

EDITORIALS



Building an Evidence Base for Survivors of Critical Illness

Daniela Lamas, M.D.

On rounds in the long-term acute care hospital, I am surprised to see a familiar name on my list — a patient with respiratory failure whom I had initially admitted to our intensive care unit (ICU). In the early days of his critical illness, we had debated ventilator management and choice of antibiotic agents, with every decision dictated by a body of evidence.

Now, months later, I am at his bedside once again. And this time he has a question for me. Gesturing impatiently to the tracheostomy tube in his neck, he asks, “When can this come out?”

I hesitate. The very presence of a tracheostomy tube — although it is necessary in approximately 15% of patients who are intubated for respiratory failure but who cannot be weaned from ventilator support¹ — can cause complications, including tracheal stenosis, bleeding, and infection.² Decannulation is a key milestone in a patient’s recovery. But if the procedure is done too soon, a failed decannulation could lead to urgent replacement of the tracheostomy tube or to endotracheal intubation; these are setbacks that involve both physiological and motivational harm. So how do we know when it is appropriate to remove a tracheostomy tube?

In contrast to the evidence that drives protocols in the ICU, when it comes to the treatment of survivors of critical illness, we are often in the dark.³ Data on decannulation methods have been limited to surveys, single-center experience, and scoring systems, without guidance from large-scale, randomized trials. As a result, decisions about decannulation are inconsistent among clinicians and among institutions.⁴ In this issue of the *Journal*, Hernández Martínez et al.⁵ report

important results that might encourage providers to be more aggressive with decannulation and that, more broadly, should lead to further high-quality research to build an evidence base for the care of survivors of critical illness.

The authors conducted a randomized trial to compare two different methods of decannulation in a cohort of 330 patients in five ICUs in Spain. All the patients had undergone weaning from mechanical ventilation. Patients in the control group underwent a capping trial, in which a cap was placed on the tracheostomy tube for 24 hours to test the patient’s ability to clear secretions and breathe around the tube and through a small fenestration in the neck of the tube (a pathway with a much higher airflow resistance than the natural airway). Although this method is one of those more commonly used for this purpose, its conservative nature might result in delays in decannulation, as the authors note. In contrast, patients in the intervention group underwent decannulation on the basis of the number of times over a 24-hour period that the care staff had to remove secretions by suctioning; these patients also received high-flow oxygen to their tracheostomy tube, although the circuit was open and patients had to make all the ventilatory efforts on their own. These patients never underwent a capping trial; rather, their tracheostomy tube was removed if they underwent suctioning fewer than two times every 8 hours.

The primary outcome, the time to decannulation, was 7 days shorter in the intervention group than in the control group, with a concomitantly lower incidence of pneumonia and tracheobronchitis and a shorter stay in the hos-

pital. Ultimately, regardless of the method used, 95% of all the enrolled patients underwent decannulation successfully, and there was no significant difference between groups in the very low incidence of replacement of the tracheostomy tube after it had been taken out.

What, then, is the conclusion we can draw? Should we shift from capping trials to suctioning frequency when it comes to deciding when to remove our patients' tracheostomy tubes? An important limitation is that in contrast to the United States, where patients are often transferred to post-acute care facilities for weaning from a mechanical ventilator and for decannulation, this trial took place in ICUs in Spain. Although the population of patients is reflective of that in the United States, the ratio of nurses and respiratory therapists to patients probably differs, and to obtain broader applicability, these results might be reproduced in a long-term care setting. In addition, as part of the trial design, the patients in the intervention group spent more time receiving high-flow oxygen therapy than those in the control group, who received high-flow oxygen therapy when the tube was not capped. As the authors note, it is possible that the heated humidification of high-flow oxygen decreased the frequency of suctioning events. It is not clear how much of a role that played in the trial outcomes. Finally, it will be a challenge to overcome clinical resistance and inertia in adopt-

ing a more aggressive protocol when the standard care does not result in clear harm.

But that is a challenge that will be worth taking. The authors have taken an important step in building an evidence base to improve care for patients with chronic critical illness. The generation of new knowledge should not end when a patient has survived acute illness. As Hernández Martínez et al. have shown, research in this population is both feasible and necessary. The next time I stand at a bedside and a patient asks me when his tracheostomy tube might come out, I should be able to answer, "Let me take a look at the evidence."

Disclosure forms provided by the author are available with the full text of this editorial at NEJM.org.

From the Division of Pulmonary and Critical Care Medicine, Brigham and Women's Hospital, Boston.

1. Abe T, Madotto F, Pham T, et al. Epidemiology and patterns of tracheostomy practice in patients with acute respiratory distress syndrome in ICUs across 50 countries. *Crit Care* 2018;22:195.
2. O'Connor HH, White AC. Tracheostomy decannulation. *Respir Care* 2010;55:1076-81.
3. Kahn JM, Carson SS. Generating evidence on best practice in long-term acute care hospitals. *JAMA* 2013;309:719-20.
4. Mitchell RB, Hussey HM, Setzen G, et al. Clinical consensus statement: tracheostomy care. *Otolaryngol Head Neck Surg* 2013; 148:6-20.
5. Hernández Martínez G, Rodríguez M-L, Vaquero M-C, et al. High-flow oxygen with capping or suctioning for tracheostomy decannulation. *N Engl J Med* 2020;383:1009-17.

DOI: 10.1056/NEJMe2024625

Copyright © 2020 Massachusetts Medical Society.

Treatment of Hemophilia — More Amazing Progress

Pier M. Mannucci, M.D.

With a prevalence of 17.1 cases per 100,000 males, hemophilia A is the most frequent inherited disorder of blood coagulation.¹ After the adoption of prophylactic replacement therapy with factor VIII administered intravenously 3 or 4 times per week, patients' life expectancy has become very close to that of unaffected males.¹ Moreover, the occurrence of spontaneous bleeding and the development of musculoskeletal damage have been minimized. In addition, in the past decade, further impressive advances have occurred.^{2,3} The arrival of factor VIII prod-

ucts with an extended plasma half-life has meant that intravenous injections that are needed to minimize bleeding can be administered twice weekly.⁴ The monoclonal antibody emicizumab, which mimics factor VIII coagulant activity, is efficacious at preventing bleeding when administered subcutaneously at weekly intervals or even every 2 weeks.^{5,6} Promising results from phase 1–2 studies of gene transfer with adeno-associated viral vectors⁷ involving adults with severe hemophilia A paved the way to phase 3 studies in an advanced phase of development.⁸

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

SEPTEMBER 10, 2020

VOL. 383 NO. 11

High-Flow Oxygen with Capping or Suctioning for Tracheostomy Decannulation

Gonzalo Hernández Martínez, M.D., Ph.D., Maria-Luisa Rodriguez, M.D., Maria-Concepción Vaquero, M.D.,
Ramón Ortiz, M.D., Ph.D., Joan-Ramon Masclans, M.D., Ph.D., Oriol Roca, M.D., Ph.D.,
Laura Colinas, M.D., Ph.D., Raul de Pablo, M.D., Ph.D., Maria-del-Carmen Espinosa, M.D., Ph.D.,
Marina Garcia-de-Acilu, M.D., Cristina Climent, M.D., and Rafael Cuenca-Boy, M.D.

ABSTRACT

BACKGROUND

When patients with a tracheostomy tube reach a stage in their care at which decannulation appears to be possible, it is common practice to cap the tracheostomy tube for 24 hours to see whether they can breathe on their own. Whether this approach to establishing patient readiness for decannulation leads to better outcomes than one based on the frequency of airway suctioning is unclear.

METHODS

In five intensive care units (ICUs), we enrolled conscious, critically ill adults who had a tracheostomy tube; patients were eligible after weaning from mechanical ventilation. In this unblinded trial, patients were randomly assigned either to undergo a 24-hour capping trial plus intermittent high-flow oxygen therapy (control group) or to receive continuous high-flow oxygen therapy with frequency of suctioning being the indicator of readiness for decannulation (intervention group). The primary outcome was the time to decannulation, compared by means of the log-rank test. Secondary outcomes included decannulation failure, weaning failure, respiratory infections, sepsis, multiorgan failure, durations of stay in the ICU and hospital, and deaths in the ICU and hospital.

RESULTS

The trial included 330 patients; the mean (\pm SD) age of the patients was 58.3 \pm 15.1 years, and 68.2% of the patients were men. A total of 161 patients were assigned to the control group and 169 to the intervention group. The time to decannulation was shorter in the intervention group than in the control group (median, 6 days [interquartile range, 5 to 7] vs. 13 days [interquartile range, 11 to 14]; absolute difference, 7 days [95% confidence interval, 5 to 9]). The incidence of pneumonia and tracheobronchitis was lower, and the duration of stay in the hospital shorter, in the intervention group than in the control group. Other secondary outcomes were similar in the two groups.

CONCLUSIONS

Basing the decision to decannulate on suctioning frequency plus continuous high-flow oxygen therapy rather than on 24-hour capping trials plus intermittent high-flow oxygen therapy reduced the time to decannulation, with no evidence of a between-group difference in the incidence of decannulation failure. (REDECAP ClinicalTrials.gov number, NCT02512744.)

From Virgen de la Salud University Hospital (G.H.M., M.-L.R., L.C.) and the Research Unit, Medical Council (R.C.-B.), Toledo, Ramón y Cajal University Hospital (M.-C.V., R.P.) and Ciber Enfermedades Respiratorias, Health Institute Carlos III (O.R.), Madrid, Ciudad Real University Hospital and Ciudad Real University, Ciudad Real (R.O., M.-C.E.), Medical Research Mar Institute (J.-R.M.), the Critical Care Department, Autònoma de Barcelona University (J.-R.M., M.G.-A.), Del Mar University Hospital (J.-R.M., C.C.), Vall d'Hebron Research Institute (O.R.), and Vall d'Hebron University Hospital (O.R., M.G.A.), Barcelona, and Alcala University, Alcalá de Henares (R.P.) — all in Spain. Address reprint requests to Dr. Hernández Martínez at the Department of Critical Care Medicine, Virgen de la Salud University Hospital, Tenerife No. 40, Fl. 2, Rm. D, 28039 Madrid, Spain, or at ghermandezm@telefonica.net.

N Engl J Med 2020;383:1009-17.

DOI: 10.1056/NEJMoa2010834

Copyright © 2020 Massachusetts Medical Society.

APPROXIMATELY 15% OF PATIENTS UNDERGOING mechanical ventilation receive a tracheostomy as part of their care,^{1,2} but experimental data regarding readiness for decannulation are limited. Evidence of decannulation readiness has been limited to expert opinion,³⁻⁵ survey studies,⁶⁻⁸ single-center experience,^{9,10} unvalidated scores to predict decannulation success,¹¹⁻¹³ and a few randomized trials that have focused on organizational concerns such as intensivist-led tracheostomy teams or the effects of specific decisions on outcomes such as dysphagia or sleep quality.¹⁴⁻¹⁷

A commonly used test to determine whether a critically ill patient with a tracheostomy tube is ready for decannulation is a capping trial, in which a cap is placed over the tracheostomy tube for a period of time to see whether the patient is able to breathe around the tracheostomy tube (or through a fenestration in the tube) through the nose and mouth.^{3,4,7} Protocol-based capping trials have led to readiness criteria with high specificity and a positive predictive value for successful decannulation,¹⁸ but their conservative nature can delay decannulation — that is, patients who do not meet the trial criteria for decannulation may still be able to undergo decannulation successfully.^{13,18} An alternative approach to assessing readiness for decannulation is to measure the number of times that secretions are suctioned from a patient's airway over a given period of time, with fewer episodes of suctioning considered to be a positive indicator of potentially successful decannulation.¹³

In the Reducing Decannulation Time Limiting Capping (REDECAP) trial, we compared an assessment of readiness for decannulation that was based on suctioning frequency with an assessment that was based on tracheostomy capping. All the patients received high-flow oxygen therapy when they could respire through their tracheostomy tube.

METHODS

TRIAL DESIGN AND OVERSIGHT

We conducted this randomized trial at five intensive care units (ICUs) in Spain. The ethics committee at each center and the departments of health of the regional governments with which these hospitals are affiliated (Madrid, Catalonia, and Castilla-La Mancha) approved the protocol

(available with the full text of this article at NEJM.org). All the patients or their relatives provided written informed consent. The only commercial support for this trial was that Fisher and Paykel Healthcare paid for writing assistance with the manuscript, but it had no role in the design or conduct of the trial or in the decision to submit the manuscript for publication.

PATIENT POPULATION

All critically ill adult patients in whom a first tracheostomy was created during an ICU stay underwent screening after being weaned from mechanical ventilation, which was defined as freedom from mechanical ventilation for 24 consecutive hours. Exclusion criteria were a contraindication for decannulation at randomization (unconsciousness, severe swallowing dysfunction, an airway patency problem, neuromuscular disease other than ICU-acquired weakness, or tracheostomy for airway control), an age of less than 18 years, or an expectation (according to the Sabadell score, which is a measure of the risk of death) that death would occur before hospital discharge.¹⁹

The following variables that were recorded at inclusion were age, sex, and body-mass index (BMI; the weight in kilograms divided by the square of the height in meters); the Acute Physiology and Chronic Health Evaluation (APACHE) II score in the first 24 hours after admission as assessed on the basis of 17 variables (scores range from 0 to 71, with higher scores indicating more severe disease); coexisting conditions, which were categorized according to the Charlson comorbidity index, on which 22 clinical conditions are scored with regard to the risk of death (with higher scores indicating a higher risk of death); and the primary diagnosis. The variables that were recorded on the day tracheostomy was performed were the indication for tracheostomy, tracheostomy technique, cannula characteristics, and the APACHE II score. The variables that were recorded at randomization were the APACHE II score, results of a swallowing test, and suctioning frequency. The following variables were recorded until discharge from the hospital: the date of decannulation, the date on which the criteria for decannulation were met, infectious complications, weaning failure or decannulation failure, reasons for capping-trial failure or delayed progression to decannulation,

ICU readmission, and duration of stay in the ICU and the hospital; and death in the ICU and in the hospital.

MECHANICAL-VENTILATION WEANING AND DECANNULATION PROTOCOLS

Patients were weaned from mechanical ventilation according to the following protocol²⁰: Patients with a tracheostomy tube underwent screening daily in order to determine readiness for weaning according to prespecified criteria. To avoid prolonged cuff deflation in patients at high risk for aspiration, we assessed the risk of aspiration by checking swallowing with a drink test involving 50 ml of water with the cuff deflated for a short period of time. After the drink test, we performed a tracheostomy-tube occlusion test to rule out tracheal airflow obstruction. In brief, we occluded the opening of the cannula with the tracheal cuff deflated for 5 minutes. Patients who had any sign that was suggestive of airflow obstruction underwent diagnostic bronchoscopy.

Patients underwent progressive weaning from mechanical ventilation according to a protocol that was based on intermittent trials of spontaneous breathing of progressively longer duration through the tracheostomy tube. Between the trials, assist-controlled ventilation was reinstated in order to allow patients to rest. Spontaneous breathing trials were attempted twice a day, with at least 2 hours of ventilatory support between trials. The attending physician stopped the trial if the patient had any sign of respiratory distress. When no signs of respiratory distress were present, the trial was continued for 12 consecutive hours. When patients were able to sustain spontaneous breathing for more than 12 consecutive hours on 2 consecutive days, they were switched to continuous high-flow oxygen therapy through their tracheostomy tube. The cuff was deflated and respiratory secretions were aspirated; the cuff remained deflated only during the periods of spontaneous breathing.

Throughout the trial period, the same style of 7-mm inner-diameter tracheostomy tube with a fenestrated inner sleeve (TRACOE twist, TRACOE Medical) was used; the cuff was deflated for all capping trials. In patients who had a BMI greater than 45 or who had anatomical abnormalities of the airway, other tracheal cannulas were allowed. In the control group, the decision to decannulate was based on a 24-hour capping trial.¹⁸

Patients were considered to be ready to undergo a capping trial when they had had no more than one aspiration every 4 hours during a 12-hour period according to prespecified indications (see below). Failure on the capping trial was defined as decapping for any reason during the 24-hour period (see the protocol).²¹ When a capping trial failed, a new capping trial was not allowed until the next day (i.e., ≥ 12 hours later in order to check criteria for eligibility). Patients in whom capping trials failed repeatedly could undergo decannulation outside the protocol on the basis of suctioning requirements if the attending physicians considered them to be ready for decannulation.

In the intervention group, the decision to decannulate was based on suctioning frequency. Patients underwent decannulation when they had had no more than two aspirations every 8 hours during a 24-hour period according to prespecified indications (see below). Patients in this group did not undergo capping trials.

Suctioning was performed when a patient presented with any of the following conditions: presence of rhonchi over the trachea, visible secretions in the airways, an inability to generate an effective spontaneous cough through the cannula despite repeated attempts, suspected aspiration of gastric or upper-airway secretions, acute respiratory distress, or deterioration of the oxygen saturation (to $\leq 92\%$) that was thought to be related to airway obstruction. When suctioning was performed, it was done according to guideline recommendations.²¹ Aspirations that were performed only to obtain sputum specimens for analyses were not considered in the decannulation protocols.

Decannulation could be delayed in patients because of pending diagnostic or therapeutic procedures and in those with a limited level of consciousness who were considered by the clinicians to be at risk for neurologic deterioration. To rule out bias related to these delays, we performed an intention-to-treat analysis. Every week, reasons for delayed decannulation were classified.

All the patients received high-flow oxygen therapy (Airvo 2, Fisher and Paykel Healthcare) with a specific interface for tracheostomy tubes (OPT870, Fisher and Paykel Healthcare) when they were breathing through the tracheostomy tube. This setup meant that patients in the control group received intermittent high-flow oxygen

therapy while the tube was decapped and patients in the intervention group received continuous high-flow oxygen therapy until decannulation. High-flow oxygen therapy was targeted to a temperature of 37°C and a flow of 60 liters per minute, and the fraction of inspired oxygen was regularly adjusted to maintain an arterial oxygen saturation, as measured by pulse oximetry, of between 92% and 95%.

Patients could be discharged from the high-dependency unit (ICU or step-down unit) before decannulation if they met the safety criteria (see the protocol). All the patients who were discharged to a ward while they had a tracheostomy tube were followed up by intensivist-led teams and trained nurses.

Both groups of patients were treated by the same medical, nursing, and respiratory therapy staff and received similar medical treatment. Attending physicians were aware of the trial groups. Within 8 hours after weaning from mechanical ventilation, eligible patients underwent simple randomization to the control group or the intervention group by means of concealed assignment with a random-number generator through a call center.

END POINTS

The primary outcome was the time to decannulation, which was defined as the time from the completion of weaning from mechanical ventilation (24 consecutive hours disconnected from the ventilator) to actual decannulation (intention-to-treat analysis). Secondary outcomes were decannulation failure, which was defined according to prespecified criteria; weaning failure; respiratory infections (pneumonia and tracheobronchitis); sepsis; multiorgan failure; durations of stay in the ICU and hospital; ICU readmission; and in-ICU and in-hospital deaths.

STATISTICAL ANALYSIS

The sample size was calculated to detect a 3-day difference in the time to decannulation (primary outcome), assuming a mean (\pm SD) time of 13 \pm 11 days in the control group.²² A sample of 165 patients per group was considered to be adequate for the trial to have 80% power, with an alpha level of 5% for two-sided tests and with no more than 15% of the patients withdrawing from the trial. All the outcomes were analyzed according to the intention-to-treat principle. The results for

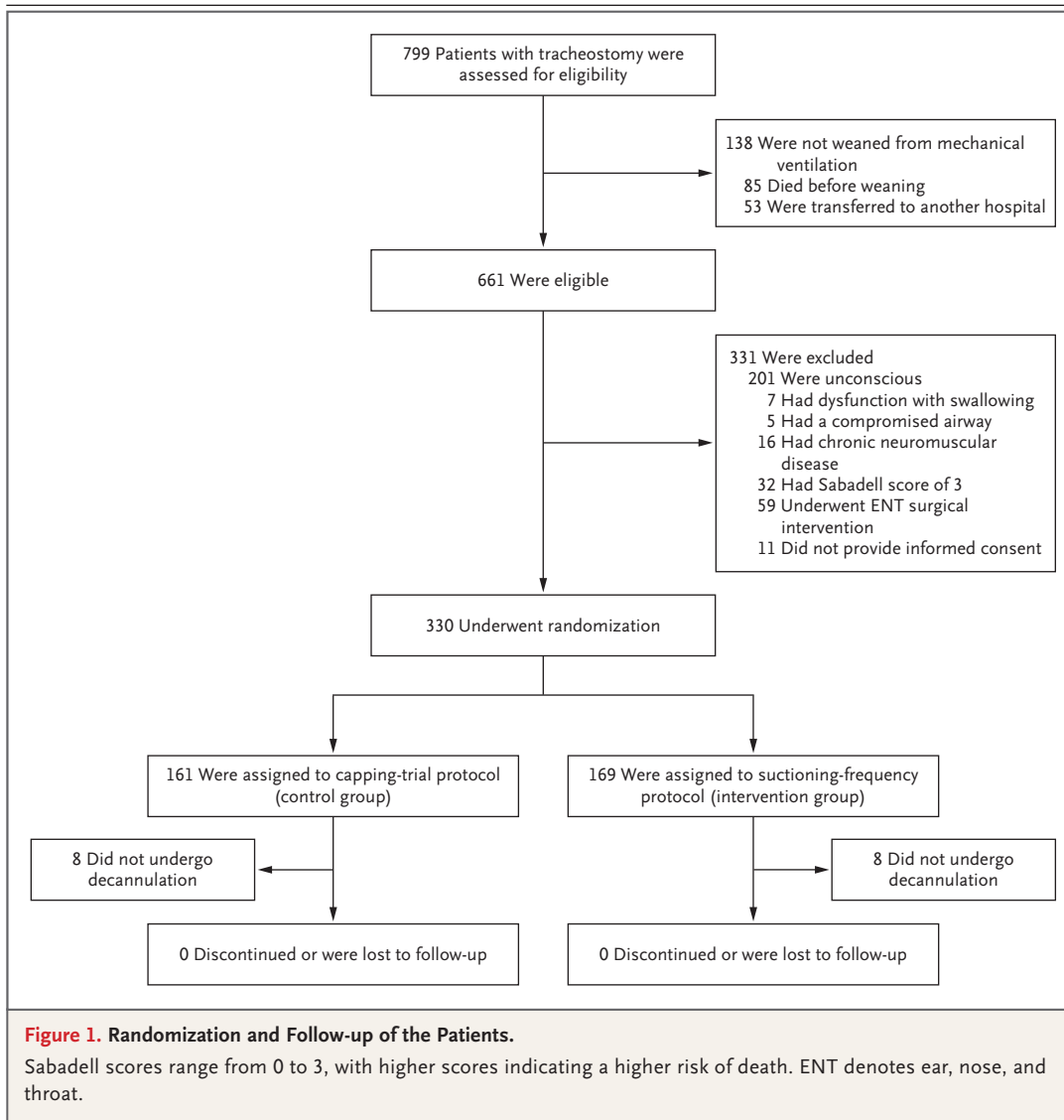
the primary outcome were also stratified according to center. Results for differences in days are reported in absolute values. Secondary and exploratory outcomes were not adjusted for multiplicity, and therefore these results should not be used to infer treatment effects.

To assess the time to decannulation, we plotted Kaplan–Meier curves and compared them using the log-rank test. Patients who did not undergo decannulation were included in the analysis and had their data censored at the date of hospital discharge, death, or withdrawal from the trial. Confidence intervals for time-to-event outcomes were calculated with the use of inference for linear function of medians,²³ and the Newcombe and Wilson hybrid score was used to calculate the interval estimation for the difference between proportions.²⁴ The two-sided level of significance was set at 0.05. We used SPSS software, version 13.0 (SPSS), for statistical analyses.

RESULTS

PATIENTS

From May 2016 through May 2018, we identified 799 patients with a tracheostomy tube; of these patients, 138 did not complete weaning from mechanical ventilation. Thus, 661 patients underwent screening for inclusion in the trial. A total of 330 patients (49.9% of those screened) underwent randomization: 161 patients were assigned to the control group (capping trial and receipt of intermittent high-flow oxygen therapy) and 169 were assigned to the intervention group (assessment of suctioning frequency and receipt of continuous high-flow oxygen therapy) (Fig. 1). Eight patients in each group did not undergo decannulation and had their data censored. Overall, the mean (\pm SD) age of the patients was 58.3 \pm 15.1 years, and 68.2% of the patients were men. The demographic and clinical characteristics of the patients were similar in the two groups (Table 1; and Table S1 in the Supplementary Appendix, available at NEJM.org). In the control group, 12 patients underwent decannulation without having met the decannulation criteria after they had repeated failures on capping trials; all these patients underwent decannulation successfully. Five patients had the cannula changed out of protocol for anatomical reasons. All the patients were followed to hospital discharge or death.



PRIMARY OUTCOME

Table 2 shows the results of the intention-to-treat analysis for the primary outcome. The median time to decannulation was shorter in the intervention group than in the control group (6 days [interquartile range, 5 to 7] vs. 13 days [interquartile range, 12 to 14]; absolute difference, 7 days [95% confidence interval {CI}, 5 to 9]) (Fig. 2 and Table S2).

SECONDARY OUTCOMES

Results regarding the secondary outcomes are shown in Table 2. Recannulation (i.e., decannulation failure) occurred in 9 patients (5.6%) in the control group and in 4 (2.4%) in the inter-

vention group (difference, 3.2 percentage points; 95% CI, -1.2 to 8.1). Weaning failure occurred in 27 patients (16.7%) in the control group and in 11 (6.5%) in the intervention group (difference, 10.3 percentage points; 95% CI, 3.4 to 17.4). The causes of and reasons for weaning failure are presented in Table 2 and Figure S1.

Pneumonia occurred in 16 patients (9.9%) in the control group and in 7 (4.1%) in the intervention group (difference, 5.8 percentage points; 95% CI, 0.2 to 11.8). Tracheobronchitis occurred in 47 patients (29.2%) in the control group and in 32 (18.9%) in the intervention group (difference, 10.3 percentage points; 95% CI, 1.0 to 19.3). The median duration of stay in the hospi-

Table 1. Characteristics of the Patients.*

Characteristic	Control Group (N=161)	Intervention Group (N=169)
Age — yr	59.3±14.8	57.3±15.4
Male sex — no. (%)	108 (67.1)	117 (69.2)
APACHE II score†	10.8±3.7	11.6±4.1
Median duration of mechanical ventilation before tracheostomy (IQR) — days	13 (10–19)	13 (10–18)
Indication for tracheostomy — no. (%)		
Mechanical ventilation for >21 days	30 (18.6)	29 (17.2)
Prolonged weaning from mechanical ventilation‡	64 (39.8)	80 (47.3)
Low level of consciousness	43 (26.7)	37 (21.9)
Management of respiratory secretions	4 (2.5)	6 (3.6)
Airway-patency problems	20 (12.4)	18 (10.7)
Percutaneous tracheostomy	126 (78.3)	133 (78.7)
Out-of-protocol tracheal cannula	3 (1.9)	2 (1.2)
Coexisting conditions — no. (%)§		
Body-mass index >25¶	122 (75.8)	126 (74.6)
Heart disease	34 (21.1)	29 (17.2)
Neurologic disease	36 (22.4)	30 (17.8)
Chronic obstructive pulmonary disease	21 (13.0)	18 (10.7)
Type of diagnosis at admission — no. (%)		
Medical	128 (79.5)	133 (78.7)
Trauma	38 (23.6)	39 (23.1)
Surgical	94 (58.4)	90 (53.3)
Swallowing dysfunction at randomization — no. (%)**	63 (39.1)	52 (30.8)
Suctioning frequency at randomization — no. of events during 8 hr before randomization	1.9±1.2	2.0±1.1

* Plus-minus values are means ±SD. IQR denotes interquartile range.

† 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.

‡ Prolonged weaning from mechanical ventilation was defined according to the Sixth International Consensus Conference in Intensive Care Medicine.²⁵

§ 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.

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

|| Patients could have had more than one type of diagnosis at admission.

** Swallowing dysfunction was defined as an abnormal result on the 50-ml drink test. Patients with severe swallowing dysfunction were excluded from the trial. No patient's condition worsened from having an abnormal result on the drink test to having severe swallowing dysfunction during the trial period.

tal was 62 days (interquartile range, 38 to 105) in the control group and 48 days (interquartile range, 33 to 71) in the intervention group (absolute difference, 14 days; 95% CI, 9 to 33).

DISCUSSION

In conscious, critically ill adult patients with a tracheostomy tube, we found that the time to

decannulation was shorter in those with decannulation based on suctioning frequency plus the use of continuous high-flow oxygen therapy than in those who received the standard of care including capping trials plus the use of intermittent high-flow oxygen therapy, with no significant difference in the incidence of recannulation. The most plausible explanation for this result is that capping trials are highly demand-

Table 2. Primary and Secondary Outcomes.*

Outcome	Control Group (N=161)	Intervention Group (N=169)	Difference (95% CI)
Primary outcome: median time to decannulation (IQR) — days†	13 (11 to 14)	6 (5 to 7)	7 (5 to 9)
Secondary outcomes			
Decannulation failure — no. (%)	9 (5.6)	4 (2.4)	3.2 (–1.2 to 8.1)
Weaning failure — no. (%)‡	27 (16.8)	11 (6.5)	10.3 (3.4 to 17.4)
Pneumonia — no. (%)	16 (9.9)	7 (4.1)	5.8 (0.2 to 11.8)
Tracheobronchitis — no. (%)	47 (29.2)	32 (18.9)	10.3 (1.0 to 19.3)
Median duration of stay (IQR) — days			
In the ICU§	35 (27 to 51)	32 (25 to 43)	3 (–1 to 11)
In the hospital	62 (38 to 105)	48 (33 to 71)	14 (9 to 33)
Death — no. (%)			
In the ICU	0	0	0 (–2.2 to 2.3)
In the hospital	8 (5.0)	4 (2.4)	2.6 (–1.7 to 7.4)
Sepsis — no. (%)	12 (7.5)	12 (7.1)	0.3 (–5.5 to 6.3)
Multiorgan failure — no. (%)	6 (3.7)	2 (1.2)	2.5 (–1.1 to 6.8)
Exploratory outcomes			
Decannulation before ICU discharge — no. (%)	104 (64.6)	139 (82.2)	–17.7 (–26.8 to –8.1)
Capping-trial failure — no. (%)¶	118 (73.3)	NA	NA
Median duration of stay (IQR) — days			
In the hospital after randomization	37 (20 to 66)	23 (14 to 36)	14 (10 to 31)
In the hospital after ICU discharge	27 (11 to 53)	16 (7 to 27)	11 (4 to 20)
ICU readmission — no. (%)	17 (10.6)	10 (5.9)	4.6 (–1.4 to 10.9)
Swallowing dysfunction at decannulation — no. (%)	16 (9.9)	15 (8.9)	1.1 (–5.4 to 7.6)

* Results for differences in days are reported in absolute values; durations in the intervention group were always shorter than those in the control group. Differences between percents are shown in percentage points and were calculated on the basis of unrounded data. The 95% confidence intervals (CIs) for the secondary and exploratory outcomes were not adjusted for multiplicity, and therefore these results should not be used to infer treatment effects. ICU denotes intensive care unit, and NA not applicable.

† The primary outcome was assessed in the intention-to-treat population and was calculated according to the day on which the patient underwent decannulation. In 81 patients who met the criteria for decannulation (30 in the control group vs. 51 in the intervention group), attending physicians delayed decannulation. The main reason for delay was therapeutic intervention in 28 patients (12 in the control group and 16 in the intervention group), expected diagnostic procedure in 24 patients (9 and 15, respectively), and fluctuating level of consciousness in 17 patients (6 and 11). The analysis according to the day on which the patients met decannulation criteria showed the following results: the median time to decannulation was 12 days (interquartile range, 7 to 12) in the control group and 4 (interquartile range, 3 to 8) in the intervention group (absolute difference, 8 days; 95% CI, 5 to 10).

‡ The causes of weaning failure were related to respiratory acidosis (in 3 patients in the control group), decreased level of consciousness (in 1 patient in the intervention group), hypoxemia (in 2 patients in the intervention group and in 13 in the control group), tachypnea (in 3 and 2, respectively), and clinical signs suggestive of respiratory-muscle fatigue (in 5 and 9) (Fig. S1).

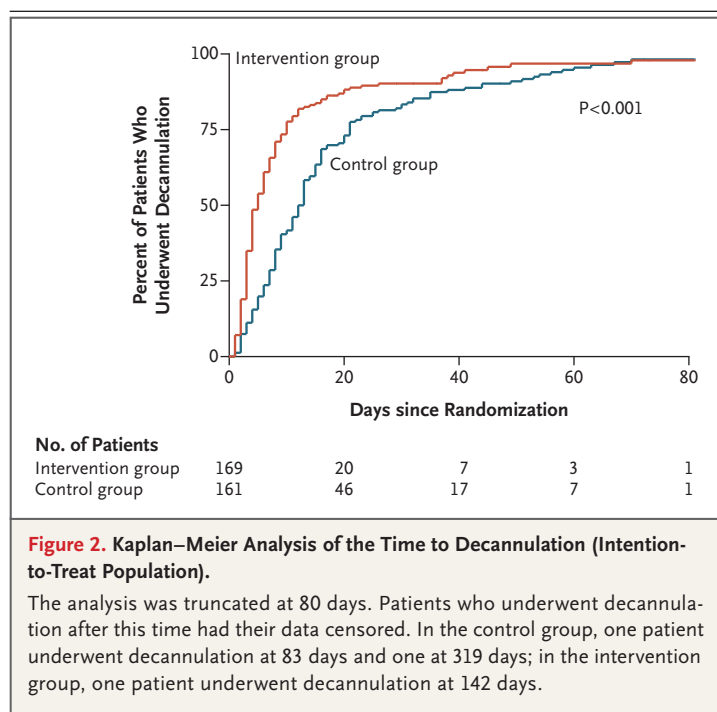
§ The median duration of stay in the ICU before randomization was 27 days (interquartile range, 17 to 36) in the control group and 24 days (interquartile range, 17 to 34) in the intervention group (difference, 3 days; 95% CI, –7 to 4).

¶ Of these 118 patients, 23 (19.5%) had the tracheostomy-tube cap removed because of deterioration in the oxygen saturation level (to $\leq 92\%$), because an increase in the fraction of inspired oxygen (F_{iO_2}) to at least 0.40 was warranted, or because an increase in the F_{iO_2} by at least 0.10 from the baseline value was warranted, and 95 patients (80.5%) had the tracheostomy-tube cap removed after the attending nursing staff considered it to be necessary in order to remove accumulated pulmonary secretions (see the protocol). The mean (\pm SD) number of failed capping trials per patient was 2.95 ± 2.45 .

ing, thus delaying the time to decannulation as reflected by the high proportions of patients with capping trials that failed and of patients with weaning failure. In addition, failure on capping trials preceded infection episodes and weaning failure, a finding that suggests that failure

on capping trials could lead to a sequence of clinical deterioration (Fig. S1).

Capping-trial protocols usually call for downsizing the tracheal cannula or deflating the cuff and switching to a fenestrated or uncuffed cannula. In this trial, whenever possible, we used



the same tracheostomy tube in both groups, thus minimizing the differences in this aspect of the patients' experience.

Our protocol included one change to a cannula with a 7-mm inner diameter, a 9.7-mm external diameter, and multiple large fenestrae in order to complete weaning from mechanical ventilation. Even under these conditions, 73.3% of the patients in the control group had at least one failure on the capping trial, and 12 patients had repeated failures on capping trials but nevertheless underwent decannulation successfully out of protocol. These results reinforce the hypothesis that prolonged capping trials require that patients with limited respiratory functional reserve overcome an excessively demanding ventilatory workload.

Patients in the intervention group may have benefited from receiving more continuous high-flow oxygen therapy than patients in the control group. Birk et al.²⁶ found that heated (37°C) humidification of oxygen administered at 30 liters per minute enhanced mucociliary transport and reduced the number of suctioning procedures in patients with a tracheostomy tube. Although data are lacking regarding clinical benefits with short-term high-flow oxygen therapy in patients with a tracheostomy tube,²⁷ when it is used with a gas flow of at least 50 liters per minute, high-

flow oxygen therapy improves oxygenation, reduces the respiratory rate, and provides a small degree of positive airway expiratory pressure.²⁸

Applying decannulation protocols on the basis of subjective criteria leads to an incidence of recannulation ranging from 2 to 5%.^{6,29} Our objective criteria led to a similar incidence of recannulation (2.4% in the intervention group and 5.6% in the control group). However, these results must be interpreted in light of the high percentage of patients who underwent decannulation (95.2%). Previous studies have shown that decannulation occurs in 56%¹² to 88%¹⁸ of patients, depending mainly on the number of patients included who had a neurocritical condition and the type of facility where decannulation was performed. Moreover, a high percentage of our patients underwent decannulation before ICU discharge.

The lower incidence of infection in the intervention group than in the control group, although not significant, is also noteworthy. The mechanisms that are involved in this difference are unclear. Factors that might have contributed to this finding include a shorter time with an invasive airway present and the continuous use of high-flow oxygen therapy until decannulation.²⁰

One limitation of our trial is the criteria affecting the time to decannulation in the two protocols. In the control group, the cutoff to determine readiness for capping trials (≤ 1 aspiration every 4 hours for 12 hours) was based on safety results in another group.¹⁸ It could be argued that this criterion was overly restrictive and thus prolonged the hospital course before the capping trial was started; however, the high proportion of patients in whom the capping trial failed (73.3%) seems to rebut this argument. Furthermore, 12 patients in the capping-trial protocol who had repeated failures on the capping trial underwent successful decannulation. In the intervention group, the cutoff to determine readiness for decannulation (≤ 2 aspirations every 8 hours for 24 hours) was based on the results of a different study that showed a hazard ratio ranging from 0.7 (95% CI, 0.54 to 0.91) to 0.81 (95% CI, 0.67 to 0.97) per aspiration in an 8-hour period.¹³ Some patients who receive more frequent suctioning can undergo decannulation, but the identification of these patients would require a more complex protocol and expertise.¹³ Both protocols included the use of high-flow oxygen therapy. However, the frac-

tion of time that the high-flow oxygen therapy was applied was much greater in the intervention group than in the control group. The role that the differential use of high-flow oxygen therapy had in our outcomes is not known. Finally, the attending teams were aware of the trial-group assignments. Although the investigators were excluded from participating in the clinical decisions, we cannot rule out the possibility that this bias may, at least in part, explain the results.

We found that in conscious, critically ill adults with a tracheostomy tube, a protocol that was based on suctioning frequency plus continuous high-flow oxygen therapy resulted in a shorter time

to decannulation than capping trials plus intermittent high-flow oxygen therapy, with no significant difference in the incidence of recannulation.

Dr. Hernández Martínez reports receiving travel support from Fisher and Paykel Healthcare; Dr. Masclans, receiving travel support from Fisher and Paykel Healthcare; and Dr. Roca, receiving consulting fees, paid to his institution, from Hamilton Medical and lecture fees from Air Liquide. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

A data sharing statement provided by the authors is available with the full text of this article at NEJM.org.

We thank all the patients and collaborators in the trial; all the medical and nursing staff for their cooperation; Pedro Beito, M.D., Ph.D., for assistance with the methods; and John Giba, B.Sc., for assistance with editing an earlier version of the manuscript.

REFERENCES

1. Abe T, Madotto F, Pham T, et al. Epidemiology and patterns of tracheostomy practice in patients with acute respiratory distress syndrome in ICUs across 50 countries. *Crit Care* 2018;22:195.
2. Esteban A, Frutos-Vivar F, Muriel A, et al. Evolution of mortality over time in patients receiving mechanical ventilation. *Am J Respir Crit Care Med* 2013;188:220-30.
3. Mitchell RB, Hussey HM, Setzen G, et al. Clinical consensus statement: tracheostomy care. *Otolaryngol Head Neck Surg* 2013;148:6-20.
4. Trouillet JL, Collange O, Belafia F, et al. Tracheotomy in the intensive care unit: guidelines from a French expert panel. *Ann Intensive Care* 2018;8:37.
5. McGrath BA, Brenner MJ, Warrillow SJ, et al. Tracheostomy in the COVID-19 era: global and multidisciplinary guidance. *Lancet Respir Med* 2020;8:17-25.
6. Stelfox HT, Crimi C, Berra L, et al. Determinants of tracheostomy decannulation: an international survey. *Crit Care* 2008;12:R26.
7. Stelfox HT, Hess DR, Schmidt UH. A North American survey of respiratory therapist and physician tracheostomy decannulation practices. *Respir Care* 2009;54:1658-64.
8. Singh RK, Saran S, Baronia AK. The practice of tracheostomy decannulation — a systematic review. *J Intensive Care* 2017;5:38.
9. Ceriana P, Carlucci A, Navalesi P, et al. Weaning from tracheotomy in long-term mechanically ventilated patients: feasibility of a decisional flowchart and clinical outcome. *Intensive Care Med* 2003;29:845-8.
10. Mah JW, Staff II, Fisher SR, Butler KL. Improving decannulation and swallowing function: a comprehensive, multidisciplinary approach to post-tracheostomy care. *Respir Care* 2017;62:137-43.
11. Santus P, Gramegna A, Radovanovic D, et al. A systematic review on tracheostomy decannulation: a proposal of a quantitative semiquantitative clinical score. *BMC Pulm Med* 2014;14:201.
12. Heidler MD, Salzwedel A, Jöbges M, et al. Decannulation of tracheotomized patients after long-term mechanical ventilation — results of a prospective multicentric study in German neurological early rehabilitation hospitals. *BMC Anesthesiol* 2018;18:65.
13. Hernández G, Ortiz R, Pedrosa A, et al. The indication of tracheotomy conditions the predictors of time to decannulation in critical patients. *Med Intensiva* 2012;36:531-9.
14. Tobin AE, Santamaria JD. An intensivist-led tracheostomy review team is associated with shorter decannulation time and length of stay: a prospective cohort study. *Crit Care* 2008;12:R48.
15. Fisher DF, Kondili D, Williams J, Hess DR, Bitner EA, Schmidt UH. Tracheostomy tube change before day 7 is associated with earlier use of speaking valve and earlier oral intake. *Respir Care* 2013;58:257-63.
16. Suntrup S, Marian T, Schröder JB, et al. Electrical pharyngeal stimulation for dysphagia treatment in tracheotomized stroke patients: a randomized controlled trial. *Intensive Care Med* 2015;41:1629-37.
17. Roche-Campo F, Thille AW, Drouot X, et al. Comparison of sleep quality with mechanical versus spontaneous ventilation during weaning of critically ill tracheostomized patients. *Crit Care Med* 2013;41:1637-44.
18. Pandian V, Miller CR, Schiavi AJ, et al. Utilization of a standardized tracheostomy capping and decannulation protocol to improve patient safety. *Laryngoscope* 2014;124:1794-800.
19. Fernandez R, Bacelar N, Hernandez G, et al. Ward mortality in patients discharged from the ICU with tracheostomy may depend on patient's vulnerability. *Intensive Care Med* 2008;34:1878-82.
20. Hernandez G, Pedrosa A, Ortiz R, et al. The effects of increasing effective airway diameter on weaning from mechanical ventilation in tracheostomized patients: a randomized controlled trial. *Intensive Care Med* 2013;39:1063-70.
21. American Association for Respiratory Care. AARC clinical practice guidelines: endotracheal suctioning of mechanically ventilated patients with artificial airways 2010. *Respir Care* 2010;55:758-64.
22. Hernandez G, Vaquero C, Gonzalez P, et al. The role of high flow conditioned oxygen therapy on reducing time to decannulation in critically ill tracheostomized patients: a preliminary cohort study. *Intensive Care Med* 2013;39:Suppl 2:S406. abstract.
23. Bonett DG, Price RM. Statistical inference for a linear function of medians: confidence intervals, hypothesis testing, and sample size requirements. *Psychol Methods* 2002;7:370-83.
24. Newcombe RG. Interval estimation for the difference between independent proportions: comparison of eleven methods. *Stat Med* 1998;17:873-90.
25. Boles JM, Bion J, Connors A, et al. Weaning from mechanical ventilation. *Eur Respir J* 2007;29:1033-56.
26. Birk R, Händel A, Wenzel A, et al. Heated air humidification versus cold air nebulization in newly tracheostomized patients. *Head Neck* 2017;39:2481-7.
27. Stripoli T, Spadaro S, Di Mussi R, et al. High-flow oxygen therapy in tracheostomized patients at high risk of weaning failure. *Ann Intensive Care* 2019;9:4.
28. Natalini D, Grieco DL, Santantonio MT, et al. Physiological effects of high-flow oxygen in tracheostomized patients. *Ann Intensive Care* 2019;9:114.
29. Choate K, Barbetti J, Currey J. Tracheostomy decannulation failure rate following critical illness: a prospective descriptive study. *Aust Crit Care* 2009;22:8-15.

Copyright © 2020 Massachusetts Medical Society.