Tracheal complications of mechanical ventilation for COVID-19: a plot twist for survivors

Badovinac, Sonja; Popović, Filip; Glodić, Goran; Baričević, Denis; Srdić, Dražena; Džubur, Feđa; Koršić, Marta; Samaržija, Miroslav

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To the Editor:

Severe COVID-19 patients require mechanical ventilation in up to 15.2% of cases [1]. Post-intubation tracheal stenosis (PITS), post-tracheostomy tracheal stenosis (PTTS) and trachea-oesophageal fistulas are tracheal complications of mechanical ventilation. The incidence of tracheal complications of mechanical ventilation was one in 200 000 patients annually before the COVID-19 pandemic [2]. The most important risk factors for these complications include prolonged mechanical ventilation, reintubation and excessive tracheal tube cuff pressure (>30 cmH_2O), all of which were common in mechanically ventilated COVID-19 patients [3, 4]. We experienced a significant increase in referrals to our interventional pulmonology unit at a tertiary teaching hospital for PITS and PTTS treatment after the most severe COVID-19 surges, and thus conducted this retrospective study with prospective follow-up aiming to describe this unique cohort of patients.

All patients referred to our interventional pulmonology unit for evaluation and treatment of PITS, PTTS or tracheo-oesophageal fistulas complicating mechanical ventilation for COVID-19 from March 2021 to June 2022 were included. Clinical and radiological data were collected from hospital records of both our and referring hospitals. Patients were followed up with flexible bronchoscopy at 4-week intervals with additional diagnostic imaging as indicated. Assessment of the severity and grading of stenosis was performed with computed tomography and flexible bronchoscopy. Based on the Myer–Cotton and McCaffrey classification systems and key features such as length, shape, location and cartilage involvement, stenoses were divided in two groups: simple and complex [5, 6]. After assessment, patients were treated either endoscopically or surgically. Endoscopic treatment was performed under general anaesthesia using rigid bronchoscopy. First, tissue incisions were made at 3, 9 and 12 o'clock using endobronchial electrocautery. Mechanical dilatation followed, with Rusch Wiruthan (Willy Rusch GmbH, Kernen, Germany) or CRE Pulmonary (Boston Scientific, Natick, MA, USA) dilatation catheters and rigid bronchoscopes with a diameter of 1.1 and 1.4 cm. Surgical treatment included cricotracheal or tracheotracheal resection and end-to-end anastomosis. Microsoft Excel (Microsoft, Redmond, WA, USA) was used to tabulate data, calculate frequencies and percentages, and perform statistical analysis. The study was approved by the ethics committee of University Hospital Centre Zagreb (class 8.1-22/21-2, number 02/013 AG).

A total of 24 patients were evaluated and 21 of them were treated during the study period. The median duration of follow up was 8 months (interquartile range (IQR) 6–9 months). Patient characteristics, intensive care unit (ICU) treatment strategies and treatment data are shown in table 1. Most patients (18 out of 24, 11 out of 14 and five out of seven of total, rigid bronchoscopy and surgical patients, respectively) were referred from a single hospital, after treatment in the same ICU. The time between extubation and clinical presentation varied widely, from 5 to 110 days. The mean±SD diameter of simple PITS/PTTS was 5.6±1.5 mm. Tracheo-oesophageal fistula developed in two patients with complex PITS/PTTS. 14 (58.3%) patients had simple and 10 (41.7%) complex PITS/PTTS. Rigid bronchoscopy was used as the initial treatment in 14 patients, who mostly had simple PITS/PTTS (85.7%), while surgery was the initial approach for seven patients with mostly complex PITS/PTTS (60%). All 14 patients treated with rigid bronchoscopy achieved complete recanalisation without any procedure related complication. Despite good initial success, restenosis occurred in 93.9% patients after a median of 32 days (IQR 22.75–61.25 days),

Shareable abstract (@ERSpublications)
Tracheal complications should be suspected in mechanically ventilated COVID-19 survivors with respiratory symptoms. Treatment requires a multimodal approach of interventional bronchoscopy and surgery with tight follow-up due to a high rate of restenosis. https://bit.ly/3iw05xQ

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TABLE 1 Patient characteristics, intensive care unit (ICU) treatment strategies and treatment data

Patient characteristics	Total	Simple PITS/PTTS	Complex PITS/PTTS	p-value[#]
Patients	24	14 (58.3%)	10 (41.7%)	
Age, years	55.5 (51–68.75)	55.5 (50–64.5)	58(53–69.5)	0.52
Male	12 (50%)	6 (42.9%)	6 (60%)	0.68
Female	12 (50%)	8 (57.1%)	4 (40%)	
Never-smoker	17 (71%)	11 (78.6%)	6 (60%)	0.39
Active/former smoker	7 (29%)	3 (21.4%)	4 (40%)	
BMI, kg·m^{-2}, mean±SD	28.8±4.8	28.5±5	28.8±4.5	0.58
Underweight	0	0	0	
Normal weight	6 (25%)	4 (28.6%)	2 (20%)	0.63
Overweight	13 (54.2%)	6 (42.9%)	7 (70%)	0.24
Obese	2 (8.3%)	1 (7.1%)	1 (10%)	0.8
Extremely obese	3 (12.5%)	2 (14.2%)	1 (10%)	0.75
Comorbidities				
Arterial hypertension	16 (67%)	9 (64.3%)	7 (70%)	0.77
Diabetes mellitus	10 (41.7%)	5 (35.7%)	5 (50%)	0.68
Heart disease	2 (8.3%)	2 (14.2%)	0	0.49
Active malignancy	3 (12.5%)	2 (14.2%)	1 (10%)	0.75
Chronic kidney disease	1 (4.2%)	1 (7.1%)	0	
ICU treatment characteristics				
Duration of MV, days	12(10–22.5)	10 (9–18.5)	16 (12–24.75)	0.14
Duration of MV >14 days	11 (45.8%)	5 (35.7%)	6 (60%)	0.41
Maximum duration of MV, days n	50	50	44	
Reintubation	3 (8.3%)	2 (14.2%)	1 (10%)	0.75
Tracheotomy	10 (41.7%)	3 (21.4%)	7 (70%)	**0.035**
Patient presentation				
Stridor	11 (45.8%)	7 (50%)	4 (40%)	0.7
Dyspnoea	12 (50%)	7 (50%)	5 (50%)	1
Food aspiration	1 (4.2%)	0	1 (10%)	0.42
Time to symptom onset, days	34 (14.5–60)	42 (14.75–60)	19.5 (7–48.75)	0.38
Time to PITS diagnosis, days	15 (2–42)	30 (11–75)	8.5 (0.75–33)	0.1
Initial PITS/PTTS treatment strategy				
Rigid bronchoscopy	14 (58.3%)	12 (85.7%)	2 (20%)	**0.003**
Thoracic surgery	7 (29.2%)	1 (7.1%)	6 (60%)	**0.009**
Tracheotomy	1 (4.2%)	0	1 (10%)	0.42
Lost to follow-up	2 (8.3%)	1 (7.1%)	1 (10%)	0.8

Data are presented as n (%) or median (interquartile range) unless otherwise stated. PITS: post-intubation tracheal stenosis; PTTS: post-tracheotomy tracheal stenosis; BMI: body mass index; MV: mechanical ventilation. [#]: Mann–Whitney, Chi-squared or Fisher's exact test as appropriate. Bold indicates statistically significant p-values.

requiring a total of 32 rigid bronchoscopies, which established airway patency in 10 (71.4%) patients, while four (28.6%) patients ultimately had to be surgically treated due to severe restenosis. Three (42.8%) patients initially treated surgically needed endoscopic interventions due to post-surgery restenosis. Successful recanalisation was achieved in all of them. Aside from the high rate of restenosis, no other major complications occurred during or after rigid bronchoscopy. A total of 39 therapeutic rigid bronchoscopies and 111 diagnostic flexible bronchoscopies were performed during the study period.

Our interventional pulmonology department is the Croatian national centre for rigid bronchoscopy, which admits patients with tracheal disease from the whole country. In the years preceding the pandemic (2017–2019), we treated an average of 12 PITS/PTTS patients annually. This number almost doubled after the COVID-19 pandemic, with 24 referrals during the 15-month study period. In concurrence with previous studies, we observed a disproportionate number of obese patients, with an even higher incidence of patients with diabetes mellitus (41.7% *versus* 17.4%) [7]. Obesity is a well described risk factor for PITS/PTTS in pre-pandemic studies and complicates the course of acute COVID-19 with a higher rate of mechanical ventilation and airway management issues among these patients [3, 8]. Diabetes could play an important role in the development of tracheal complications due to the changes in the microvasculature and impaired wound healing [3, 9, 10]. The median and maximum duration of mechanical ventilation, reintubation and tracheostomy rates were similar to other cohorts and higher than in non-COVID-19

patients [7, 8, 11]. The wide time window between extubation, clinical presentation and diagnosis was also almost identical to previous reports [7]. Interestingly, more patients in our study presented with simple stenosis than in previous reports, where complex stenosis was more common [7, 12]. Complex stenosis was significantly more common among PTTS patients.

We used the same management strategy for both simple and complex stenosis after COVID-19 as in non-COVID-19 patients. However, the treatment course of PITS/PTTS after COVID-19 was complicated with an extremely high rate of restenosis requiring a multimodal approach. Initial rigid bronchoscopy was preferred for patients with simple stenosis, while complex stenosis was treated surgically whenever possible. The reported success rate of endoscopic procedures of 40–82% depends on the length and complexity of stenosis. Surgical procedures have a success rate as high as 95% [13]. Despite the high rate of restenosis in our cohort (93.9%), we ultimately had a high treatment success rate of 71.4% among the 14 patients initially treated with rigid bronchoscopy, after an average of 2.3 endoscopic procedures per patient. We avoided stent placement as per usual institutional protocol due to potential complications, similarly to the protocol reported by Freitas *et al.* [12] who treated simple PITS with more than four dilatations in some cases. We observed a substantial rate of restenosis after surgery (42.8%) requiring endoscopic management of restenosis. This high failure rate could be attributed to the complexity of stenosis and impaired healing after surgery, which is most likely a consequence of chronic inflammation, low tissue quality after prolonged critical illness and patient comorbidities such as diabetes [9, 10, 14].

The most intriguing finding is that the majority of patients (18 out of 24) were referred from a single hospital, after treatment in the same ICU, from an area that experienced the most severe COVID-19 surge in Croatia. The extremely high number of patients that required ICU treatment presented unique organisational challenges. Physician and nurse shortages led to fatigue and stress that could have contributed to suboptimal ICU care. This highlights the fact that PITS and PTTS are, despite some contributing intrinsic patient characteristics, in essence, iatrogenic diseases preventable by meticulous ICU care.

In conclusion, rigid bronchoscopy was successfully used for post-COVID-19 PITS and PTTS as the primary treatment and pre- and post-surgery, which emphasises the importance of multidisciplinary management. Given the high restenosis rate and complicated treatment course, care should be given to prevent tracheal complications with maintenance of high ICU quality standards. Finally, delayed accurate diagnosis emphasises the importance of awareness of tracheal complications among mechanically ventilated COVID-19 survivors, since respiratory symptoms could be misattributed to parenchymal lung disease or neuromuscular disease in long COVID-19 syndrome.

Sonja Badovinac[1], Filip Popović[1], Goran Glodić[1], Denis Baričević[1], Dražena Srdić[1], Feđa Džubur[1], Marta Koršić[1] and Miroslav Samaržija[1,2]

[1]Clinic for Lung Diseases Jordanovac, University Hospital Centre Zagreb, Zagreb, Croatia. [2]School of Medicine, University of Zagreb, Zagreb, Croatia.

Corresponding author: Goran Glodic (glodic.goran@gmail.com)

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