Early tracheostomy for managing ICU capacity during the COVID-19 outbreak: a propensity-matched cohort study

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ABSTRACT

BACKGROUND: During the first wave of the COVID-19 pandemic, shortages of ventilators and intensive care unit (ICU) beds overwhelmed healthcare systems. Whether early tracheostomy reduces the duration of mechanical ventilation and ICU stay is controversial.

RESEARCH QUESTION: Can “failure-free days” outcomes focused on ICU resources could help decide the optimal timing of tracheostomy in overburdened healthcare systems during viral epidemics?

STUDY DESIGN AND METHODS: This retrospective cohort study included consecutive patients with COVID-19 pneumonia tracheostomized in 15 Spanish ICUs during the surge, when ICU occupancy modified clinicians criteria to perform tracheostomy in COVID-19 patients. We compared ventilator-free days at 28 and 60 days and ICU- and hospital bed-free days at 28 and 60-days in propensity-score-matched cohorts tracheostomized at different timings (≤7 days, 8–10 days, 11–14 days after intubation).

RESULTS: Of 1939 patients admitted with COVID-19 pneumonia, 682 (35.2%) were tracheostomized, 382 (56%) within 14 days. Earlier tracheostomy was associated with more ventilator-free days at 28 days [≤7 vs. >7d (116 patients included in the analysis): median 9 days (IQR 0–15) vs. 3 (0–7), difference between groups 4.5 days, 95%CI (2.3 to 6.7); 8–10 vs. >10d (222 patients analysed): 6 (0–10) vs. 0 (0–6), difference 3.1 days, 95%CI (1.7 to 4.5); 11–14 vs. >14d (318 patients analysed): 4 (0–9) vs. 0 (0-2), difference 3 days, 95%CI (2.1 to 3.9)]. Except hospital bed-free days at 28 days, all other endpoints were better in early tracheostomy.

INTERPRETATION: Optimal timing of tracheostomy may improve patient outcomes and alleviate ICU capacity strain during the COVID-19 pandemic without increasing mortality. Tracheostomy within the first work on ventilator may particularly improve ICU availability.

Key words: tracheostomy, timing, capacity, resource, failure-free.

Abbreviations: ANOVA = ANalysis Of VAriance; APACHE II = Acute Physiology And CHronic Evaluation II; BFD = Bed Free-Days; COVID-19 = COronaVIrus Disease 2019; ECMO = ExtraCorporeal Membrane Oxygenation; ICU = Intensive Care Unit; FiO2 = Fraction of Inspired Oxygen; LOESS = LOcally Estimated Scatterplot Smoothing; LOS = Length Of Stay; PCR = Polymerase Chain Reaction; PEEP = Positive End Expiratory Pressure; SARS = Severe Acute Respiratory Syndrome; VFD = Ventilator Free-Days.

The severe acute respiratory syndrome (SARS) CoV-2 coronavirus that is responsible for coronavirus disease 2019 (COVID-19) pandemic overwhelmed critical care resources, making the management of intensive care unit (ICU) capacity a crucial challenge worldwide. Up to 20% of patients hospitalized with COVID-19 require ICU admission,[1] more than 50% of those admitted to ICUs need invasive ventilatory support,[2] and 30% of those undergoing mechanical ventilation are eventually tracheostomized,[3] due to the requirement for relatively prolonged respiratory support, or airway problems (eg. laryngeal edema associated with COVID-19 complicating airway management),[4] making it essential to optimize the patient´s prognosis and the use of ICU beds and ventilators. Various strategies have been suggested to overcome the shortage of these resources during the pandemic.[1,2]

Some data from studies done before the COVID-19 pandemic suggest that early tracheostomy reduces the length of mechanical ventilation and ICU stay,[,5,6,7,8] reduces ventilator-associated pneumonia,[8] and improves cost-effectiveness,[7] without modifying the mortality rate. However, methodological pitfalls in these studies preclude firm conclusions, and scant data are available in COVID-19 patients.[9] Furthermore, performing tracheostomy and post-tracheostomy care generate aerosols, placing healthcare professionals at risk, making it essential to protect them too.[10]

General guidelines on managing critically ill patients with COVID-19 include recommendations regarding tracheostomy,[11,12] and clinical decisions have been guided by recommendations based on expert opinion.[10,13–17] Expert recommendations on timing tracheostomy during the COVID-19 pandemic vary widely. One panel concluded that no specific timing could be recommended[17]; other panels recommend 7,[18] 10,[10] 14,[14,19] or 21 days[13,16,20] after intubation. These recommendations aim to balance benefits of earlier tracheostomy for patients and healthcare systems based on pre-COVID-19 evidence while minimizing risk for healthcare professionals, because infectivity declines over time.[10]

Pre-COVID-19 studies preclude definitive conclusions on the best timing of tracheostomy because they used heterogeneous outcome measures and definitions of early tracheostomy (2–14 days); moreover, they relied on physicians' predictions of which patients would require prolonged mechanical ventilation, limiting the ability of randomized trials[21-23] and of meta-analyses[5,6,8] to demonstrate a clear benefit for early tracheostomy.

Studies done after the appearance of COVID-19 have additional methodological pitfalls. Given the difficulties in performing randomized trials under pandemic conditions, all available evidence comes from observational studies. Moreover, the time-dependent outcomes of these studies are especially prone to selection, immortal-time, and competing-risk biases.[24] However, some characteristics of the COVID-19 pandemic actually favor the analysis of tracheostomy timing. COVID-19 is a more homogeneous clinical condition in which it is easier to predict whether a patient will require prolonged mechanical ventilation.[3,25] The surge in ICU admissions resulted in a high volume of tracheostomies, and tracheostomies were done earlier to allow patients to be discharged to wards. Finally, about 30-50% of patients with COVID-19 die under mechanical ventilation powering the failure-free days outcome but making it futile for many of these patients.[17,26]

Specific measures of the impact of different treatment strategies on the availability of ICU resources under these conditions are lacking. Composite outcome measures based on the "failure-free days" concept summarize the effect of an intervention on morbidity in the presence of the competing event of death.[26] Thus, we used ventilator-free days

(VFD) and ICU and hospital bed-free days (BFD) as measures of the effectiveness of tracheostomy in freeing up ICU and hospital resources during the COVID-19 outbreak to determine best timing of tracheostomy to optimize the clinical course of patients and the use of ventilators and beds during the surge.

STUDY DESIGN AND METHODS:

Study design:

This retrospective cohort study included all consecutive patients in 15 Spanish ICUs diagnosed with hypoxemic respiratory failure secondary to RT-PCR-confirmed COVID-19 pneumonia who were tracheostomized between February 15 and May 15, 2020. During the outbreak, attending physicians decided who, when, and how to tracheostomize based on ICU occupancy and anticipated benefit to the patient from tracheostomy. Criteria for tracheostomy included anticipated need for prolonged mechanical ventilation (≥10 days since tracheostomy); ventilator parameters (positive end-expiratory pressure ≤12 cm H_2O, FiO_2 ≤60%); no anticipated need for future prone positioning; any patient within24-36 hours of being placed on extra corporeal membrane oxygenation; and absence of negative prognostic indicators (i.e. high probability of death, coagulopathy, extra-pulmonary organ dysfunction other than acute renal failure on dialysis).

Outcomes were compared with patients who underwent early versus late tracheostomy, with the following cutoffs: ≤ 7 days, 8–10 days, and 11–14 days. The institutional review boards of the participating hospitals approved the study, waiving the need for written informed consent due to the retrospective and observational nature of the study

(CEIM Complejo Hospitalario de Toledo, 10/7/2020 Nº546). The STROBE guidelines for reporting observational studies were followed.

Cohorts:

To prevent competing-risk bias, we excluded patients with factors associated with tracheostomy: admission to the ICU with a PCR positive for COVID-19 but without indications for mechanical ventilation for COVID-19 pneumonia; admission after otorhinolaryngology surgery; low level of consciousness; swallowing dysfunction; neuromuscular disease other than ICU-acquired weakness; tracheostomy; advanced directives to withhold life-sustaining interventions; or expected to die before hospital discharge.

To prevent residual selection bias due to the lack of randomization of the timing of tracheostomy, we matched cohorts based on propensity scores. Propensity scores were calculated using variables predictive of the timing of tracheostomy in the ICU (age, sex, comorbidities, APACHE II at ICU admission, extrapulmonary organ failures at ICU admission, type of ICU), additional covariates for COVID-19 patients (date of ICU admission, time from clinical presentation to invasive mechanical ventilation, and medical treatment with corticoids or remdesivir), and variables predictive of tracheostomy or prolonged mechanical ventilation (need for reintubation prior to tracheostomy, neurologic failure at ICU admission, and underlying chronic respiratory disease).

We excluded post-tracheostomy factors that could lead to immortal-time bias, except the use of high-flow oxygen therapy during weaning. For matched comparisons, patients in the late tracheostomy cohort were selected according to the propensity score from among the remaining patients (≥8, ≥11, ≥15 days, respectively).

Data Collection:

We collected data regarding patients' characteristics; course of COVID-19; ICU and hospital admission; severity of illness at ICU admission and at tracheostomy; respiratory and COVID-19 treatments; extubation episodes before tracheostomy (counting this time off ventilator in the calculation of VFD); weaning or decannulation failure (counting the time off ventilator before weaning failure in the calculation of VFD); ICU and hospital length of stay (LOS); ICU readmission (counting the time between admissions in the calculation of BFD); course of mechanical ventilation and tracheostomy; vital status at ICU and hospital discharge; and cause of death. We also recorded tracheostomy- and post-tracheostomy-related ICU complications (see Supp mat.).

Outcomes:

The primary outcome was VFD at 28 days, calculated as $VFD_{28} = 28 - x$, where x represents the number of days from intubation to liberation from ventilation or death.

Secondary outcomes included VFD at 60 days ($VFD_{60} = 60 - x$, where x represents the number of days from intubation to liberation from ventilation or death) and modified ICU/hospital BFD at 28 days ($BFD_{28} = 28 - y$, where y represents the number of days from ICU/hospital admission to discharge to the ward/home or death) and at 60 days ($BFD_{60} = 60 - y$, where y represents the number of days from ICU/hospital admission to discharge to the ward/home or death). Therefore, the value of these variables is 0 when the patient uses the resource (ventilator or bed) for longer than the specified period (28 or 60 days).

Statistical analyses:

To compare groups of patients tracheostomized in different timeframes (<7, 8–10, 11–14 days after intubation) within the entire cohort (unmatched patients), we used chi-square tests or Fisher's exact test for categorical variables and analysis of variance (ANOVA) or Kruskal-Wallis for continuous variables, as appropriate. We used Kaplan-Meier plots to determine the probability of being mechanically ventilated in each tracheostomy-timing group, and we used the log-rank test to compare this probability among groups. To analyze the relationship between the timing of tracheostomy, duration of mechanical ventilation, ICU LOS, and hospital LOS, we used locally estimated scatterplot smoothing (LOESS).

To determine the effect of timing of tracheostomy on outcomes (VFD$_{28}$, VFD$_{60}$, BFD$_{28}$, and BFD$_{60}$) we compared propensity-score-matched cohorts of patients tracheostomized at different time points after intubation (≤7 days, 8 10 days, and 11 14 days). The supplementary material presents detailed information about the variables included in the propensity-score matching. In constituting all propensity-score matched cohorts to be compared, we used 1:1 nearest-neighbor matching without replacement and a caliper (maximum permitted difference between matched subjects) of 0.2 standard deviation of the logit of the propensity score. An exploratory analysis also compared outcomes between two additional matched cohorts to assess differences among different timings of early tracheostomy (≤7 days vs. 8–10 days and ≤7 days vs. 11–14 days).

We used Stata Statistical Software, release 14 (StataCorp LLC, College Station, TX, USA) and R version 3.6.3 (R Core Team, Vienna, Austria) for all analyses, using the MatchIt package from R for propensity-score matching. Two-tailed p-values ≤0.05 were considered statistically significant.

RESULTS:

Participating ICUs admitted a total of 1939 patients with COVID-19 pneumonia during the study period; 682 (35.2%) of these underwent tracheostomy during the ICU stay, 382 (56%) within 14 days of intubation. The centers where and dates when tracheostomies were performed are presented in e-Table 1 and e-Figure 1.

Table 1 summarizes the baseline characteristics of the entire population classified according to the timing of tracheostomy (≤7 days, 8–10 days, 11–14 days, 15–20 days, ≥21 days) (see detailed data in e-Table 2). Figure 1 shows the probability of remaining on mechanical ventilation for the groups of tracheostomized patients according to the timing of tracheostomy, as a surrogate for total time on mechanical ventilation.

Primary and secondary outcomes in non-matched and matched cohorts:

Primary and all the secondary outcomes except hospital BFD_{28} differed significantly depending on the timing of tracheostomy. LOESS showed that time under mechanical ventilation, ICU LOS, and hospital LOS increased with the time from intubation to tracheostomy (e-Figures 2, 3, and 4).

e-Table 3 summarizes the outcomes for the entire population broken down by timeframes in which tracheostomy was performed after intubation (unmatched cohorts). Tables 2–4 report the results of the comparisons between the matched cohorts (≤7 days vs. >7 days; 8–10 days vs. >10 days; 11–14 days vs. >14 days, respectively); the detailed characteristics of the patients in these cohorts are detailed in e-Tables 4–6. No significant differences in mortality were found between cohorts.

Exploratory outcomes.

In the exploratory analysis to assess differences between the three early timings analyzed, the comparison between ≤7 days vs. 8–10 days (matching cohorts of 88 patients) did not find a significant difference only for VFD_{28} [6 (0–13) days in the group tracheostomized ≤7 days after intubation vs. 8 (1–13) in the group tracheostomized 8–10 days after intubation; mean difference between groups -0.5, 95%CI (-3.0 to 2.0)], whereas the comparison between ≤7 days vs. 11–14 days (matching cohorts of 106 patients) found significant differences in VFD_{28} [8 (0–15) days in the group tracheostomized ≤7 days after intubation vs. 2 (0–6) days in the group tracheostomized 11–14 days after intubation; mean difference between groups 4.2, 95%CI (2 to 6.4)] and in ICU BFD_{28} [3 (0–10) days vs. 0 (0–3) days, respectively; mean difference between groups 3.8, 95%CI (2.1 to 5.5)].

DISCUSSION:

To our knowledge, this is the largest multicenter study to examine the timing of tracheostomy in COVID-19 patients with a propensity-matched score. We found that early tracheostomy increased VFD and BDF attributed mainly to a reduction in the time on mechanical ventilation as no differences in mortality between the groups tracheostomized at different timings were observed.

Our early tracheostomy group is similar to that reported in the Large Observational Study to Understand the Global Impact of Severe Acute Respiratory Failure (LUNG-SAFE) study. LUNG SAFE authors found that 13% of patients with acute respiratory distress syndrome were tracheostomized in the ICU; these patients were on mechanical ventilation for a median of 21.5 (13–33) days, and 29.5% died within 60 days.[27] In our study, the surge conditions meant that physicians decided who to tracheotomize, when to do the procedure, and what technique to use based on weekly burden in ICUs (e-Figure 1). Thus, the COVID-19 outbreak represents a unique opportunity to advance our knowledge about the effectiveness of tracheostomy in managing ICU resources.

The propensity score took into account all variables that were associated with the duration of mechanical ventilation and/or mortality in previous studies in general critically ill populations[28–30] or COVID-19 patients.[31–38] Moreover, considering the date of ICU admission reflects the strain on ICU resources during the surge, thus strengthening the model by improving its ability to elucidate the relationships between the timing of tracheostomy and the availability of ICU resources.[39]

Although a previous, single-center study also found that early tracheostomy reduced the duration of mechanical ventilation,[9] the reduction was achieved by shortening the time patients were ventilated before tracheostomy without shortening the time from tracheostomy to successful weaning from mechanical ventilation. By contrast, in our study, early tracheostomy also reduced weaning time. This discrepancy can be explained by differences in patients' baseline characteristics as suggested by the short time to definitive weaning achieved in that study. Our results are in line with those of a national study in Spain,[40] where 52.1% of patients were liberated from mechanical ventilation within 30 days. Additional reasons for the reduced weaning time with early tracheostomy include our failure to take into account previously reported benefits of early tracheostomy (e.g., reduced sedative administration and respiratory infection rate).[41]

Our results confirm that the increases in VFD and BFD with early tracheostomy were not related to differences in mortality rates. Possible explanations for the lack of associations with mortality include the higher complications rates during the ICU stay in the matched cohorts of patients who were tracheostomized later. These differences reached significance in the (>14 days) delayed cohort (see e-Tables 4, 5, and 6), suggesting that some prevalent COVID-19 complications become more common as time on mechanical ventilation increases, leading to increases in ICU LOS and hospital LOS.[39] The LOESS analysis showed that ICU LOS and hospital LOS increased with increased duration of mechanical ventilation according to the timing of tracheostomy, reinforcing the idea that the duration of mechanical ventilation hampers recovery in COVID-19 patients. Furthermore, very early tracheostomy was probably performed in response to emergency situations, which could explain the U-shaped curves suggesting that both very early and delayed tracheostomies might be associated with the development of clinical complications.

Regardless of the timing, tracheostomy had a positive impact on the availability of ICU resources. The earlier the tracheostomy, the higher the improvement; the greatest benefits for ICU resources were found in the group tracheostomized within 7 days after intubation, suggesting that the mechanisms involved are time dependent. Some aspects related to very early tracheostomy deserve mention. It can be argued that this timing selects less severe patients, given that tracheostomy is usually delayed until the needs for increased FiO_2 and PEEP are reduced and that prone position is a relative contraindication for tracheostomy. However, to avoid this bias, the propensity matching took into account rescue therapies (prone positioning and ECMO) applied before tracheostomy; most patients requiring prone positioning were definitively turned to the supine position before tracheostomy and some tracheostomized patients were prone. There is no consensus about the respiratory settings that compromise the safety of patients and healthcare professionals performing tracheostomy, but patients with COVID-19 seldom require high PEEP, so this not a valid reason to delay tracheostomy in patients with persistent hypoxemia.[10, 18, 39]

Limitations of the study:

The most important limitation is the retrospective design, which precludes definite conclusions about the causality of the associations observed and cannot totally exclude selection bias. Because the conditions during the outbreak precluded carrying out a prospective randomized study, we opted for a retrospective study based on propensity matching. Furthermore, the cohort of patients tracheostomized ≤7 days after intubation is relatively small, limiting the ability of the analyses to extract definitive conclusions and included 1 patient on mechanical ventilation less than 10 days. Nevertheless, VFB and ICU BFD were higher in patients tracheostomized within <7 days than in those patients tracheostomized 11–14 days after intubation. These results correspond to the time ranges reported for general critically-ill patients by Chorath et al.[8] Given the lack of larger studies on the timing of tracheostomy in COVID-19 patients, the information from the present study may be crucial for managing ICU resources in future surges.

Our high percentage of tracheostomized patients compared to other cohorts (REVA, Martin-Villares) can be explained by specific time-frames during the first wave as learning on COVID-19 evolved rapidly,[40, 41] and previous experience in high-volume and high-complexity recruiting centers for this study. However, recent evidence for early tracheostomy supports our results.[8]

The only post-tracheostomy variable that differed significantly between the cohorts tracheostomized at different timings was the use of high-flow oxygen therapy during weaning. Despite the risk of introducing an immortal time bias by including this variable in the matching because this therapy shortens the time to weaning,[37] we decided to include it because its use depended only on its availability and did not modify the indication for early tracheostomy.

The results cannot be extrapolated to settings other than overwhelming periods. Life-support measures were withheld in many patients, making time to death highly dependent on local practices during this first wave in an outbreak of a poorly understood disease, thereby increasing the heterogeneity of the results. However, the large number of patients included from 15 ICUs improves the external validity of the results. Finally, the overwhelming conditions in ICUs during the first wave may have limited professionals' ability to apply standard care protocols.

Interpretation: Optimal timing of tracheostomy may improve patient outcomes and alleviate ICU capacity strain during the COVID-19 pandemic without increasing mortality. Tracheostomy within the first work on ventilator may particularly improve ICU availability.

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Take-Home points

Study question

What is the best timing for tracheostomy in patients with COVID-19 pneumonia with patient´s prognosis and ICU capacity maintenance in mind?

Results

Early tracheostomy was associated with a significantly higher number of ventilator-free days in the first 28 and 60 days after intubation and higher number of ICU and hospital bed-free days in the first 28 and 60 days after ICU/hospital admission. Moreover, the results suggest that the earlier the tracheostomy, the better the patient´s prognosis and the higher the ICU resources capacity maintenance.

Interpretation

Early tracheostomy can help optimize clinical course of patients and critical care resources during future viral pandemic and probably other overwhelming situations in ICUs.

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Author contributions:

Dr. Hernandez contributed to the conception, design, analysis, and interpretation of the data, as well as to drafting, critical revision, reading, and approval of the manuscript.

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Dr. Hernandez and Dr. Roca take responsibility for the integrity of the work as a whole.

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Figure 1.- Kaplan-Meier curves for groups of tracheostomized patients according to the timing of tracheostomy (≤7d, 8–10d, 11–14d, 15–21d, >21d after intubation) related to the probability of remaining on mechanical ventilation in the entire population.

MV = mechanical ventilation; ETI = endotracheal intubation.

Table 1.- Baseline patient characteristics in the entire population (unmatched samples), according to time from intubation to tracheostomy (detailed information in Table S2).

Time to tracheostomy, in days from intubation	**≤ 7 (n=65)**	**8–10 (n=126)**	**11–14 (n=191)**	**15–20 (n=197)**	**≥21 (n=103)**	***p***
Age, y, median (IQR)	62 (55-70)	65 (56-69)	64 (57-71)	64 (57-69)	65 (56-72)	0.863
Male sex, nº (%)	42 (64.6)	88 (69.8)	136 (71.2)	149 (73.8)	74 (75.5)	0.563
Comorbidities[1]:						

BMI^2 >30, nº (%)	28 (43.1)	52 (41.3)	88 (46.1)	74 (36.6)	41 (41.8)	0.450
Heart disease, nº (%)	6 (9.2)	10 (7.9)	16 (8.4)	15 (7.4)	20 (20.4)	0.005
COPD, nº (%)	2 (3.1)	2 (2.4)	11 (5.8)	8 (4)	4 (4.1)	0.651
Other respiratory disease, nº (%)	6 (9.2)	6 (4.8)	24 (12.6)	31 (15.3)	15 (15.3)	0.042
COVID-19 course:						
Time from symptom onset to ICU admission, d, median (IQR)	9 (6-12)	8 (6-12)	9 (7-12)	10 (7-14)	9 (6-14)	0.217
Time from intubation to tracheostomy, d, median (IQR)	6 (5-7)	9 (8-10)	13 (12-13)	17 (16-19)	24 (22-29)	<0.001
Time from tracheostomy to weaning^3, d, median (IQR)	7 (1-19)	7 (0-17)	6 (0-12)	8 (0-22)	11 (0-19)	0.213
Treatments:						
HFOT during weaning, n (%)	23 (35.4)	45 (35.7)	53 (27.8)	36 (17.8)	25 (25.5)	0.003
Remdesivir, n (%)	2 (3.1)	13 (10.3)	13 (6.8)	10 (5)	9 (9.2)	0.217
Steroids, n (%)	51 (78.5)	107 (84.9)	153 (80.1)	149 (73.8)	79 (80.6)	0.177
Rescue ARDS therapy^4, nº (%)	58 (89.2)	120 (95.2)	172 (90.1)	179 (88.6)	90 (91.8)	0.336
Severity at ICU admission:						
Hemodynamic failure, nº (%)	21 (33.9)	51 (42.2)	73 (41)	95 (48)	49 (56.3)	0.043
Renal failure, nº (%)	22 (33.9)	36 (28.6)	73 (38.2)	59 (29.2)	35 (35.7)	0.274
Nº failed organs, median (IQR)	2 (1-3)	2 (1-3)	2 (1-3)	2 (1-3)	2 (1-3)	0.687

APACHE II[4], median (IQR)	13 (8-16)	13 (9-18)	15 (10-18)	15 (11-18)	15 (11-17)	0.212
Complications during ICU stay:						
Weaning failure[8], nº (%)	5 (7.7)	12 (9.5)	26 (13.6)	14 (7.1)	27 (26.2)	<0.001
VAP, nº (%)	22 (33.9)	52 (41.3)	68 (35.6)	86 (42.6)	55 (56.1)	0.012
Sepsis, nº (%)	13 (20)	34 (27)	53 (27.8)	58 (28.7)	52 (53.1)	<0.001
Hematological[11], nº (%)	15 (23.1)	40 (31.8)	47 (24.6)	66 (32.7)	43 (43.9)	0.009
Death, nº (%)	18 (27.7)	47 (37.3)	71 (37.2)	76 (37.6)	30 (30.6)	0.468

ARDS = acute respiratory distress syndrome; BMI = body mass index; CI = confidence interval; COPD = chronic obstructive pulmonary disease; HFOT = high-flow oxygen therapy; ICU = intensive care unit; IQR = interquartile range; VAP = ventilator-associated pneumonia; VFD = ventilator-free days; SD = standard deviation.

[1] Coexisting conditions were assessed according to the Charlson comorbidity index, on which 22 clinical conditions are scored with regard to the risk of death; scores range from 0 to 37, with higher scores indicating a higher risk of death.

[2] The body-mass index is the weight in kilograms divided by the square of the height in meters.

[3] Weaning was defined as 24 consecutive hours disconnected from mechanical ventilation.

[4] The Acute Physiology and Chronic Health Evaluation (APACHE) II score was calculated from 17 variables recorded on the day of admission to the intensive care unit; scores range from 0 to 71 points, with higher scores indicating more severe disease.

Table 2.- Results for the primary and secondary outcomes in the propensity-matched cohorts of patients with tracheostomy performed ≤7 days vs. >7 days after intubation.

Time from intubation to tracheostomy	**≤7 days (n=58)**	**>7 days (n=58)**	**Difference between groups (95%CI)**
Days using a ventilator, median (IQR)	20 (13-32)	26 (21-36)	-5.8 (-10 to -0.6)
ICU length of stay, d, median (IQR)	23 (16-39)	33 (24-47)	-6.9 (-13.4 to -0.4)
Hospital length of stay, d, median (IQR)	40 (26-60)	55 (32-66)	-8 (-15.2 to -0.7)
VFD at 28 days, d, median (IQR)	9 (0-15)	3 (0-7)	4.5 (2.3 to 6.7)
ICU BFD at 28 days, d, median (IQR)	5 (0-12)	0 (0-4)	3.9 (2 to 5.8)
Hospital BFD at 28 days, d, median (IQR)	0 (0-2)	0 (0-0)	.3 (-1.3 to 1.8)
VFD at 60 days, d, median (IQR)	41 (28-47)	35 (24-39)	5.4 (.6 to 10.2)
ICU BFD at 60 days, d, median (IQR)	37 (21-44)	27 (12-36)	7.3 (2.1 to 12.6)
Hospital BFD at 60 days, d, median (IQR)	20 (0-34)	5 (0-28)	5.9 (.8 to 11)

BFD = bed-free days; CI = confidence interval; ICU = intensive care unit; IQR = interquartile range; VFD = ventilator-free days.

Table 3.- Results for the primary and secondary outcomes in the propensity-matched cohorts of patients with tracheostomy performed 8-10 days vs. >10 days after intubation.

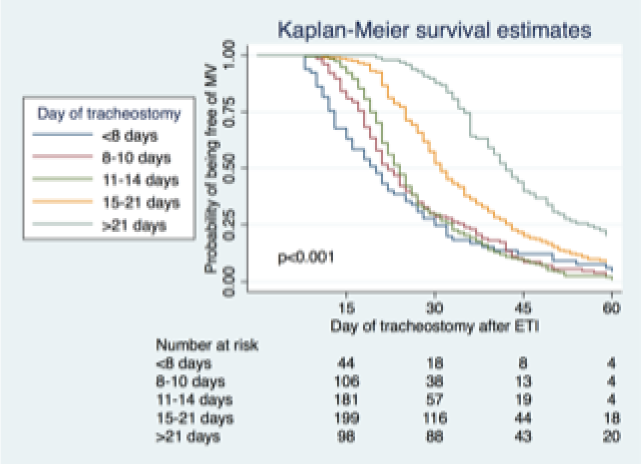
Time from intubation to tracheostomy	**8-10 days (n=111)**	**>10 days (n=111)**	**Difference between groups (95%CI)**
Days using a ventilator, median (IQR)	22 (18-34)	31 (22-41)	-6.8 (-11.2 to -2.3)
ICU length of stay, d, median (IQR)	26 (19-37)	35 (25-47)	-7.9 (-12.5 to -3.2)
Hospital length of stay, d, median (IQR)	39 (28-57)	49 (34-69)	-9.1 (-15.2 to -3.1)
VFD at 28 days, d, median (IQR)	6 (0-10)	0 (0-6)	3.1 (1.7 to 4.5)
ICU BFD at 28 days, d, median (IQR)	2 (0-9)	0 (0-3)	2.4 (1.2 to 3.7)
Hospital BFD at 28 days, d, median (IQR)	0 (0-1)	0 (0-0)	0.8 (-0.9 to 2.5)
VFD at 60 days, d, median (IQR)	38 (26-42)	29 (18-38)	6.2 (2.7 to 9.7)
ICU BFD at 60 days, d, median (IQR)	34 (22-40)	25 (6-35)	8.2 (4.4 to 12)
Hospital BFD at 60 days, d, median (IQR)	21 (3-32)	11 (0-26)	6.4 (2.8 to 10)

BFD = bed-free days; CI = confidence interval; ICU = intensive care unit; IQR = interquartile range; VFD = ventilator-free days.

Table 4.- Results for the primary and secondary outcomes in the propensity-matched cohort for patients with tracheostomy performed 11–14 days vs >14 days after initiation of mechanical ventilation.

Timing of tracheostomy, in days	**11–14 (n=159)**	**> 14 (n=159)**	**Difference between groups (95%CI)**
Days using a ventilator, median (IQR)	24 (20-33)	35 (26-46)	-10.9 (-14.1 to -7.7)
ICU length of stay, d, median (IQR)	28 (22-40)	41 (30-57)	-12.6 (-16.2 to -9)
Hospital length of stay, d, median (IQR)	46 (32-61)	61 (42-76)	-14.2 (-19.4 to -9.1)
VFD at 28 days, d, median (IQR)	4 (0-9)	0 (0-2)	3 (2.1 to 3.9)
ICU BFD at 28 days, d, median (IQR)	0 (0-6)	0 (0-0)	1.9 (1.2 to 2.6)
Hospital BFD at 28 days, d, median (IQR)	0 (0-0)	0 (0-0)	-0.3 (-1.5 to 0.9)
VFD at 60 days, d, median (IQR)	36 (27-41)	25 (15-33)	9 (6.4 to 11.6)
ICU BFD at 60 days, d, median (IQR)	32 (18-38)	17 (10-29)	11.2 (8.2 to 14.3)
Hospital BFD at 60 days, d, median (IQR)	13 (0-28)	0 (0-18)	7.1 (4.2 to 9.9)

BFD = bed-free days; CI = confidence interval; ICU = intensive care unit; IQR = interquartile range; VFD = ventilator-free days.



Number at risk				
<8 days	44	18	8	4
8-10 days	106	38	13	4
11-14 days	181	57	19	4
15-21 days	199	116	44	18
>21 days	98	88	43	20