CHEST Online Supplement

# Early Tracheostomy for Managing ICU Capacity During the COVID-19 Outbreak

## A Propensity-Matched Cohort Study

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**e-Appendix 1.**

**Detailed protocol.**

Study design:

This retrospective cohort study included all 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, the peak of the pandemic in Spain. In all participating hospitals, pre-COVID-19 protocols for timing tracheostomy indicated early tracheostomies only for patients with neurologic dysfunction. However, during the outbreak, attending physicians determined who, when, and how to tracheostomize based on weekly ICU burden (the number of ICU admissions and the accumulated number of COVID-19 patients in the ICU): the greater the burden, the earlier tracheostomy was indicated, resulting in higher tracheostomy rates and greater proportions of surgical tracheostomies. To determine the impact of early tracheostomy on ICU resources, this study compared measures of ventilator and bed usage after early tracheostomy (variably defined as ≤7 days, 8–10 days, and 11–14 days after intubation). The study was approved by the review boards of the hospitals participating in the study; informed consent was waived due to the retrospective and observational nature of the study.

Cohorts:

To prevent competing-risk bias, patients who had the following factors were excluded: admission to the ICU with a PCR positive for COVID-19 but without indications for mechanical ventilation for COVID-19 pneumonia; admission after ear, nose, or throat surgical procedures; low level of consciousness; swallowing dysfunction; neuromuscular disease other than ICU-acquired weakness; prior 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 a tracheostomy, cohorts were matched based on propensity scores. Propensity scores were calculated using variables predictive of the timing of a tracheostomy in the ICU. To identify those variables, the Medline database was searched for the following MeSH terms: tracheostomy, timing, risk factors, and intensive care unit. Relevant studies reported that the following variables were associated with the timing of a tracheostomy in general ICU populations: age, sex, comorbidities, APACHE II at ICU admission, extrapulmonary organ failures at ICU admission, type of ICU *(1, 2, 3)*; moreover, a separate search identified the following 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 *(4, 5, 6, 7, 8, 9, 10, 11)*.

When building a propensity score, it is important to ensure that there are no important unmeasured variables that are not accounted for in the propensity regression. Thus, the score also included additional variables predictive of tracheostomy and prolonged mechanical ventilation *(12)*: need for reintubation prior to tracheostomy, neurologic failure at ICU admission, and underlying chronic respiratory disease. It is also important to exclude events developing after tracheostomy that could lead to immortal-time, selection, or competing-risk

bias (e.g., complications related to tracheostomy or complications during the ICU stay). However, patients who received high-flow oxygen therapy (HFOT) during weaning were not excluded because HFOT shortens the time to weaning. This decision was justified because whether HFOT was administered depended solely on the availability of a device (all patients received HFOT if a device was available) and because using HFOT did not modify the indication for early tracheostomy. All those events were excluded in the propensity score and used for exploratory analyses only. In effect, the propensity score represented the probability that a patient would receive a tracheostomy in a specific timeframe measured from the initiation of mechanical ventilation. For all comparisons, patients included in the cohorts were matched according to the propensity score.

Data Collection:

The following data were collected: date of onset of COVID-19 symptoms; calendar week of ICU admission; type of hospital (with or without neurointensive care unit); level of surge; age; sex; body mass index; comorbidities, assessed according to the Charlson index, in which 22 clinical conditions are scored for the risk of dying, with higher scores indicating a greater risk of dying; severity of illness at ICU admission, according to the Acute Physiology and Chronic Health Evaluation II (APACHE II) score in the first 24 hours of admission, calculated from 17 variables, with scores ranging from 0 to 71 points and higher scores indicating more severe disease *(13)*; organ dysfunctions, according to the definitions of the third International Consensus *(14)*; the need for surgical intervention at ICU admission; COVID-19 treatments (corticoids or remdesivir); rescue respiratory therapies during the ICU stay and timing of their administration (prone positioning, extracorporeal membrane oxygenation (ECMO)); respiratory status on the day of tracheostomy; tracheostomy technique, classified as surgical or percutaneous; extubation episodes before tracheostomy (counting these days off ventilator in the calculation of ventilator-free days (VFD)); tracheostomy-related complications (classified as airway problems, including airway emergencies that required changing the tracheal cannula due to airway obstruction, dislodgement, or air leaks; bleeding that required transfusion or surgical control of the source; or stoma infection episodes); use of HFOT to facilitate weaning from mechanical ventilation; weaning failure, defined as the need to reinitiate mechanical ventilation for any reason within 7 days after being disconnected from mechanical ventilation for ≥ 24 h; decannulation failure, defined as the need to recannulate for any reason between decannulation and hospital discharge (days off ventilator before weaning failure counted in the calculation of VFD); lengths of ICU and hospital stays, defined as time from ICU/hospital admission to ICU/hospital discharge); ICU readmission, defined as readmission before hospital discharge (days between ICU discharge and readmission counted in the calculation of bed-free days (BFD)); duration of mechanical ventilation and time from tracheotomy to decannulation; vital status at ICU and hospital discharge; cause of death; and orders to withhold or withdraw life-sustaining treatments.

ICU events associated with ICU mortality in mechanically ventilated patients were also collected. Healthcare-associated respiratory infections were diagnosed according to the ATS/IDSA guidelines *(15)*. Briefly, pneumonia was defined as the presence of fever or altered leukocyte count plus new onset of purulent endotracheal secretions or change in sputum, with new and progressive or persistent infiltrate or consolidation or cavitation. Tracheobronchitis was defined by the same criteria but without new infiltrates. Extra-pulmonary infections were

recorded. Sepsis and multiorgan failure were defined according to the third International Consensus *(14)*. ICU-acquired weakness was defined as clinically detected weakness with no plausible cause other than critical illness and classified according to the Medical Research Council sum score, ranging from 0 to 60 points with higher scores indicating greater weakness *(16)*. Bleeding episodes were classified according to whether they required transfusion, modification of medical treatment, or surgical control of the source. Thrombotic episodes were classified according to whether they required modification of medical treatment or endovascular treatment for clinical instability. The presence of air leaks, including pneumothorax, pneumomediastinum, bronchopleural fistula, or subcutaneous emphysema was also recorded. Also collected were episodes of ICU-acquired delirium, defined as the presence of a new-onset and fluctuating disturbance of consciousness associated with a change in cognition or perception.

Outcomes:

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

Secondary outcomes included (a) VFD at 60 days calculated as $VFD_{60} = 60 - x$, where $x$ represents the number of days from intubation to liberation from ventilation or death, (b) modified ICU bed-free days at 28 days ($BFD_{28}$) calculated as $BFD_{28} = 28 - x$, where $x$ represents the number of days from intubation to discharge to the ward or death, and (c) ICU bed-free days at 60 days ($BFD_{60}$), calculated as $BFD_{60} = 60 - x$, where $x$ represents the number of days from intubation to discharge to the ward or death.

According to these definitions, the value of VFD or BFD will be 0 for patients who remain under mechanical ventilation or occupying an ICU bed for longer than the period considered (>28 or >60 days).

Statistical analyses:

Categorical variables are expressed as frequencies and percentages. Continuous variables are expressed as means and standard deviations (±SD) when normally distributed and as medians and interquartile range (IQR) when non-normally distributed. To compare unmatched cohorts in the entire population, chi-square tests or Fisher's exact tests were used as appropriate for categorical variables, and analysis of variance (ANOVA) or the Kruskal-Wallis test were used as appropriate for continuous variables. To determine the probability of remaining under mechanical ventilation for the four groups according to timing of tracheostomy, Kaplan-Meier curves were plotted; to assess differences in this probability, the log-rank test was used. To analyze the relationship between the timing of tracheostomy and (a) the time under mechanical ventilation, (b) ICU length of stay (LOS), and (c) hospital LOS, locally estimated scatterplot smoothing (LOESS) was used.

To determine the effect of timing of tracheostomy on outcomes ($VFD_{28}$, $VFD_{60}$, $BFD_{28}$, and $BFD_{60}$), propensity-score-matched cohorts of patients tracheostomized at different timepoints after intubation (☐7 days vs. >7 days; 8–10 days vs. >10 days; 11–14 days vs. >14 days)

were compared. In constituting all propensity-score matched cohorts to be compared, 1:1 nearest-neighbor matching without replacement was used, with a caliper (maximum permitted difference between matched subjects) of 0.2 standard deviation of the logit of the propensity score. The balance between matched cohorts was assessed by the standardized differences of each independent variable used in the propensity score estimation. To analyze the differences in the matched cohorts, McNemar's test was used for categorical variables, paired t-tests were used for normally distributed continuous variables, and the Wilcoxon signed-rank test was used for non-normally distributed continuous variables. 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).

Stata Statistical Software, release 14 (StataCorp LLC, College Station, TX, USA), and R version 3.6.3 (R Core Team, Vienna, Austria) were used for all analyses, with the MatchIt package from R being used for propensity score matching *(17)*. Two-tailed p-values ≤0.05 were considered statistically significant.

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**e-Table 1.** Pooled data, by participating hospital.

| | **Pre-COVID-19 Nº of ICU-beds** | **Nº of COVID-19 ICU patients** | **Tracheostomies n (%)** | **Tracheostomies ≤ 14d n (%)** |
|---|---|---|---|---|
| Hospital 1 | 28 | 121 | 51 (42.1) | 31 (60.8) |
| Hospital 2 | 20 | 158 | 43 (27.2) | 37 (86) |
| Hospital 3 | 56 | 342 | 154 (45) | 119 (77.3) |
| Hospital 4 | 16 | 110 | 54 (49.1) | 12 (22.2) |
| Hospital 5 | 24 | 129 | 35 (27.1) | 21 (60) |
| Hospital 6 | 30 | 250 | 110 (44) | 57 (51.8) |
| Hospital 7 | 20 | 114 | 28 (24.6) | 18 (64.3) |
| Hospital 8 | 14 | 85 | 19 (22.4) | 3 (15.8) |
| Hospital 9 | 12 | 60 | 5 (8.3) | 1 (20) |
| Hospital 10 | 16 | 32 | 10 (31.3) | 1 (10) |
| Hospital 11 | 30 | 51 | 23 (45.1) | 11 (47.8) |
| Hospital 12 | 12 | 150 | 36 (24) | 18 (50) |
| Hospital 13 | 30 | 131 | 37 (28.2) | 18 (48.6) |
| Hospital 14 | 16 | 83 | 29 (34.9) | 10 (34.5) |
| Hospital 15 | 50 | 123 | 48 (39) | 25 (52.1) |
| Entire population | 374 | 1939 | 682 (35.2) | 382 (56) |

**e-Table 2.** Detailed baseline patient characteristics in the entire population, by timing of tracheostomy.

| **Time to tracheostomy, in days from intubation** | **≤7 (n=65)** | **8–10 (n=126)** | **11–14 (n=191)** | **15–20 (n=202)** | **≥21d (n=98)** | ***p*** |
|---|---|---|---|---|---|---|
| Age, y, median (IQR) | 62 (55-70) | 65 (56-69) | 64 (57-71) | 64 (57-69) | 65 (56-72) | .863 |
| Male sex, nº (%) | 42 (64.6) | 88 (69.8) | 136 (71.2) | 149 (73.8) | 74 (75.5) | .563 |
| **Comorbidities:** | | | | | | |
| BMI >30, nº (%) | 28 (43.1) | 52 (41.3) | 88 (46.1) | 74 (36.6) | 41 (41.8) | .450 |
| Arterial hypertension, nº (%) | 22 (33.9) | 49 (38.9) | 77 (40.3) | 84 (41.6) | 48 (49) | .373 |
| Heart disease, nº (%) | 6 (9.2%) | 10 (7.9) | 16 (8.4) | 15 (7.4) | 20 (20.4) | .005 |
| Neurologic disease, nº (%) | 2 (3.1) | 3 (2.4) | 5 (2.6) | 8 (4) | 6 (6.1) | .550 |
| COPD, nº (%) | 2 (3.1) | 2 (2.4) | 11 (5.8) | 8 (4) | 4 (4.1) | .651 |
| Other respiratory disease, nº (%) | 6 (9.2) | 6 (4.8) | 24 (12.6) | 31 (15.3) | 15 (15.3) | .042 |
| Diabetes mellitus, nº (%) | 14 (21.5) | 30 (23.8) | 40 (20.9) | 48 (23.8) | 25 (25.5) | .910 |
| Cancer, nº (%) | 5 (7.7) | 9 (7.1) | 15 (7.9) | 14 (6.9) | 5 (5.1) | .938 |
| Vascular disease, nº (%) | 4 (6.2) | 6 (4.8) | 6 (3.1) | 5 (2.5) | 4 (4.1) | .631 |
| Chronic renal failure, nº (%) | 3 (4.7) | 9 (7.1) | 8 (4.2) | 10 (5) | 5 (5.1) | .836 |
| Chronic hepatic failure, nº (%) | 5 (7.7) | 6 (4.8) | 7 (3.7) | 5 (2.5) | 2 (2) | .292 |
| Other diseases, nº (%) | 9 (13.9) | 8 (6.4) | 19 (10) | 27 (13.4) | 13 (13.3) | .274 |
| **COVID-19 course:** | | | | | | |
| Time symptoms–ICU admission, d, median (IQR) | 9 (6-12) | 8 (6-12) | 9 (7-12) | 10 (7-14) | 9 (6-14) | .217 |
| Delayed intubation, d, median (IQR) | 1 (0-2) | 1 (0-2) | 1 (0-2) | 1 (0-2) | 1 (0-2) | .395 |
| Time intubation–TR, d. median (IQR) | 6 (5-7) | 9 (8-10) | 13 (12-13) | 17 (16-19) | 24 (22-29) | <.001 |
| Time TR–weaning, d, median (IQR) | 7 (1-19) | 7 (0-17) | 6 (0-12) | 8 (0-22) | 11 (0-19) | .213 |
| Time weaning–-decannulation, d, median (IQR) | 3 (0-8) | 2 (0-4) | 2 (0-5) | 2 (0-6) | 2 (0-4) | .370 |
| **Indication for tracheostomy:** | | | | | | |
| Prolonged MV, nº (%) | 59 (90.8) | 116 (92.1) | 170 (89) | 186 (92.1) | 76 (77.6) | <.001 |
| Weaning, nº (%) | 4 (6.2) | 10 (7.9) | 21 (11) | 16 (7.9) | 22 (22.5) | |
| Airway, nº (%) | 2 (3.1) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Surgical technique, nº (%) | 34 (54.8) | 68 (58.6) | 82 (45.8) | 108 (56) | 43 (46.2) | .076 |
| **Treatments:** | | | | | | |
| HFOT during weaning, nº (%) | 23 (35.4) | 45 (35.7) | 53 (27.8) | 36 (17.8) | 25 (25.5) | .003 |
| Remdesivir, nº (%) | 2 (3.1) | 13 (10.3) | 13 (6.8) | 10 (5) | 9 (9.2) | .217 |
| Steroids, nº (%) | 51 (78.5) | 107 (84.9) | 153 (80.1) | 149 (73.8) | 79 (80.6) | .177 |
| Rescue therapy for ARDS, nº (%) | 58 (89.2) | 120 (95.2) | 172 (90.1) | 179 (88.6) | 90 (91.8) | .336 |
| **Severity at ICU admission:** | | | | | | |
| $PaO_2/FiO_2$ ≤200, nº (%) | 55 (84.6) | 113 (89.6) | 168 (87.9) | 171 (84.6) | 86 (87.7) | .428 |
| Hemodynamic failure, nº (%) | 21 (33.9) | 51 (42.2) | 73 (41) | 95 (48) | 49 (56.3) | .043 |
| Renal failure, nº (%) | 22 (33.9) | 36 (28.6) | 73 (38.2) | 59 (29.2) | 35 (35.7) | .274 |
| Nº failed organs, median (IQR) | 2 (1-3) | 2 (1-3) | 2 (1-3) | 2 (1-3) | 2 (1-3) | .687 |
| APACHE II, median (IQR) | 13 (8-16) | 13 (9-18) | 15 (10-18) | 15 (11-18) | 15 (11-17) | .212 |
| **Complications related to tracheostomy:** | | | | | | |
| Bleeding, nº (%) | 14 (21.5) | 16 (12.7) | 31 (16.2) | 15 (7.4) | 6 (6.1) | .003 |
| Infection, nº (%) | 2 (3.1) | 2 (1.6) | 11 (5.8) | 8 (4) | 3 (3.1) | .460 |
| Airway compromise, nº (%) | 10 (15.4) | 17 (13.5) | 26 (13.6) | 25 (12.4) | 12 (12.2) | .973 |
| Weaning failure, nº (%) | 5 (7.7) | 12 (9.5) | 26 (13.6) | 14 (7.1) | 27 (26.2) | <.001 |
| Decannulation failure, nº (%) | 4 (6.2) | 3 (2.4) | 3 (1.6) | 6 (3) | 1 (1) | .294 |
| **Complications during ICU stay:** | | | | | | |
| VAT, nº (%) | 18 (27.7) | 26 (20.6) | 64 (33.5) | 65 (32.2) | 33 (33.7) | .108 |
| VAP, nº (%) | 22 (33.9) | 52 (41.3) | 68 (35.6) | 86 (42.6) | 55 (56.1) | .012 |
| Infection from other source, nº (%) | 29 (47.5) | 71 (62.8) | 92 (51.4) | 137 (69.5) | 80 (84.2) | <.001 |
| Sepsis, nº (%) | 13 (20) | 34 (27) | 53 (27.8) | 58 (28.7) | 52 (53.1) | <.001 |
| Multiorgan failure, nº (%) | 10 (15.4) | 26 (20.6) | 37 (19.4) | 442 (20.8) | 27 (27.6) | .392 |
| Hematological, nº (%) | 15 (23.1) | 40 (31.8) | 47 (24.6) | 66 (32.7) | 43 (43.9) | .009 |
| Severe ICU-acquired weakness, nº (%) | 45 (69.2) | 78 (61.9) | 116 (60.7) | 137 (67.8) | 73 (74.5) | .134 |
| Delirium, nº (%) | 31 (47.7) | 45 (35.7) | 70 (36.7) | 92 (45.5) | 38 (38.8) | .197 |
| Air leak, nº (%) | 10 (15.4) | 19 (15.1) | 31 (16.2) | 42 (20.8) | 24 (24.5) | .278 |
| Withholding life-support measures, nº (%) | 12 (18.5) | 31 (24.6) | 53 (27.8) | 45 (22.3) | 20 (30.6) | .468 |
| Death, nº (%) | 18 (27.7) | 47 (37.3) | 71 (37.2) | 76 (37.6) | 30 (30.6) | .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; TR = tracheostomy.

[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 on the basis of 17 variables on the day of admission to the intensive care unit. Scores range from 0 to 71 points, with higher scores indicating more severe disease

**e-Table 3.** Primary and secondary outcomes, by time from intubation to tracheostomy, in the entire population.

| **Time to tracheostomy, in days from intubation** | **≤7 (n=65)** | **8–10 (n=126)** | **11–14 (n=191)** | **15–20d (n=202)** | **≥21 (n=98)** | ***p*** |
|---|---|---|---|---|---|---|
| Days using a ventilator, median (IQR) | 20 (13-30) | 22 (18-35) | 24 (19-33) | 31 (25-43) | 42 (35-56) | <.001 |
| ICU length of stay, d, median (IQR) | 23 (16-38) | 27 (19-38) | 27 (22-38) | 36 (28-48) | 47 (39-64) | <.001 |
| Hospital length of stay, d, median (IQR) | 40 (25-60) | 40 (28-57) | 44 (31-61) | 55 (36-73) | 68 (54-91) | <.001 |
| | | | | | | |
| VFD at 28 days, d, median (IQR) | 8 (0-15) | 6 (0-10) | 5 (0-9) | 0 (0-3) | 0 (0-0) | <.001 |
| ICU BFD at 28 days, d, median (IQR) | 5 (0-12) | 2 (0-9) | 0 (0-6) | 0 (0-0) | 0 (0-0) | <.001 |
| Hospital BFD at 28 days, d, median (IQR) | 0 (0-3) | 0 (0-0) | 0 (0-0) | 0 (0-0) | 0 (0-0) | .048 |
| VFD at 60 days, d, median (IQR) | 40 (30-47) | 38 (25-42) | 36 (27-41) | 29 (18-35) | 18 (7-25) | <.001 |
| ICU BFD at 60 days, d, median (IQR) | 37 (22-44) | 33 (21-40) | 32 (21-38) | 20 (0-31) | 7 (0-20) | <.001 |
| Hospital BFD at 60 days, d, median (IQR) | 20 (0-35) | 20 (3-32) | 15 (0-29) | 5 (0-24) | 0 (0-6) | <.001 |

**e-Table 4.** Baseline patients characteristics in the propensity-matched cohorts of patients with tracheostomy performed <7 days vs. >7 days after intubation.

| **Time to tracheostomy, in days from intubation** | **≤7 (n=58)** | **>7 (n=58)** | **Difference between groups (95%CI) or *p*** |
|---|---|---|---|
| Age, y, median (IQR) | 63 (57-70) | 67 (61-72) | -1.3 (-5 to 2.4) |
| Male sex, nº (%) | 38 (65.5) | 36 (62.1) | 3.4 (-14 to 20.9) |
| Outbreak week ICU admission date, nº (%)* | | | .259 |
| February 18–23 | 0 (0) | 1 (1.7) | |
| February 24–29 | 0 (0) | 0 (0) | |
| March 1–6 | 1 (1.7) | 2 (3.5) | |
| March 7–12 | 3 (5.2) | 4 (6.9) | |
| March 13–18 | 15 (25.9) | 17 (31) | |
| March 19–24 | 18 (31) | 14 (24.1) | |
| March 25–31 | 4 (6.9) | 0 (0) | |
| April 1–6 | 7 (12.1) | 11 (19) | |
| April 7–12 | 5 (8.6) | 2 (3.5) | |
| April 13–18 | 4 (6.9) | 6 (10.3) | |
| April 19–24 | 1 (1.7) | 1 (1.7) | |
| April 25–30 | 0 (0) | 0 (0) | |
| May 1–6 | 0 (0) | 0 (0) | |
| May 7–12 | 0 (0) | 0 (0) | |
| **Comorbidities:** | | | |
| BMI >30, nº (%) | 24 (41.4) | 24 (41.4) | 0 (-17.9 to 17.9) |
| Arterial hypertension, nº (%) | 22 (37.9) | 24 (41.4) | -3.4 (-21.2 to 14.3) |
| Heart disease, nº (%) | 6 (10.3%) | 10 (17.2) | -6.9 (-19.3 to 5.6) |
| Neurologic disease, nº (%) | 2 (3.5) | 5 (8.6) | -5.1 (-13.8 to 3.4) |
| COPD, nº (%) | 2 (3.5) | 2 (3.5) | 0 (-6.6 to 6.6) |
| Other respiratory disease, nº (%) | 6 (10.3) | 4 (6.9) | 3.4 (-6.7 to 13.6) |
| Diabetes mellitus, nº (%) | 13 (22.4) | 17 (29.3) | -6.9 (-22.8 to 9) |
| Cancer, nº (%) | 4 (6.9) | 4 (6.9) | 0 (-9.2 to 9.2) |
| Vascular disease, nº (%) | 4 (6.9) | 5 (8.6) | -1.7 (-11.5 to 8) |
| Chronic renal failure, nº (%) | 3 (5.2) | 3 (5.2) | 0 (-8.1 to 8.1) |
| Chronic hepatic failure, nº (%) | 3 (5.2) | 5 (8.6) | -3.4 (-12.6 to 5.6) |
| Other diseases, nº (%) | 9 (15.5) | 11 (19) | -3.4 (-17.2 to 10.3) |
| **COVID-19 course:** | | | |
| Time symptoms-ICU admission, d, median (IQR) | 9 (6-12) | 9 (6-12) | -0.5 (-2.5 to 1.5) |
| Delayed intubation, d, median (IQR) | 1 (0-2) | 1 (0-2) | 0.1 (-0.9 to 1) |
| Time intubation-TR, d (IQR) | 6 (5-7) | 15 (12-18) | -9.3 (-10.6 to -8.1) |
| Time TR-weaning, d, median (IQR) | 7 (0-19) | 8 (0-18) | 1.6 (-3.6 to 6.8) |
| Time weaning-decannulation, d (IQR) | 3 (0-8) | 3 (0-8) | 1.4 (0.9 to 3.7) |

| | | | |
|---|---|---|---|
| **Indication for tracheostomy:** | | | |
| Prolonged MV, nº (%) | 56 (93.1) | 55 (94.8) | -1.7 (-10.4 to 6.9) |
| Percutaneous technique, nº (%) | 26 (44.8) | 24 (41.4) | 3.4 (-14.6 to 21.5) |
| **Treatments:** | | | |
| HFOT during weaning, nº (%) | 19 (32.8) | 15 (25.9) | 6.9 (-9.6 to 23.4) |
| Remdesivir, nº (%) | 2 (3.5) | 2 (3.5) | 0 (-6.6 to 6.6) |
| Steroids, nº (%) | 46 (79.3) | 43 (74.1) | 5.6 (-9.8 to 21.1) |
| Rescue therapy for ARDS, nº (%) | 51 (87.9) | 50 (86.2) | 1.7 (-10.5 to 13.9) |
| **Severity at ICU admission:** | | | |
| Hemodynamic failure, nº (%) | 17 (29.3) | 21 (36.2) | -6.9 (-23.9 to 10.1) |
| Renal failure, nº (%) | 17 (29.3) | 15 (25.9) | -3.4 (-12.8 to 19.7) |
| Nº failed organs, median (IQR) | 2 (1-2) | 2 (1-3) | 0 (-0.3 to .4) |
| APACHE II, median (IQR) | 13 (8-16) | 14 (10-17) | -0.5 (-2.6 to 1.6) |
| **Complications related to tracheostomy:** | | | |
| Bleeding, nº (%) | 12 (20.7) | 6 (10.3) | 10.3 (-2.7 to 23.4) |
| Infection, nº (%) | 2 (3.5) | 4 (6.9) | -3.4 (-11.5 to 4.6) |
| Airway compromise, nº (%) | 7 (13.8) | 8 (13.8) | -1.7 (-13.9 to 10.5) |
| Weaning failure, nº (%) | 5 (8.6) | 5 (8.6) | 0 (-10.2 to 10.2) |
| Decannulation failure, nº (%) | 4 (6.9) | 1 (1.7) | 5.2 (-2.2 to 12.5) |
| **Complications during ICU stay:** | | | |
| VAT, nº (%) | 14 (24.1) | 13 (22.4) | 1.7 (-13.7 to 17.1) |
| VAP, nº (%) | 18 (31) | 21 (36.2) | -5.2 (-22.3 to 12) |
| Sepsis, nº (%) | 12 (20.7) | 17 (29.3) | -8.6 (-24.3 to 7.1) |
| Multiorgan failure, nº (%) | 9 (15.5) | 11 (19) | -3.4 (-17.2 to 10.3) |
| Hematological, nº (%) | 13 (22.4) | 18 (31) | -8.6 (-24.6 to 7.4) |
| Severe ICU-acquired weakness, nº (%) | 40 (69) | 39 (67.2) | 1.7 (-15.2 to 18.7) |
| Delirium, nº (%) | 27 (46.6) | 24 (41.4) | 5.2 (-12.9 to 23.2) |
| Air leak, nº (%) | 8 (13.8) | 14 (24.1) | -10.3 (-24.5 to 3.8) |
| Withholding life-support measures, nº (%) | 11 (19) | 11 (19) | 0 (-14.3 to 14.3) |
| Death, nº (%) | 16 (27.6) | 17 (29.3) | -1.7 (-18.1 to 14.7) |

**e-Table 5.** Baseline patient characteristics in the propensity-matched cohorts of patients with tracheostomy performed 8–10 days and >10 days after intubation.

| Time to tracheostomy, in days from intubation | 8–10 (n=111) | > 10 (n=111) | Difference between groups (95%CI) or *p* |
|---|---|---|---|
| Age, y, mean (±SD) | 64 (56-69) | 62 (56-68) | 0.1 (-2.5 to 2.8) |
| Male sex, nº (%) | 79 (71.2) | 84 (75.7) | -0.5 (-16.1 to 7.1) |
| Outbreak week ICU admission date, median (IQR)* | | | .099 |
| February 18–23 | 0 (0) | 0 (0) | |
| February 24–29 | 0 (0) | 0 (0) | |
| March 1–6 | 1 (.9) | 0 (0) | |
| March 7–12 | 3 (2.7) | 5 (4.5) | |
| March 13–18 | 28 (25.2) | 29 (26.1) | |
| March 19–24 | 39 (35.1) | 29 (26.1) | |
| March 25–31 | 10 (9) | 11 (9.9) | |
| April 1–6 | 19 (17.1) | 24 (21.6) | |
| April 7–12 | 7 (6.3) | 9 (8.1) | |
| April 13–18 | 3 (2.7) | 4 (3.6) | |
| April 19–24 | 1 (.9) | 0 (0) | |
| April 25–30 | 0 (0) | 0 (0) | |
| May 1–6 | 0 (0) | 0 (0) | |
| May 7–12 | 0 (0) | 0 (0) | |
| **Comorbidities:** | | | |
| BMI >30, nº (%) | 44 (39.6) | 50 (45.1) | -0.7 (-9.4 to 7.9) |
| Arterial hypertension, nº (%) | 40 (36) | 34 (30.6) | 1.8 (-7.6 to 11.1) |
| Heart disease, nº (%) | 9 (8.1) | 9 (8.1) | 0 (-7.2 to 7.2) |
| Neurologic disease, nº (%) | 3 (2.7) | 0 (0) | 2.7 (-0.3 to 0.6) |
| COPD, nº (%) | 2 (1.8) | 2 (1.8) | 0 (-0.3 to 0.3) |
| Other respiratory disease, nº (%) | 5 (4.5) | 7 (6.3) | -1.8 (-7.7 to 4.1) |
| Diabetes mellitus, nº (%) | 26 (23.4) | 33 (29.7) | -6.3 (-17.9 to 5.3) |
| Cancer, nº (%) | 7 (6.3) | 6 (5.4) | -0.9 (-5.2 to 7) |
| Vascular disease, nº (%) | 4 (3.6) | 6 (5.4) | -1.8 (-7.3 to 3.6) |
| Chronic renal failure, nº (%) | 5 (4.5) | 7 (6.3) | -1.8 (-7.7 to 4.1) |
| Chronic hepatic failure, nº (%) | 4 (3.6) | 4 (3.6) | 0 (-4.9 to 4.9) |
| Other diseases, nº (%) | 7 (6.3) | 9 (8.1) | -1.8 (-8.6 to 5) |
| **COVID-19 course:** | | | |
| Time symptoms–ICU admission, d, median (IQR) | 8 (6-11) | 8 (6-12) | .4 (-1.1 to 1.8) |
| Delayed intubation, d, median (IQR) | 1 (0-2) | 1 (0-2) | 0 (-0.4 to 0.5) |
| Time intubation–TR, d (IQR) | 9 (8-10) | 15 (13-19) | -7.2 (-8.2 to -6.3) |
| Time TR–weaning, d, median (IQR) | 9 (0-17) | 8 (0-17) | -0.5 (-4 to 5) |
| Time weaning–decannulation, d (IQR) | 2 (0-4) | 2 (0-5) | -0.1 (-1.4 to 1.3) |
| **Indication for tracheostomy:** | | | |
| Prolonged MV, nº (%) | 101 (91) | 98 (88.3) | 2.7 (-5.3 to 10.7) |
| Percutaneous technique, nº (%) | 46 (41.4) | 46 (41.4) | 0 (-13 to 13) |

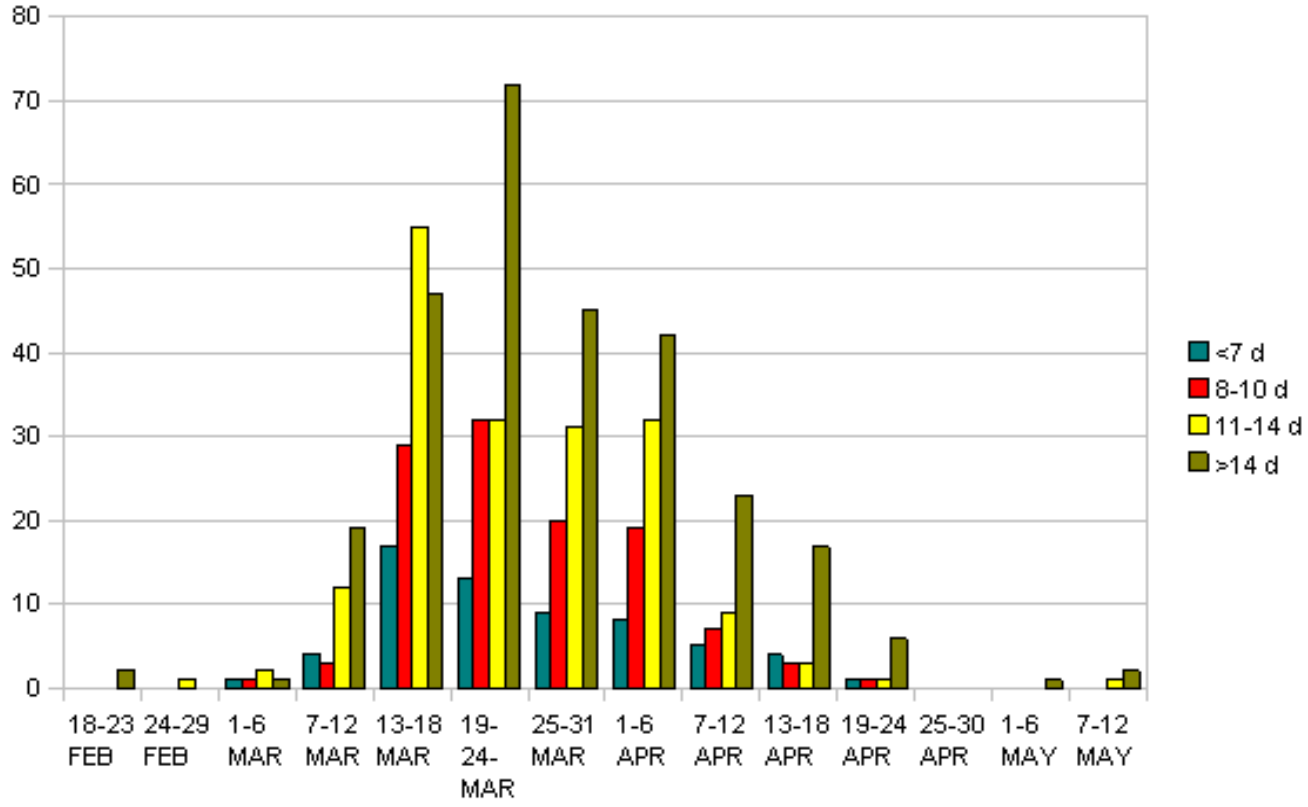
| | | | |
|---|---|---|---|
| **Treatments:** | | | |
| HFOT during weaning, nº (%) | 41 (36.9) | 44 (24.9) | .9 (-11.7 to 13.6) |
| Remdesivir, nº (%) | 11 (9.9) | 10 (9) | .9 (-6.8 to 8.6) |
| Steroids, nº (%) | 93 (83.8) | 95 (85.6) | -1.8 (-11.3 to 7.7) |
| Rescue therapy for ARDS, nº (%) | 105 (94.6) | 109 (98.2) | -3.6 (-8.5 to 1.3) |
| **Severity at ICU admission:** | | | |
| Hemodynamic failure, nº (%) | 42 (37.8) | 33 (29.7) | 8.1 (-4.3 to 20.5) |
| Renal failure, nº (%) | 28 (25.2) | 25 (22.5) | -2.7 (-8.5 to 13.9) |
| Nº failed organs, median (IQR) | 2 (1-3) | 2 (1-3) | -0.1 (-0.2 to 0.4) |
| APACHE II, median (IQR) | 13 (9-18) | 13 (9-17) | -0.6 (-0.8 to 2.1) |
| **Complications related to tracheostomy:** | | | |
| Bleeding, nº (%) | 13 (11.7) | 9 (8.1) | 3.6 (-4.2 to 11.5) |
| Infection, nº (%) | 1 (1.8) | 7 (6.3) | -4.5 (-9.7 to .6) |
| Airway compromise, nº (%) | 12 (10.8) | 15 (13.5) | -2.7 (-11.3 to 5.9) |
| Weaning failure, nº (%) | 11 (9.9) | 11 (9.9) | 0 (-7.9 to 7.9) |
| Decannulation failure, nº (%) | 3 (2.7) | 0 (0) | 2.7 (-0.3 to 0.6) |
| **Complications during ICU stay:** | | | |
| VAT, nº (%) | 17 (15.3) | 28 (25.2) | -9.9 (-20.4 to 0.5) |
| VAP, nº (%) | 46 (41.1) | 56 (50.5) | -9 (-22.1 to 4) |
| Sepsis, nº (%) | 26 (23.4) | 32 (28.8) | -5.4 (-16.9 to 6.1) |
| Multiorgan failure, nº (%) | 19 (17.1) | 23 (20.7) | -3.6 (-13.9 to 6.7) |
| Hematological, nº (%) | 35 (31.5) | 35 (31.5) | 0 (-12.2 to 12.2) |
| Severe ICU acquired weakness, nº (%) | 68 (61.3) | 74 (66.7) | -5.4 (-18 to 7.2) |
| Delirium, nº (%) | 38 (34.2) | 39 (35.1) | -0.9 (-13.4 to 11.6) |
| Air leak, nº (%) | 17 (15.3) | 19 (17.1) | -1.8 (-11.5 to 7.9) |
| Withholding life-support measures, nº (%) | 25 (22.5) | 27 (24.3) | -1.8 (-12.9 to 9.3) |
| Death, nº (%) | 40 (36) | 42 (37.8) | -1.8 (-14.5 to 10.9) |

**e-Table 6.** Baseline patient characteristics in the propensity–matched cohorts of patients with tracheostomy performed 11–14 days vs. >14 days after intubation.

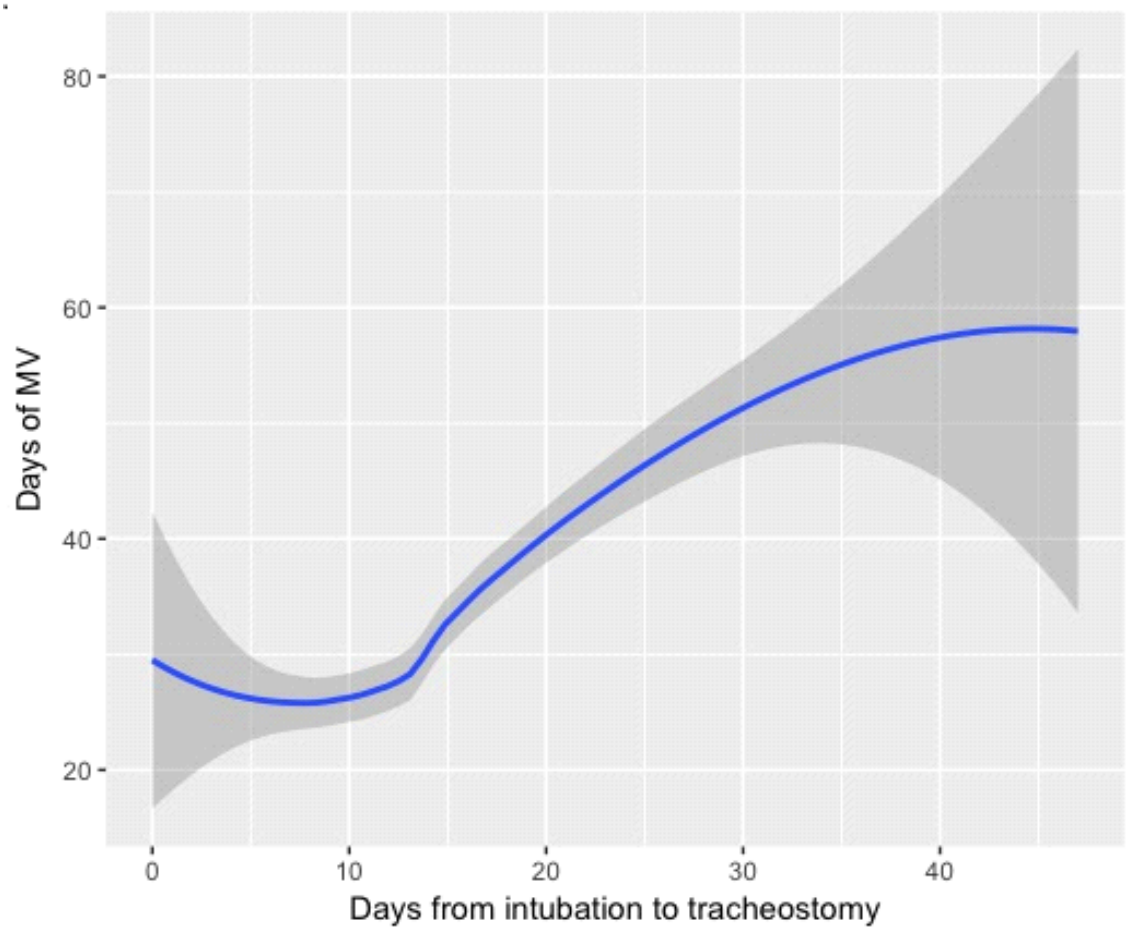
| **Time to tracheostomy, in days from intubation** | **11–14 (n=159)** | **>14 (n=159)** | **Difference between groups (95%CI) or *p*** |
|---|---|---|---|
| Age, y, mean (±SD) | 63 (56-70) | 63 (56-70) | 0.3 (-2 to 2.6) |
| Male sex, nº (%) | 111 (69-8) | 115 (72.3) | -2.5 (-12.5 to 7.4) |
| Outbreak week ICU admission date, nº (%) | | | .943 |
| February 18–23 | 0 (0) | 0 (0) | |
| February 24–29 | 0 (0) | 0 (0) | |
| March 1–6 | 1 (.6) | 1 (.6) | |
| March 7–12 | 12 (7.6) | 12 (7.6) | |
| March 13–18 | 45 (28.3) | 40 (25.2) | |
| March 19–24 | 43 (27) | 48 (30.2) | |
| March 25–31 | 15 (9.4) | 13 (8.2) | |
| April 1–6 | 29 (18.2) | 30 (18.9) | |
| April 7–12 | 9 (5.7) | 9 (5.7) | |
| April 13–18 | 3 (1.9) | 3 (1.9) | |
| April 19–24 | 1 (.6) | 2 (1.2) | |
| April 25–30 | 0 (0) | 0 (0) | |
| May 1–6 | 1 (.6) | 1 (.6) | |
| May 7–12 | 0 (0) | 0 (0) | |
| **Comorbidities:** | | | |
| BMI >30, nº (%) | 68 (42.8) | 65 (40.9) | 1.9 (-8.9 to 12.7) |
| Arterial hypertension, nº (%) | 64 (40.3) | 66 (41.5) | -1.2 (-12.1 to 9.5) |
| Heart disease, nº (%) | 14 (8.8) | 14 (8.8) | 0 (-6.2 to 6.2) |
| Neurologic disease, nº (%) | 5 (3.1) | 2 (1.2) | 1.9 (-1.3 to 5.1) |
| COPD, nº (%) | 8 (5) | 9 (5.7) | -0.7 (-5.6 to 4.3) |
| Other respiratory disease, nº (%) | 18 (11.3) | 21 (13.2) | -1.9 (-9.1 to 5.3) |
| Diabetes mellitus, nº (%) | 34 (21.4) | 35 (22) | -0.6 (-9.7 to 8.4) |
| Cancer, nº (%) | 10 (6.3) | 13 (8.2) | -1.9 (-7.6 to 3.8) |
| Vascular disease, nº (%) | 5 (3.1) | 4 (2.5) | .6 (-3 to 4.3) |
| Chronic renal failure, nº (%) | 6 (3.8) | 9 (5.6) | -1.8 (-6.5 to 2.8) |
| Chronic hepatic failure, nº (%) | 4 (2.5) | 5 (3.1) | -0.6 (-4.3 to 3) |
| Other diseases, nº (%) | 15 (9.4) | 19 (11.9) | -2.5 (-9.3 to 4.3) |
| **COVID-19 course:** | | | |
| Time symptoms–ICU admission, d, median (IQR) | 9 (7-12) | 9 (6-12) | 0.2 (-1 to 1.3) |
| Delayed intubation, d, median (IQR) | 1 (0-2) | 1 (0-2) | 0 (-0.3 to 0.4) |
| Time intubation–TR, d (IQR) | 13 (12-14) | 19 (16-22) | -7.5 (-8.4 to -6.6) |
| Time TR–weaning, d, median (IQR) | 6 (0-12) | 9 (0-22) | -4.9 (-8.3 to 1.5) |
| Time weaning–decannulation, d (IQR) | 2 (0-4) | 2 (0-5) | -1.4 (-2.9 to .1) |
| **Indication for tracheostomy:** | | | |
| Prolonged MV, nº (%) | 139 (87.4) | 139 (87.4) | 0 (-7.3 to 7.3) |
| Percutaneous technique, nº (%) | 79 (49.7) | 79 (49.7) | 0 (-11 to 11) |

| | | | |
|---|---|---|---|
| **Treatments:** | | | |
| HFOT during weaning, nº (%) | 40 (25.2) | 37 (23.3) | 1.9 (-7.5 to 11.3) |
| Remdesivir, nº (%) | 10 (6.3) | 10 (6.3) | 0 (-5.3 to 5.3) |
| Steroids, nº (%) | 124 (78) | 124 (78) | 0 (-9.1 to 9.1) |
| Rescue therapy for ARDS, nº (%) | 143 (89.9 | 145 (91.2) | -1.3 (-7.7 to 5.2) |
| **Severity at ICU admission:** | | | |
| Hemodynamic failure, nº (%) | 59 (37.1) | 63 (39.6) | -2.5 (-13.2 to 8.2) |
| Renal failure, nº (%) | 51 (32.1) | 52 (32.7) | -0.6 (-10.9 to 9.7) |
| Nº failed organs, median (IQR) | 2 (1-3) | 2 (1-3) | -0.3 (-0.3 to 0.2) |
| APACHE II, median (IQR) | 14 (9-18) | 14 (10-17) | 0.1 (-1.1 to 1.3) |
| **Complications related to tracheostomy:** | | | |
| Bleeding, nº (%) | 24 (15.1) | 13 (8.2) | 6.9 (-0.1 to 13.9) |
| Infection, nº (%) | 9 (5.7) | 7 (4.4) | 1.3 (-3.5 to 6.1) |
| Airway compromise, nº (%) | 17 (10.7) | 17 (10.7) | 0 (-6.8 to 6.8) |
| Weaning failure, nº (%) | 19 (11.9) | 17 (10.7) | 1.3 (-5.7 to 8.2) |
| Decannulation failure, nº (%) | 3 (1.9) | 4 (2.5) | 0 (-3.8 to 2.6) |
| **Complications during ICU stay:** | | | |
| VAT, nº (%) | 44 (27.7) | 46 (28.9) | -1.2 (-11.2 to 8.6) |
| VAP, nº (%) | 60 (37.7) | 78 (49.1) | -11.3 (-22.1 to -0.5) |
| Sepsis, nº (%) | 43 (27) | 61 (38.4) | -11.3 (-21.6 to -1.1) |
| Multiorgan failure, nº (%) | 31 (19.5) | 34 (21.4) | -1.9 (-10.7 to 7) |
| Hematological, nº (%) | 35 (22) | 58 (36.5) | -14.5 (-24.3 to -4.6) |
| Severe ICU-acquired weakness, nº (%) | 95 (59.8) | 115 (72.3) | -12.6 (-22.9 to -2.3) |
| Delirium, nº (%) | 52 (32.7) | 65 (40.9) | -8.2 (-18.7 to 2.4) |
| Air leak, nº (%) | 22 (13.8) | 29 (18.2) | -4.4 (-12.5 to 3.6) |
| Withholding life-support measures, nº (%) | 42 (26.4) | 27 (17) | 9.4 (0.4 to 18.4) |
| Death, nº (%) | 61 (38.4) | 51 (32.1) | 6.3 (-4.2 to 16.8) |

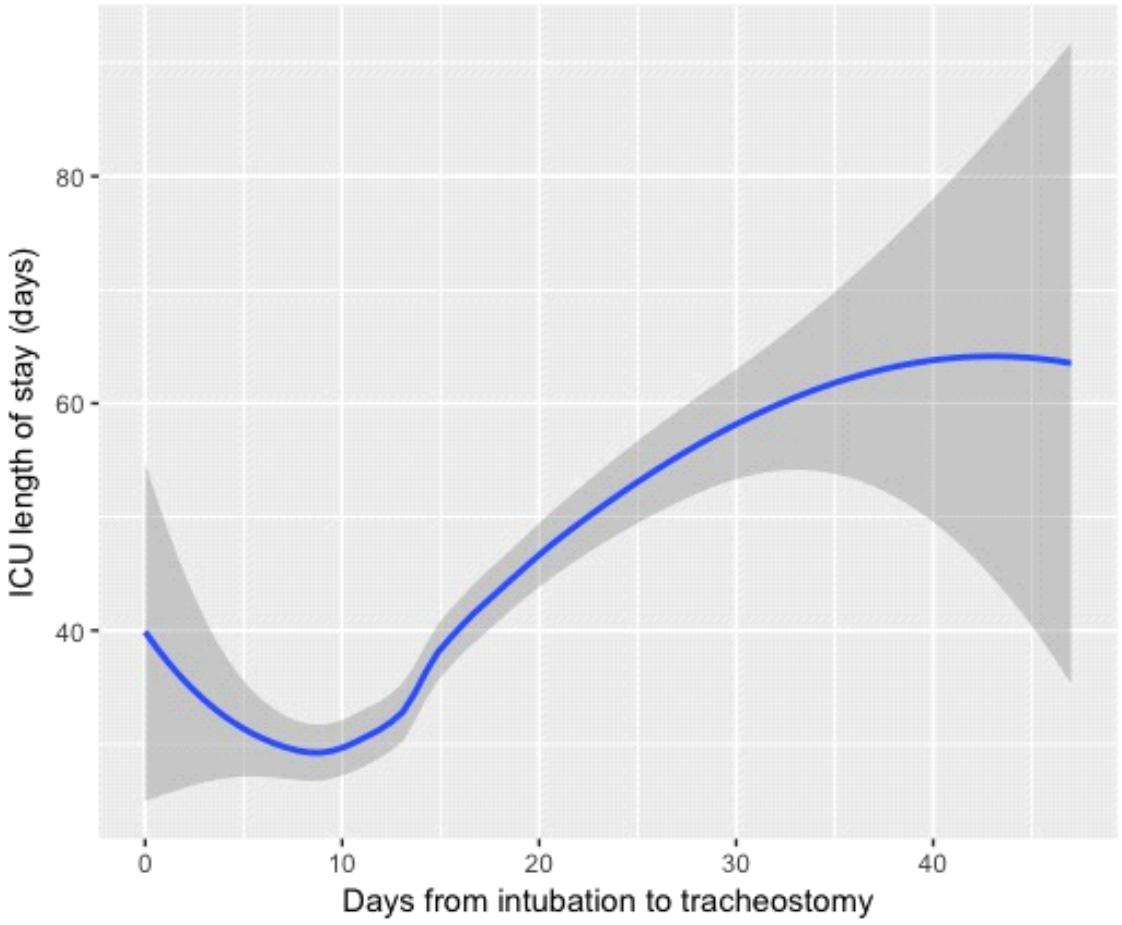
**e-Figure 1.** Number of tracheostomies performed in different timeframes from intubation according to week of admission to the ICU.



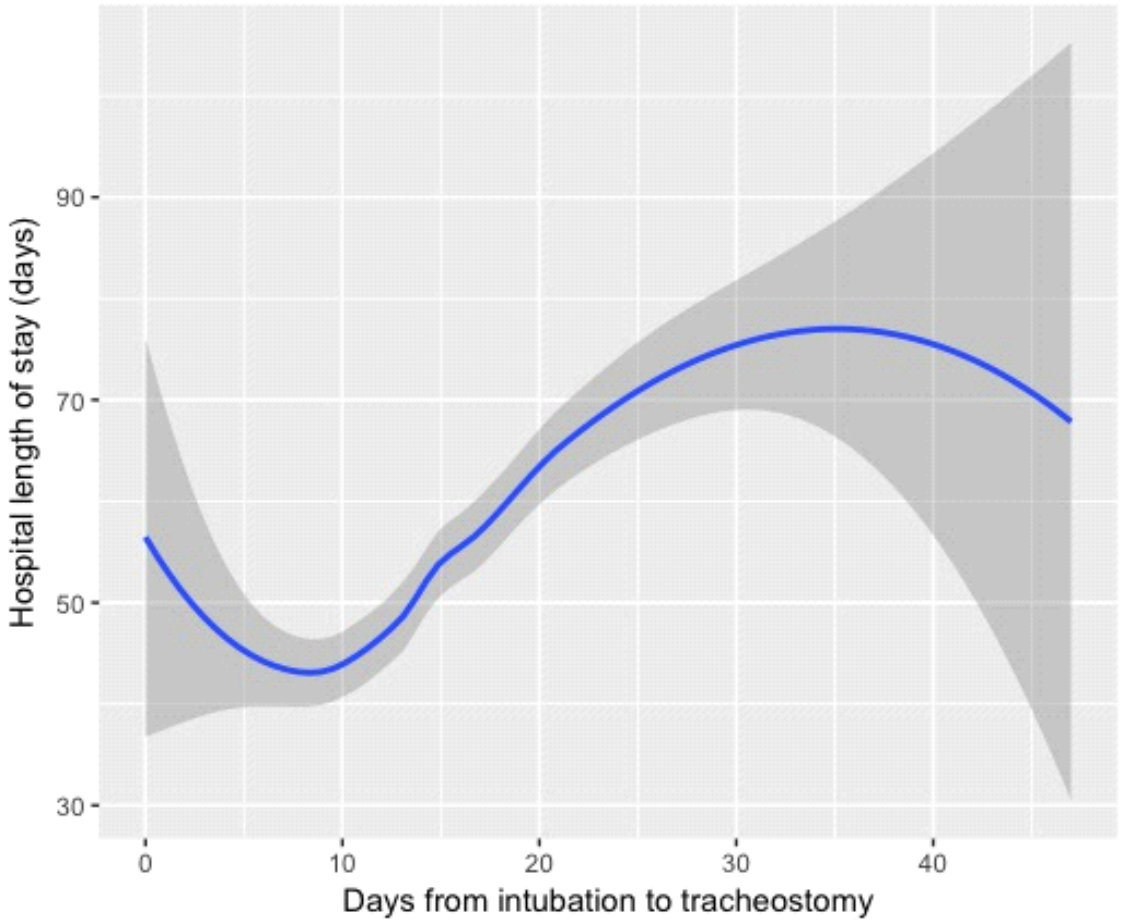
**e-Figure 2.** Days on mechanical ventilation according to timing of tracheostomy in the entire population.



**e-Figure 3.** ICU length of stay according to timing of tracheostomy in the entire population.



**e-Figure 4.** Hospital length of stay according to timing of tracheostomy in the entire population.

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