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Case Report

Tracheobronchial Stent Insertion Under Venovenous Extracorporeal Membrane Oxygenation in a Patient With Coronavirus Disease 2019

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CORONAVIRUS DISEASE 2019 (COVID-19) is a respiratory disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus is highly infectious and mainly is transmitted from person-to-person via close contact and respiratory droplets.[1] Airborne transmission is an important route of infection, especially in cases in which many droplets are generated.[2] Thus, the virus can be spread in hospital settings if the infection control measures applied are inadequate. It is crucial to prevent infection of medical staff who are taking care of patients with COVID-19.

Tracheobronchial stent placement is a relatively safe and effective treatment for tracheobronchial stenosis. The silicone stent insertion typically is performed via rigid bronchoscopy under general anesthesia with positive-pressure ventilation.[3] However, this procedure requires high-frequency ventilation, and a large number of respiratory droplets are expelled due to air leakage from the side port used in rigid bronchoscopy during ventilation. Therefore, the risk of droplet transmission is extremely high during tracheobronchial stenting of patients with COVID-19.

Extracorporeal membrane oxygenation (ECMO) is a useful technique for maintaining oxygenation and adequate ventilation while simultaneously removing carbon dioxide. However, it conventionally is considered a relative contraindication in patients with advanced malignancy due to a poor outcome despite ECMO.[4] ECMO only is used for high-risk patients

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with asphyxia who are difficult to manage under conventional ventilation during the tracheal stent placement.[5]

In this report, the authors describe the case of a patient with COVID-19 with an obstructive tracheal tumor that degenerated rapidly into respiratory failure. Silicone Y-tracheal stenting was performed under venovenous ECMO (VV-ECMO) with general anesthesia. This method ensured oxygenation while also stopping ventilation and shortening the surgery time to reduce the risk of SARS-CoV-2 infection of the operating staff.

Case Report

Written informed consent for publication was obtained from the patient. A 59-year-old man (height 165 cm, weight 55 kg) with two years of dry cough was screened for COVID-19 due to close contact with a patient with COVID-19. The antigen test showed a positive result for SARS-CoV-2, and this prompted his hospitalization. At that time, computed tomography (CT) revealed a 40-mm tumor adjacent to the trachea, causing severe stenosis and right bronchial obstruction accompanied by right upper atelectasis. Radiologic findings characteristic of COVID-19 were not found in the lung fields. On the same day, the patient's fever increased, and intravenous remdesivir and oral dexamethasone were administered due to the onset of suspected COVID-19 symptoms. However, oxygenation continued to worsen gradually, and mechanical ventilation through an orotracheal tube was initiated six days after the onset of symptoms. After starting ventilation, SpO_2 was 95% under fraction of inspired oxygen (F_IO_2) at 80%, and positive end-expiratory pressure (PEEP) was 5 cmH_2O. High-flow nasal oxygenation or noninvasive ventilation was not performed before mechanical ventilation. On the seventh day after his initial hospitalization, the patient was transferred to the authors' hospital.

At the time of admission to the intensive care unit (ICU), assist-control mechanical ventilation settings with deep sedation and muscle relaxants, such as propofol, dexmedetomidine, fentanyl, and rocuronium were as follows: F_IO_2, 50%; PEEP, 8 cmH_2O; tidal volume, 310 mL (inspiratory pressure, 12 cmH_2O); and respiratory rate, 15 breaths per minute. The depth of an 8.0-mm inner-diameter standard tracheal tube was 24 cm from the interincisor gap, and the tube tip was placed just before the tumor. Noradrenaline was infused to maintain hemodynamics. Under these conditions, blood gas analysis showed that the pH was 7.24, PaO_2 was 92 mmHg, and $PaCO_2$ was 68 mmHg. The neoplastic lesion near the trachea was reevaluated by CT. The lesion was 47 × 43 × 15 mm in size and arose from the right posterior wall of the lower third of the trachea, causing thickening of the tracheal wall and stenosis of the bilateral main bronchus (Fig 1, A). The narrowest part of the trachea was 5 mm (Fig 1, B), and the right upper bronchi were completely obstructed. Although localized ground-glass opacities were observed in the lingual area and the lower lobe of the left lung on CT (Fig 1, C), they were not considered to be caused by SARS-CoV-2 infection. After discussion with a thoracic surgeon, infectious disease doctor, pulmonologist, cardiovascular surgeon, intensivist, and anesthesiologist, the authors concluded that the deterioration of the patient's respiratory condition was due to tracheal stenosis. The authors were concerned that the tumor had grown more rapidly and obstructed the trachea and bronchi, leading to asphyxia and making tracheal stenting difficult. Thus, the authors decided to perform tracheobronchial stent insertion immediately under general anesthesia with VV-ECMO. A positive result for SARS-CoV-2 via polymerase chain reaction was confirmed just before the procedure.

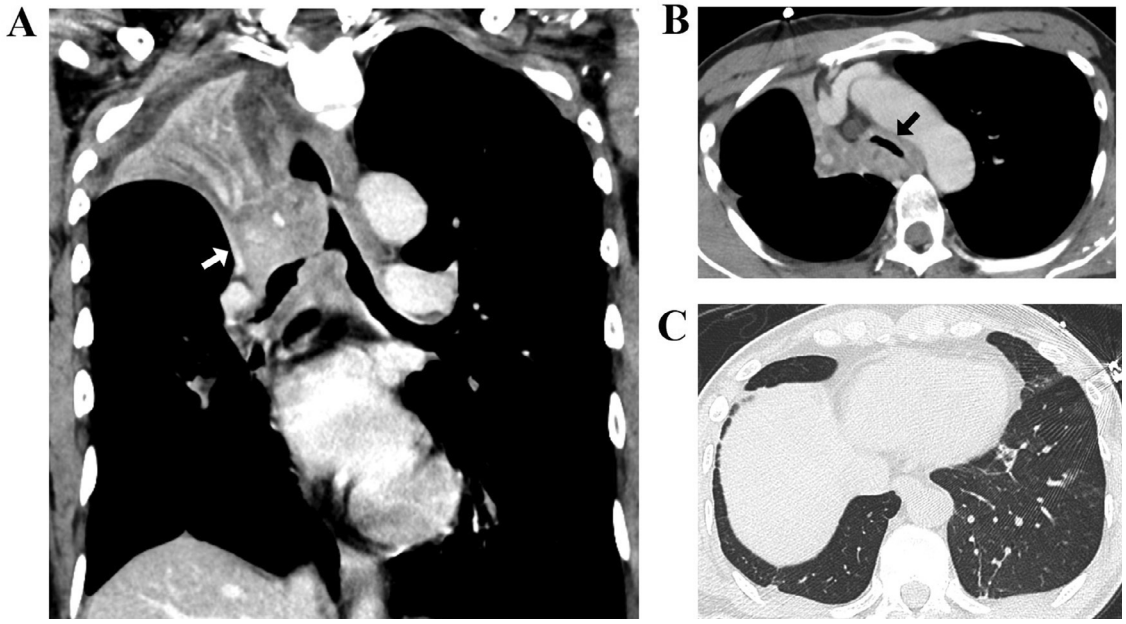

Fig 1. (A) Coronal section image shows tracheobronchial stenosis via the neoplasm with right upper lobe atelectasis (*white arrow*). (B) The diameter of the narrowest part of the trachea was 5 mm (*black arrow*). (C) Transverse section image of the lung field shows localized ground-glass opacities.

All staff in the operating room wore appropriate personal protective equipment (PPE) (N95 respirator mask, goggles, face mask, hair and foot coverings, hood, gown, and double gloves) throughout the procedure. General anesthesia was maintained using 1.0 mg/kg/h of remimazolam, ultra-short-acting benzodiazepine, and 0.5 μg/kg/min of remifentanil. Rocuronium, 7.0 μg/kg/min, was infused continuously to maintain a deep neuromuscular blockade. VV-ECMO was established before stenting. A 22-Fr drainage cannula was introduced into the femoral vein and advanced at the junction between the inferior vena cava and the right atrium. A 16-Fr reinjection cannula was introduced into the right internal jugular vein and advanced through the superior vena cava into the right atrium. A heparin-coated ECMO circuit was used without intravenous anticoagulants to reduce the risk of bleeding from the endotracheal tumor during the procedure. The activated partial thromboplastin time before the procedure was 30.2 seconds. After starting VV-ECMO, blood flow immediately reached 3.0-3.5 L/min (1.9-2.2 L/min/m^2), and the F_IO_2 and outflow PaO_2 of VV-ECMO were 80% and 445 mmHg, respectively. Blood temperature was set at 35.5°C to reduce oxygen consumption. Dopamine and noradrenaline were infused to maintain adequate cardiac output and blood pressure, and patient hemodynamics were stable during VV-ECMO (blood pressure 115-135/65-70 mmHg and heart rate 85 beats per minute). The patient's hemoglobin was 13.8-to-15.3 g/dL; therefore, transfusion was not required. Mechanical ventilation was stopped, and the surgeons began the procedure after waiting for the end of exhalation (approximately 90 seconds), determined by end-tidal carbon dioxide. The tumor completely obstructed the right bronchi, and there was a lot of bleeding from the tumor. After careful suctioning of the blood, bougie and balloon dilations were used to relieve the bronchial obstruction under fiberoptic bronchoscopy guidance. Subsequently, a Dumon silicone Y-stent (Novatech, La Ciotat, France) was placed using rigid bronchoscopy. No lung ventilation was required throughout the procedure, and an antivirus filter was not connected to the rigid bronchoscope because of the likelihood of apnea during the procedure. The SpO_2 was maintained between 88% and 94%.

After stenting, tracheal intubation was performed using an 8.0-mm inner-diameter standard tube, and mechanical ventilation was restarted. Tidal volume was increased to approximately 500-to-550 mL (inspiratory pressure, 12 cmH_2O), and the patient was weaned successfully from VV-ECMO. The time from asphyxia to completion of all procedures was 68 minutes.

At ICU admission after surgery, mechanical ventilation settings were as follows: F_IO_2, 0.3; PEEP, 8 cmH_2O; tidal volume, 550 mL (inspiratory pressure, 10 cmH_2O); and respiratory rate, 12 breaths per minute. Blood gas analysis showed that the pH was 7.40, PaO_2 was 74 mmHg, and $PaCO_2$ was 44 mmHg. A little bleeding from the tumor continued even after ICU admission, but it gradually decreased. On postoperative day two, tracheal extubation was performed, and the patient was moved out of the ICU. The number of viral RNA copies in the polymerase chain reaction test in intratracheal sputum samples was 387,710 copies/5 μL on the same day, and none of the healthcare providers involved in the stent insertion was infected with COVID-19. The tumor was diagnosed via bronchial biopsy as an adenoid cystic carcinoma, and radiation therapy was started on postoperative day ten. The therapy was stopped on postoperative day 48, and the patient was discharged home on postoperative day 52. The size of the tracheal tumor gradually decreased after radiation, and right upper lobe aeration was restored.

Discussion

One indication for airway stenting is airway stenosis caused by endotracheal and extrinsic tumors.[6] Tracheobronchial stent insertion should be performed immediately if the patient's respiratory condition is exacerbated by tumor growth. Tracheobronchial stenting that requires open access to the airway is accompanied inherently by aerosol-generating procedures such as bag-mask ventilation, tracheal intubation/extubation, airway suctioning, high-frequency ventilation via the side port used in rigid bronchoscopy, and laser excision/ablation. High-frequency ventilation via the side port used in rigid bronchoscopy causes a substantial amount of droplet and aerosol shedding due to air leakage around the rigid bronchoscope. Therefore, airway stenting for patients with COVID-19 bears an extremely high risk of infection for airway surgeons, anesthesiologists, and all other healthcare providers in the operating room.

Theoretically, it may be best to postpone any kind of airway surgery in patients with COVID-19 until after the recovery from COVID-19 to avoid nosocomial infections among hospital staff. Indeed, according to several bronchology societies, bronchoscopy is contraindicated relatively in a patient with COVID-19.[7] In the present patient, asymptomatic tracheobronchial stenosis on the verge of complete occlusion was identified fortuitously during the COVID-19 screening survey. It was uncertain how rapidly the tumor would grow to occlude the airway completely and when the infectivity of SARS-CoV-2 would become negative. After a thorough multidisciplinary discussion, a decision was made to immediately perform tracheobronchial stenting. Based on chest CT findings, exacerbation of the respiratory condition mainly was due to the tracheobronchial stenosis that caused atelectasis, but not due to SARS-CoV-2 infection. The survival rate after inserting tracheobronchial stents in patients with malignant airway disease has been reported to be only three-to-four months; the one-year survival rate is 15%.[6,8] However, early discharge from the ICU and continued tumor therapy are independent predictors of survival time.[8] This may indicate that tumor therapy (radiation and/or chemotherapy) after immediate stent insertion prolongs patient survival. If the authors had waited for the patient to recover completely from COVID-19, it might have become impossible to place a stent due to further enlargement of the tumor. Additionally, rapid discharge from the ICU and weaning from mechanical ventilation after stent insertion help preserve medical resources, which has been imperative during the COVID-19 pandemic.

Generally, silicone stents have some advantages over metallic stents for the management of malignant tracheal tumors. The patient with a silicone stent can avoid recurrent obstruction by tumor ingrowth and allow radiation or chemotherapy to exert its effect.[9] Silicone stents can be removed if the size of the tumor reduces after the therapies.[10] Additionally, silicone stents can cover fistulae caused by radiation therapy or malignancy itself.[9] For these reasons, the authors chose silicone stent insertion in this patient. However, rigid bronchoscopy under general anesthesia is required to insert a silicone stent,[9,10] and the risk of droplet and aerosol transmission is high during the procedure.

ECMO generally is performed for severe acute respiratory distress syndrome in a patient with COVID-19 with poor oxygenation and hypercapnia.[11] Considering the respiratory condition, VV-ECMO was not an absolute necessity for stent insertion in this patient. However, the use of VV-ECMO for stent insertion in a patient with COVID-19 has several benefits. First, although respiratory insufficiency in this patient was caused mainly by airway stenosis rather than acute respiratory distress syndrome caused by COVID-19, SARS-CoV-2 infection also may have been involved in the pathology, considering that oxygenation worsened rapidly in a short time. VV-ECMO ensured adequate oxygenation and carbon dioxide removal, increasing the safety of the stent-insertion procedure. Second, the droplets and aerosols were expelled during ventilation, and it showed that aerosol-generating procedures, including short-time manual ventilation before intubation, increase the risk of infection to healthcare workers.[12] Therefore, as a general rule, no ventilation will reduce the spread of droplets, thereby decreasing the risk of transmission. VV-ECMO eliminated the need for lung ventilation during the procedure, thereby reducing the risk of SARS-CoV-2 infection of the medical staff in the operating room via patient droplets or aerosols. Third, any procedures requiring full PPE are extremely difficult for medical staff compared to those without PPE. Full PPE makes the medical staff working temperature high, which obstructs their vision and renders their work difficult. Under VV-ECMO, the surgery time was shorter because the surgeons did not need to stop the procedure due to desaturation. The static surgical field facilitated the proper placement of the stent, especially in a hemorrhagic tumor. The bleeding tendency of the tumor can be a risk factor for emergent requirement of ECMO during airway stenting; moreover, emergent conversion to ECMO is not easy and is stressful for the medical staff even under normal situations, and especially more under full PPE. Therefore, tracheal stenting under planned VV-ECMO without lung ventilation ensured the patient oxygenation, minimized the risk of SARS-CoV-2 infection of the medical staff, facilitated the procedure, shortened the surgery time, and avoided the emergent introduction of ECMO. Additionally, these measures also helped to alleviate the physical and mental stress of the medical staff.

Nevertheless, the cost-benefit and associated complications of VV-ECMO should be considered, because it is very expensive to perform ECMO. However, the costs vary depending on the region. Additionally, the risk of infection might not be high if appropriate infection control measures, including PPE use, are implemented. Furthermore, VV-ECMO also has a high rate of complications (40.2%), and 73% of the complications include bleeding.[13] Therefore, the performance of VV-ECMO is not necessary for all tracheal stent insertions, including in a patient with COVID-19. High risk of conversion (eg, severe hypoxia, hemorrhagic tumor, or bleeding tendency) or expected long procedure time due to the difficulty of stent insertion may be a good indication for planned VV-ECMO in a patient with COVID-19. However, these are not general indications, and the authors decided it was better to insert a tracheal stent under planned VV-ECMO in this patient, by comprehensive judgment.

As a limitation, in this patient the procedure was started after waiting for the end of exhalation determined by end-tidal carbon dioxide, but there was no scientific evidence whether this waiting period was enough to suppress the transmission. Normal speech generates thousands of oral droplets, which can be transmitted for more than ten minutes.[14] Additionally, it is recommended that the interventional room be cleaned 20 minutes after all aerosol-generating procedures to stabilize or disperse airborne droplets.[15] Thereby, it may be necessary to wait for a longer period than the end of exhalation determined by end-tidal carbon dioxide to suppress transmission, as was done in this patient. However, the respiratory circuit with an antivirus filter was closed completely until the end of exhalation, and there was no ventilation during the procedure. Therefore, the risk of generating droplets or aerosols under the procedure condition was lesser than that under a ventilated condition.

Lung ventilation can be necessary even when VV-ECMO is applied. To achieve complete respiratory support by VV-ECMO without lung ventilation, sufficient pump flow (>60 mL/kg/min) and low recirculation rate (ratio of ECMO blood flow-to-cardiac output >60%) are important.[16] As a judgment criterion for sufficient oxygenation, SaO_2 ≥80% is recommended during VV-ECMO management for acute respiratory failure.[4] If SaO_2 cannot be maintained under adequate pump flow, sedation, use of muscle relaxants and/or beta-blockers, and decreasing body temperature are recommended to suppress cardiac output and metabolic oxygen requirement.[16] Suppression of cardiac output occasionally can improve the ratio of ECMO blood flow-to-cardiac output. Fortunately, SaO_2 was maintained at approximately 90% in this patient during the use of VV-ECMO. Therefore, the authors infused dopamine and noradrenaline to maintain adequate hemodynamics. In the present patient, a deep muscular blockade by continuous rocuronium infusion helped avoid inadvertent spontaneous breathing or diaphragm contraction during the procedure. A heparin-coated ECMO circuit without anticoagulant use was useful in reducing the bleeding. Anticoagulants may exacerbate bleeding, which makes the procedure more difficult. Differential hypoxia is one of the problems during ECMO, and it can occur under venoarterial ECMO. In this patient, VV-ECMO was performed by a drainage cannula into the femoral vein and a reinjection cannula into the right

internal jugular vein. Thus, it was not necessary to consider the possibility of differential hypoxia during the procedure.

In conclusion, the authors described a successful case of intraoperative management of tracheobronchial stenting under VV-ECMO to treat tracheobronchial stenosis caused by a neoplasm in a patient with COVID-19. The indications for tracheobronchial stenting were discussed carefully from a multidisciplinary perspective. The authors minimized the risk of SARS-CoV-2 droplet transmission during the procedure by obtaining a nonbreathing condition under VV-ECMO with general anesthesia.

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Declarations of interest

None.

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