New Perspectives on Tracheal Resection for COVID-19-related Stenosis: a Propensity Score Matching Analysis

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New Perspectives on Tracheal Resection for COVID-19-related Stenosis: a Propensity Score Matching Analysis

February 2020 - March 2022
n = 147 consecutive tracheal resections for tracheal stenosis:
- n= 24 Post-COVID patients
- n=123 Non-COVID patients

1:1 propensity score matching analysis, considering age, gender, BMI (Body Mass Index), and length of stenosis (1-4 cm).

After matching:
- n= 24 Post-COVID group
- n=24 Non-COVID group

-Post-tracheostomy etiology of stenosis more frequent in post-COVID patients (p=0.03)

-Need for postoperative re-intubation for glottic edema with respiratory failure and ICU admission in the postoperative period higher in the Post-COVID Group (p=0.04)

-Postoperative dysphonia increased in post-COVID patients (p=0.03)

Tracheostomy seems to be a more frequent cause of tracheal stenosis compared to prolonged intubation in post-COVID-19 patients.

ICU admission rate and postoperative complications seem to be higher in post-COVID-19 patients who underwent tracheal resection compared to non-COVID-19 patients.
New Perspectives on Tracheal Resection for COVID-19-related Stenosis: a Propensity Score Matching Analysis

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Word count: 2683
Glossary:

COVID-19: COronaVIrus Disease-19

BMI: Body Mass Index

COPD: Chronic Obstructive Pulmonary Disease

ICU: Intensive Care Unit

IMV: Invasive Mechanical Ventilation

ENT: Ear Nose Throat

ETT: Endo Tracheal Tube

STROBE: STrengthening the Reporting of OBservational studies in Epidemiology

FBO: Fiberoptic Bronchoscopy

CT: Computed Tomography

LMA: Laryngeal Mask Airway

HFOT: High Flow Oxygen Therapy

SD: Standard Deviation

ASA: American Society of Anesthesiologists

PSM: Propensity Score Matching

SMD: Standardized Mean Difference

Central Picture Legend: Tracheal surgery after COVID-19

Central Message: Post-COVID-19 patients affected by tracheal stenosis who underwent tracheal resection showed higher postoperative complications rate and increased ICU admission stay compared to non-COVID-19 patients.

Perspective statement: COVID-19 and mechanical ventilation significantly affected the tracheal stenosis etiology. The aim of the present study is to investigate how COVID-19 could impact on tracheal surgery in terms of postoperative outcomes.
ABSTRACT

Objective: The large number of COVID-19 patients subjected to prolonged invasive mechanical ventilation has been expected to result in a significant increase of tracheal stenosis in the next years. The aim of the study was to evaluate and compare postoperative outcomes of survived COVID-19 critical illness patients who underwent tracheal resection for post-intubation/post-tracheostomy tracheal stenosis with those of non-COVID patients.

Methods: It is single-center retrospective study. All consecutive patients affected by post-intubation/post-tracheostomy tracheal stenosis who underwent tracheal resection from February 2020 to March 2022 were enrolled. A total of N=147 tracheal resections were performed: n=24 were Post-COVID patients and n=123 were Non-COVID patients. A 1:1 propensity score matching analysis was performed, considering age, gender, BMI (Body Mass Index), and length of stenosis. After matching, two groups of 24 patients each were identified: Post-COVID Group and Non-COVID Group.

Results: No mortality after surgery was registered. Post-tracheostomy etiology of stenosis resulted more frequently in post-COVID patients (n=20 in Post-COVID Group vs n=11 in NON-COVID Group, p=0.03), as well as the ICU admission in the postoperative period (n=16 vs n=9 patients, p=0.04). Need for postoperative re-intubation for glottic edema and respiratory failure was higher in the Post-COVID Group (n=7 vs n=2 postoperative re-intubation procedures, p=0.04). Postoperative dysphonia was observed in n=11 (46%) patients of Post-COVID Group vs n=4 (16%) patients of NON-COVID Group (p=0.03).

Conclusions: Tracheal resection still continue to be safe and effective in COVID-19-related tracheal stenosis scenario. ICU admission rate and postoperative complications seem to be higher in post-COVID-19 patients who underwent tracheal resection compared to non-COVID-19 patients.

Keywords: tracheal stenosis, tracheal surgery, COVID-19
Objective

Coronavirus disease 2019 (COVID-19) pandemic, outbroken during early 2020, embodied a challenge for surgery worldwide [1]. Although the clinical presentation of COVID-19 could be extremely heterogeneous, varying from asymptomatic to severe respiratory failure, invasive mechanical ventilation (IMV) has been necessary in 9.8%–15.2% of patients [2-3]. The mechanical and ischemic damage caused by prolonged intubation and tracheostomy on the tracheal wall is a well-known risk factor for the production of fibrotic tracheal scarring [4–5]. Moreover, the SARS-CoV-2 has proved to worsen this ischemic tracheal mucosa damage by causing a prothrombotic and antifibrinolytic state, producing microvascular injury and necrosis and requiring chronic high dose systemic steroids use [6–7]. As already published, the supine-to-prone position change, frequently used in the intensive care setting to improve the prognosis in intubated COVID-19 patients with respiratory distress, induces modification of endotracheal tube cuff pressure associated to tube displacement [8]. In addition, tracheal epithelial changes caused by the SARS-CoV-2 virus itself should be considered as a predisposing factor for tracheal stenosis in a COVID-19 patient [9-10]. Prolonged need for IMV in COVID-19 patients, along with the intrinsic capacity of the virus itself to damage the tracheal mucosa, have led to an increased incidence in post-intubation/tracheostomy airways complications, including tracheal stenosis, tracheomalacia and tracheoesophageal fistulas [11].

Concurrently, if elective surgery has been recommended to be postponed during pandemic [12], some diseases could potentially become life-threatening and could not be delayed [13]. Among these conditions, tracheal stenosis, that usually becomes symptomatic when reach 50% obstruction, has become an unavoidable surgical entity culminating their incidence in the last two years. Thus, considering a dual etiology of post-intubation of tracheal stenosis, COVID-19 survivors could have a different postoperative course after tracheal surgery. The aim of this study was to report our experience with post-COVID-19 patients who underwent tracheal resection and reconstruction, comparing the postoperative outcomes with those of non-COVID patients (Figure 1).
**Methods**

**Patients**

This is single-center retrospective study performed following the STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) guidelines. IRB approval was granted for this study (RIF. CE 6451_2021, 09/15/2021). Individual written informed consent was obtained from each patient or legally authorized representative or parent(s) for this study.

From February 2020 to March 2022, n=147 consecutive patients affected by post-intubation/post-tracheostomy tracheal stenosis underwent to tracheal or laryngo-tracheal resection and reconstruction with an end-to-end anastomosis via cervicotomy at Thoracic Surgery Unit - Sant’Andrea Hospital – Sapienza University of Rome, the referral center for tracheal surgery in the country. Generally, cases arrive from the north to the south of Italy. A significant part of the study population has transferred from Intensive Care Units or rehabilitation institutions of the central regions of Italy after brain injury, state of coma, heart/respiratory failure. ENT specialists do not address tracheal surgery in Italy.

Patients affected by idiopathic tracheal stenosis or neoplastic tracheal stenosis, patients who underwent to an extended tracheal resection for long-segment tracheal stenosis (> 5 cm), as well as patients who underwent to a tracheal replacement by a cryopreserved aortic graft, were not considered in this series. Of these N=147 patients, n=24 were Post-COVID-19 patients, survived to a critical illness that required an IMV through intubation or tracheostomy during pandemic, while n=123 were patients affected by tracheal stenosis who received a ETT (Endo Tracheal Tube) or a tracheostomy for other causes and not for COVID-19 respiratory failure. Preoperative assessment included fiberoptic bronchoscopy (FBO) and neck-thorax CT (Compute Tomography) scan to verify the vocal cords motility and to evaluate the tracheal stenosis, its length from vocal cords, the extent, the site, and the severity grade according to Cotton-Meyer classification (Figure 2). Tracheal resection-anastomosis was performed in accordance with Pearson’s technique. Intraoperative ventilation was achieved by endotracheal intubation with a wire-reinforced small caliber tube (4-4.5 mm) passed
through the stenosis or by the insertion of a laryngeal mask airway (LMA) device. The choice to use a ETT or LMA was done according to patients’ physical characteristics and clinic history, features of the stenosis (distance from vocal cords, grade of stenosis). During surgery, all patients underwent traditional cross-field ventilation after tracheal resection by an armored 5 mm ETT. When possible, immediate extubation or removal of the LMA would be attempted for every patient in the operating room. However, at the end of the cross-field ventilation, when the end-to-end anastomosis is performed, the anesthesiologist could decide to place a naso-tracheal tube, with a 7-7.5 mm caliber ETT, as described in our previous series [14] defined as a traditional early re-intubation, also when a LMA was used during the first phases of the surgical procedure (induction, resection, anastomosis). This anesthesiologist’s choice is based on the individual evaluation of patient, on the anatomical glottis status, on the patient’s stability and preoperative cooperation. Thus, the patient can be moved to the ICU or to the Thoracic Surgery Unit with a 7-7.5 mm naso-tracheal tube in place and deflated cuff, awake, spontaneously breathing. The tube is removed after 24 hours under broncoscopic vision. The unexpected re-intubation was defined as a new EET positioning, occurring because of a respiratory failure, after the removal of the LMA or the EET at the end of surgery in the operating room or within the first 24-48 hours from surgery (delayed re-intubation).

During the postoperative period, according to non-invasive protocols, patients received steroids administration, air humidification, diuretics therapy, nebulized epinephrine and High Flow Oxygen Therapy (HFOT, AIRVO2®) to prevent and to treat laryngeal oedema. FBO was performed when necessary and at discharge, and then after 1, 3, 6 and 12 months after surgery for every patient. Specimens of the trachea resected from the patients who underwent tracheal surgery were sent for pathologic examination. Squamous metaplasia, ulceration, dense fibrosis, acute flogosis, gigantocellular flogosis, necrosis, gland atrophy and neoangiogenesis were evaluated on surgical specimens.

Propensity score matching and statistical analysis
To identify two balanced groups according to potential confounding baseline variables, a 1:1 propensity score matching (PSM) analysis was performed using a logistic regression model and considering age, gender, BMI (Body Mass Index), and length of stenosis (1-4 cm). A greedy algorithm with calipers of 0.2 of the SD of the logit of the propensity score was used. The distributions of the propensity score matched results between groups were evaluated using standardized mean difference (SMD). Groups were defined comparable for all confounders if SMD <0.10. After matching, two groups of 24 patients each were identified: a Post-COVID Group and a Non-COVID Group (Figure 3). Characteristics of patients and postoperative results were analyzed before and after matching. For the Estimation of treatment effect matched data were analysed using procedures for matched analyses, such as paired t tests for continuous variable, while McNemar’s test, conditional logit, doubly robust and mixed effect (matched pairs as random effect) logistic regression were used for binary outcomes. Tracheal specimens resected from patients of both groups were evaluated to assess possible similarities or differences. Data were collected and stored in an Excel database (Microsoft Corp, Redmond, Wash) and were analyzed using statistical package SPSS, version 25.0 (SPSS Software, IBM Corp., Armonk, NY, USA). Quantitative variables were expressed as mean ± standard deviation (SD), whereas nominal variables were expressed binarily as presence (1) or absence (0) of the event. Comparison of categorical variables was performed by Chi-squared test using Fischer exact test. Comparison of continuous variables was performed by Student t-test. Significance was defined as a P value of less than 0.05. No missing data are present in the dataset.

Results

Pre- and post-matching characteristics of patients and intraoperative variables are shown in Table 1. Post-matching results are shown in Table 2. Male patients were n=14 (58%) in Post-COVID Group and n=14 (58%) in Non-COVID Group (p=1.00). The mean age was 59.29±9.84 in Post-COVID
Group and 52.33±18.28 in Non-COVID Group (p=0.10). All the other preoperative characteristics, including ASA score, BMI, distance from vocal cords and preoperative dilation procedures (rigid bronchoscopy, laser vaporization) did not present statistically significant differences between the two groups (p=0.69, p=0.18, p=0.23 and p=0.41 respectively), except for the etiology of the stenosis: n=4 (17%) patients of Post-COVID Group vs n=13 (54%) patients of Non-COVID Group had a post-intubation stenosis, while n=20 (83%) patients of Post-COVID Group vs n=11 (46%) patients of Non-COVID Group had a post-tracheostomy stenosis (p=0.03). In Post-COVID Group n=14 (58%) patients required laryngo-tracheal, versus n=12 (50%) in Non-COVID Group (p=0.76). In Post-COVID Group, n=22 (92%) patients were operated with LMA intraoperative assistance, whereas n=2 (8%) patients were operated with traditional ETT. In Post-COVID Group, n=19 (79%) patients were operated with LMA intraoperative assistance, whereas n=5 (21%) patients were operated with traditional ETT (p=0.20). Early re-intubation was reported in n=9 (37%) patients in Post-COVID Group and in n=8 (32%) patients in Non-COVID Group (p=0.12). Preoperative comorbidities such as Chronic Obstructive Pulmonary Disease (COPD), diabetes and Charlson Comorbidity Index were analysed before and after matching, not showing statistically significant differences (p=0.72, p=0.11, p=0.21 respectively before matching, and p=0.89, p=1.00 and p=0.34 after matching). Variables as preoperative smoking history and diabetes mellitus were analysed before and after matching and no statistically significant differences were found (Table 1). The mean time from intubation or tracheostomy and surgery was 7.67±4.71 months in Post-COVID Group and 5.69±4.29 months in the Post-COVID Group (p=0.31). Results are shown in Table 2. The mean operative time was not different between groups: 93.70±24.45 minutes in Post-COVID Group vs 100.83±32.12 in Non-COVID Group (p=0.48). Mortality was 0% in both groups and minor complications (vocal roughness, mild early temporary swallowing difficulty, surgical incision dehiscence) were 8% in both groups. Postoperative dysphonia was reported in n=11 (46%) patients in Post-COVID Group and n=4 (16%) patients in Non-COVID Group (p=0.03). Delayed re-intubation rate for laryngeal oedema and respiratory failure was higher in Post-COVID Group (n=7; 29%) vs Non-COVID Group (n=2; 8%).
with a statistically significant difference, \( p=0.04 \). ICU admission rate was higher in Post-COVID Group (\( n=16, \ 67\% \) vs \( n=9, \ 37\% \); \( p=0.04 \)). At the end, mean hospital stay was not different between groups (\( 7.42\pm4.21 \) days in Post-COVID Group vs \( 6.67\pm3.11 \) days in Non-COVID Group, \( p=0.39 \)), with a median of 7 vs 6 days. No differences in re-stenosis occurrence rate that was 8\% in both groups.

N=1 patient of Post-COVID Group received a permanent tracheostomy (4\%). N=1 patient of Post-COVID Group and n=2 patients of Non-COVID Group are still managing the re-stenosis with airways stenting. Mean follow-up was 12.23\pm4.12 months.

Histological macroscopic findings showed an intense hyaline fibrosis extended to the peritracheal soft tissue at the Hematoxylin-Eosin staining, with acute inflammation demonstrated by the presence of lymphocytes and plasma cells infiltrate in specimens from both groups (Figure 2 and Figure 4). Occasional giant cell granulomas were present. However, no statistically significant differences were reported between groups (\( p>0.05 \) for each histological variable analyzed).

**Conclusions**

Historical recourses showed us how similar situations that happened in the past can recur in the future. Lessons learned from what happened during the pandemic should remain clear to deal with the consequences and to manage any future outbreaks. Cooper [15] highlighted how the worldwide epidemic of poliomyelitis in the early 1950s initiated the era of positive pressure ventilation through cuffed endotracheal or tracheostomy tubes, developing the application of ventilatory assistance in specialized medical and surgical intensive care units. Amongst the survivors, more than 20\% developed airway complications, primarily tracheal stenosis.

More recently, Fiacchini showed that the 48\% of ventilated patients during the severe phase of the COVID-19 illness reported a tracheal stenosis [10]. Accordingly, the clinical numbers are often confirmed by histological findings: very hard and peculiar inflammatory tissues persisted in the peritracheal area during the dissection, with an infiltration of multinuclear giant cell granulomas and
intravascular fibrin thrombi with perivascular mononuclear infiltrate of CD3 T lymphocytes [16]. Fiacchini [17] showed in n=8 patients that a subepithelial inflammatory lymphomonocyte infiltrate was observed in tracheal biopsies of both COVID-19 and non-COVID-19 patients, associated with vasculitis of small subepithelial vessels associated with foci of coagulative necrosis. Two gene sets (HALLMARK_INFLAMMATORY_RESPONSE and HALLMARK_ESTROGEN_RESPONSE_LATE) were significantly deregulated in COVID-19 patients compared to the control group. The authors conclude that the altered inflammatory response of the COVID-19 patients could be another possible explanation of the increasing number of laryngotracheal complications. On the contrary, Ward [18] examined the histological findings of tracheal tissue samples obtained from COVID-19 positive mechanically ventilated patients (n=33), to assess the degree of tracheal inflammation/ulceration present, comparing samples obtained from COVID-19 negative patients (n=5). Histological findings were similar between mechanically ventilated COVID-19 positive and negative patients.

It is clear that deeper histological and mechanistic studies, evaluating the interleukines, IgG4-secreting plasma cells and Th2 response, are needed to highlight the potential implication of the virus itself on the tracheal mucosa in the pathogenesis of the stenosis.

Although, clinical reviews and case reports have been published in the last 2 years [2,19-20] showing the state of the art of COVID-19-related tracheal stenosis, the incidence and the management, they result often circumstantial and poor of comparison. The exact number of intubated COVID-19 patients developing tracheal stenosis is unknown, ranging from 3 to 40% [20]. However, the worldwide incidence of tracheal stenosis is reported to be higher in COVID-19 patients than in pre-COVID-19 era, as our group experienced, and the medical community has been alerted.

The present study tries to evaluate a pure surgical aspect, considering a unique high-volume center for tracheal surgery in the country: the postoperative complications in patients with a COVID-19-
related tracheal stenosis who underwent tracheal resection (Figure 6). Following laryngo-tracheal
and tracheal resection-anastomosis, laryngeal oedema is one of the most challenging intra and
postoperative non-anastomotic complications, eventually requiring the re-intubation of patient.
Postoperative care for patients after tracheal surgery included judicious use of steroids, ambient
humidity, and diuretics to prevent the risk of oedema of the glottis. All the published series
demonstrated that tracheal resection is a safe and effective procedure [14,21]. The laryngeal oedema
can be the main cause for the unexpected re-intubation after extubation or laryngeal mask removal
(“delayed re-intubation”). The present study suggests that, comparing to the control group, the
COVID-19 etiology could increase the delayed re-intubation occurrence, ICU admission rate and
postoperative dysphonia. These data could be a consequence of the increased delayed re-intubation
in this set of patients. The laryngo-tracheal resection, required for very high and subglottic stenosis,
can be a direct risk factor for intra- and postoperative laryngeal oedema, the closeness to vocal cords,
the involvement of lymphatic vessels and the need for extending resection to the cricoid are the major
difficulties, especially in idiopathic or acquired subglottic stenosis. In fact, the closer to vocal cords
is the stenosis, the greater is the risk for inflammation involving vocal cords, and so a consequent
oedema and a consequent respiratory failure. However, the matching analysis of the present study
and the exclusion of the patients affected by idiopathic stenosis from the study should overcome this
bias. Moreover, the use of LMA seems not to be a variable with a clinical impact or a potential risk
factor, as demonstrated in a previous study [22]. Preoperative comorbidities were accurately analyzed
before and after matching. However, no statistically significant differences were found.
Comorbidities seems not to influence postoperative outcomes in this cohort of patients.

To the best of our knowledge, this is the first study exploring the potential impact of COVID-19
etiology on postoperative complications in patients who underwent tracheal surgery, compared to a
control group (NON-COVID patients). However, several limitations are present. It is a single-centre
retrospective study, and it deals with a small group of patients, although it is the largest in the
literature. Post-intubation tracheal stenosis is a rare condition with an estimated incidence of 4.9 cases per million per year in the general population [23]. There are still no reliable data about the occurrence of Post-intubation tracheal stenosis in recovered COVID-19 patients. Actually, this is the largest report of post-COVID-19-related tracheal stenosis. In literature, no more than case-series are present, not exceeding a dozen patients. Nevertheless, limitations are present: 1. PSM was chosen to allow regression on multiple variables in a small sample size, which is an imperfect method of controlling confounders, but at least a way to attempt to increase comparability between groups; 2. PSM cannot account for unmeasured variables (for example, maybe those who survived COVID are more robust than average, and this is why outcomes were similarly good), however no statistical methods analysing retrospective data could be representative of the population as a whole; 3. Acknowledging that tracheal stenosis is a rare disease, there is an increased likelihood of a Type II error occurring when the cohort of the study is small.

The tracheostomy etiology seems to have an implication because is more frequent preoperative variable in the COVID-19 patients, due to both cuff damage and cartilage injury caused during the stoma procedure with no differences. However, this is a fact that should be taken into account by the surgeon at the preoperative evaluation time, explaining to the patient the potential risks. Further prospective multicentric studies would be useful to confirm the results and to identify a real preventive strategy.

Finally, the severe COVID disease is becoming more infrequent at the moment. However, the disease and its consequences are still present. Moreover, the current experience may represent a know-how useful in future, unpredictable situations involving intracellular respiratory infection with intense local inflammation and requiring prolonged intubation, determining tracheal stenosis.

In conclusion, tracheal resection still continues to be effective in COVID-19-related tracheal stenosis scenario, with no differences in long-term postoperative outcomes. ICU admission rate and
postoperative complications seem to be higher in post-COVID-19 patients who underwent tracheal resection compared to non-COVID-19 patients.

References:


## Table 1

<table>
<thead>
<tr>
<th></th>
<th>Post-COVID Group (original)</th>
<th>Non-COVID Group (original)</th>
<th>SMD before matching</th>
<th>Post-COVID Group (matched)</th>
<th>Non-COVID Group (matched)</th>
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<td>62 (51)</td>
<td></td>
<td>20 (83)</td>
<td>11 (46)</td>
<td></td>
</tr>
<tr>
<td>Etiology, n (%)</td>
<td></td>
<td></td>
<td>0.161</td>
<td></td>
<td></td>
<td>0.011</td>
</tr>
<tr>
<td>Cuff (ETT or tracheostomy)</td>
<td>15 (62)</td>
<td>91/ (74)</td>
<td></td>
<td>15 (62)</td>
<td>14 (58)</td>
<td></td>
</tr>
<tr>
<td>Stoma</td>
<td>9 (38)</td>
<td>32 (26)</td>
<td></td>
<td>9 (38)</td>
<td>10 (42)</td>
<td></td>
</tr>
<tr>
<td>BMI (mean±SD)</td>
<td>23.87 ± 4.44</td>
<td>26.02±5.12</td>
<td>0.092</td>
<td>23.87 ± 4.44</td>
<td>24.29±3.97</td>
<td>0.002</td>
</tr>
<tr>
<td>Intraoperative airway, n (%)</td>
<td>22 (92)</td>
<td>82 (67)</td>
<td>0.149</td>
<td>22 (92)</td>
<td>19 (79)</td>
<td>0.095</td>
</tr>
<tr>
<td>Laryngeal mask</td>
<td>2 (8)</td>
<td>41 (33)</td>
<td></td>
<td>2 (8)</td>
<td>5 (21)</td>
<td></td>
</tr>
<tr>
<td>ETT</td>
<td></td>
<td></td>
<td>0.027</td>
<td></td>
<td></td>
<td>0.014</td>
</tr>
<tr>
<td>Early re-intubation, n (%)</td>
<td>9 (37)</td>
<td>60 (49)</td>
<td></td>
<td>9 (37)</td>
<td>8 (33)</td>
<td></td>
</tr>
</tbody>
</table>

ASA: American Society of Anesthesiologists; BMI: body mass index; CCI: Charlson Comorbidity Index; CI: confidence interval; COPD: Chronic obstructive pulmonary disease; DM: Diabetes Mellitus; ETT: EndoTracheal Tube; SD: Standard Deviation; SMD: standardized mean difference.

## Table 2
<table>
<thead>
<tr>
<th></th>
<th>Post-COVID Group (original)</th>
<th>Non-COVID Group (original)</th>
<th>SMD before matching</th>
<th>Post-COVID Group (matched)</th>
<th>Non-COVID Group (matched)</th>
<th>SMD after matching</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
<td>24</td>
<td>123</td>
<td>24</td>
<td>24</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Operative time (minutes, mean±SD)</td>
<td>93.70±24.45</td>
<td>106.41±42.77</td>
<td>0.282</td>
<td>93.70±24.45</td>
<td>100.83±32.12</td>
<td>0.252</td>
</tr>
<tr>
<td>Postoperative Length of stay (days, mean±SD)</td>
<td>7.42±4.21</td>
<td>8.57±3.64</td>
<td>0.312</td>
<td>7.42±4.21</td>
<td>6.67±3.11</td>
<td>0.202</td>
</tr>
</tbody>
</table>

Estimation of treatment effect

<table>
<thead>
<tr>
<th></th>
<th>P-value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality, n (%)</td>
<td>0 (0)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Delayed re-intubation, n (%)</td>
<td>0.052</td>
<td>7 (29)</td>
</tr>
<tr>
<td>Re-stenosis, n (%)</td>
<td>0.061</td>
<td>2 (8)</td>
</tr>
<tr>
<td>Postoperative Dysphonia, n (%)</td>
<td>0.024</td>
<td>11 (46)</td>
</tr>
<tr>
<td>Permanent Tracheostomy, n (%)</td>
<td>0.881</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Minor complications, n (%)</td>
<td>0.899</td>
<td>2 (8)</td>
</tr>
<tr>
<td>ICU admission rate, n (%)</td>
<td>0.039</td>
<td>16 (67)</td>
</tr>
<tr>
<td>Fully adjusted logistic, OR (95% CI)</td>
<td>0.87 (0.56–1.05)</td>
<td>0.045</td>
</tr>
<tr>
<td>Conditional logit, OR (95% CI)</td>
<td>0.71 (0.54–0.98)</td>
<td>0.039</td>
</tr>
<tr>
<td>Doubly robust logistic, OR (95% CI)</td>
<td>0.77 (0.49–0.88)</td>
<td>0.043</td>
</tr>
<tr>
<td>Mixed effect logistic, OR (95% CI)</td>
<td>0.72 (0.52–0.91)</td>
<td>0.038</td>
</tr>
</tbody>
</table>

CI: confidence interval; ICU: Intensive Care Unit; OR: odds ratio; SD: Standard Deviation; SMD: standardized mean difference.

**Figure 1**
New Perspectives on Tracheal Resection for COVID-19-related Stenosis: a Propensity Score Matching Analysis

Legend:

Figure 1: Graphical abstract of the study

Figure 2: Endoscopic view (A) and CT findings (C) of a post-intubation non-COVID tracheal stenosis; Endoscopic view (B) and CT findings (D) of a post-COVID tracheal stenosis

Figure 3: Patients’ inclusion/exclusion flow diagram

Figure 4: 1X original magnification, Hematoxylin-Eosin staining. A) In the specimen of a patient from Post-COVID Group severe hyaline fibrosis restricting the tracheal lumen can be seen. Hyaline fibrosis extends to the peritracheal soft tissues and disrupts the cartilaginous arch; B) A milder fibrosis with a lower lumen restriction can be appreciated in the specimen of a patient from Non-COVID Group. The fibrosis mostly involves the pars membranacea and rear portion of the trachea.
Figure 5: Surgical specimen of a tracheal resection in a post-COVID-19 patient

Figure 6: Central Picture showing the postoperative findings of the study. ICU: intensive care unit; COVID-19: Coronavirus disease 2019

Table 1: Patients’ characteristics and intraoperative variables before and after matching

Table 2: Postoperative results before and after matching, and logistic regression for ICU admission rate
TRACHEAL STENOSIS

ETIOLOGY:
- COVID-RELATED
- NON-COVID-RELATED

Surgery

POSTOPERATIVE OUTCOMES:
ICU admission rate and postoperative complications seem to be higher in post-COVID-19 patients who underwent tracheal resection compared to non-COVID-19 patients.
New Perspectives on Tracheal Resection for COVID-19-related Stenosis: a Propensity Score Matching Analysis

Post-COVID-19 tracheal stenosis

February 2020 - March 2022
n = 147 consecutive tracheal resections for tracheal stenosis:
- n= 24 Post-COVID patients
- n=123 Non-COVID patients

1:1 propensity score matching analysis, considering age, gender, BMI (Body Mass Index), and length of stenosis (1-4 cm).

After matching:
- n= 24 Post-COVID group
- n=24 Non-COVID group

-Tracheostomy etiology of stenosis more frequent in post-COVID patients (p=0.03)

-Need for postoperative re-intubation for glottic edema with respiratory failure and ICU admission in the postoperative period higher in the Post-COVID Group (p=0.04)

-Postoperative dysphonia increased in post-COVID patients (p=0.03)

Tracheostomy seems to be a more frequent cause of tracheal stenosis compared to prolonged intubation in post-COVID-19 patients.

ICU admission rate and postoperative complications seem to be higher in post-COVID-19 patients who underwent tracheal resection compared to non-COVID-19 patients.
February 2020 - March 2022

n = 147 consecutive tracheal or laryngo-tracheal resections via cervicotomy for post-intubation/post-tracheostomy tracheal stenosis, excluding:

- Idiopathic tracheal stenosis
- Neoplastic tracheal stenosis
- Extended tracheal resection for long-segment tracheal stenosis (> 5 cm)
- Tracheal replacement by a cryopreserved aortic graft

1:1 propensity score matching analysis, considering age, gender, BMI (Body Mass Index), and length of stenosis (1-4 cm).

After matching:

- n = 24 Post-COVID group
- n = 24 Non-COVID group
TRACHEAL STENOSIS

ETIOLOGY:
- COVID-RELATED
- NON-COVID-RELATED

Surgery

POSTOPERATIVE OUTCOMES:
ICU admission rate and postoperative complications seem to be higher in post-COVID-19 patients who underwent tracheal resection compared to non-COVID-19 patients.
HISTOLOGY

A

Post-COVID 19 patient

B

Non-COVID 19 patient

p > 0.05