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Lung: Short Report

Tracheal Stenosis and Airway Complications in the Coronavirus Disease 2019 Era

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ABSTRACT

BACKGROUND Severe coronavirus disease 2019 (COVID-19) infection is associated with prolonged intubation and its complications. Tracheal stenosis is 1 such complication that may require specialized surgical management. We aimed to describe the surgical management of post–COVID-19 tracheal stenosis.

METHODS This case series describes consecutive patients with tracheal stenosis from intubation for severe COVID-19 infection at our single, tertiary academic medical center between January 1, 2021, and December 31, 2021. Patients were included if they underwent surgical management with tracheal resection and reconstruction (TRR) or bronchoscopic intervention. Operative through 6-month symptom-free survival and histopathologic analysis of resected trachea were reviewed.

RESULTS Eight patients are included in this case series. All patients are female, and most (87.5%) are obese. Five patients (62.5%) underwent TRR; 3 patients (38.5%) underwent non–resection-based management. Among patients who underwent TRR, 6-month symptom-free survival is 80%; 1 patient (20%) required tracheostomy after TRR for recurrent symptoms. Of the 3 patients who underwent non–resection-based management, 2 (66.7%) experienced durable relief from symptoms of tracheal stenosis with tracheal balloon dilation; the remaining patient required laser excision of tracheal tissue before experiencing symptomatic relief.

CONCLUSIONS The incidence of tracheal stenosis may increase as patients recover from severe COVID-19 infection requiring intubation. Management of tracheal stenosis with TRR is safe and effective, with comparable rates of success to TRR for non–COVID-19 tracheal stenosis. Non–resection-based management is an option to manage tracheal stenosis in patients with less severe stenosis or in poor surgical candidates.

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Critically ill patients suffering from coronavirus disease 2019 (COVID-19) infection face high rates of intubation in the setting of acute respiratory distress syndrome.[1-3] Given the profound lung injury and the high burden of multisystem organ failure with severe COVID-19 infection and concerns about exposure to health care workers associated with airway procedures, many of these patients require prolonged intubation.[3]

Prolonged intubation can lead to severe airway complications, including post-intubation tracheal stenosis (PITS).[4] This risk may be elevated in severe COVID-19 infection, given that medical comorbidities such as obesity and diabetes mellitus are mutual risk factors for

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both critical illness in COVID-19 and PITS.[5] Furthermore, the inflammation and profibrotic effects of COVID-19 may be additional predisposing factors for development of PITS in intubated COVID-19 patients.

Tracheal resection and reconstruction (TRR) is a widely accepted surgical approach to treating PITS, with excellent long-term freedom from restenosis.[6] As the COVID-19 pandemic continues, it is reasonable to expect an increase in the presentation of PITS in the setting of intubation for severe COVID-19 and a subsequent increase in the performance of TRR. Herein we share our early experience with TRR for PITS in patients who recovered from severe COVID-19 infection.

IN SHORT

- The incidence of tracheal stenosis may increase as patients recover from severe COVID-19 infection requiring intubation.
- Management of tracheal stenosis with tracheal resection and reconstruction is safe and effective, with comparable rates of success to tracheal resection and reconstruction for non–COVID-19–related tracheal stenosis.
- Non–resection-based management is an option for tracheal stenosis in patients with less severe stenosis or in those who are not surgical candidates.

PATIENTS AND METHODS

PATIENTS. This is a single-center case series of consecutive patients with a diagnosis of COVID-19-related PITS cared for at Stanford University Medical Center between January 1, 2021, and December 31, 2021. Demographic characteristics, medical comorbidities, and history of tracheal stenosis diagnosis and management were reviewed. In patients who underwent TRR, postoperative course and short-term outcomes were reviewed. This study was approved by the Stanford University School of Medicine institutional review board.

SURGICAL PROCEDURE. TRR was performed in a standardized fashion in all patients who underwent resection. For each patient, flexible bronchoscopy was performed in the operating room before the start of the procedure; balloon dilation was performed if necessary, and a 5.0- to 6.0-mm endotracheal tube was inserted. The patient was positioned supine with the neck gently extended. A low transverse cervical incision was made, the strap muscles were separated, and the anterior trachea was exposed. The level and extent of tracheal stenosis were identified with bronchoscopic guidance and dissected circumferentially. The stenotic segment was resected, keeping the vascular supply to the remaining healthy trachea intact. Reconstruction was performed according to the surgeon's preference, either interrupted 4-0 Vicryl or PDS sutures to anastomose the 2 ends of the trachea. Cross-table ventilation was used during suturing of the anastomosis (Figure 1). Postoperatively, patients were maintained in a neutral or slightly flexed neck position with the assistance of a stitch from the chin to the chest at the manubrium. Patients were admitted to the intensive care unit for 24 hours for airway monitoring. Flexible bronchoscopy was performed once more between postoperative days 5 and 7. Outcomes are reported out to 6 months after the procedure.

PATHOLOGIC EXAMINATION. Resected tracheal tissue was obtained from each patient and histopathologically characterized by hematoxylin-eosin staining, Masson trichrome staining, pentachrome staining, and elastic tissue fibers Verhoeff-Van Gieson staining (Figure 2).

STATISTICAL ANALYSIS. Descriptive statistics are used to summarize patient characteristics and outcomes. Continuous variables are expressed as mean ± SD or median (interquartile range). All analyses were completed with Stata version 16.1 software (StataCorp LLC).

RESULTS

Eight patients with PITS after intubation for COVID-19 are included in this series (Table). All patients were female, and 4 (50%) patients were Hispanic/Latino. The average age at time of presentation to our center was 46.1 ± 16.4 years. Seven (87.5%) patients were obese, with a mean body mass index of 40.3 ± 8.7 kg/m^2, and 6 (75%) patients had type 2 diabetes. All

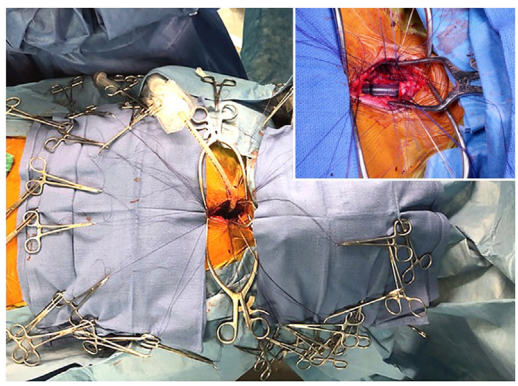

FIGURE 1 Cross-table ventilation before completion of the anastomosis. A sterile cuffed endotracheal tube is used to provide ventilation intermittently while sutures are placed in the cut ends of the trachea. After all of the anastomotic sutures have been placed, the endotracheal tube is advanced to the distal trachea (inset)

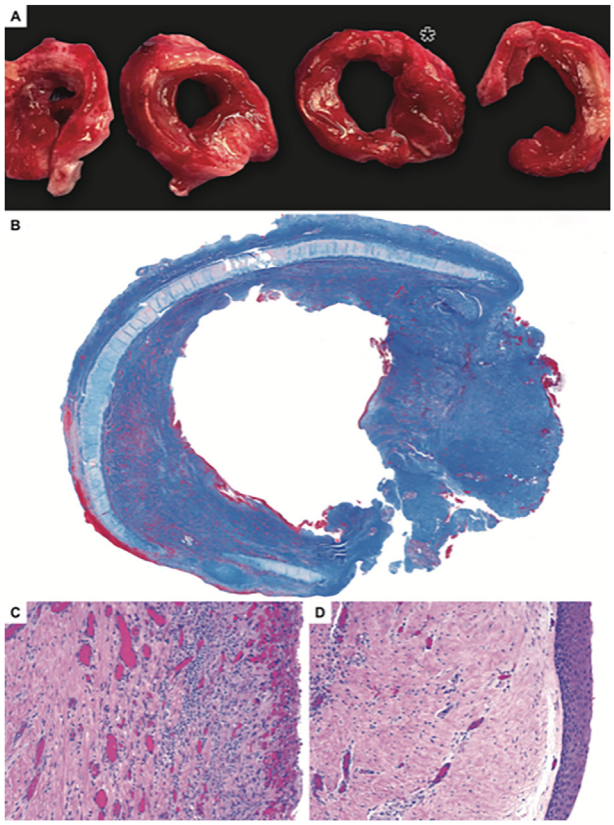

FIGURE 2 Histopathologic evaluation of resected tracheal tissue. (A) Axial sections of tracheal segment showing luminal stenosis and peritracheal expansion of connective tissue. (B) Low-power image of the tracheal segment marked by * in (A) demonstrating both luminal and peritracheal expansion by collagenous connective tissue (blue staining elements) on the Masson trichrome stain (magnification ×10). (C) In some areas, the mucosal layer was ulcerated and replaced by granulation tissue (hematoxylin and eosin, magnification ×200). (D) In other regions, the mucosal lining consisted of squamous metaplastic cells (hematoxylin and eosin, magnification ×200).

patients presented with stridor and shortness of breath and were formally diagnosed with PITS through rigid or flexible bronchoscopy. All patients had endotracheal tube-related strictures without any tracheostomy stoma-related stenosis apparent.

Five (62.5%) patients underwent TRR during the study period. Among them, the median length of time spent intubated with an endotracheal tube was 14.75 (13-15) days, and 3 (60%) patients underwent tracheostomy. The median time from diagnosis to tracheal operation was 12 (8-27) days. Four (80%) patients underwent tracheal balloon dilation before undergoing TRR. All patients had symptomatic improvement in shortness of breath in the immediate postoperative period and improved or resolved stridor on phonation. Some degree of stridor redeveloped during follow-up in 4 of 5 patients (80%), requiring repeated bronchoscopy for removal of granulation tissue at the anastomosis. Of these patients, 3 (75%) experienced durable symptomatic relief at 6 months after TRR, whereas 1 required repeated tracheostomy. All patients survived to 6 months.

Three (37.5%) patients in the series have been managed nonoperatively. All 3 underwent tracheostomy during their initial admission for COVID-19. For their tracheal stenosis, all 3 underwent tracheal balloon dilation, of whom 2 (66.7%) experienced significant symptomatic relief. The remaining patient who did not experience symptomatic relief underwent CO_2 laser excision of granulation tissue at the stenosis site and corticosteroid injections, which resulted in symptomatic relief. Of these 3 patients, 1 patient is not a surgical candidate because of medical comorbidities, and 2 are still potential future candidates for TRR.

Histopathologic evaluation was performed in 5 cases. The tracheal segments all showed varying degrees of luminal stenosis by dense collagenous scar tissue (Figures 2A, 2B). The mucosal layer showed various types of coverage ranging from ciliated respiratory epithelium to squamous metaplasia to mucosal erosions with granulation tissue (Figures 2C, 2D). The submucosal layer contained abundant scar tissue with scattered collections of chronic inflammatory cells and dilated capillary blood vessels. The composition and distribution of cellular and connective tissue elements were similar to the changes observed in idiopathic tracheal stenosis (not shown).

COMMENT

PITS is a well-characterized pathologic process that frequently occurs in the setting of prolonged intubation. The COVID-19 pandemic may exacerbate its presentation, given the prevalence of intubation for severe COVID-19, reported to range from 12.5% to 30% in unvaccinated patients admitted to the hospital because of COVID-19 infection, with a median intubation time nearing 17 days.[1,3]

Our cohort represents the largest series to date of TRR performed for PITS in the setting of COVID-19 infection requiring intubation. All but 1 patient was obese, which is similar to prior reports of TRR for COVID-19-related PITS and a known risk factor for PITS and COVID-19.[4,5,7] Notably, all of our patients with COVID-19-related PITS were female. Given the limitations of a small series, it is impossible to draw conclusions about sex-related risk of PITS in COVID-19, although it is possible that female sex is a risk factor for development of PITS in COVID-19, as it is in idiopathic tracheal stenosis.[6]

TABLE Demographic Characteristics of the Patients

Patient	Age, y	Sex	BMI, kg/m^2	Race	Comorbidities	TRR	Medical Treatments Received for COVID-19	Length of Laryngotracheal Intubation, d	Tracheostomy	Interventions Before Resection	Time to Intervention, d	Length of Stay, d	Follow-up Intervention
A	59	F	35.7	White	OSA, obesity, T2DM, CAD, HTN, former smoker	Y	Racemic epinephrine and dexamethasone	19	Y	Tracheal balloon dilation	29	10	Bronchoscopic removal of granulation tissue before discharge
B	38	F	30.8	Asian; non-Hispanic/ non-Latino	Group 1 pulmonary hypertension, obesity, systemic sclerosis	Y	Remdesivir, dexamethasone, Symbicort	10	N	Tracheal balloon dilation	12	8	Bronchoscopic removal of granulation tissue before discharge
C	49	F	42.4	Hispanic/ Latino	OSA, obesity, T2DM, CAD, HTN, former smoker	Y	Dexamethasone	21	N	Tracheal balloon dilation	8	10	Bronchoscopy with débridement of granulation tissue (after discharge)
D	55	F	42.1	Hispanic/ Latino	HTN, obesity T2DM	Y	Albuterol	15	Y	Bronchoscopy with tracheal balloon dilation	1	13	Bronchoscopy with débridement of granulation tissue (after discharge)
E	26	F	42	Hispanic/ Latino	Asthma, OSA, anxiety, obesity	Y	Albuterol, remdesivir	13	Y	NA	27	5	None
F	35	F	41.6	White	Obesity	N		24	Y	Balloon dilation of trachea, tracheal stenting, corticosteroid injection, CO_2 laser excision			
G	75	F	29.8	Hispanic/ Latino	No significant PMH	N	Remdesivir	Unclear	Y	Bronchoscopy with tracheal balloon dilation, granulation tissue removal			
H	32	F	57.6	Black/African American	Obesity, OSA, T2DM, HTN	N	Albuterol, dexamethasone	Unclear	Y	Bronchoscopic dilation			

BMI, body mass index; CAD, coronary artery disease; F, female; HTN, hypertension; N, no; NA, not applicable; OSA, obstructive sleep apnea; PMH, past medical history; T2DM, type 2 diabetes mellitus; TRR, tracheal resection and reconstruction; Y, yes.

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Notably, the median intubation time in our cohort was less than the median intubation time overall for COVID-19 patients and can be considered borderline for prolonged intubation before initiation of tracheostomy or extubation. This may suggest that there is an accelerating feature toward PITS present in COVID-19 infection, which may be explained by the profibrotic changes associated with severe COVID-19 infection. Irritation from the endotracheal tube may initiate an inflammatory process in the trachea that cascades into fibrosis and devascularization, accelerated by global inflammatory changes caused by COVID-19.

Stenosis-free, long-term survival after TRR has been described at expert centers to be >90%.[6] In our cohort of patients with COVID-19-related TRR, short-term freedom from durable restenosis and survival are comparable. Given the small sample size and the limited follow-up available at this time, this study is limited in drawing conclusions about durability of TRR in COVID-19-related PITS.

The length of the proinflammatory state associated with COVID-19 infection is still under investigation. Although none of the patients had active COVID-19 infection at the time of tracheal intervention, it is reasonable to consider temporizing measures such as tracheostomy with T-tube until patients are well out of the critical illness window. Timing on when to intervene in our patient cohort was based on patient-centered discussions, including most patients' desire to avoid a long-term tracheostomy tube, as well as an institutional preference for definitive management when feasible. Bronchoscopic management over surgical management was determined with shared decision-making factoring in immediate surgical candidacy, overall health status, patient preference, and degree of symptoms/stenosis.[8]

Finally, in the span of 1 year, our center performed 5 TRRs for COVID-19-related complications compared with 1 for non-COVID-19-related complications. Most patients were diagnosed with tracheal stenosis within months of the COVID-19 surge in December 2020 in California. This may reflect a widespread increase in the presentation of PITS, accelerated by the pandemic, although multi-institutional corroboration is required before conclusions can be drawn about the increased incidence of PITS during the COVID-19 pandemic. Strategies to mitigate the risk of PITS in patients suffering from COVID-19 may include early tracheostomy, within 1 week of intubation. Multidisciplinary evaluation of intubated patients with discussions involving respiratory therapists and the critical care team can identify patients at risk of prolonged intubation, especially those who have proinflammatory conditions like COVID-19.

In conclusion, PITS may become more common, given the prevalence of severe COVID-19 infection requiring intubation. The factors that may predispose patients to severe COVID-19 requiring intubation may also be associated with development of tracheal stenosis, such as obesity and diabetes. TRR is a well-tolerated surgical treatment of tracheal stenosis. Our series suggests that COVID-19-related PITS may be appropriately treated with TRR, with early outcomes showing favorable results, although further monitoring and larger multi-institutional cohorts are needed to confirm these findings.

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DISCLOSURES

The authors have no conflicts of interest to disclose.

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