Short term outcomes for patients and providers following elective tracheostomy in COVID-19 positive patients

Short Title: Tracheostomy in COVID-19 positive patients

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Abstract

Importance: Urgent guidance is needed on the safety for providers of percutaneous tracheostomy in patients diagnosed with COVID-19.

Objective: Demonstrate that percutaneous dilational tracheostomy (PDT) with a period of apnea in patients requiring prolonged mechanical ventilation due to COVID-19 is safe and can be performed for the usual indications in the ICU. We hypothesize that the usual indications for tracheostomy including prolonged mechanical ventilation, high sedative requirements, and copious secretions apply to patients with COVID-19 and thus this diagnosis should modify tracheostomy technique but not change clinical indications.

Design: Observational case series

Setting: Single center medical intensive care unit at a Level-1 Trauma center

Participants: Patients diagnosed with COVID-19 who were assessed for tracheostomy

Main outcomes and measures: Success of a modified technique included direct visualization of tracheal access by bronchoscopy and a blind dilation and tracheostomy insertion during a period of patient apnea to reduce aerosolization. Secondary outcomes include transmission rate of COVID-19 to providers and patient complications.

Results: From April 6th, 2020 to July 21st, 2020, 2,030 patients were admitted to the hospital with COVID-19, 615 required ICU care (30.3%), and 254 patients required mechanical ventilation (12.5%). The mortality rate for patients requiring mechanical ventilation was 29%. 18 patients were assessed for PDT and 11 (61%) underwent the procedure. The majority had failed extubation at least once (72.7%) and the median duration of intubation prior to tracheostomy was 15 days (IQR 13-24). The median PEEP at time of tracheostomy was 10.8. The median PaO2/FiO2 ratio on the day of tracheostomy was 142.8 (IQR 104.5-224.4). Two patients had bleeding complications. At 1 week follow-up 8 patients still required ventilator support (73%). At the most recent follow-up 8 patients (73%) have been liberated from the ventilator, 1 patient (9%) died as a result of respiratory/multi-organ failure, and 2 were discharged on the ventilator (18%). Average follow-up was 20 days. None of the surgeons performing PDT have symptoms of or have tested positive for COVID-19.

Conclusions and Relevance: Percutaneous dilational tracheostomy for COVID-19 patients is safe for healthcare workers and patients despite higher PEEP requirements, and should be performed for the same indications as other causes of respiratory failure.

Introduction

The COVID-19 pandemic has presented many challenges to the medical community as we constantly adapt treatment guidelines based on what is learned daily about this novel virus. For surgeons, indications for tracheostomy for patients on prolonged mechanical ventilation due to COVID-19 has generated some controversy. Mechanical ventilation is required for the most severe cases of acute respiratory syndrome coronavirus-2 (COVID-19).[1] Recent reports estimate 10%-15% of hospitalized patients required mechanical ventilation, and the median duration of mechanical ventilation was 7 days.[1,2] However, for patients who have failed ventilator weaning and require prolonged intubation, tracheostomy must be considered. Prolonged endotracheal intubation has numerous detrimental effects including the potential for tracheal trauma, accidental extubation without a secure airway, difficulty weaning the ventilator, inability to communicate, continued delirium, and patient discomfort leading to high sedative and analgesic requirements.[3] The goal of elective tracheostomy is to eliminate or reduce these risks to the patient while balancing the risk of an additional procedure.[4] Generally accepted indications for elective tracheostomy include long-term mechanical ventilation, ventilator weaning failure, copious secretions, and airway obstruction and are typically performed at 1-2 weeks. Major complications of tracheostomy are rare. Risk of mortality, tracheo-innominate fistula, and tracheo-esophageal fistula from this procedure are all less than 1%. Early bleeding complications at the stoma are more common with rates around 5%.[3]

Elective tracheostomies in patients with COVID-19 present unique potential challenges: severe hypoxia due to high FiO2 and PEEP requirements,[1,5,6] and risk of viral transmission to healthcare personnel. Early in the pandemic, several societies including the American Academy of Otolaryngology-Head and Neck Surgery published recommendations against performing elective tracheostomies in COVID-19.[7,8] Concerns include unclear duration of viral shedding, risk of viral transmission to healthcare workers, and potential futility in the patients' outcomes.

Other guidelines recommended waiting 2-3 weeks, requiring one or two negative COVID-19 nasopharyngeal swabs and to consider performing the procedure open rather than percutaneous to decrease aerosolization.[7,9] Guidelines thus far have not been based on clinical data, but rather on caution due to uncertain risk, and experience with similar epidemics, namely the Severe Acute Respiratory Syndrome (SARS) outbreak in the early 2000s.[7,10]

After the initial surge of patients with COVID-19 were admitted to the MICU in March 2020, it became evident that recovery from this disease requires prolonged mechanical ventilation for some. After a multidisciplinary meeting between our division of acute care and trauma surgery, the medical ICU director, and respiratory therapy, we concluded that the usual indications for elective tracheostomy for prolonged mechanical ventilation would have the same benefits in patients with COVID-19,[11] and developed a protocolized procedure for tracheostomy for COVID-19 positive patients.

Now several months into the pandemic, more of the medical community, including the Society of Critical Care Medicine, has published that tracheostomies for patients with COVID-19 are unavoidable in order to provide the standard of care.[9] Every institution should develop practice guidelines to perform this procedure safely for their patients. In this paper we report on our experience of patient selection, procedure technique, and short-term patient and provider outcomes.

Methods

Patient Population

This is a retrospective observational study evaluating all tracheostomy consults for mechanically ventilated patients who were COVID-19 positive at a tertiary care, academic, Level-1 trauma center in Indianapolis, Indiana from April 6th, 2020 to July 21st, 2020. COVID-19 infection was confirmed by nasal pharyngeal swab for reverse transcriptase polymerase chain

reaction (rtPCR) assay. Indiana University institutional review board approval (IRB # 2004142964) was obtained prior to data collection. Informed consent was waived by the IRB.

Patient Selection

This study included all mechanically ventilated patients who were both COVID-19 positive and received a consult for tracheostomy. Patients were cared for by the Medical Intensive Care Unit (MICU) and if the intensivist felt a tracheostomy was indicated he/she consulted the trauma surgeon on call. There were no predetermined criteria for tracheostomy. Each patient was evaluated individually by the trauma surgeon and appropriateness for tracheostomy was assessed by considering the patient prognosis and goals of care, potential benefit of the procedure, and stability to tolerate the procedure. A negative COVID test was not required. Patients with high ventilator settings (FiO2 ≥ 60%, PEEP ≥ 15 mmHg) and those in multi-organ failure with hemodynamic instability were deferred and re-assessed daily. For patients who had higher settings, a trial of apnea with paralysis for up to 3 minutes was performed to ensure they would tolerate apnea for the PDT. This was performed at the surgeon's discretion.

Tracheostomy Technique

Percutaneous dilational tracheostomy (PDT) with a period of apnea was the preferred technique, performed at the patient's bedside in a negative pressure ICU room, (Figure 1A). Personnel included two board-certified trauma surgeons who are surgical intensivists and also are the general surgeons for the hospital (one performed bronchoscopy and the other the PDT), a respiratory therapist (operating the ventilator) and two nurses (one administered medications and documented the procedure while the other was a runner that stood outside the room by a procedure cart). Extra sedation and paralytic medication was drawn up and ready in the room to avoid personnel entering and leaving during the procedure. All of the surgeons wore an N95

mask under a Powered Air-Purifying Respirator (PAPR). The other personnel remaining in the room for the duration of the procedure wore the following Personal Protective Equipment (PPE): N95 mask under a regular surgical mask OR a P100 reusable facemask with eye-protection, hair cover, isolation gown and single layer of gloves.

The patient was placed supine with a shoulder roll to extend the neck and was given sedation and paralytic medication. The cricoid cartilage was identified by palpation and a vertical incision was made. The subcutaneous tissue was bluntly dissected until the 2nd tracheal ring was identified. At this point a disposable bronchoscope was inserted into the endotracheal tube (ETT) through a bronchoscope adapter which was already attached to the ventilator tubing (Figure 1B). The ETT was retracted with the cuff down and the trachea was palpated to identify the entry point on bronchoscopy. A large bore needle was used to enter the trachea under direct visualization and a guidewire was threaded. The cuff was reinflated. At this time the inspiratory filter on the short corrugated tubing was disconnected from the ventilator and the patient was apneic (Figure 1C). The bronchoscope was removed and the rest of the procedure performed blind. The tract was dilated with a short dilator, then with the “Blue Rhino” dilator (COOK Medical). The tracheostomy was then inserted and the cuff inflated. The bronchoscope was inserted to confirm placement and the ETT was removed and placed into a medical waste bag. The inspiratory limb was then reattached.

Outcomes

The endpoints for this study were the short-term safety and feasibility for both patients and providers when performing PDT. Baseline demographics, comorbidities, ventilator data, indications for tracheostomy, timing of the procedure, pre-procedural, intra-procedural and post-procedural complications are reported. We also collected patient status at last follow-up and provider symptoms of or positive testing for COVID-19. Descriptive patient characteristics are described using medians (range) and frequencies.

Results

From April 6th, 2020 to July 21st, 2020, 2,030 patients were admitted with COVID-19, 615 required ICU level care and 254 patients (12.5%) required intubation and mechanical ventilation for respiratory failure due to COVID-19. We were consulted on 18 patients and 11 underwent PDT (61%). Patient characteristics including demographics and Charlson Comorbidity Index are found in Table 1. The majority of these patients experienced shock (requiring vasopressor medications) prior to tracheostomy consult (11 of 18, 84.6%) and 13 required prone positioning (72.2%) for acute respiratory distress syndrome (ARDS). The majority of patients who underwent PDT failed extubation at least once (72.7%) and the median time to tracheostomy was 15 days (IQR 13-24) after initial intubation. The median time to tracheostomy after a COVID+ diagnosis was 19 days (IQR 15-24). Additionally, of the 11 patients who underwent PDT, 5 (45.5%) developed ventilator-associated pneumonia (VAP) prior to the procedure. The median PaO2/FiO2 ratio on the day of tracheostomy was 142.8 (IQR 104.5-224.4) and the average PEEP was 10.8 (SD 3.4). The median SOFA score during ICU stay was 8 (IQR 5-11). The median CAM-ICU and RASS scores on the day of tracheostomy were 7 (IQR 6-7) and -3 (IQR -4, -2), respectively. Table 3 describes comorbidities and non-procedure related complications for all 18 patients who received a tracheostomy consult. Reasons for not performing tracheostomy were varied but the most common was that the patient was able to be extubated (57.1%). The described technique was successful in 100% of patients.

At 1-week follow-up, 8 (72.7%) of the tracheostomy patients remained ventilator-dependent and none had died. Two patients had intra-procedural complications (18.2%) and 1 patient had post-procedural complications (9.1%). During their hospital course, 8 (72.7%) of the patients who underwent tracheostomy were downsized and liberated from the ventilator, 1 died (9.1%), and 2 (18.2%) were discharged on the vent. Hospital course after tracheostomy can be found in Table 2. None of the surgeons have demonstrated symptoms of COVID-19.

Discussion

We have demonstrated the feasibility and safety of a modified technique for bedside percutaneous tracheostomy including a period of apnea and the use of PAPRs for PPE. PDT was performed for usual indications for respiratory failure. All tracheostomies were performed in patients requiring prolonged mechanical ventilation due to COVID-19. This was accomplished with a multi-disciplinary team of surgeons, intensivists, nurses and respiratory therapists.

Development of Tracheostomy Technique

Our technique was refined and informed by key observations during the initial tracheostomies. Isolation precautions highlighted the importance of preparation, particularly in case of unforeseen equipment failure or complications (e.g. bending of wire, contamination of instruments, unexpected bleeding). We adapted and created a role of a designated “runner” to address this need. The “runner” was a nurse who stood outside the room and was ready to address unanticipated needs with a procedure cart with additional supplies, including an extra tracheostomy kit. In addition, communication emerged as a critical component. The PAPR motor is quite loud and limited intraprocedural communication. To address this, we performed a huddle with the procedure team prior to starting the tracheostomy to clarify each person’s role, position, and appropriate time to disconnect the ventilator. This huddle minimized confusion and procedure time. Finally, several techniques were initially employed in order to minimize aerosolization. During the first tracheostomy, the long limb tubing to the endotracheal tube was disconnected and the end of the tubing was then covered by the respiratory therapists’ hand while the airway was serially dilated and the tracheostomy was placed. Another technique initially employed was turning off the ventilator completely and bagging the patient up until the airway was accessed and dilated. The ventilator was then turned on and connected to the

tracheostomy after placement. After discussions between the surgeons and respiratory therapists after these initial tracheostomies, the preferred technique to minimize aerosolization through apnea during the procedure was to disconnect the inspiratory limb of the ventilator after gaining wire access to the trachea, and to minimize the amount of time the bronchoscope is in place after confirming appropriate tracheal access. This technique is simple, does not require shutting off the ventilator and restarting it, and only clean air from the vent itself is expelled into the room. Other principles of the protocol to improve staff safety included minimizing personnel in the room, use of appropriate PPE, and keeping the room door closed during and then after the procedure for 45 minutes. No trainees were involved in these procedures.

Indications and Timing of Percutaneous Tracheostomy

Given the limited data available about COVID-19 infection, our institution relied on data describing traditional benefits of percutaneous tracheostomy for prolonged ventilation for acute respiratory distress syndrome from other causes.[10,11] These potential benefits include ability to wean sedation and increase patient communication, management of secretions, and to facilitate long-term vent weaning with decreased ventilator days.[12] Given that the duration of viral shedding and infectivity of COVID-19 is unknown and that early tracheostomy has no established mortality benefit,[11] patients were generally not considered for tracheostomy until they were mechanically ventilated for 10-14 days. Recent evidence suggests that maximum viral shedding occurs within the 5 days after symptom onset.[13] When considering tracheostomy, the ability to wean sedation was of particular importance due to medication shortages. PPE shortages were not a consideration, as protocols were instituted early to conserve and re-use PPE in the hospital. When determining the next steps for patients requiring prolonged ventilation, goals of care discussions were vital. This was especially pertinent for patients 65 years of age or older, as studies have shown that tracheostomy for non-surgical causes is associated with a higher 1-year mortality.[14] The healthcare team along with the palliative care

team held discussions with family and the patient if possible, surrounding tracheostomy and the implications of prolonged mechanical ventilation. This ensured that plans of care were consistent with the patient's wishes.

Reluctance to perform tracheostomy for prolonged mechanical ventilation in COVID-19 positive patients has in part been driven by perceived lack of beneficence, as mortality rates for critically ill and ventilated patients were reportedly high. A single-center experience in Wuhan China reported a 61.5% mortality rate in 28 days of follow-up.[4] A report from the Lombardy, Italy region reported a 26% mortality rate for critically ill patients in the ICU.[3] The largest study from New York initially reported mortality rates of 76.4% and 97.2% for those who received mechanical ventilation in the 18-65 year old age group and those older than 65 years old, respectively. These results have since been corrected to an overall mortality rate of 24.5% for patients who required mechanical ventilation.[1] At our institution the mortality rate for patients with COVID-19 requiring mechanical ventilation is 29%. This is better than recently reported mortality rates for ARDS of all etiologies since 2010: 45% in-hospital, 38% ICU, 30% 28/30-day, and 32% 60-day mortality.[15] Tracheostomies are inevitably required in order to provide comprehensive care to those on prolonged mechanical ventilation. We have shown that with proper PPE, precautions, and a structured team approach[16], healthcare providers can safely perform percutaneous tracheostomy for COVID-19 positive patients.

Preference for Percutaneous Technique

Aerosolization risk during tracheostomy has led other groups to consider novel techniques of tracheostomy,[17] or to preferentially perform an open tracheostomy.[18] We were successful in performing bedside percutaneous tracheostomy in all our patients with few modifications to the traditional technique. The benefits of using the percutaneous technique include using the patient's ICU room for the procedure, thus not requiring operating room personnel to be in contact with the patient, conserving operating room resources, and limiting

patient travel which can theoretically lead to increased viral exposure and also compromise the patients' tenuous respiratory status. In addition, the percutaneous technique is the preferred technique by the surgeons at this institution, leading to comfort and skill with the procedure. Procedure set-up time including patient positioning, the team huddle, time-out, and donning of PPE took about 30 minutes. Total time of the procedure excluding set-up time was 3-5 minutes, and time in the actual airway was 1-2 minutes.

Observations

While the sample size is small, some observations are notable. Ventilator-associated pneumonia was common, noted in 9 (50.0%) of the patients consulted for tracheostomy and in 7 (63.6%) of patients who underwent the procedure. In addition, all of the patients who required percutaneous tracheostomy were Hispanic/Latino or African-American. The median age was 54 (25-74) years old and most patients were male, 90%. Finally, the median CAM-ICU-7 and RASS scores on the day of percutaneous tracheostomy were 7 (IQR 6-7) and -3 (IQR -4, -2), respectively. These scores indicate severe delirium and a moderate level of sedation, both of which are linked to worsening outcomes.[19] At 1-week follow-up, 6 of the 11 tracheostomy patients continued to have positive CAM-ICU-7 scores. As previous studies have shown, COVID-19 patients have an estimated delirium prevalence rate of 73.6%.[20] Future studies should investigate underlying factors for the disproportionately higher number of cases and more severe cases of COVID-19 observed in ethnic minority groups.

Strengths and Limitations

Our study is not without limitations. There is a clear selection bias for who received a tracheostomy favoring patients who are expected to recover. Notably, only 11 of 18 patients we were consulted on received a tracheostomy. Further, our sample was small and limited to a single center, reducing generalizability and external validity. Also, due to ethical limitations we

do not have confirmation on the absence of symptoms for respiratory therapy and nursing staff. Our hospital has performed random mitigation testing and no tracheostomy providers have tested positive. Finally, we do not have a comparison group to establish the potential benefits of tracheostomy, although this has been established in similar disease processes.[10]

Of note, a series of 96 patients who underwent a novel percutaneous tracheostomy utilizing the bronchoscope outside of the ETT has established safety and efficacy of their technique in short-term follow-up (average 18 days) and has comparable patient outcomes to our institution.[17] In addition, a recent publication has described a protocol for percutaneous tracheostomy with a period of apnea to minimize aerosolization. This series focuses on the description of the technique.[21] We describe a different technique utilizing apnea to minimize aerosolization, which was performed only on patients with COVID-19 infection, and with a PEEP cut-off of 15, which is higher than previously described thresholds. Our description of outcomes is the first to include delirium and delirium severity in patients with respiratory failure due to COVID-19 who require tracheostomy. In addition, to our knowledge, we are the first to describe the routine use of PAPRs for PPE during tracheostomy. In later follow-up studies, comparison of effectiveness of PPE types will be important in limiting infection transmission and conserving resources. This paper is an important addition to early literature regarding care for the COVID-19 positive patient. We provide a thorough description of considerations for and a safe modified technique of percutaneous tracheostomy despite a higher PEEP threshold.

Conclusions

Percutaneous tracheostomy can be safely performed in patients diagnosed with COVID-19 *for the usual indications*, with a modified technique to minimize aerosolization. As we continue to care for more patients with COVID-19, development of institutional protocols for safe performance of tracheostomy will be required for prolonged ventilator weaning. Comparison of

outcomes from described protocols can help establish evidence-based standards of care for patients with respiratory failure from COVID-19.

Figure 1: (A) Personnel and positioning for percutaneous tracheostomy. (B) Bronchoscopy performed to directly visualize needle access to trachea. (C) Inspiratory filter disconnected for apnea period to limit aerosolization.

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Table 1 – Patient characteristics of patients diagnosed with COVID-19 considered for PDT

Pt	Age	Sex	Race	Ethnicity	CCI	BMI (kg/m^2)	Trach indication	PDT	Treatment	Died
1	25	M	White	Hispanic/Latino	0	35	Prolonged ventilation, failed extubation	Y	HQ + AZ, IV steroids, Lasix	N
2	51	M	Multirace	Hispanic/Latino	0	24	Prolonged ventilation, secretions, failed extubation	Y	HQ + AZ, IV steroids, Lasix	N
3	74	M	White	Hispanic/Latino	0	29	Prolonged intubation, secretions	Y	HQ + AZ, Tocilizumab, IV steroids, Lasix, CVVH, convalescent plasma	Y
4	43	F	White	Hispanic/Latino	1	27	Prolonged ventilation	Y	HQ + AZ, IV steroids	N
5	68	M	White	Hispanic/Latino	1	24	Prolonged ventilation, failed extubation	Y	HQ + AZ, tocilizumab, IV steroids, Lasix	N
6	55	M	Black	Not Hispanic/Latino	1	24	Prolonged ventilation	Y	HQ + AZ, IV steroids, Lasix	N
7	52	M	White	Hispanic/Latino	1	40	Prolonged ventilation, failed extubation	Y	HQ + AZ, tocilizumab, IV steroids, Lasix, CVVH	N
8	67	M	White	Hispanic/Latino	0	25	Prolonged ventilation, failed extubation	Y	HQ + AZ, IV IV steroids, Lasix	N
9	53	M	White	Hispanic/Latino	1	21	Prolonged ventilation	Y	HQ + AZ, Lasix	N
10	77	M	Black	Not Hispanic/Latino	3	22	Prolonged ventilation, failed extubation	Y	HQ + AZ, tocilizumab, full anticoagulation, Lasix	N
11	60	F	Black	Not Hispanic/Latino	0	27	Prolonged ventilation	Y	Remdesivir, IV steroids, full anticoagulation, Lasix,	N

									convalescent plasma	
12	52	M	White	Not Hispanic/Latino	0	30	Prolonged ventilation	N	HQ + AZ, Lasix	N
13	65	F	Black	Not Hispanic/Latino	6	36	Prolonged ventilation	N	HQ + AZ, IV steroids, Lasix	Y
14	66	F	White	Not Hispanic/Latino	4	63	Prolonged ventilation	N	HQ + AZ, full anticoagulation, Lasix, CVVH	N
15	72	M	Asian	Not Hispanic/Latino	1	28	Prolonged ventilation	N	HQ + AZ, tocilizumab, Lasix	N
16	48	M	White	Hispanic/Latino	1	24	Prolonged ventilation	N	HQ + AZ, IV steroids, full anticoagulation, Lasix	Y
17	59	F	White	Hispanic/Latino	1	28	Prolonged ventilation	N	HQ + AZ, IV steroids, full anticoagulation, Lasix	N
18	51	M	White	Hispanic/Latino	1	25	Prolonged ventilation	N	Remdesivir, IV steroids, full anticoagulation, Lasix	N

CCI=Charlson Comorbidity Index; HQ=hydroxychloroquine; AZ=azithromycin; CVVH=continuous veno-venous hemofiltration; BMI = Body Mass Index

Table 2 – Outcomes of patients diagnosed with COVID-19 undergoing elective PDT

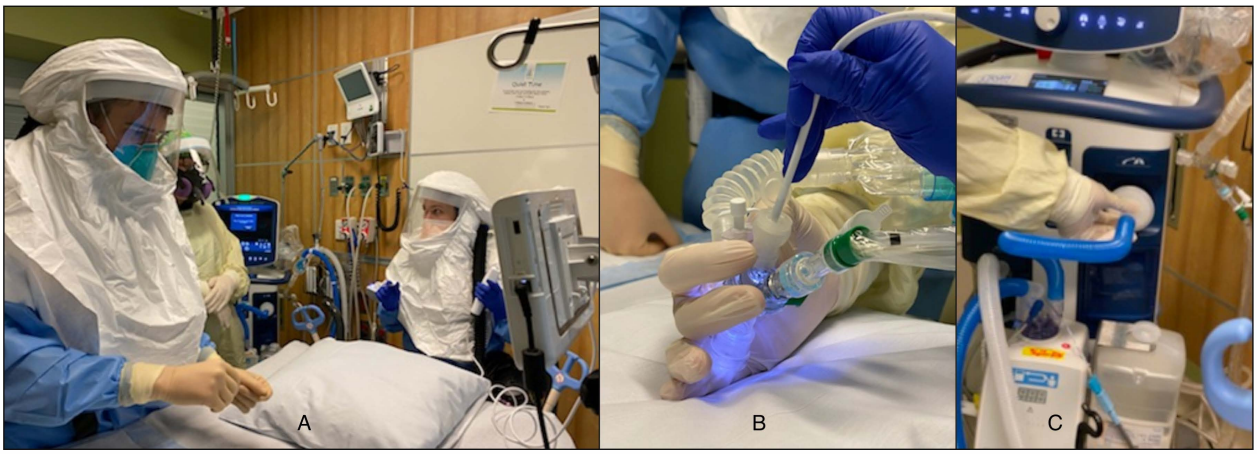
Patient	Days of MV prior to PDT	Extubation Attempts	Intra-op complication	Complication within follow-up	Status at 1-week post-PDT	Hospital course after trach	Length of follow-up, days
1	13	3	Bleeding	None	On vent, AC/VC	Developed VAP. Trach downsized on HD 30. Discharged home on RA on HD 31	18
2	23	1	None	None	On vent, AC/VC	Discharged home on 3L oxygen on HD 74	52
3	14	0	None	None	On vent, AC/VC	Died from COVID complications on HD 26	12
4	13	1	None	None	On vent, PSV	Trach downsized on HD 26. Discharged home on RA on HD 30	14
5	14	1	None	None	No ventilator	Trach downsized on HD 25. Discharged home on RA on HD 33	19
6	24	0	None	None	On vent, AC/VC	Trach downsized on HD 35. Discharged to inpatient rehabilitation with trach collar 30% O_2 on HD 48	26
7	21	2	None	None	No ventilator	Discharged on RA to acute rehab on HD 37.	15
8	15	1	None	Bleeding during trach change	On vent, AC/VC	Trach downsized on HD 27. Decannulated on HD 39, discharged to SNF on HD 51	36
9	24	1	None	None	No ventilator	Trach downsized on HD 30. Discharged on RA to LTACH on HD 35	11
10	28	1	None	None	On vent, AC/VC	Developed VAP, sepsis. Discharged on ventilator to LTACH on HD 44	14
11	8	0	Pneumothorax	None	On vent, AC/VC	Discharged on ventilator to LTACH on HD 33	12

VAP=ventilator-acquired pneumonia; HD=hospital day; RA=room air; SAR=sub-acute rehab; LTAC=long-term acute care hospital; HFNC=high-flow nasal cannula

Table 3 – Comorbidities and non-procedural complications

Condition	Total (n=18)	Tracheostomy (n=11)	No Tracheostomy (n=7)
Asthma, n (%)	2 (11.1)	1 (9.1)	1 (14.3)
Diabetes, n (%)	10 (55.6)	5 (45.5)	5 (71.4)
Hypertension, n (%)	11 (61.1)	7 (63.6)	4 (57.1)
Liver disease or cirrhosis, n (%)	2 (11.1)	1 (9.1)	1 (14.3)
Obesity (BMI ≥30 kg/m^2) , n (%)	5 (27.8)	2 (18.2)	3 (42.9)
Evidence of bacterial or viral co-infection at admission, n (%)	4 (22.2)	2 (18.2)	2 (28.6)
Pulmonary embolism, n (%)	1 (5.6)	0 (0.0)	1 (14.3)
DVT, n (%)	4 (22.2)	4 (36.4)	0 (0.0)
Sepsis, n (%)	7 (38.9)	4 (36.4)	3 (42.9)
Septic shock, n (%)	14 (77.8)	7 (63.6)	7 (100.0)
VAP, n (%)	9 (50.0)	7 (63.6)	2 (28.6)

BMI=Body Mass Index; DVT=Deep Vein Thrombosis; VAP=Ventilator associated pneumonia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