Tracheotomy in ventilator-dependent patients with COVID-19: a cross-sectional study of analgesia and sedative requirements

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Abstract

Objective: During March 2020 in the United States, demand for sedatives increased by 91%, that for analgesics rose by 79%, and demand for neuromuscular blockers increased by 105%, all owing to the number of COVID-19 cases requiring invasive mechanical ventilation (MV). We hypothesize that analgesic and sedative requirements decrease following tracheotomy in this patient population.

Methods: In this cross-sectional study, we conducted a retrospective chart review to identify patients with COVID-19 who underwent tracheotomy (T) at an academic medical center between March 2020 and January 2021. We used a paired Student t-test to compare total oral morphine equivalents (OMEs), total lorazepam equivalents, 24-hour average dexmedetomidine dosage in μg/kg/hour, and 24-hour average propofol dosage in μg/kg/minute on days T−1 and T+2 for each patient.

Results: Of 50 patients, 46 required opioids before and after tracheotomy (mean decrease of 49.4 mg OMEs). Eight patients required benzodiazepine infusion (mean decrease of 45.1 mg lorazepam equivalents). Fifteen patients required dexmedetomidine infusion (mean decrease 0.34 μg/kg/hour). Seventeen patients required propofol (mean decrease 20.5 μg/kg/minute).

Conclusions: When appropriate personal protective equipment is available, use of tracheotomy in patients with COVID-19 who require MV may help to conserve medication supplies in times of extreme shortages.
Introduction

Mechanical ventilation (MV) is commonly used in modern intensive care units (ICUs), with approximately 800,000 patients in the United States requiring mechanical ventilatory support each year. Among mechanically ventilated patients, between 10% to 34% will undergo tracheostomy. The incidence of tracheotomy performed in the United States has increased in the past 20 years, with approximately 100,000 tracheostomies performed per year.

Randomized control trials (RCTs), systematic reviews, and meta-analyses of RCTs have repeatedly shown that early tracheotomy decreases the duration of MV, shortens the ICU length of stay (LOS), lowers long-term mortality, and reduces sedation requirements. This last benefit is important in patients with COVID-19 because early tracheotomy may decrease sedation and analgesic requirements at a time when there are critical shortages of many of these medications.

As the COVID-19 pandemic spread in the United States, nationwide shortages of necessary critical care medications were becoming increasingly common. During 6 months in 2020, 27 new medication shortages were announced by the US Food and Drug Administration, including fentanyl, sufentanil, hydromorphone, morphine, propofol, dexmedetomidine, midazolam, and lorazepam. Such shortages force providers to rely on alternative agents with greater adverse effects and less desirable overall pharmacologic profiles to achieve the same effects as the preferred therapy. By March 2020, with a growing number of patients with COVID-19 requiring MV, the demand for sedatives increased by 91%, that for analgesics increased by 79%, and the demand for neuromuscular blockers rose by 105%. Use of these medications can cause many adverse effects, not limited to depression of the cardiovascular, respiratory, and immunological systems, thereby potentially negatively influencing overall outcomes in critically ill patients. To preserve supplies of these critical medications, it may be beneficial to shift the practice guidelines toward interventions that can decrease reliance on sedative and analgesic medications, especially as further waves of COVID-19 cases will likely worsen current medication shortages.

We hypothesized that the amount of sedative and analgesic medications required after tracheotomy in patients with COVID-19 is significantly lower than the amount required prior to tracheostomy. This hypothesis is important because the United States may face increasing medication shortages as the COVID-19 pandemic progresses.

Methods

This was a retrospective cross-sectional study performed via chart review at a single academic medical center with 72 cumulative ICU beds. The Institutional Review Board of the University of New Mexico Health Sciences Center Human Research Review Committee reviewed and approved this study.
20-644, assigned on 31 January 2021). Owing to the study design, consent was not required from patients.

**Patient identification**

Inclusion criteria were MV-dependent patients with COVID-19 who underwent tracheotomy between March 2020 and January 2021. Exclusion criteria were opioid or benzodiazepine dependence, concurrent extracorporeal membrane oxygenation (ECMO) therapy, performance of tracheotomy at a referring institution, and COVID-19 as an incidental diagnosis rather than the primary reason for ICU admission. The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

**Data collection**

Baseline characteristics were recorded for each patient and included age, sex, ethnicity, body mass index, and medical comorbidities. Baseline data pertaining to the COVID-19 disease course were also obtained, including date of most recent positive COVID-19 test and whether the patient had concurrent bacterial pneumonia (defined as positive sputum culture 5 days prior to the date of tracheotomy or 2 days after tracheostomy). Lastly, data regarding the overall hospital and disease course were recorded, including transfer from a referring facility and LOS at the referring facility, where applicable; the number of days on MV prior to tracheostomy; MV settings at the time of tracheostomy; and MV settings 48 hours after tracheotomy was performed (Table 1). From these baseline characteristics, population data were recorded, including average hospital LOS, ICU LOS, mortality rate, and incidence of ventilator-associated pneumonia (Table 2). All patient details were de-identified.

### Table 1. Baseline demographic information.

| Age (years) | n (%) |
|-------------|-------|
| 18–39       | 4 (8%) |
| 40–59       | 19 (38%) |
| 60–79       | 27 (54%) |
| 80 or older | 0 (0%) |
| Sex         |       |
| Male        | 27 (54%) |
| Female      | 23 (46%) |
| Ethnicity   |       |
| White       | 18 (36%) |
| Native American | 17 (35%) |
| Black       | 0 (0%) |
| Other       | 15 (30%) |
| BMI (kg/m²) |       |
| <18         | 0 (0%) |
| 18–25       | 8 (16%) |
| 25–35       | 30 (60%) |
| 35–45       | 7 (14%) |
| >45         | 3 (6%) |
| Unable to calculate | 2 (4%) |
| Number of medical comorbidities* |       |
| 0           | 4 (8%) |
| 1–2         | 19 (38%) |
| 3+          | 27 (54%) |
| Transferred from referring facility? |       |
| Yes | 30 (60%) |
| No  | 20 (40%) |
| Concurrent bacterial pneumonia? |       |
| Yes | 25 (50%) |
| No  | 25 (50%) |

*Most commonly recorded comorbidities, in descending order: diabetes mellitus (n = 28), hypertension (n = 24), obesity (n = 14), hyperlipidemia (n = 12), hypothyroidism (n = 4), chronic kidney disease (n = 4), and end-stage renal disease (n = 4).

BMI, body mass index.

**Raw medication data**

The amount of each medication required 24 hours before and 48 hours after tracheotomy (T) was extracted. A binary method of analysis (patients requiring versus not requiring a given medication) was used for clonidine, antipsychotics, valproate, and vasopressors. The cumulative dosage of each medication used over the 24-hour period on day T–1
and day T+2 was calculated for the following agents: oxycodone, hydromorphone, fentanyl, morphine, lorazepam, midazolam, dexmedetomidine, and propofol.

**Sedation analysis**

From the above data, the cumulative amount of oxycodone, hydromorphone, fentanyl, and morphine was converted into total oral morphine equivalents (OME). The amount of lorazepam and midazolam was converted into lorazepam equivalents. The total dosages of dexmedetomidine and propofol were summed and then converted to the mean rates, in a standard dose of μg/kg/hour and μg/kg/minute, respectively. Patients receiving dexmedetomidine or propofol on day T−1 and who were switched to the opposite agent on day T+2 were excluded from the analysis comparing these specific medications. A paired Student’s t-test was used to compare total OMEs, total lorazepam equivalents, 24-hour cumulative average dexmedetomidine dosage (μg/kg/hour), and 24-hour cumulative average propofol dosage (μg/kg/minute) on days T−1 and T+2 for each patient. A p-value <0.05 was considered statistically significant.

**Results**

In a chart review, we initially identified 71 MV-dependent patients with COVID-19 who underwent tracheotomy between March 2020 to January 2021. Of these 71 patients, nine were excluded owing to concurrent ECMO because the confounding effects of this therapy are outside the scope of this study. We excluded one additional patient in whom tracheotomy was performed at a referring facility prior to admission at the study center because the medications pre- and post-tracheotomy could not be obtained. Eleven patients were excluded because COVID-19 was incidentally found and not the primary reason for ICU admission; these included patients with trauma and head and neck cancer. Thus, 50 patients were retained for analysis in this retrospective chart review. The mean (standard deviation) patient age was 57.8 (11.7) years, and 54% were men (Table 1).

Of the 50 patients included in the analysis, 46 required opioids before and after tracheostomy. The amount of OMEs required for patient analgesia showed a statistically significant decrease post-tracheostomy, with a mean decrease of 49.4 mg OMEs (p = 0.014). On review of sedation data, eight patients required benzodiazepine infusion before and after tracheostomy. The mean lorazepam equivalents were significantly decreased following tracheostomy, with a mean decrease of 45.1 mg lorazepam equivalents (p = 0.031). In the 15 patients requiring dexmedetomidine infusion before and after tracheostomy, there was a significant decrease in mean dosage on day T+2 by 0.34 μg/kg/hour (p = 0.012). A decrease was also seen in the propofol dosage required for sedation on day T+2. In the 17 patients on propofol before and after tracheostomy, there was a significant mean decrease of 20.5 μg/kg/minute (p <0.0001) (Table 3).

**Discussion**

During the study period of 1 March 2020 to 31 January 2021, there were a total of 1557
patients with COVID-19 infection at our academic institution. Of these, 1226 patients were admitted primarily for COVID-19, of which 399 required ICU-level care and 258 required tracheostomy. Only 60 patients who were positive for COVID-19 during the study period were intubated and subsequently successfully extubated without requiring tracheostomy.

Tracheotomy is thought to decrease sedation requirements in all populations requiring MV in a multifactorial manner. First, tracheotomy leads to several physiological changes to the patient’s airway owing to the larger cannulae, in comparison with endotracheal tubes (ETT). These changes include improved expiratory flow, reduced dead space and airway resistance, and enhanced secretion clearance.2,9,10 When compared with ETT, tracheotomy also better facilitates oral and bronchopulmonary care.4

Recent psychological data in ICU populations have suggested that MV is a major cause of patient anxiety. This psychological symptom, experienced by 30% to 80% of all patients in the ICU, is driven in part by dyspnea and respiratory dyssynchrony.4 Patient-ventilator dyssynchrony is defined as any state in which “ventilator assistance does not match the patient’s demand.”5 Essentially, respiratory dyssynchrony drives patient anxiety, which in turn increases the amount of sedatives and analgesics provided to patients receiving MV.4 Patient anxiety and comfort has often been used as a proxy for studying respiratory dyssynchrony.4,9,12

Current conjecture among critical care physicians postulates that tracheotomy decreases respiratory dyssynchrony owing to improved patient comfort; however, the published literature is conflicting. A recent observational study involving 72 patients on MV undergoing tracheotomy at a tertiary care ICU showed a significant decrease in fentanyl and midazolam administration with no increase in patient agitation time post-procedure.9 A systemic review reiterated this decrease in sedation for patients undergoing early tracheotomy (defined here as <10 days but >4 days from the time of intubation) with a corresponding cost savings of USD 4316 per patient across their ICU stay.1 Conversely, a recent retrospective analysis on the use of morphine, midazolam, and propofol in 117 patients before and after tracheotomy found no such significant decrease.4 Regardless of the effect on sedation, systematic reviews and meta-analyses have not shown that early tracheostomy, defined as within 10 days of intubation, is associated with any improvement in mortality, ICU LOS, or incidence of ventilator-associated pneumonia.3 Whereas the data here were not sufficiently powered to permit analysis of these outcomes, anecdotally, the present results did not show any of these differences, thus aligning with the current literature.

Limitations of this study include a relatively small sample size with a wide

| Table 3. Summary of results. |
|-----------------------------|
| Patients requiring agent     | Mean change in dosage after tracheostomy | P-value |
| Opioids 46                  | −49.4 mg OMEs                              | 0.0137* |
| Benzodiazepines 8           | −45.1 mg lorazepam equivalents             | 0.0313* |
| Dexmedetomidine infusion 15 | −0.34 μg/kg/hour                           | 0.0124* |
| Propofol infusion 17        | −20.5 μg/kg/minute                         | <0.0001* |

*Denotes statistical significance.

OME, oral morphine equivalent.
range of age groups, which may restrict the reliability of the results and external validity of the study. Ultimately, the data from the cohort studied here overwhelmingly show that tracheotomy in patients with COVID-19 is associated with decreased requirements for analgesic and sedative medications, including oxycodone, hydromorphone, fentanyl, lorazepam, midazolam, dexmedetomidine, and propofol.

**Conclusion**

The ongoing COVID-19 pandemic and its respiratory sequelae in affected patients have dramatically increased the importance of discussion around use of tracheotomy in the ICU. Reports estimate that 14% of COVID-19-positive patients are diagnosed with acute hypoxic respiratory failure, with 5% of all patients with COVID-19 infection requiring MV.6,7 Institutional guidelines regarding tracheotomy in this population urge caution and careful timing as the procedure is aerosol-generating and thus confers an infection risk to involved providers.13 In light of current national medication shortages in the setting of an ongoing pandemic, the data presented here take on additional importance. Tracheotomy in patients with COVID-19 is associated with statistically significant decreases in OMEs and total lorazepam equivalents, as well as lower average rates of dexmedetomidine and propofol infusion. Therefore, we contend that providers can consider early tracheotomy for all patients receiving MV who are admitted primarily for COVID-19 infection to lessen the burden of medication shortages.

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**Author contributions**

Each author significantly contributed to the manuscript by participating in project proposal, data collection, data analysis, writing, and editing. All four authors made substantial contributions to the concept and design as well as acquisition of data. Brianne Wiemann and Richard Miskimins made further substantial contributions to analysis and interpretation of the data. Brianne Wiemann drafted the article. All authors participated in revising the manuscript. All authors gave their final approval of the version to be submitted.

**Data availability statement**

Original research data to support the results and tables presented in this manuscript are available upon request.

**Declaration of conflicting interests**

The authors declare that there is no conflict of interest.

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