Contents lists available at ScienceDirect

# Journal of Cardiothoracic and Vascular Anesthesia
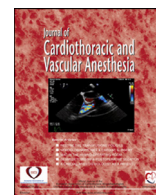
Original Article

# Tracheal Stenosis After Prolonged Intubation Due to COVID-19

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*Objectives:* The authors aimed to evaluate the characteristics and management outcomes of patients who developed tracheal stenosis after invasive mechanical ventilation (IMV) due to COVID-19.

*Design, Setting, and Participants:* The data of 7 patients with tracheal stenosis and 201 patients without tracheal stenosis after IMV due to COVID-19 between March 2020 and October 2021 were retrospectively analyzed.

*Interventions:* Flexible bronchoscopy was performed for the diagnosis of tracheal stenosis and the evaluation of the treatment's effectiveness, and rigid bronchoscopy was applied for the dilatation of tracheal stenosis.

*Measurements and Main Results:* In the follow-up period, tracheal stenosis was observed in 7 of 208 patients (2 women, 5 men; 3.3%). The patients were divided into 2 groups as patients with tracheal stenosis (n = 7) and patients without tracheal stenosis (n = 201). There were no statistically significant differences between the 2 groups in terms of age, sex, body mass index, and comorbidities (p > 0.05). The mean duration of IMV of the patients with tracheal stenosis was longer than patients without tracheal stenosis (27.9 ± 13 *v* 11.2 ± 9 days, p < 0.0001, respectively). Three (43%) of the stenoses were web-like and 4 (57%) of them were complex-type stenosis. The mean length of the stenoses was 1.81 ± 0.82 cm. Three of the patients were treated successfully with bronchoscopic dilatation, and 4 of them were treated with tracheal resection.

*Conclusions:* Tracheal stenosis developed in 7 of 208 (3.3%) patients with COVID-19 who were treated with IMV. The most important characteristic of patients with tracheal stenosis was prolonged IMV support.
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*Key Words:* COVID-19; tracheal stenosis; invasive mechanical ventilation; bronchoscopic dilatation; tracheal resection

TRACHEAL STENOSIS is a potentially life-threatening condition that generally develops iatrogenically as a result of endotracheal intubation or tracheostomy. It has long been known that ischemia, secondary to prolonged intubation, is the primary source of scarring injury in tracheal stenosis.[1] The COVID-19 pandemic, caused by a new coronavirus (SARS-CoV-2) in December 2019, has become the most important reason for intensive care unit (ICU) admissions worldwide due to respiratory failure. Approximately 88% of the patients followed and treated in the ICU due to COVID-19 needed invasive mechanical ventilation (IMV) and received IMV support for an average of 18 days with an endotracheal tube at high positive end-expiratory pressures.[2] While tracheostomy generally is performed 7-to-14 days after endotracheal intubation in order to increase weaning success and reduce the risk of

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complications and death in patients with IMV support, the generally accepted global clinical practice for COVID-19 intubation is the opposite. The suggested management for patients with COVID-19 is to postpone the tracheostomy until it is determined that the patient is cleared from the virus and the patient does not need to be ventilated in the prone position. This practice means that patients remain intubated for up to 3-to-4 weeks and have an increased risk of tracheal stenosis.[3]

The authors' hospital is one of the first pandemic clinics in their country and is one of the centers with the highest number of patients with COVID-19. During the pandemic, the authors' hospital served 5 ICUs with a total bed capacity of 40. In this study, the authors aimed to evaluate the characteristics and management outcomes of patients who developed tracheal stenosis after IMV due to respiratory failure caused by COVID-19. The authors compared the clinical characteristics of patients with and those without tracheal stenosis after IMV.

## Methods

The data of 7 patients who developed tracheal stenosis and 201 patients who did not develop tracheal stenosis after IMV due to critical COVID-19 in the ICUs of the authors' hospitals between March 2020 and October 2021 were retrospectively analyzed. All patients with COVID-19 were diagnosed using next-generation sequencing or real-time reverse transcription polymerase chain reaction (PCR). The demographic features of the patients, comorbidities, duration of mechanical ventilator support, time from endotracheal intubation to tracheostomy, duration of tracheostomy, time from extubation to diagnosis, the type, size, and localization of the stenosis, categories of the endoscopic interventions and surgeries applied, and their success rates were analyzed using the patients' medical records. The same extubation criteria were used for other patients without COVID-19. Ethical approval for the study was obtained from the Umraniye Training and Research Hospital Ethics Committee (October 18, 2021/326).

### Diagnosis and Description of the Stenosis

The diagnosis of tracheal stenosis was confirmed with flexible bronchoscopy (FB) (Olympus BF1T150, Tokyo, Japan) when clinical and radiologic signs led to the suspicion of tracheal stenosis. The type of stenosis was classified as web-like or complex. The size and length of the stenosis were measured using chest tomography and during FB evaluation. The localization of stenosis was classified as subglottic, one-third of the upper part of the trachea, middle part of the trachea, and one-third lower part of the trachea. The size of the stenosis was classified according to the degree of stenosis of the tracheal lumen in 4 grades as follows: grade I (≤50%), grade II (51%-70%), grade III (>70%), and grade IV (complete obstruction). FB was performed to evaluate the effectiveness of the treatment and during follow-ups, and rigid bronchoscopy (Novotech rigid bronchoscope, Dutau Novotech, Marseille, France) was applied for the dilatation of stenosis. Patients with tracheal

stenosis who could not be treated with rigid bronchoscopy were treated by surgery.

### Follow-up of Patients

All patients were followed up after discharge using the hospital electronic medical records system and the national medical database called "E pulse," which includes all the medical records of the patients (epicrisis, anamnesis, physical examination, laboratory parameters, and radiological images). Symptoms related to tracheal stenosis or tracheal stenosis diagnosed radiologically or clinically in a different health institution were not observed in the national medical database called "E pulse" of 201 patients who did not develop tracheal stenosis.

## Statistical Analysis

Parametric tests were used without normality tests because of the suitability of the central limit theorem. While performing statistical data of continuous structure, average, standard deviation, and minimum and maximum values were used. When defining categorical variables, frequency and percentage values were used. Chi-square test statistics were used to evaluate the relationships between categorical variables. The Student $t$ test was used to compare the means of the 2 groups. The statistical significance level of the data was considered at $p < 0.05$. The MedCalc statistics package program (MedCalc Software, Ostend, Belgium) and E-PICOS software (MedicReS, New York, NY) were used to evaluate the data.[4]

## Results

During the study period, 586 patients were followed up with IMV due to respiratory failure caused by COVID-19 in the ICU of the authors' hospital. Of these patients, 350 died in the ICU (59.7%). Approximately 28 patients died during the follow-up period after discharge from the ICU. During the follow-up period, tracheal stenosis was observed in 7 of 208 patients (2 female, 5 male; 3.3%) who were successfully discharged from the hospital after being extubated. The mean age of the patients was $61.7 \pm 13$ years. The patients were divided into 2 groups as follows: patients with tracheal stenosis (n = 7) and patients without tracheal stenosis (n = 201). The demographics and clinical characteristics of the patients are summarized in Table 1. There were no statistically significant differences between the 2 groups in terms of age, sex, body mass index, and comorbidities ($p > 0.05$) (Table 1). Twenty patients (9.6%) underwent tracheostomy during the weaning phase and were discharged from the ICU after their tracheostomy was closed. All patients who underwent tracheostomy had negative PCR results before tracheostomy. The frequency of tracheostomy in patients with tracheal stenosis (57.1%, n = 4) was higher than that in patients without tracheal stenosis (8%, n = 16) ($p < 0.0001$). The mean follow-up duration of patients after discharge from the ICU was $358.2 \pm 158$ days. There were no statistical differences between the 2 groups in terms of tracheostomy duration (days) and time from

Table 1
Demographics and Clinical Characteristics of Patients

| Variable | | Total Number of Patientsn = 208 (%) | Patients with Tracheal Stenosisn = 7 (%) | Patients Without Tracheal Stenosisn = 201 (%) | p Value[*] |
|---|---|---|---|---|---|
| Sex | Male | 139 (67.1) | 5 (71.4) | 134 (67) | 0.81 |
| | Female | 68 (32.9) | 2 (28.6) | 66 (33) | |
| Age (y) | Mean ± SD | 61.7 ± 13 | 57.4 ± 10 | 61.9 ± 13 | 0.38 |
| BMI (kg/m$^2$) | Mean ± SD | 27.89 ± 5 | 27.41 ± 2 | 27.91 ± 5 | 0.63 |
| Comorbidities | Yes | 143 (68.8) | 3 (42.9) | 140 (69.7) | 0.13 |
| | No | 65 (31.3) | 4 (57.1) | 61 (30.3) | |
| Hypertension | Yes | 105 (50.5) | 2 (28.6) | 103 (51.2) | 0.24 |
| | No | 103 (49.5) | 5 (71.4) | 98 (48.8) | |
| Diabetes | Yes | 75 (36.1) | 1 (14.3) | 74 (36.8) | 0.22 |
| | No | 133 (63.9) | 6 (85.7) | 127 (63.2) | |
| CAD | Yes | 36 (17.3) | 1 (14.3) | 35 (17.4) | 0.83 |
| | No | 172 (82.7) | 6 (85.7) | 166 (82.6) | |
| COPD | Yes | 42 (20.2) | 2 (28.6) | 40 (19.9) | 0.63 |
| | No | 166 (79.8) | 5 (71.4) | 161 (80.1) | |
| CRF | Yes | 22 (10.6) | - | 22 (10.9) | 0.36 |
| | No | 186 (89.4) | 7 (100) | 179 (89.1) | |
| Tracheostomy | Yes | 20 (9.6)) | 4 (57.1) | 16 (8) | <0.0001 |
| | No | 188 (90.4) | 3 (42.9) | 185 (92) | |
| Tracheostomy duration (d) | Mean ± SD | 21.8 ± 12 | 25.3 ± 6 | 20.9 ± 13 | 0.54 |
| Follow-up duration of patients (d) | Mean ± SD | 358.2 ± 158 | 239.7 ± 180 | 362.3 ± 156 | 0.04 |
| Time from endotracheal intubation to tracheostomy (d) | Mean ± SD | 17.9 ± 5 | 16.75 ± 2 | 18.1 ± 5 | 0.67 |
| Total IMV duration (endotracheal tube and tracheostomy) (d) | Mean ± SD | 38.3 ± 14 | 27.9 ± 13 | 11.2 ± 9 | <0.0001 |
| ICU length of stay (d) | Mean ± SD | 17.9 ± 11 | 39.9 ± 16 | 17.1 ± 10 | <0.01 |
| Total length of stay (ICU + clinic) (d) | Mean ± SD | 25.9 ± 15 | 48.7 ± 19 | 25.1 ± 14 | <0.0001 |

Abbreviations: BMI, body mass index; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure; ICU, intensive care unit; IMV, invasive mechanical ventilation; SD, standard deviation.

   * The p value is significant at the level of <0.05 (Student $t$/chi-square test).

endotracheal intubation to tracheostomy (day) (p = 0.54 and p = 0.67, respectively) (Table 1). The mean duration of IMV was 38.3 ± 14 days. The mean duration of IMV was longer in patients with tracheal stenosis than in those without tracheal stenosis (27.9 ± 13 $v$ 11.2 ± 9, p < 0.0001, respectively). ICU length of stay (39.9 ± 16 days $v$ 17.1 ± 10 days, p < 0.01) and total (ICU plus clinic) length of stay (48.7 ± 19 days $v$ 25.1 ± 14 days, p < 0.0001) were longer in patients with tracheal stenosis (Table 1).

All patients with tracheal stenosis had complaints of dyspnea, wheezing, and stridor on physical examination. Five patients (71%) were admitted to the emergency department, and 2 patients (29%) were admitted to the outpatient clinic. The time from extubation to diagnosis of tracheal stenosis was 114.57 ± 85 days. Three (43%) of the stenoses were web-like and 4 (57%) were complex type (Fig 1). The majority of stenoses (n = 6, 86%) were localized in the upper one-third of the trachea and were grade 3 (n = 4, 58%). The mean length of the stenoses was 1.81 ± 0.82 cm. The characteristics of the patients with tracheal stenosis are summarized in Table 2.

Bronchoscopic dilatation was performed once in patients with web-like stenosis. Restenosis was not observed in any of the patients with FB control 1 month after dilatation. In patients with complex stenosis, at least 1 bronchoscopic dilatation was performed before surgery. Bronchoscopic dilatation was performed at 2 different times in patients 1 and 6, whose

surgery was delayed due to COVID-19 and restenosis. Furthermore, bronchoscopic dilatation was performed 5 times on patient 5, who did not accept surgery at first but later was amenable to surgery. Tracheal resection was performed in 4 patients with complex-type stenosis (Table 3). There were no procedural complications in patients who underwent bronchoscopic dilatation. No complications were encountered in 4 of the 7 patients who underwent tracheal resection. The mean follow-up period of the patients was 239.7 ± 180 days. During this period, none of the patients had any symptoms or signs related to restenosis or late complications secondary to surgery.

## Discussion

Although this study included only 7 patients with tracheal stenoses, to the authors' knowledge it was the largest series evaluating tracheal stenoses caused by COVID-19. The primary disease causing mechanical ventilation, airway interventions in the ICU, and accompanying comorbidities are the most important risk factors in the development of postintubation tracheal stenosis and posttracheostomy tracheal stenosis. The stenosis group in which the course of COVID-19 was worse included patients with advanced age and accompanying comorbidities.[5] In this group, there was a 3-fold difference between the hospitalization times of the patients followed in
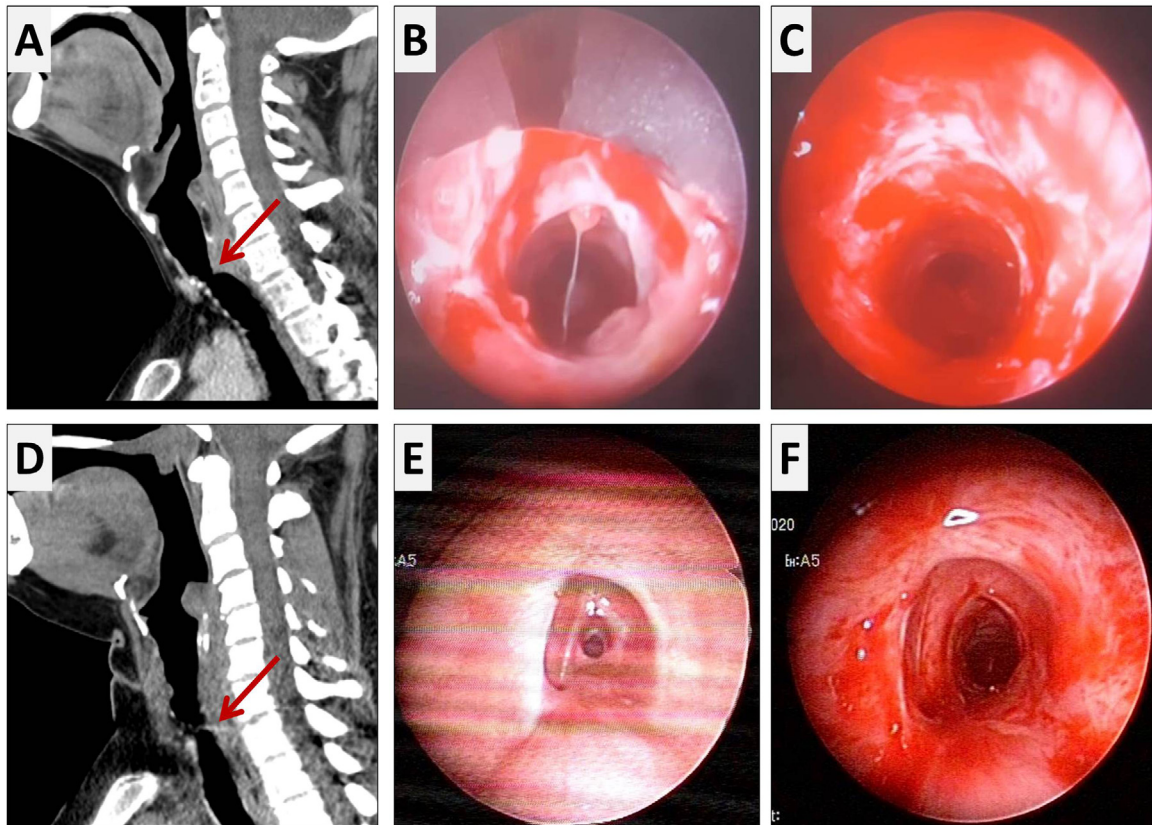
Fig 1. (A) Image of stenosis in sagittal section of patient 2 via computed tomography. (B) Bronchoscopic view of patient 2 before dilatation of stenosis. (C) Bronchoscopic view of patient 2 after dilatation of stenosis. (D) Image of stenosis in sagittal section of patient 4 via computed tomography. (E) Bronchoscopic view of patient 4 before dilatation of stenosis. (F) Bronchoscopic view of patient 4 after dilatation of stenosis.

the clinic and the ICU (5 days [3-7] $v$ 15 days [9-23], p < 0.001).[6] Patients who develop respiratory failure due to COVID-19 subsequently are on a long-term (mean, 18 days) mechanical ventilator support with high positive end-expiratory pressures.[2] In this study, there were no statistically significant differences between patients with tracheal stenosis and those without tracheal stenosis in terms of age, sex, body mass index, and comorbidities, and the mean duration of IMV was quite high (38.3 $\pm$ 14 days). The mean duration of IMV in patients with tracheal stenosis was longer than that in patients without tracheal stenosis (27.9 $\pm$ 13 $v$ 11.2 $\pm$ 9, p < 0.0001, respectively), and this prolonged IMV support was the main risk factor for the development of tracheal stenosis. Moreover, ICU length of stay (39.9 $\pm$ 16 days $v$ 17.1 $\pm$ 10 days, p < 0.01) and total (ICU plus clinic) length of stay (48.7 $\pm$ 19 days $v$ 25.1 $\pm$ 14 days, p < 0.0001) were longer in patients with tracheal stenosis.

In this study, despite long-term IMV follow-up with an endotracheal tube, tracheostomy was performed in only 9.6% (n = 20) of the patients. This situation may be related to the high risk of virus transmission during tracheostomy, the prolongation of virus clearance, the continuation of the need for prone position ventilation, or the death of most patients within the first 14 days. The authors could not provide clear information on this subject because of the inadequacy of medical records, including the virus clearance time and the frequency and duration of prone position ventilation of the patients.

Although the overall mechanical ventilation time was much higher in the tracheal stenosis group, the time to tracheostomy and the tracheostomy duration was no different between the groups. The lack of difference between the groups in the time to tracheostomy may have been related to the waiting for PCR negativity before the tracheostomy procedure in patients planned for tracheostomy. Also, this may have been related to other factors not measured that might have contributed to the tracheal stenosis, such as much greater vasopressor use, or longer periods of hypoxia in the tracheal stenosis group that contributed to tissue ischemia.

Although the frequency of postintubation tracheal stenosis in intubated patients is reported to be−1%-to- 21%, symptomatic cases with severe stenosis constitute 1% to 2% of patients.[7] Symptoms and signs of tracheal stenosis may appear immediately after extubation or within a few years.[8] The work of breathing in the central airway obstruction and tracheal stenosis depends on the pressure change and mainly is affected by the degree of obstruction and airflow rate. Mild tracheal narrowing (ie, $\leq$ 50% reduction in cross-sectional area [CSA]) is unlikely to cause symptoms, as the pressure is similar to that at the normal glottic opening. Moderate obstruction (51%-70% reduction in CSA) produces variable symptoms, with significant pressure drops occurring, especially in situations requiring high flow such as exertion. Sedentary patients may have been asymptomatic during this stage. Severe stenosis (> 71% reduction in CSA) causes a significant pressure drop, and

Table 2
Characteristics of the Patients With Tracheal Stenoses

| | |
|---|---|
| **Symptoms and signs of patients, n (%)** | |
| Dyspnea | 7 (100) |
| Wheezing | 7 (100) |
| Stridor | 7 (100) |
| **How to apply to the hospital, n (%)** | |
| Emergency service | 5 (71) |
| Outpatient clinic | 2 (29) |
| **Time from extubation to diagnosis/day, mean ± SD** | 114.57 ± 85 |
| **Tracheostomy, n (%)** | 4 (57) |
| **Type of stenosis, n (%)** | |
| Web-like | 3 (43) |
| Complex | 4 (57) |
| **Localization, n (%)** | |
| Subglottic | - |
| One-third upper part of trachea | 6 (86) |
| Middle part of trachea | 1 (14) |
| One-third lower part of trachea | - |
| **Length (cm), mean ± SD** | 1.81 ± 0.82 |
| **Degree of stenosis, n (%)** | |
| Grade 1 | 2 (28) |
| Grade 2 | 1 (14) |
| Grade 3 | 4 (58%) |
| Grade 4 | - |
| **Number of procedures, mean ± SD** | |
| Flexible bronchoscopy | 1.71 ± 0.95 |
| Rigid bronchoscopy | 1.86 ± 1.46 |
| **Treatment, n (%)** | |
| Dilatation | 7 (100) |
| Stent | - |
| Dilatation + surgery | 4 (57) |

Abbreviation: SD, standard deviation.

most of these patients are symptomatic even at rest.[9,10] The actual incidence of postintubation tracheal stenosis and PETS in asymptomatic patients is unknown. In this study, 208 of 586 patients who were intubated during the COVID-19 pandemic were successfully discharged, and 7 of these 208 patients (3.3%) were diagnosed with tracheal stenosis. Although 2 patients had mild tracheal narrowing ($\leq$ 50% reduction in CSA), they were symptomatic. This may have been related to the severity of COVID-19 and delayed functional recovery.

Because pulmonary function tests cannot be performed for a long time under pandemic conditions, the duration and degree of functional recovery of the patients are unknown. The duration of the patients from extubation to diagnosis was quite long (114.57 ± 85 days). This long diagnosis period was thought to be caused by many factors, such as the late development of stenosis, the unwillingness of patients to come to the hospital after long-term intensive care follow-up, the disruptions experienced in the outpatient clinic examinations and health system due to COVID-19, and the inability of patients to distinguish stenosis-related symptoms from COVID-19 related symptoms.

Endoscopic procedures are accepted as the first treatment option in the treatment of web-like stenosis smaller than 1 cm and not accompanied by tracheal malacia.[11] Approximately 60% success is achieved in these patients after 1 ± 3 interventions with endoscopic procedures and the mucosa-sparing technique.[12] In complex-type stenoses, endoscopic procedures are contraindicated because the risk of recurrence is high and the stenosis length can increase, which can reduce the chance of surgery. Nevertheless, these endoscopic procedures can be applied before surgery.[13,14] In complex-type stenosis, tracheal resections can be performed up to 4-to-6 cm, but in longer stenoses, surgery is not recommended due to the high frequency of anastomotic complications.[15] In this study, the mean stenosis length was 1.81 ± 0.82 cm, and the majority of stenoses (n = 6, 86%) were observed in the one-third proximal part of the trachea. Dilatation was performed once in 3 patients with web-like stenosis. Restenosis was not observed in the control flexible bronchoscopy at the first month follow-up after dilatation. In patients with complex stenosis, dilatation was performed to save time for surgery. No surgical complications or postoperative restenosis were observed in 4 patients who underwent tracheal resection.

The most important limitation of this study was the retrospective analysis of the cases. Therefore, only patients with symptoms suggestive of tracheal stenosis in the postintensive care follow-up were recruited for the study. However, symptoms related to tracheal stenosis or tracheal stenosis diagnosed radiologically or clinically in a different health institution

Table 3
Personal Characteristics of Patients With Tracheal Stenosis

| Patient | Age/Sex | BMI | IMV Duration | Time From Extubation to Diagnosis | Tracheostomy Duration | Type | Localization | Length | Degree | Procedure FB/RB | Treatment (Dilatation or Surgery) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 53/M | 27.6 kg/m² | 38 d | 265 d | 25 d | C | One-third upper | 2 cm | 80% | 1/2 | D+S |
| 2 | 60/M | 26.7 kg/m² | 30 d | 23 d | - | W | One-third upper | 1 cm | 40% | 3/1 | D |
| 3 | 69/F | 24 kg/m² | 15 d | 126 d | - | W | One-third upper | 1 cm | 70% | 3/1 | D |
| 4 | 44/F | 32 kg/m² | 40 d | 93 d | 17 d | C | One-third upper | 2.2 cm | 80% | 1/5 | D+S |
| 5 | 45/M | 26.2 kg/m² | 21 d | 134 d | 32 d | C | One-third upper | 2.5 cm | 85% | 1/1 | D+S |
| 6 | 67/M | 28.3 kg/m² | 42 d | 13 d | 27 d | C | Middle | 3 cm | 85% | 1/2 | D+S |
| 7 | 64/M | 27.1 kg/m² | 148 d | 134 d | - | W | One-third upper | 1 cm | 50% | 1/1 | D |

Abbreviations: BMI, body mass index; C, complex; D, dilatation; F, female; FB, flexible bronchoscopy; IMV, invasive mechanical ventilation; M, male; RB, rigid bronchoscopy; S, surgery; W, web-like.

were not observed in the national medical database called "E pulse" of 201 patients who did not develop tracheal stenosis.

## Conclusion

In this single-center retrospective study, tracheal stenosis developed in 7 of 208 patients (3.3%) who were successfully discharged from the hospital after being extubated. The most important characteristic of patients who developed tracheal stenosis was prolonged IMV support. Three of the patients were successfully treated with bronchoscopic dilatation and 4 underwent tracheal resection.

## Conflict of Interest

None.

## Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1053/j.jvca.2022.02.009.

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