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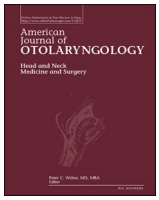

Nine-month outcomes of tracheostomy in patients with COVID-19: A retrospective study

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ABSTRACT

Purpose: The outcome of performing a tracheostomy in patients with coronavirus disease (COVID-19) seems promising based on the reported 30-day survival rate. However, long-term outcomes are still lacking. Therefore, our aim in this study was to evaluate the long-term outcomes of tracheostomy performed in critically ill COVID-19 patients.

Methods: This was a retrospective analysis of 27 COVID-19 patients on whom tracheostomy was performed between February 28, 2020, and April 7, 2020, at Tongji Hospital (Wuhan, China). Patients' clinical characteristics, complications, and outcomes were analyzed.

Results: All patients underwent successful bedside tracheostomy. Thirteen patients (48.1%) were successfully weaned off ventilation within 1 month. The survival rate at one, three, and nine months after tracheostomy were 63.0%, 37.0%, and 29.6%, respectively. At nine months after tracheostomy, 8/27 patients had survived, with five (62.5%) being discharged home while the remaining were dependent on nursing care.

Conclusion: The survival rate of COVID-19 patients who underwent tracheotomy decreased markedly from 1 to 3 months after tracheotomy, remaining stable between 3 and 9 months. Medical support is much needed for COVID-19 patients over the first 90 days after tracheotomy.

1. Introduction

Coronavirus disease (COVID-19) is spreading globally. As of Feb 12, 2021, more than 408 million people have been infected globally, with over 5 million deaths. The disease may cause acute progressive respiratory failure and even death. Early studies revealed that approximately 20–25% of patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection developed acute respiratory distress syndrome (ARDS) and required admission to the intensive care unit (ICU) [1–3]. Invasive mechanical ventilation, including endotracheal intubation, is required for some critically ill patients. For patients who require prolonged intubation, tracheostomy may be considered important for optimal respiratory care. Recent studies have reported on the short-term outcomes [4–6], with a higher 30-day survival and shorter ICU stay for patients who received tracheostomy than non-tracheostomized patients [6]. To the best of our knowledge, no previous study has described the long-term (>3 months) outcomes of tracheostomy among COVID-19 patients. In this study, we retrospectively analyzed 27 critically ill patients with COVID-19, who underwent tracheostomy in a medical center in Wuhan, focusing on the long-term outcomes.

2. Methods

2.1. Statement of ethics

Our study was approved by the Ethics Committee of Tongji Hospital and written informed consent was obtained from patients' legal representative.

2.2. Study design and group

This was a retrospective descriptive case series on long-term outcome after tracheostomy. Twenty-seven patients with a confirmed COVID-19 diagnosis who underwent tracheostomy between February

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28, 2020, and April 7, 2020, at Tongji Hospital affiliated with Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, were documented.

2.3. Clinical cases

The clinical characteristics of the patients in our study group are detailed in Table 1. All patients received invasive mechanical ventilation on admission to the ICU, with 10 treated using extracorporeal membrane oxygenation (ECMO). Anticoagulant therapy was administered to all patients owing to increased coagulation activity; of note, anticoagulant therapy was suspended in five cases after occurrence of cerebral hemorrhage or gastrointestinal bleeding.

2.4. Outcomes

The endpoint of follow-up was 9 months after tracheotomy or death, whichever occurred earlier. The primary outcome was the survival rate at 9 months. Secondary outcomes were successful weening from mechanical ventilation within 1 month of tracheostomy, survival rate at 1 and 3 months after tracheostomy, and cause of death. Variables associated with death and liberation from mechanical ventilation with one month were analyzed. We performed propensity score matching (PSM) in 27 patients undergoing tracheostomy to compare long-term survival with case-matched cohort consisting of patients with closely matched clinical characteristics who received mechanical ventilation but had no tracheostomy. Twelve variables for PSM matching were selected, including demographic data, duration from illness onset to intubation, laboratory test results, and comorbidities (Table 3). The propensity scores for receiving one treatment option (tracheostomy or no tracheostomy) were calculated using the logistic regression model. The continuous variables in groups were compared using Student's *t*-tests (normally distributed) or Mann-Whitney *U* test (non-normally distributed), while the categorical variables were analyzed by the Fisher's exact test or $\chi 2$ test. The Kaplan-Meier method was used to assess survival with significance calculated using the log rank test.

2.5. Medical staff, instruments, and procedures

The medical staff included two skilled surgeons and an intensive care specialist responsible for administering anesthesia and monitoring patients. Tracheostomies were performed in a single, well-ventilated ICU room to avoid unnecessary transportation. The procedures for bedside open tracheostomy and percutaneous tracheostomy have been detailed in previous literature, including one of our previous studies [7,8].

3. Results

The median age of the patients in our study group was 67 (range, 38–86) years. Twenty-two (81.5%) patients had at least one underlying comorbidity, the most common being hypertension (59.3%), diabetes (37.0%), cerebrovascular disease (33.3%), coronary heart disease (22.2%), and malignancy (7.4%). The median duration from the onset of illness to tracheostomy was 43 (range, 10–90) days. The median intubation period was 26 (range, 5–50) days. No deaths were attributed to the tracheostomy procedure.

The overall survival rate at 1, 3, and 9 months after tracheostomy were 63.0%, 37.0%, and 29.6%, respectively (Fig. 1). The median time from tracheostomy to death was 29 (range, 4–236) days. At the final time-point of follow-up at 9 months, 8 of 27 (29.6%) patients had survived, resulting in a 9-month mortality rate of 70.4%. Among the eight patients who survived, five (62.5%) were discharged home. The other three remained dependent on nursing care, two of whom remained cannulated. Within 30 days after tracheostomy, 10 patients had died of respiratory failure (9/10) and cerebral hemorrhage (1/10). Between 30 and 90 days after tracheostomy, seven patients died of respiratory failure (cases 2, 10, and 24), gastrointestinal hemorrhage (case 14), cerebral hemorrhage (case 17), sepsis (case 8), and acute myocardial infarction (case 23). At the 3-month follow-up, two more patients had died of cerebral hemorrhage (cases 4 and 6). Among the 13 out of 27 patients who were successfully weaned off ventilation within 30 days, eight patients died. Among the other 14 patients who failed to be liberated from ventilation in the first month, only one survived until the 9th month. Accordingly, there was a significant correlation between mortality and the incidence of weaning success within 30 days ($P < 0.05$, Table 2).

We were able to match 27 COVID-19 patients (tracheostomy group) to 27 patients (no tracheostomy group) at a ratio of 1:1 (Table 3), using the nearest neighboring method. Before propensity score matching, the neutrophil count was lower in the no tracheostomy group, compared with the tracheostomy group ($P = 0.001$) (Table 3). Hypertension tended to be more common in the tracheostomy group ($P = 0.08$) (Table 3). After matching, the two groups showed no significant differences in age, gender, duration from illness onset to intubation, laboratory test results, and comorbidities ($P > 0.05$). In the PSM cohort, the Kaplan-Meier survival of the two groups showed a significant difference ($P = 0.03$). The 9-month survival rate of the two groups was similar (29.2% in tracheostomy group vs. 25.9% in no tracheostomy group, $P = 1.00$).

4. Discussion

Recent retrospective studies have evaluated 1-month outcomes of tracheostomy in COVID-19 patients [5,6,8,9]. The 30-day survival of patients receiving tracheostomy was higher than that of non-tracheostomized patients [6]. However, no long-term outcome data are available yet. We observed that seven of 17 survivors at the 30-day follow-up died in the subsequent 2 months, highlighting the difficulty and complexity of the medical treatment of critically ill COVID-19 patients.

Prolonged intubation ($\geq$14 days) remains the most common indication for tracheostomy in critically ill COVID-19 patients [10,11]. In our study, 22 of 27 patients were intubated for >14 days. Our findings revealed a marked decrease in the survival rate from 1-month follow-up (62.9%) to the 3-month (37.1%) follow-up (Fig. 1). The cause of death for seven of 17 patients who died between the 1- and 3-month follow-up included respiratory failure (three patients), gastrointestinal or cerebral hemorrhage (two patients), and acute myocardial infarction (one patient). Autopsy of a COVID-19 patient lung tissue showed diffuse alveolar damage with cellular fibromyxoid exudates and hyaline membrane formation [12]. Moreover, a recently published elegant study showed that a considerable proportion COVID-19 patients who were discharged showed impaired pulmonary diffusion capacities and abnormal chest imaging manifestations at 5 months after symptom onset [13]. Our data also showed that respiratory failure is a leading cause of death (11/15) within 2 months after tracheostomy, especially within the first month (9/10).

Three months after tracheostomy, the survival rate was relatively stable. The cause of death among patients after the 3-month follow-up were varied. Two patients (cases 4 and 6) died of cerebral hemorrhage. Case 4 was of a 70-year-old male who had hypertension, diabetes, and coronary disease. Case 6 was of a 42-year-old male who developed multiple organ failure and had required repeated ECMO salvage. Considering that two other patients (case 17, 23) died of hemorrhage within 3 months after tracheostomy suggests that hemorrhage is a critical cause of death, especially after the 2-month time-point after tracheostomy (3/4 patients). According to a recent large cohort study, over 10% of COVID-19 patients discharged from hospital died within the subsequent 5 months [14]. The incidence of major adverse cardiovascular event (MACE, a composite of heart failure, myocardial infarction, stroke, and arrhythmia) is significantly higher among COVID-19 patients than the general population (24.4% vs 5.6%, respectively) over this 5-month period after discharge [14]. In agreement with these

Table 1
Clinical characteristics of patients.

Case No.	Age (years)	Gender	Duration from illness onset to intubation (days)	Duration of endotracheal intubation (days)	Comorbidity	Methods	ECMO	Duration since tracheotomy (days)	Cause of death	Duration of mechanical ventilation (days)	Duration from intubation to decannulation (days)	Weaning from ventilator in 30 days after tracheostomy	Outcome
1	60	M	20	9	None	PT	Yes	29	Respiratory failure, infectious shock	NA	NA	No	Deceased
2	70	M	27	5	Diabetes	PT	No	44	Respiratory failure	NA	NA	No	Deceased
3	55	F	13	27	Hypertension, diabetes	OT	No	NA	NA	34	NA	Yes	Partial recovery
4	70	M	10	27	CD, hypertension, diabetes	OT	No	236	Cerebral hemorrhage	45	NA	Yes	Deceased
5	65	F	13	21	CD, hypertension, diabetes	OT	No	NA	NA	41	201	Yes	Recovery
6	42	M	20	25	None	PT	Yes	91	Cerebral hemorrhage	62	64	No	Deceased
7	42	M	14	29	None	PT	Yes	NA	NA	34	36	Yes	Recovery
8	67	F	16	17	Hypertension, CHD, malignancy	OT	No	43	Sepsis	NA	NA	Yes	Deceased
9	55	F	24	26	Hypertension, diabetes	PT	No	NA	NA	46	56	Yes	Recovery
10	66	M	27	15	Hypertension, diabetes, CHD	PT	No	72	Respiratory and circulatory failure	NA	NA	Yes	Deceased
11	45	F	22	16	None	PT	Yes	10	Respiratory failure	NA	NA	No	Deceased
12	79	F	28	13	Hypertension	OT	Yes	24	Respiratory failure, multiple organ failure	NA	NA	No	Deceased
13	47	M	12	29	None	PT	Yes	21	Respiratory failure	NA	NA	No	Deceased
14	69	M	22	24	Hypertension, diabetes	OT	No	41	Gastrointestinal hemorrhage	NA	NA	Yes	Deceased
15	56	M	21	32	Hypertension	OT	Yes	NA	NA	112	116	No	Recovery
16	69	M	11	36	CD	OT	No	NA	NA	54	NA	Yes	Partial recovery
17	68	F	24	9	CD, hypertension, diabetes	OT	No	86	Cerebral hemorrhage	NA	NA	Yes	Deceased
18	67	M	20	33	CD	OT	No	18	Respiratory failure	NA	NA	No	Deceased
19	86	M	3	50	Hypertension, CHD, CD	PT	No	NA	NA	62	NA	Yes	Partial recovery
20	80	F	41	15	Hypertension	OT	Yes	6	Respiratory failure, infectious shock	NA	NA	No	Deceased
21	74	F	29	27	Hypertension, CHD	OT	No	13	Respiratory failure	NA	NA	No	Deceased
22	38	M	3	7	CD, Hypertension	PT	No	4	Cerebral hemorrhage	NA	NA	No	Deceased
23	47	M	27	26	Hypertension, diabetes	OT	Yes	44	Acute myocardial infarction	NA	NA	Yes	Deceased
24	81	F	34	37	CD	PT	No	32	Respiratory failure	NA	NA	No	Deceased
25	77	M	65	25	CD, CHD	OT	No	12	Respiratory failure	NA	NA	No	Deceased
26	69	M	10	32	CHD, malignancy	OT	No	NA	NA	52	55	Yes	Recovery
27	58	F	37	33	Hypertension, diabetes	OT	Yes	23	Respiratory failure, Multiple organ failure	NA	NA	No	Deceased

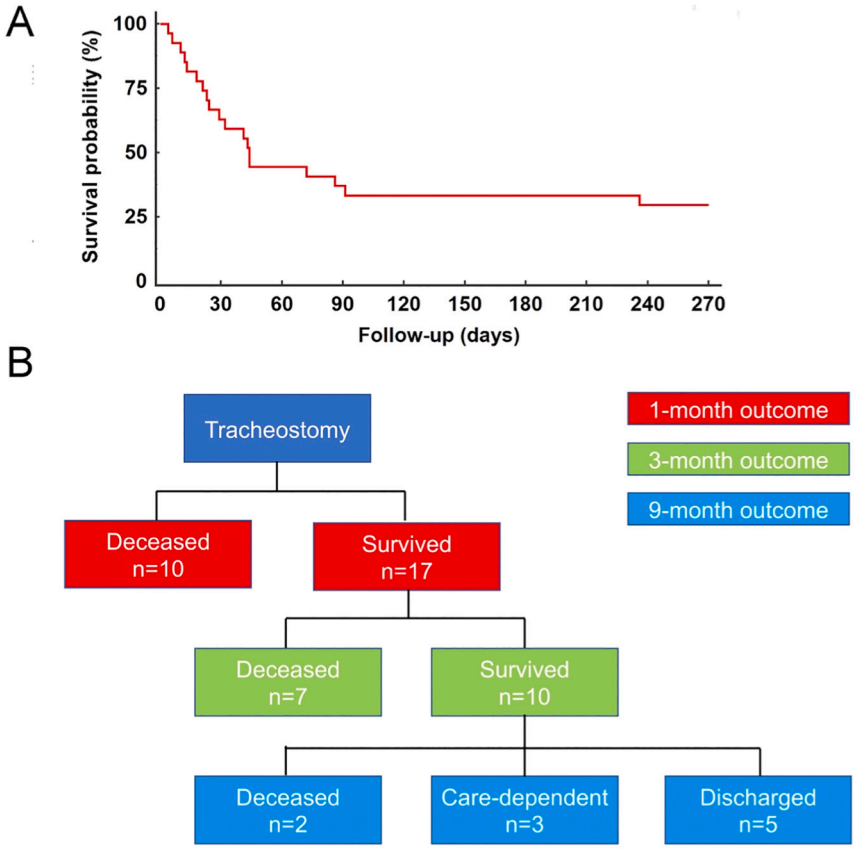

Fig. 1. Kaplan-Meier curve (A) and flowchart (B) of overall survival for patients from date of tracheostomy.

Table 2
Variables associated with nine-month outcome.

	Survived n = 8	Deceased n = 19	P
Age	62.13 ± 13.19	63.42 ± 13.58	0.82
Gender			1.00
Male	5	11	
Female	3	8	
Hypertension			0.67
Yes	6	11	
No	2	8	
Diabetes			1.00
Yes	3	7	
No	5	12	
Coronary heart disease			0.66
Yes	3	5	
No	5	14	
Cerebrovascular disease			0.63
Yes	1	6	
No	7	13	
Malignancy			1.00
Yes	1	2	
No	7	17	
Extracorporeal membrane oxygenation			0.67
Yes	2	8	
No	6	11	
Liberated from ventilation within 1 month[#]			
Yes	7	6	0.01
No	1	13	

The data was presented as means±standard error of the mean.
[#] $P < 0.05$.

findings, four of 17 patients in our study group died of organ hemorrhage after the 30-day follow-up. This finding emphasizes the importance of managing the coagulation system for long-term tracheostomized COVID-19 patients.

Evidence is lacking regarding whether performing tracheostomy contributes to better prognosis at 9-month follow-up. The prolonged life-sustaining treatment of critically ill COVID-19 is extremely resource intensive. Regarding mechanical ventilation for respiratory failure, it is generally accepted that a tracheostomy should not be considered in a person who cannot readily benefit from the advantages that the airway may offer [15]. Our data showed that liberation from ventilation with 1 month is the only risk-factor that is associated with the 9-month mortality. In the present study, 13 patients (48.1%) were successfully weaned off ventilation within 30 days, which is similar to the proportion (56.6%) reported by another group [5]. Thirteen out of 14 patients who failed to be weaned from ventilation in the first month died by the endpoint of follow-up at 9 months after tracheostomy. This may aid us in predicting the prognosis and evaluating the benefit of tracheostomy.

According to our paired adjustment for COVID-19 patients who were intubated for >14 days, compared with non-tracheostomy group, the tracheostomy group did not show statistically significant difference on 9-month mortality ($P > 0.05$, Fig. 2). The survival advantage of COVID-19 patients receiving a tracheostomy was seen significantly in 30-day outcomes in a previous study [6], which is also the scenario in our present study. However, this advantage was attenuated significantly due to increased death after one month in our tracheostomized group. There may be confounding factors including a selection bias of healthier patients for the non-tracheostomy group, and tracheostomy in patients with questionable prognoses. However, our data revealed that the advantage of performing tracheostomy in COVID-19 patients may need to be evaluated at a longer than 30-day follow-up.

This study has several limitations which should be acknowledged. First, our case series included only 27 patients, a relatively small sample,

Table 3
Characteristics of patients stratified by tracheostomy before and after propensity score matching.

	Unmached			Matched(1:1)		
	Tracheostomy (n = 27)	No tracheostomy (n = 64)	*P*	Tracheostomy (n = 27)	No tracheostomy (n = 27)	*P*
Age, median (IQR)	67 (55, 70)	68 (59.25, 73)	0.235	67 (55,70)	64 (55,73)	0.742
Male gender, n (%)	16(59.3%)	36(56.3%)	0.682	16(59.3%)	18(66.7%)	0.778
Duration from illness onset to intubation (days)	21 (13, 27)	19 (15,28)	0.814	21(13,27)	21(15, 28)	0.723
Leukocyte, median (IQR)	9.6 (7.28, 15.21)	15.42 (10.58, 19.55)	0.004	9.6(7.28, 15.21)	12.2(8.25, 17.59)	0.183
Neutrophil, median (IQR)	7.62 (6.25, 13.4)	13.76 (9.54, 18.10)	0.001	7.62(6.25,13.4)	11.34(7.57, 15.56)	0.085
lymphocyte, median (IQR)	0.71 (0.47, 0.79)	0.57 (0.42, 0.75)	0.328	0.71(0.47,0.79)	0.57(0.44, 0.76)	0.489
Procalcitonin, median (IQR)	0.58 (0.21, 1.26)	0.33 (0.11, 0.93)	0.192	0.58(0.21, 1.26)	0.36(0.1, 2.69)	0.533
Any comorbidity, n (%)						
Hypertension	16(59.3%)	26 (40.2%)	0.08	16(59.2%)	13(48.1%)	0.384
Diabetes	10(37%)	14 (21.9%)	0.215	10(37%)	7(25.9%)	0.558
Cardiovascular disease	5 (22.2%)	5 (7.8%)	0.155	5(22.2%)	4(14.8%)	1.000
Malignancy	2(7.4%)	5 (7.8%)	1.000	2(7.4%)	2(7.4%)	1.000
Cerebrovascular disease	9 (33.3%)	15 (23.4%)	0.796	9(33.3%)	8(29.6%)	1.000

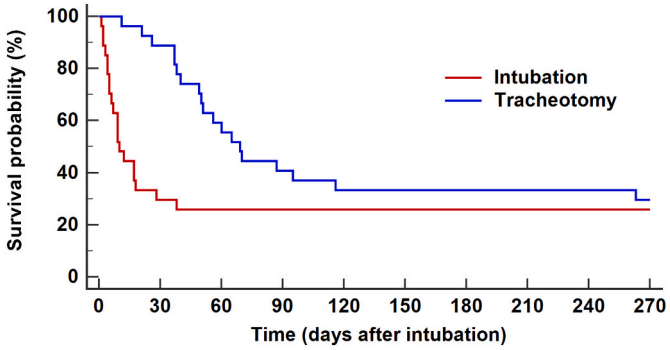

Fig. 2. Kaplan-Meier curves of overall survival for patients with or without tracheostomy from date of intubation.

from one center in Wuhan, China. Further recruitment, within the timeframe of our study, was not possible due to the fast resolution of the COVID-19 outbreak in Wuhan. Second, this is a retrospective and observational study. Third, due to the lack of knowledge and treatment guidelines when we encountered this newly identified disease, some of our treatments were empirical which may have influenced the final outcome. Multicenter collaborations with a larger sample size are better to address the entire picture as to long-term outcomes of tracheostomy for COVID-19 patients.

5. Conclusion

Our study showed that the survival rate of COVID-19 patients after tracheotomy decreased steadily in the first 90 days after tracheostomy, and patients stayed relatively stable after 90 days. Medical support is much needed for COVID-19 patients over the first 90 days after tracheotomy. Respiratory failure was the leading cause of death within the first 2 months after tracheotomy and organ hemorrhage thereafter. Whether tracheostomy in COVID-19 patients contributes to better clinical outcomes needs further investigation in future large-scale cohort studies.

Ethics approval and consent to participate

Ethics approval for this study was obtained from the Tongji hospital Ethics Board prior to the start of the study.

Consent for publication

All authors have reviewed the manuscript and consent for publication.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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CRediT authorship contribution statement

XL and ZL devised the project. XHZ, XBL, KX performed the surgery and collected patient data for study. XHZ, KX wrote the manuscript. ZL supervised the project and edited the manuscript. All authors read and approved the final manuscript.

Declaration of competing interest

The authors declare that they have no competing interests.

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