retrospective study of 63 patients who underwent corrective surgery: cervical tracheoplasty, Montgomery T-tube, or tracheostomy. This report is the first published cohort of patients with TS after COVID-19 infection in Peru; and one of the first series reported in Latin America, confirming the role of surgery as the treatment of choice in tracheal pathology.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Institutional Ethics Committee of NIT (No. 1141-2021-123), and individual consent for this retrospective analysis was waived.

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