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Optimal timing and outcomes among COVID-19 patients undergoing tracheostomy

Steven K.M. Vuu, MD\textsuperscript{a,b,*}, Tandis Soltani, MD\textsuperscript{a,b}, Huazhi Liu, MS\textsuperscript{b}, Jennifer DeMuro, MD\textsuperscript{a,b}, Laura Mena Albors, MD\textsuperscript{a,b}, Ettore Crimi, MD\textsuperscript{a,b}, Darwin N. Ang, MD, PhD, MPH\textsuperscript{a,b,c}

\textsuperscript{a} Department of Surgery, University of Central Florida College of Medicine, Orlando, FL
\textsuperscript{b} Department of Surgery, Ocala Regional Medical Center, Ocala, FL
\textsuperscript{c} Department of Surgery, University of South Florida Morsani College of Medicine, Tampa, FL

\section*{A B S T R A C T}

\textbf{Background:} Patients who require mechanical ventilation secondary to severe COVID-19 infection have poor survival. It is unknown if the benefit of tracheostomy extends to COVID-19 patients. If so, what is the optimal timing?

\textbf{Methods:} Retrospective cohort study within a large hospital system in the United States. The population included patients with COVID-19 from January 1, 2020 to September 30, 2020. In total, 93,918 cases were identified. They were excluded if no intubation or tracheostomy, underwent tracheostomy before intubation, \textless 18 years old, hospice patients before admission, and bacterial pneumonia. In total, 5,911 patients met the criteria. Outcomes between patients who underwent endotracheal intubation only versus tracheostomy were compared. The primary outcome was inpatient mortality. All patients who underwent tracheostomy versus intubation only were compared. Three cohort analysis compared early (\textless 10 days) versus late (>10 days) tracheostomy versus control. Eight cohort analysis compared days 0–2, days 3–6, days 7–10, days 11–14, days 15–18, days 19–22, and days 23+ to tracheostomy versus control.

\textbf{Results:} There was an overall inpatient mortality rate of 37.5\% in the tracheostomy cohort compared to 54.4\% in the control group (\textit{P} < .0001). There was an early tracheostomy group inpatient mortality rate of 44.7\% (adjusted odds ratio 0.73, 95\% confidence interval 0.52–1.01) compared to 33.1\% (adjusted odds ratio 0.44, 95\% confidence interval 0.34–0.58) in the late tracheostomy group.

\textbf{Conclusion:} COVID-19 patients with tracheostomy had a significantly lower mortality rate compared to intubated only. Optimal timing for tracheostomy placement for COVID-19 patients is 11 days or later. Future studies should focus on early tracheostomy patients.

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\section*{Introduction}

Acute respiratory failure is a known complication of COVID-19. This subset of critically ill patients may require endotracheal intubation and mechanical ventilation as rescue therapy. COVID-19 may progress to acute respiratory distress syndrome (ARDS). This may be secondary to viral shedding in the airways or a large cytokine inflammatory response resulting in diffuse alveolar damage.\textsuperscript{1} Many of these patients may require prolonged intubation and subsequent tracheostomy.\textsuperscript{2,3} Tracheostomy is commonly performed when it is anticipated that a patient will require prolonged mechanical ventilation. Up to one-third of patients requiring prolonged mechanical ventilation now undergo a tracheostomy.\textsuperscript{4}

Advantages of tracheostomy compared to prolonged endotracheal intubation includes less sedation, expedited weaning from mechanical ventilation, and improved patient comfort. This may result in a lower risk of ventilator-associated pneumonia, fewer hospital days, and promotion of early mobility.\textsuperscript{5,6} Other benefits include decreased risk of subglottic stenosis and laryngeal complications.\textsuperscript{7,8} Within the context of a global pandemic such as COVID-19, health care systems have been overwhelmed and underresourced. Multiple studies have shown that tracheostomies performed either early or late are associated with early weaning of mechanical ventilation, progressing to decannulation, liberating health care resources and ICU beds.\textsuperscript{1,9} On the other hand, particularly early in the pandemic, concerns were raised for potential exposure to health care providers who are part of the team in

\* Reprint requests: Steven K.M. Vuu, MD, Department of Surgery, University of Central Florida College of Medicine, 6850 Lake Nona Blvd, Orlando, FL 32827.
E-mail addresses: steven.vuu@gmail.com, steven.vuu@ucf.edu (S.K.M. Vuu);
Twitter: @svuuMD

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tracheostomy creation. Several studies have demonstrated the risk to clinicians participating in the procedures is minimal while using a protocol-driven approach and donning adequate personal protective equipment.

Our study aims to examine the clinical outcomes of patients with COVID-19 who underwent tracheostomy and to investigate the optimal timing for tracheostomy. We hypothesized that patients with COVID-19 who underwent tracheostomy would have lowered inpatient mortality and that there is an optimal time to perform tracheostomy in these patients. Our study seeks to add to the body of existing knowledge related to this topic by providing results from a large hospital system within the United States.

Methods

Study design

A retrospective cohort study of a clinical database within a large hospital system in the United States was performed, selecting for patients diagnosed with COVID-19 from January 1, 2020 to September 30, 2020. All participating hospitals are a part of a single health care system and use the same electronic medical record (EMR) software. The data were entered into a centralized data set in a secured server within the hospital system’s clinical data warehouse and subsequently abstracted as deidentified data. A formal institutional review board process deemed this study as exempt.
There was a total of 93,918 patients with confirmed cases of COVID-19 within the period of study. Patients were excluded if they did not undergo intubation or tracheostomy, underwent tracheostomy before intubation, were <18 years old, were hospice patients before admission, or those with bacterial pneumonia. Critically ill patients were defined as COVID-19-positive patients admitted to the ICU who underwent endotracheal intubation (ICD-10 31500, OBH17EZ) or tracheostomy (ICD-10 31600, Z93.0, Z93.9, OBH18EZ, OBH113F4). A total of 5,911 patients met the criteria for the study (Figure 1).

Laboratory confirmation of COVID-19 infection was performed using the following tests: the Sofia SARS Antigen Fluorescent Immunoassay (FIA) (Quidel, San Diego, CA) was used for qualitative detection of the nucleocapsid protein from SARS-CoV-2. Direct nasal swabs were used as samples. The protocol provided by Quidel was used. Positive samples were confirmed using ID NOW COVID-19 (Abbott Diagnostics, Scarborough, ME), a nucleic acid amplification protocol. Furthermore, positive samples were also sent to North Florida Laboratory and confirmed using Simplexa COVID-19 (DiaSorin Molecular, Cypress, CA) Direct real-time RT-PCR assay. Only laboratory-confirmed cases were included in this analysis.

**Study cohorts and variables**

The control group included 5,516 COVID-19 positive patients who underwent endotracheal intubation only. The exposure group included 395 COVID-19 positive patients who underwent endotracheal intubation and then subsequently tracheostomy. The timing of tracheostomy patients is widely variable; as a result, the study (Figure 1).

Mortality was then evaluated by stratiﬁed analysis by time to tracheostomy, 3 to 6 days after intubation, 7 to 10 days, 11 to 14 days, 15 to 18 days, 19 to 22 days, and 23 days and beyond after intubation.

**Statistical analysis**

Continuous data were expressed as mean with standard deviation (SD) or median, and the difference between the 2 groups was compared. Parametric data expressed as proportions were evaluated by χ2 tests and Student’s t tests for continuous variables. Nonparametric data were evaluated by Fisher exact test for proportions and the Wilcoxon rank sum test for continuous variables. Logistic regression was used for binary outcomes, and linear

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| Table I | Tracheostomy versus endotracheal cohort demographics and comorbidities |
|---------|-------------------------------------------------------------|
|         | Tracheostomy (N = 395) | Endotracheal intubation only (N = 5,516) | P values |
| Age, y  |                                 |                                 |         |
| 18–44   | 9.1% 9.2% .95 |                                 |         |
| 45–54   | 18.2% 13.2% .005 |                                 |         |
| 55–64   | 27.9% 22.3% .01 |                                 |         |
| 65–74   | 28.9% 27.9% .67 |                                 |         |
| 75–84   | 13.7% 20.4% .001 |                                 |         |
| ≥85     | 2.3% 7.0% .0003 |                                 |         |
| Age, y (mean) | 61.9 (±12.7) 64.9 (±14.4) | <.0001 | |
| Age, y (median) | 63 66 |                                 |         |
| Age, y (mode) | 63 71 |                                 |         |
| Sex     |                                 |                                 |         |
| Male    | 56.2% 59.9% .15 |                                 |         |
| Female  | 43.8% 40.1% .15 |                                 |         |
| Race    |                                 |                                 |         |
| White   | 50.4% 49.9% .86 |                                 |         |
| Black   | 16.2% 20.7% .03 |                                 |         |
| Asian   | 5.3% 2.9% .01 |                                 |         |
| Other   | 23.5% 23.2% .86 |                                 |         |
| Unknown | 4.6% 3.3% .17 |                                 |         |
| Insurance |                                 |                                 |         |
| Blue Cross/Cost | 4.3% 2.5% | .01 | |
| Commercial | 18.0% 12.4% | .001 | |
| Government | 7.6% 11.9% | .01 | |
| Medicaid | 15.2% 10.4% .003 |                                 |         |
| Medicare | 49.9% 56.9% .01 |                                 |         |
| Other   | 4.1% 4.6% .62 |                                 |         |
| Self-pay | 0.5% 0.9% | .39 | |
| Workers comp. | 0.5% 0.4% | .75 | |
| Hospital disposition |                                 |                                 |         |
| Home    | 2.8% 9.2% <.0001 |                                 |         |
| Home under care | 2.8% 4.4% | .12 | |
| Inpatient rehab facility (IRF) | 7.6% 3.9% | .0004 | |
| Long-term acute care hospital (LTACH) | 33.9% 3.8% <.0001 | |
| Short-term general hospital | 2.8% 6.1% | .01 | |
| Skilled nursing facility (SNF) | 3.3% 5.1% | .11 | |
| Expired | 37.5% 54.4% <.0001 |                                 |         |
| Hospice | 9.1% 11.8% .1 |                                 |         |
| Others  | 0.3% 1.2% | .1 | |
| Comorbidities |                                 |                                 |         |
| Coronary artery disease (CAD) | 17.7% 22.2% | .04 | |
| Congestive heart failure (CHF) | 25.8% 25.7% | .94 | |
| Malignant neoplasm | 0.3% 0.2% | .67 | |
| Chronic obstructive pulmonary disease (COPD) | 2.5% 2.0% | .50 | |
| Asthma | 7.6% 6.7% | .48 | |
| History of stroke (CVA) | 2.0% 1.3% | .26 | |
| Alzheimer's disease | 0.3% 1.3% | .07 | |
| Diabetes | 14.4% 14.0% | .79 | |
| Chronic kidney disease (CKD) | 10.6% 10.0% | .67 | |
| Cannabis use | 0.8% 0.6% | .73 | |
| Alcohol abuse | 1.8% 1.7% | .85 | |
| Obesity (BMI >30) | 28.6% 22.1% | .003 | |
| Tobacco smoker | 3.8% 4.6% | .47 | |

BMI, body mass index.
regression methods were used for continuous outcomes. Mortality was adjusted by age, race, sex, insurance status, obesity, tobacco smoking status, and Charlson Comorbidity Index. To account for potential survival bias, we also included ICU LOS and ventilator days in separate multivariable regression models. For LOS and ventilator days, the regression model included age, race, sex, insurance status, BMI, tobacco smoker, and Charlson Comorbidity Index. All statistical analyses were performed using SAS 9.4. Outcomes were determined to be statistically significant if the adjusted odds ratios did not overlap with 1.00.

Results

There was a total of 93,918 patients with confirmed cases of COVID-19 within the study period. A total of 5,911 patients underwent only endotracheal intubation. The exposure group included 395 COVID-positive patients who underwent only endotracheal intubation. The control group included 5,516 COVID-19 within the study period. A total of 5,911 patients met the inclusion criteria for the study. The control group included 5,516 COVID-19 patients. The exposure group included 395 COVID-19-positive patients who underwent only endotracheal intubation.

Tables 1 and 2 provide descriptive analyses between the 2 cohorts: exposure (N = 395) versus control (N = 5,516). In total, 395 patients underwent tracheostomy and 5,516 patients were intubated only. Inpatient mortality rate was 37.5% compared to 54.4%, respectively (adjusted P value <.0001). The sociodemographic variables were similar between groups, including age, sex, race, insurance status, and comorbidities. There were some differences noted; for example, the tracheostomy group had a slightly higher proportion of younger patients compared to the intubation-only group. For both cohorts, the majority of patients in both groups were in the age 55–74 bracket. The mean age in the tracheostomy group was 61.9 years old (SD ± 12.7 years) compared to 64.9 years old (SD ± 14.4 years) (P value .0001). There were more Asian

patients in the tracheostomy group (5.3% vs 2.9%, P value .01) and more Black patients (20.7% vs 16.2%, P value .03) in the intubation-only group. Hospital discharge destinations differed, with fewer patients going home in the tracheostomy group compared to the intubation-only group (2.8% vs 9.2%, P value .0001). Patients who underwent tracheostomy were more likely to be discharged to an inpatient rehab facility (IRF) (7.6% vs 3.9%, P value .0004), long term acute care hospital (LTACH) (33.9 vs 38.9%, P value .0001), or short-term general hospital (2.8% vs 6.1%, P value .01). Interestingly, more of the tracheostomy patients were obese (28.6% vs 22.1%, P value .003). The tracheostomy group had more cases of VAP, PE, AKI, and ARDS. In total, 9.9% of the tracheostomy group had VAP compared to 1.9% of the control group, with an adjusted odds ratio (aOR) of 5.57, 95% confidence interval (CI) of 3.75 to 8.26, and P value of <.0001. The tracheostomy cohort had higher rates of PE, 5.3% vs 3.2% (aOR 1.83, 95% CI 1.14–2.92, P value .01), AKI (aOR 1.36, 95% CI 1.08–1.84, P value .01), and ARDS (aOR 1.41, 95% CI 1.08–1.84, P value .01). The tracheostomy cohort also had a longer mean HLOS, 35.8 days (SD ± 16.8) compared to 16.4 days (SD ± 13.0) (P value <.0001). The tracheostomy group had more cases of VAP, PE, AKI, and ARDS. In total, 9.9% of the tracheostomy group had VAP compared to 1.9% of the control group, with an adjusted odds ratio (aOR) of 5.57, 95% confidence interval (CI) of 3.75 to 8.26, and P value of <.0001. The tracheostomy cohort had higher rates of PE, 5.3% vs 3.2% (aOR 1.83, 95% CI 1.14–2.92, P value .01), AKI (aOR 1.36, 95% CI 1.08–1.84, P value .01), and ARDS (aOR 1.41, 95% CI 1.08–1.84, P value .01). The tracheostomy cohort also had a longer mean HLOS, 35.8 days (SD ± 16.8) compared to 16.4 days (SD ± 13.0) with a P value <.0001. The tracheostomy cohort also had a longer mean total days on mechanical ventilation, 21.6 (SD ± 15.8) compared to 7.4 (SD ± 8.7) with a P value <.0001.

Tables 3 and 4 subanalyzed these patients into 3 groups, an early tracheostomy group (days 0–10 after intubation) compared to a late group (days 11+ after intubation), compared to the control group. The early tracheostomy group contained 150 patients, and the late tracheostomy group contained 245 patients. The early tracheostomy group had a mortality rate of 44.7% vs 33.1% for the late group and 54.4% for the endotracheal intubation-only group. The adjusted likelihood of mortality for the early tracheostomy group was aOR 0.73 (95% CI 0.52–1.01) and for the late group an aOR of 0.44 (95% CI 0.34–0.58). The early tracheostomy group’s mean age was 62.5 years old (SD ± 13.5). The late tracheostomy group’s mean age was 61.5 years old (SD ± 12.2). The intubation-only group mean age was 64.9 years old (SD ± 14.4). Again, both early and late tracheostomy groups were less likely to be discharged home (P value <.0001) and more likely to be discharged to IRF (P value .001), LTACH (P value <.0001), or short-term general hospital (P value .02). Differences in comorbidities were not statistically significant. However, patients in both the early and late tracheostomy groups had a higher BMI compared to the control group (P value .01). There were higher rates of VAP in both early (6.7%, aOR 3.79, 95% CI 1.94–7.42) and late tracheostomy groups (11.8%, aOR 7.13, 95% CI 4.62–11.00), compared to 1.9% in the control group. There were higher rates of PE in the early group (6.0%, aOR 2.06, 95% CI 1.03–4.13) and similar PE rates in the late tracheostomy group (4.9%, aOR 1.68, 95% CI 0.92–3.08), compared to 3.2% in the control group. There were also higher rates of ARDS in the late group (22.9%, aOR 1.75, 95% CI 1.28–2.40) and no differences in the ARDS rates in the early tracheostomy groups (12.7%, aOR 0.90, 95% CI 0.55–1.46), compared to 13.8% in the control group. The early tracheostomy group had a longer mean HLOS of 31.6 days (SD ± 16.7 days) with an adjusted P value <.0001 compared to the intubation-only group’s 16.4 days (SD ± 13 days). The late tracheostomy group had an average HLOS of 38.4 days (SD ± 16.3 days) with an adjusted P value <.0001 compared to the intubation-only group’s 7.4 days (SD ± 8.7 days). The late tracheostomy group also had a longer mean TMVD of 23.6 days (SD ± 16.4 days) with an adjusted P value <.0001 compared to the intubation-only group.

Table II

| Tracheostomy (N = 395) | Endotracheal intubation only (N = 5,516) | P values | Adjusted P values* |
|------------------------|-----------------------------------------|----------|--------------------|
| **Inpatient mortality**|                                        |          |                    |
| Ventilator-associated pneumonia (VAP) | 37.5% | 54.4% | <.0001 | <.0001 |
| Pulmonary embolism (PE) | 5.3% | 1.9% | <.0001 | <.0001 |
| Acute myocardial infarction (MI) | 12.2% | 14.6% | .019 | .13 |
| Cerebral infarction (CVA) | 2.0% | 1.3% | .26 | .22 |
| Acute kidney injury (AKI) | 72.4% | 67.0% | .03 | .01 |
| Acute respiratory distress syndrome (ARDS) | 19.0% | 13.8% | .004 | .01 |
| Mean hospital length of stay (HLOS) | 35.8 (±16.8) | 16.4 (±13.0) | <.0001 | <.0001 |
| Mean total mechanical ventilation days (TMVD) | 21.6 (±15.8) | 7.4 (±8.7) | <.0001 | <.0001 |

BMI, body mass index; * Adjusted by age, race, sex, insurance status, BMI, tobacco smoker, Charlson Comorbidity Index.
Tables 5 and 6 further subanalyze these patients into 8 cohorts based on the day of tracheostomy after intubation compared to the control group. In total, 60 patients were included in the days 0–2 after intubation group, 39 patients in the days 3–6 group, 51 patients in the days 7–10 group, 76 patients in the days 11–14 group, 58 patients in the days 15–18 group, 47 patients in the days 19–22 group, and 64 patients in the day 23+ group. Ages were similar in all groups except for more patients over 85 years old in the control group (P value .03). More patients were discharged to LTACH in all tracheostomy groups compared to the control group (P value <.001). In terms of inpatient mortality, days 0–2 had a statistically significantly lower inpatient mortality rate of 36.7% (aOR 0.51, 95% CI 0.30–0.88). Days 3–6 and days 7–10 had no differences in inpatient mortality. Days 11–14 had a statistically significantly lowered inpatient mortality rate of 32.9% (aOR 0.45, 95% CI 0.27–0.73), and days 19–22 had a statistically significantly lowered inpatient mortality rate of 29.8% (aOR 0.39, 95% CI 0.21–0.73), while days 23 and beyond had the lowest statistically significant inpatient mortality rate of 26.6% (aOR 0.31, 95% CI 0.18–0.55) (Figure 2).

Comparing the early versus late tracheostomy groups, the lowest inpatient mortality rate in the early tracheostomy group was between days 0 and 2 (36.7%, aOR 0.51, 95% CI 0.30–0.88), and the highest was between days 3 and 6 (53.9%, aOR 1.10, 95% CI 0.58–2.10). In the late tracheostomy group, the lowest inpatient mortality rate was on days 23 and beyond (26.6%, aOR 0.31, 95% CI 0.18–0.55), whereas the highest inpatient mortality rate appeared

### Table III

Early versus late versus control cohort demographics and comorbidities

|                   | Tracheostomy days 0–10 after intubation (early) (N = 150) | Tracheostomy days 11+ after intubation (late) (N = 245) | Endotracheal intubation only (N = 5,516) | P values |
|-------------------|----------------------------------------------------------|-------------------------------------------------------|----------------------------------------|----------|
| **Age, y**        |                                                          |                                                       |                                        |          |
| 18–44             | 10.0%                                                    | 8.6%                                                  | 9.2%                                   | .89      |
| 45–54             | 17.3%                                                    | 18.8%                                                 | 13.2%                                  | .02      |
| 55–64             | 24.0%                                                    | 30.2%                                                 | 22.3%                                  | .01      |
| 65–74             | 29.3%                                                    | 28.6%                                                 | 27.9%                                  | .90      |
| 75+               | 16.0%                                                    | 12.2%                                                 | 20.4%                                  | .004     |
| ≥85               | 3.3%                                                     | 1.6%                                                  | 7.0%                                   | .001     |
| **Age, y (mean)** | 62.5 (±13.5)                                             | 61.5 (±12.2)                                          | 64.9 (±14.4)                           | .0002    |
| **Age, y (median)** | 64                                                      | 62                                                   | 66                                     |          |
| **Age, y (mode)** | 55                                                       | 63                                                   | 71                                     |          |
| **Sex**           |                                                          |                                                       |                                        |          |
| Male              | 53.3%                                                    | 58.0%                                                 | 59.9%                                  | .24      |
| Female            | 46.7%                                                    | 42.0%                                                 | 40.1%                                  | .24      |
| **Race**          |                                                          |                                                       |                                        |          |
| White             | 54.7%                                                    | 47.8%                                                 | 49.9%                                  | .40      |
| Black             | 19.3%                                                    | 14.3%                                                 | 20.7%                                  | .05      |
| Asian             | 3.3%                                                     | 6.5%                                                  | 2.9%                                   | .01      |
| Other             | 16.0%                                                    | 28.2%                                                 | 23.2%                                  | .02      |
| Unknown           | 6.7%                                                     | 3.3%                                                  | 3.3%                                   | .08      |
| **Insurance**    |                                                          |                                                       |                                        |          |
| Blue Cross/Cost   | 6.0%                                                     | 3.3%                                                  | 2.5%                                   | .02      |
| Commercial        | 13.3%                                                    | 20.8%                                                 | 12.4%                                  | .001     |
| Government        | 8.0%                                                     | 7.4%                                                  | 11.9%                                  | .03      |
| Medicaid          | 14.0%                                                    | 15.9%                                                 | 10.4%                                  | .01      |
| Medicare          | 54.0%                                                    | 47.4%                                                 | 56.9%                                  | .01      |
| Other             | 4.0%                                                     | 4.1%                                                  | 4.6%                                   | .88      |
| Self-pay          | 0.7%                                                     | 0.4%                                                  | 0.9%                                   | .67      |
| Worker’s comp.    | 0.0%                                                     | 0.8%                                                  | 0.4%                                   | .44      |
| **Hospital disposition** |                                                       |                                                       |                                        |          |
| Home              | 4.0%                                                     | 2.0%                                                  | 9.2%                                   | <.0001   |
| Home under care   | 2.0%                                                     | 3.3%                                                  | 4.4%                                   | .25      |
| Inpatient rehab facility (IRF) | 6.0%                      | 8.6%                                                 | 3.9%                                   | .001     |
| Long-term acute care hospital (LTACH) | 24.7%                      | 39.6%                                                | 3.8%                                   | <.0001   |
| Short-term general hospital | 4.0%                      | 2.0%                                                 | 6.1%                                   | .02      |
| Skilled nursing facility (SNF) | 2.7%                      | 3.7%                                                 | 5.1%                                   | .25      |
| Expired           | 44.7%                                                    | 33.1%                                                 | 54.4%                                  | <.0001   |
| Hospice           | 12.0%                                                    | 7.4%                                                  | 11.8%                                  | .1       |
| Others            | 0.0%                                                     | 0.4%                                                  | 1.2%                                   | .22      |
| **Comorbidities**|                                                          |                                                       |                                        |          |
| Coronary artery disease (CAD) I25.10 | 20.0%                      | 16.3%                                                | 22.2%                                  | .08      |
| Congestive heart failure (CHF) I50 | 28.7%                      | 24.1%                                                | 25.7%                                  | .60      |
| Malignant neoplasm C80.1 | 0.7%                      | 0.0%                                                  | 0.2%                                   | .27      |
| Chronic obstructive pulmonary disease (COPD) J44.9 | 0.7%                      | 3.7%                                                  | 2.0%                                   | .1       |
| Asthma I45        | 6.0%                                                     | 8.2%                                                  | 6.7%                                   | .66      |
| History of stroke (CVA) I63.9 | 1.3%                      | 2.5%                                                  | 1.3%                                   | .35      |
| Alzheimer’s disease G30.9 | 0.0%                      | 0.4%                                                  | 1.3%                                   | .19      |
| Diabetes E11.9    | 16.7%                                                    | 13.1%                                                 | 14.0%                                  | .58      |
| Chronic kidney disease (CKD) N18.9 | 10.7%                      | 10.6%                                                | 10.0%                                  | .91      |
| Cannabis use F12.90 | 1.3%                      | 0.4%                                                  | 0.6%                                   | .50      |
| Alcohol abuse F10.1 | 2.0%                      | 1.6%                                                  | 1.7%                                   | .95      |
| Obesity (BMI >30) E66.9 | 27.3%                      | 29.4%                                                | 22.1%                                  | .01      |
| Tobacco smoker F17.200 | 2.7%                      | 4.5%                                                  | 4.6%                                   | .54      |

BMI, body mass index.
In terms of secondary outcomes, VAP was statistically significantly higher in all groups compared to the control group, with the highest contained in the group of patients who underwent tracheostomy between days 7 and 10 (3.9%, aOR 2.25, 95% CI 1.22–1.40) and days 11–14 (6.6%, aOR 4.86, 95% CI 1.88–12.51). In contrast, we noted a statistically significantly lower incidence of VAP in the days 1–6 group (1.13%) compared to the control group (3.72%).

To be between days 15 and 18 (43.1%, aOR 0.67, 95% CI 0.39–1.13). Overall, the lowest inpatient mortality rate among all days was on days 23 and beyond. The highest inpatient mortality rate among all days was between days 3 and 6.

In terms of secondary outcomes, VAP was statistically significantly higher in all groups compared to the control group, with the highest contained in the group of patients who underwent tracheostomy between 19 and 22 days (17.0%, aOR 10.13, 95% CI 4.54–22.59) and the lowest contained in the group who underwent tracheostomy between days 7 and 10 (3.9%, aOR 2.25, 95% CI 0.54–9.47) compared to 1.9% in the control group. The rest of the VAP secondary outcomes are as follows: days 0–2 (8.3%, aOR 4.86, 95% CI 1.88–12.51), days 3–6 (7.7%, aOR 4.10, 95% CI 1.22–13.73), days 11–14 (6.6%, aOR 4.86, 95% CI 1.88–12.51), days 15–18 (13.8%, aOR 7.64, 95% CI 3.46–16.88), days >23 (12.5%, aOR 6.86, 95% CI 3.14–14.99). PE was statistically significantly higher in days 3–6 (10.3%, aOR 3.56, 95% CI 1.24–10.24) and days 15–18 (8.6%, aOR 3.37, 95% CI 1.32–8.65) compared to 3.2% in the control group. There were no differences in the other groups. MI was statistically significantly lower in the days 11–14 group (6.6%, aOR 0.37, 95% CI 0.15–0.95) compared to 14.6% in the control group. There were no differences in the other groups. MI was statistically significantly lower in the days 11–14 group (6.6%, aOR 0.37, 95% CI 0.15–0.95) compared to 14.6% in the control group. There were no differences in the other groups. MI was statistically significantly lower in the days 11–14 group (6.6%, aOR 0.37, 95% CI 0.15–0.95) compared to 14.6% in the control group. There were no differences in the other groups. MI was statistically significantly lower in the days 11–14 group (6.6%, aOR 0.37, 95% CI 0.15–0.95) compared to 14.6% in the control group. There were no differences in the other groups. MI was statistically significantly lower in the days 11–14 group (6.6%, aOR 0.37, 95% CI 0.15–0.95) compared to 14.6% in the control group. There were no differences in the other groups. MI was statistically significantly lower in the days 11–14 group (6.6%, aOR 0.37, 95% CI 0.15–0.95) compared to 14.6% in the control group. There were no differences in the other groups. MI was statistically significantly lower in the days 11–14 group (6.6%, aOR 0.37, 95% CI 0.15–0.95) compared to 14.6% in the control group. There were no differences in the other groups. MI was statistically significantly lower in the days 11–14 group (6.6%, aOR 0.37, 95% CI 0.15–0.95) compared to 14.6% in the control group. There were no differences in the other groups. MI was statistically significantly lower in the days 11–14 group (6.6%, aOR 0.37, 95% CI 0.15–0.95) compared to 14.6% in the control group. There were no differences in the other groups. MI was statistically significantly lower in the days 11–14 group (6.6%, aOR 0.37, 95% CI 0.15–0.95) compared to 14.6% in the control group. There were no differences in the other groups. MI was statistically significantly lower in the days 11–14 group (6.6%, aOR 0.37, 95% CI 0.15–0.95) compared to 14.6% in the control group. There were no differences in the other groups. MI was statistically significantly lower in the days 11–14 group (6.6%, aOR 0.37, 95% CI 0.15–0.95) compared to 14.6% in the control group. There were no differences in the other groups.

**Table IV**

| Early versus late versus control cohort outcomes | Tracheostomy days 0–10 after intubation (early) (N = 150) | Tracheostomy days 11+ after intubation (late) (N = 245) | Endotracheal intubation only (N = 5,516) |
|-------------------------------------------------|----------------------------------------------------------|---------------------------------------------------------|----------------------------------------|
| **Inpatient mortality**                          |                                                          |                                                          |                                        |
| Odds ratio                                       | 0.68 (0.49, 0.94)                                        | 0.41 (0.32, 0.54)                                        | 0.91 (0.73, 1.24)                      |
| Adjusted ratio*                                  | 0.72 (0.52, 1.01)*                                        | 0.44 (0.34, 0.58)*                                       | 0.82 (0.64, 1.05)*                     |
| Ventilator-associated pneumonia                 | 6.7%                                                     | 11.8%                                                   | 1.9%                                   |
| Pulmonary embolism (PE)                         | <0.001 (<0.001, >999)                                    | <0.001 (<0.001, >999)                                    |                                        |
| Acute myocardial infarction (MI)                | 6.0%                                                     | 4.9%                                                    | 3.2%                                   |
| Cerebral infarction (CVA)                       | 0.70 (0.42, 1.18)                                        | 0.88 (0.60, 1.29)                                        | 14.6%                                 |
| Acute kidney injury (AKI)                       | 0.72 (0.42, 1.23)*                                       | 0.82 (0.55, 1.22)*                                       | 1.3%                                   |
| Acute respiratory distress syndrome (ARDS)     | 1.3%                                                     | 1.3%                                                    | 67.0%                                  |
| Ventilator associated pneumonia (VAP)           | 0.99 (0.24, 4.09)                                        | 1.85 (0.80, 4.29)                                        | 22.9%                                  |
| Mean hospital length of stay (HLOS)             | 31.6 (±16.7)                                             | 38.4 (±16.3)                                             | 16.4 (±13.0)                           |
| P value                                         | .0001                                                    | .0001                                                   |                                        |
| Adjusted P value                                | .0001                                                    | .0001                                                   |                                        |
| Mean total mechanical ventilation days (TMVD)    | 18.3 (±14.1)                                             | 23.8 (±16.4)                                             | 7.4 (±8.7)                             |
| P value                                         | .0001                                                    | .0001                                                   |                                        |
| Adjusted P value                                | .0001                                                    | .0001                                                   |                                        |
| Mean additional mechanical ventilation days     | 8.3–18.3                                                 | 0–12.6                                                  |                                        |

BMI, body mass index.

* Adjusted by age, race, sex, insurance status, BMI, tobacco smoker, Charlson Comorbidity Index.

Discussion

Our study represents a large multicenter experience with COVID-19 and outcomes of patients who have had the benefit of guidance from earlier studies on the timing and indications for tracheostomy among COVID-19 patients.14–16 We hypothesized that COVID-19 tracheostomy patients would have lowered inpatient mortality and that there may be an optimal time for tracheostomy placement.

Out of 5,516 critically ill COVID-19 patients requiring endotracheal intubation, there was an overall inpatient mortality rate of 54.4%. In contrast, 395 tracheostomy patients had a significantly lower inpatient mortality rate of 37.5% (adjusted P value <.0001). Our results are similar to a previous study that suggested an improved 30-day survival among 164 total COVID-19 patients (with similar APACHE-III scores) who underwent tracheostomy placement (85% vs 42% in the non-tracheostomy group).16

In terms of best timing, a recent study of 80 COVID-19 infected patients who underwent tracheostomy found that tracheostomies placed within 14 days were associated with increased mortality.17
Contrary to this, a Cochrane review showed lowered mortality rates in the early (tracheostomy in less than 10 days) compared with the late tracheostomy group (RR 0.83, 95% CI 0.70–0.98; P value .03).\textsuperscript{15}

Before COVID-19, studies such as the multicenter randomized TracMan trial found no difference in 30-day mortality when they compared 455 patients undergoing early tracheostomy within 4...
days and 454 patients undergoing late tracheostomy after 10 days. Although there are limited data and some discordance as to when to perform an early or late tracheostomy, our data does provide additional insight as to timing. While both our early (<10 days) and late (>10 days) had lower overall mortality rate compared to the control (endotracheal intubation-only) cohort, inpatient mortality was significantly lower only in the late tracheostomy (>10 days) group OR 0.44 95% CI (0.34–0.58). In our subset 8 cohort interval time analysis, the raw percentage of inpatient mortality was lower in all exposure groups compared to the control group. Three of the 4 intervals in the late group were significantly lower for mortality compared to the control group (11–14 days, 19–22 days, and 23+ days), compared to 1 of the 3 intervals in the early group (0–2 days) (Table 6).

Critics of tracheostomy creation in patients with COVID-19 have emphasized the potential risk of transmission to health care workers as well as higher risk of surgical bleeding due to coagulopathy and anticoagulant use associated with COVID-19. However, multiple studies have suggested that tracheostomy in actively infected COVID-19 patients is safe for patients and surgeons. In a study that included 98 COVID-19 patients with tracheostomy (mean time from intubation to procedure 10.6 ± 5 days) from March 10th to April 15th, 2020, during the peak of the pandemic, only 5 of the 98 patients had tracheostomy-related bleeding, and no cases of health care workers transmission were found. Another study performed a tracheostomy on 62 patients at 10 to 14 days after intubation and found that there were no signs of transmission to health care workers. A study from Brazil reported tracheostomy on 98 patients within 4 to 5 days of intubation. None of their team members were symptomatic or found to have COVID-19 despite early tracheostomy. In a recent study, 50 patients underwent tracheostomies with a median time from intubation to tracheostomy at 9 days, and no infections among surgeons were identified at the end of the study.

Although our results contribute to the discussion of optimal timing, we believe that this is a highly individualized and systems-based practice. While ICUs become overwhelmed with COVID-19 patients, clinicians may be faced with decisions to alleviate resource shortages that continue to uphold a high quality of patient care. Taking this into consideration, tracheostomy at 11 days or later is associated with overall lower inpatient mortality. While the overall mortality was not lower for the early cohort, subset analysis suggests that the earliest period (0–2 days) would be the optimal time to perform an early tracheostomy. Regardless of timing, it is important to minimize the risk of transmission to the surgical team. We support the recommendations by the global multidisciplinary consortium for proper preparation of tracheostomy in these patients. Their recommendations include preoxygenation followed by a trial of apnea in the ICU, putting the patient in the supine position, with an FiO2 of 100% and passive end-expiratory pressure (PEEP) of 5 to assess if the patient can tolerate the procedure. Also recommended are enhanced PPE, such as N95 masks, eye protection, surgical gown, and gloves. The discharge destination differences between patients with tracheostomy versus those without are likely because places such as inpatient rehabilitation facilities would require tracheostomy as part of their acceptance criteria. Second, with more patients surviving in the tracheostomy cohort, they would likely need higher acuity posthospitalization care IRF (7.6% vs 3.9%, P value .0004), LTACH (33.9 vs 3.8%, P value .0001), and short-term general hospital (2.8% vs 6.1%, P value .01). It is also logical to assume that patients with COVID-19 who survived would have had a longer hospital length of stay. This is evident in the tracheostomy cohort (35.8 ± 16.8 days vs 16.4 ± 13.0 days, P value <.0001). However, better survival, longer HLOS, and longer TMVD will predispose patients to competing risks, where patients who live longer will be more likely exposed to complications. This was seen in the tracheostomy cohort where they endured significantly more complications such as VAP, PE, MI, and ARDS.

There are several limitations to this study. First, this is a retrospective cohort study; thus we cannot attribute cause and effect toward our results. Specifically, we cannot say that performing tracheostomy in COVID-19 patients will cause a decrease in mortality. However, we can state that there is a significant association toward deceased death even after adjusting for age, race, sex, insurance status, obesity, smoking status, and Charlson Comorbidity Index. Second, our data set did not allow for adjustment of the severity of critical illness such as the SOFA score or APACHE II score. It is possible that the control group had patients who were more severely ill and that they simply died sooner than the tracheostomy group. While this may have been true, the tracheostomy group did have significantly more severe cardiopulmonary complications such as ventilator-associated pneumonia, pulmonary embolism, and ARDS. Thus, the degree of severity of illness may not have been greatly different between the 2 cohorts. Third, COVID-19 positivity at the time of tracheostomy was not routinely documented. The Centers for Disease Control and Prevention (CDC) states that isolation can be discontinued after 10 days after symptom onset. It is possible that our results and other studies whose results showed that mortality is significantly lower at 11 days after intubation may merely have been reporting resolution of COVID-19 infection rather than the benefits of tracheostomy placement. However, patients who require tracheostomy after 2 or more weeks after COVID-19 infection can also be classified as experiencing the long-term symptoms of COVID-19. Regardless, a survivor bias should be considered when interpreting our results. Finally, our sample size may have been too small to see a significant difference in the early tracheostomy cohort. We did see a trend toward decreased mortality, but the lack of significance suggests that the survival benefit is much smaller than the late tracheostomy group and would require a larger sample size to discern significant differences. Lastly, we did include patients who underwent tracheostomy within days 0–2 of intubation. Although this may represent a unique population with specific comorbidities, we chose to include this subset in the analysis to compare with the TracMan randomized control trial, which compared early versus late tracheostomy patients, where the early tracheostomy patients underwent tracheostomy within 4 days.

In conclusion, tracheostomy in COVID-19 patients appears to be safe and may be associated with lower mortality. Our results suggest that late tracheostomy at day 11 is associated with lower mortality. However, it is uncertain whether the decreased mortality is due to the resolution of COVID-19 infection or the benefits of tracheostomy placement itself. In addition, the smaller sample size in the early tracheostomy patients may not have underpowered to observe a significant difference. Future studies should focus on the early tracheostomy patients as there was a trend toward decreased mortality in this cohort of patients in comparison to patients who had endotracheal intubation only.

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**Conflict of interest/Disclosure**

The authors have no related conflicts of interest to declare.
Supplementary materials

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