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Effect of Pressure Support vs Unassisted Breathing Through a Tracheostomy Collar on Weaning Duration in Patients Requiring Prolonged Mechanical Ventilation

A Randomized Trial

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Importance Patients requiring prolonged mechanical ventilation (>21 days) are commonly weaned at long-term acute care hospitals (LTACHs). The most effective method of weaning such patients has not been investigated.

Objective To compare weaning duration with pressure support vs unassisted breathing through a tracheostomy collar in patients transferred to an LTACH for weaning from prolonged ventilation.

Design, Setting, and Participants Between 2000 and 2010, a randomized study was conducted in tracheotomized patients transferred to a single LTACH for weaning from prolonged ventilation. Of 500 patients who underwent a 5-day screening procedure, 316 did not tolerate the procedure and were randomly assigned to receive weaning with pressure support (n=155) or a tracheostomy collar (n=161). Survival at 6- and 12-month time points was also determined.

Main Outcome Measure Primary outcome was weaning duration. Secondary outcome was survival at 6 and 12 months after enrollment.

Results Of 316 patients, 4 were withdrawn and not included in analysis. Of 152 patients in the pressure-support group, 68 (44.7%) were weaned; 22 (14.5%) died. Of 160 patients in the tracheostomy collar group, 85 (53.1%) were weaned; 16 (10.0%) died. Median weaning time was shorter with tracheostomy collar use (15 days; interquartile range [IQR], 8-25) than with pressure support (19 days; IQR, 12-31), $P=.004$. The hazard ratio (HR) for successful weaning rate was higher with tracheostomy collar use than with pressure support (HR, 1.43; 95% CI, 1.03-1.98; $P=.033$) after adjusting for baseline clinical covariates. Use of the tracheostomy collar achieved faster weaning than did pressure support among patients who did not tolerate the screening procedure between 12 and 120 hours (HR, 3.33; 95% CI, 1.44-7.70; $P=.005$), whereas weaning time was equivalent with the 2 methods in patients who did not tolerate the screening procedure within 0 to 12 hours. Mortality was equivalent in the pressure-support and tracheostomy collar groups at 6 months (55.92% vs 51.25%; 4.67% difference, 95% CI, −6.4% to 15.7%) and at 12 months (66.45% vs 60.00%; 6.45% difference, 95% CI, −4.2% to 17.1%).

Conclusion and Relevance Among patients requiring prolonged mechanical ventilation and treated at a single long-term care facility, unassisted breathing through a tracheostomy, compared with pressure support, resulted in shorter median weaning time, although weaning mode had no effect on survival at 6 and 12 months.

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Patients requiring prolonged mechanical ventilation, defined as more than 21 days,[1-3] account for more than 13% of ventilated patients[4] and 37% of intensive care unit (ICU) costs.[5] Because of changes in US reimbursement practices, these patients are usually transferred to centers that specialize in weaning, also known as long-term acute care hospitals (LTACHs).[6,7] The number of LTACHs increased from 192 to 408 between 1997 and 2006,[8] and costs increased by 267%, reaching $1.3 billion in 2006.[8]

With aging of the US population, demand for intensivist services is predicted to increase by 38% over the next decade.[9] Consequently, the number of ICU patients transferred to LTACHs for weaning from prolonged ventilation is expected to increase substantially.[10]

In studies of ICU patients, randomized trials have revealed that ventilator duration was influenced by weaning methods.[11-13] The 2 most common weaning methods are pressure support and spontaneous breathing trials. The relative efficacy of these methods has undergone little or no scrutiny in patients receiving care at LTCAHs.[14,15]

Accordingly, we performed a randomized study in patients transferred to an LTACH for weaning from pro-

For editorial comment see p 719.

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longed ventilation to compare the length of time required for weaning with pressure support vs unassisted breathing through an oxygen-delivery device connected to a tracheostomy collar. We also determined the 6- and 12-month survival of patients transferred to an LTACH for weaning from prolonged ventilation.

METHODS

Setting

The study was conducted in RML Specialty Hospital in Hinsdale, Illinois, a 90-bed free-standing LTACH in which 62% of beds are devoted to ventilator weaning (eAppendix, Methods, available at http://www.jama.com).

Patients

Consecutive patients with tracheotomy and transferred to RML Hospital for ventilator weaning were screened. Patients were eligible if they received mechanical ventilation for at least 21 days. Patients were excluded for the following reasons: cardiopulmonary instability, profound neurological deficits, bilateral phrenic-nerve injury, previous admission to RML Hospital, and life expectancy of less than 3 months (eAppendix, Methods). The study was approved by the institutional review board of RML Hospital and written informed consent was obtained from patients or authorized surrogates.

Measurements at Study Enrollment

Physiological Variables. Ventilation was stopped and patients were allowed to breathe spontaneously for 1 minute while respiratory frequency and tidal volume were measured.[16,17] Mechanical ventilation was reinstituted for measurements of resistance and compliance.[18-20] Maximal inspiratory pressure ($P_I$max) was measured as previously described.[21,22]

Screening Procedure. After measuring physiological variables, patients underwent a screening procedure that consisted of unassisted breathing for 5 days (120 hours). During this procedure, humidified oxygen was delivered through a tracheostomy collar. Patients who did not develop distress (eTable 1) during the 5 days were considered to have been successfully weaned and were not randomized. Patients who developed respiratory distress during the 5-day period were considered to have failed the screening procedure and were eligible for randomization.

Randomization. Eligible patients were stratified into 2 groups based on time taken to fail the 5-day screening procedure: early-failure group (0-12 hours) or late-failure group (12-120 hours). Within each group, patients were further stratified into 1 of 4 categories according to underlying disease.[11] Within each category, patients were randomly assigned, using a block size of 4, to pressure support or tracheostomy collar use in a blinded fashion using opaque envelopes (eFigure).

Weaning Protocol

Tracheostomy Collar Group. Patients randomized to tracheostomy collar use were disconnected from the ventilator and allowed to breathe through the tracheostomy. During the first day, the patient was allowed to breathe unassisted for a maximum of 12 hours. The patient was then reconnected to the ventilator and assist-control ventilation was instituted for the next 12 hours. On the second day, the 12-hour tracheostomy collar challenge, followed by assist-control ventilation was repeated. On the third day, the 5-day process of discontinuing mechanical ventilation was commenced; after disconnection from the ventilator, the patient was allowed to breathe unassisted through the tracheostomy up to a maximum of 24 hours each day (eAppendix, Methods).

Pressure-Support Group. A patient's ability to tolerate a decrease in pressure support was assessed 3 times per day: 8 AM, 2 PM, and 8 PM (eAppendix, Methods). On the first day, the initial level of pressure support was titrated to achieve a total respiratory frequency of less than 30 breaths per minute (telephone conversation with L Brochard, MD, March 2000).[11,23] The initial pressure setting was 14 cm H_2O (median interquartile range [IQR], 10-16 cm H_2O). If the patient displayed no respiratory distress (eTable 1) over the ensuing 6 hours, pressure support was decreased by 2 cm H_2O at 2 PM. At 8 PM, if the patient had not displayed any sign of distress at the preceding level of pressure support, pressure was decreased by another 2 cm H_2O. The maximum decrement in pressure support permitted in a single day was 6 cm H_2O (eAppendix, Methods).[11,12] When a patient was able to tolerate pressure support of less than 6 cm H_2O for at least 12 hours, the 5-day process of ventilator discontinuation was commenced whereby the ventilator was disconnected and the patient allowed to breathe unassisted through the tracheostomy up to a maximum of 24 hours each day (eAppendix, Methods).

Outcome Measures

The primary outcome was weaning duration, defined from the first day of randomization to the day the patient was successfully weaned. Weaning was considered successful when patients breathed without ventilator assistance for at least 5 days (eAppendix, Methods). Weaning was determined as a failure when the patient was not successfully weaned by 45 days after randomization. The secondary outcome, mortality status at 6 and 12 months for the overall group (n = 500), was assessed using phone calls, home visits, and searches within the Social Security Death Index (eAppendix, Methods).

Statistical Analysis

Based on data from Scheinhorn et al[2] and pilot data, ventilator duration for successfully weaned patients was estimated to be 22 days. A 20% difference in time to wean between pressure support and tracheostomy collar use was considered clinically meaningful (eAppendix, Methods).[12,14,15] To detect a 20% difference between the 2 methods with a power of 0.80 and 2-tailed α of .05, a sample of 316 patients was needed.

Data were analyzed with an intention-to-treat approach. Because wean-

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ing duration could not be calculated for patients who died or were withdrawn, such patients were right censored; time to study exit for this subgroup was calculated from the date a patient was randomized until the date the patient died or was withdrawn. Categorical variables were reported as percentages and continuous variables as medians and IQRs. Comparison of continuous variables between 2 subgroups was performed using the Mann-Whitney *U* test. Comparison between categorical variables was performed using the χ^2 test. The proportion of patients remaining ventilator dependent was calculated using the Kaplan-Meier estimate. Comparison of weaning time between pressure support and tracheostomy collar was made using the log-rank test.[24]

A Cox proportional hazards model was performed with and without adjusting for baseline characteristics (chosen a priori) that could influence weaning duration: weaning method, timing of screening failure (coded 0 for early failure [0-12 hours]; 1 for late failure [12-120 hours]), age, underlying cause of respiratory failure, ventilator duration before randomization, frequency to tidal volume ratio (f/V_T), maximal inspiratory pressure, resistance, and compliance.[11,12,16,25,26] The assumption that the proportional hazard would remain constant over time was tested by examining Schoenfeld residuals. Kaplan-Meier estimates were also used to assess survival at 6 and 12 months for the overall group; survival in pressure-support and tracheostomy collar groups was compared using the log-rank test. SPSS statistical software was used for all statistical analyses except Cox regression analysis, which was performed with S-plus software (Version 6.1). *P* values were 2 sided and those of less than .05 were considered statistically significant.

RESULTS

There were 2267 patients screened between 2000 and 2010, of whom 500 were enrolled and 316 were randomized (FIGURE 1). Four patients (3 in pressure-support group, 1 in tracheostomy collar group) were withdrawn before initiating the weaning protocol and were excluded from analyses (eAppendix, Results).

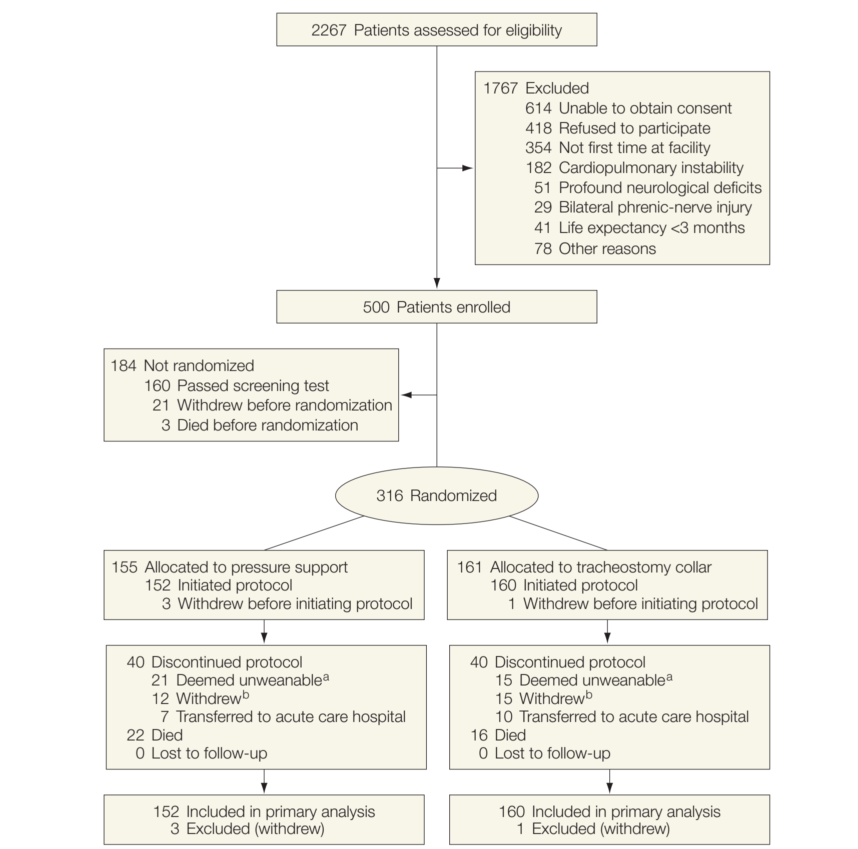
Of 312 randomized patients who entered the weaning protocol, 56 in the tracheostomy collar group (35%; 95% CI, 27.6%-42.4%) and 62 in the pressure-support group (40.8%; 95% CI, 33.0%-48.6%) died or were withdrawn (*P*=.29; eAppendix, Results). Baseline characteristics in the 2 groups were equivalent (eTable 2). All 312 patients were included in the analysis (Figure 1). Patients enrolled in the 2 study groups were similar with respect to demographics, physiological variables, indication for ventilation, ventilator duration at randomization, and timing of randomization (TABLE 1).

Weaning Outcome

Among the entire group of randomized patients (n=312), median weaning time was shorter with tracheostomy collar use than with pressure support: 15 days (IQR, 8-25) vs 19 days (IQR, 12-31), *P*=.004 (TABLE 2). Among patients who completed the study (n=194), median weaning time was shorter with tracheostomy collar use than with pressure support: 13 days (IQR, 8-30) vs 19 days (12-43), *P*=.006. A Kaplan-Meier plot of proportion of patients remaining ventilator dependent in the 2 groups is shown in FIGURE 2.

A Cox proportional hazards model was performed to determine the influence of weaning techniques on weaning duration (eAppendix, Results).

Figure 1. Flow of Patients in Study Cohort



[a]A patient was judged to be unweanable by the attending physician (who was not part of the research team) and the attending physician then transferred the patient to another facility or to home.
[b]Patients were withdrawn based on their request, surrogate request, or the request of the attending physician who was not part of the research team.

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Schoenfeld residual analysis revealed that the assumption of proportional hazards was not met. A subsequent more detailed Cox model, which adjusted for baseline clinical covariates, uncovered 5 covariates associated with the time required for successful weaning: age (hazard ratio [HR], 0.982; 95% CI, 0.969-0.995; $P < .005$), ventilator duration before randomization (HR, 0.982; 95% CI, 0.97-0.993; $P < .002$), frequency to tidal volume ratio (HR, 0.997; 95% CI, 0.995-0.999; $P < .01$), maximal inspiratory pressure (HR, 1.015; 95% CI, 1.004-1.028; $P < .01$), and weaning technique (HR, 1.43; 95% CI, 1.03-1.98); $P = .033$; eTable 3).

Schoenfeld residual analysis revealed that the proportional effect of 2 covariates, timing of screening failure and weaning method, on weaning duration was not constant over time. Separate Cox models were performed for the early-failure and late-failure groups using the same covariates that were included in the original model. The assumption of proportional hazards was tested for both models and was upheld. For the early-failure group, 4 covariates were associated with weaning duration: age (HR, 0.982; 95% CI, 0.968-0.995; $P < .01$), ventilator duration before randomization (HR, 0.976; 95% CI, 0.961-0.99; $P < .01$), frequency to tidal volume ratio (HR, 0.997; 95% CI, 0.995-0.999; $P < .02$), and maximal inspiratory pressure (HR, 1.016; 95% CI, 1.003-1.029; $P < .02$; eTable 4). For the late-failure group, weaning method was the only covariate that was associated with weaning duration ($P = .005$); the HR adjusted for baseline covariates for rate of successful weaning was higher with tracheostomy collar use than with pressure support (HR, 3.33; 95% CI, 1.44-7.77; eTable 5).

For the late-failure group, time to wean was 2.2 times longer in the pressure-support group than in the tracheostomy collar group: 20 days (IQR, 10-31) vs 9 days (IQR, 7-19), $P = .008$ (FIGURE 3A). More patients were weaned in the tracheostomy collar group than in the pressure-support group (71.0% vs 38.5%; $P = .01$); but survival was similar in the 2 groups. In the early-failure group, time to wean was not significantly longer in the pressure-support group than in the tracheostomy collar group: 19 days (IQR, 12-31) vs 16 days (9-30), $P = .058$ (Figure 3B); and the percentage of successfully weaned patients and survival were similar in the 2 groups (eAppendix, Results).

Table 1. Characteristics of Study Population at Randomization

Variable	Median (IQR) Pressure Support (n = 152)	Median (IQR) Tracheostomy Collar (n = 160)
Age, y	70 (62-79)	70 (63-77)
Sex, women/men (% women)	64/88 (42)	80/80 (50)
Duration of mechanical ventilation at randomization, d	34 (25-47)	34 (27-45)
APACHE II score[a]	15 (13-18)	15 (12-18)
Glasgow Coma Scale	15 (13-15)	15 (14-15)
Variables measured at enrollment		
$P_I$max, cm H_2O	40 (32-46)	40 (30-51)
f/V_T, breaths/min/L	113 (78-183)	102 (75-161)
Resistance, cm H_2O/L/s	16 (12-20)	15 (11-20)
Compliance, mL/cm H_2O	38 (27-52)	37 (28-47)
Timing of screening failure		
Early/late, No. of patients	126/26	129/31
Cause of respiratory failure, No. (%)		
Postoperative	70 (46)	74 (46)
Acute lung injury	53 (35)	55 (34)
Chronic obstructive pulmonary disease	19 (13)	21 (13)
Neuromuscular	10 (7)	10 (6)

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; f/V_T, frequency to tidal volume ratio; IQR, interquartile range; $P_I$max, maximal inspiratory pressure.
[a] This score has not been validated as an index of disease severity in patients managed at long-term acute care hospitals.

Table 2. Outcome Between Study Groups

	No. (%) Pressure Support (n = 152)	No. (%) Tracheostomy Collar (n = 160)	P Value
Successfully weaned	68 (45)	85 (53)	.14
Requiring reconnection to ventilator after successfully weaning	12 (8)	14 (9)	.79
Weaning duration, median (IQR), d			
All patients	19 (12-31)	15 (8-25)	.004
Patients with weaning success	16 (10-20)	11 (8-17)	.004
Length of hospital stay, median (IQR), d	41 (30-62)	42 (28-63)	.66
During mechanical ventilation	34 (17-53)	32 (14-56)	.44
After weaning	0 (0-19)	0 (0-19)	.57
After weaning, mean (SD), d	10 (14)	10 (14)	.75
Withdrew	40 (26)	40 (25)	.79
Deaths during the study	22 (15)	16 (10)	.23
Deaths during hospital	39 (26)	41 (26)	.99
Deaths at 6 mo	85 (56)	82 (51)	.41
Deaths at 12 mo	101 (66)	96 (60)	.24

Adverse Events

Frequency of adverse events (new episode of pneumonia, arrhythmias, pneumothorax) was similar in the 2 groups (eAppendix, Results).

Long-term Mortality

Mortality was equivalent in the pressure-support and tracheostomy collar

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groups at 6 months (55.92% vs 51.25%; 4.67% difference; 95% CI, −6.4% to 15.7%) and 12 months (66.45% vs 60.00%; 6.45% difference; 95% CI, −4.2% to 17.1%). Of the 500 enrolled patients, 230 (46%) died at 6 months and 275 (55%) died at 12 months. Mortality was higher among randomized patients than among nonrandomized patients at 6 months (53.5% vs 32.4%; 21.1% difference, 95% CI, 12.4%-29.8%, $P<.001$) and 12 months (63.1% vs 41.5%; 21.7% difference; 95% CI, 12.8% to 30.5%; $P<.001$).

COMMENT

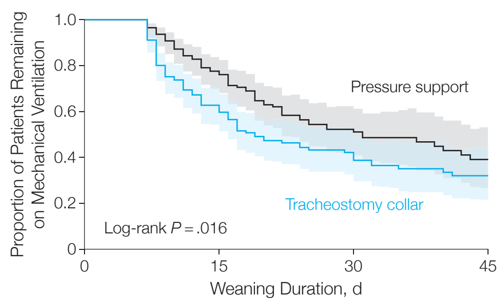
This study has 3 major findings. First, tracheostomy collar use resulted in earlier weaning than did pressure support in patients who required prolonged mechanical ventilation. Second, the influence of weaning method on rate of successful weaning was related to time taken to fail the screening procedure: weaning was faster with tracheostomy collar use than with pressure support in the late-failure group but not in the early-failure group. Third, mortality was equivalent in the pressure-support and tracheostomy collar groups at 6 and 12 months.

Critique of Methods

When this study was began, there was no consensus on how best to define weaning success among patients requiring prolonged ventilation. Based on pilot studies, we concluded that ability to sustain 5 days of unassisted breathing constituted a pragmatic definition of weaning success. Subsequently, consensus conference panelists[27] defined successful weaning as breathing unassisted for 7 days. The data were reanalyzed using the 7-day criterion standard. Outcomes were equivalent for both the 7-day and 5-day criteria (eAppendix, Results). Because fewer than 10% of patients in this study required reconnection to the ventilator following successful weaning (Table 2), 5 days of unassisted breathing appears to be a robust definition of weaning success in patients who require prolonged ventilation.

It is unlikely that the slower rate of weaning with pressure support resulted from the manner in which it was adjusted. The algorithm for weaning with pressure support was similar to that used by Brochard et al,[11] who concluded that pressure support was the best weaning method in ICU patients. Moreover, the start of the 5-day process of ventilator discontinuation occurred when a patient could tolerate 12 hours of unassisted breathing for 2 days in the tracheostomy collar group or pressure support of 6 cm H_2O for 12 hours in the pressure-support group. As such, patients in the tracheostomy collar group who performed at the fastest possible pace would have taken

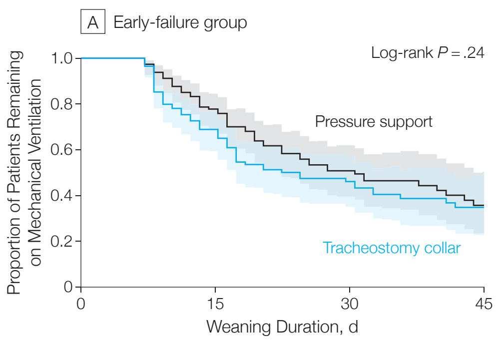
Figure 2. Proportion of Patients Remaining Ventilator Dependent in the Pressure-Support and Tracheostomy Collar Groups



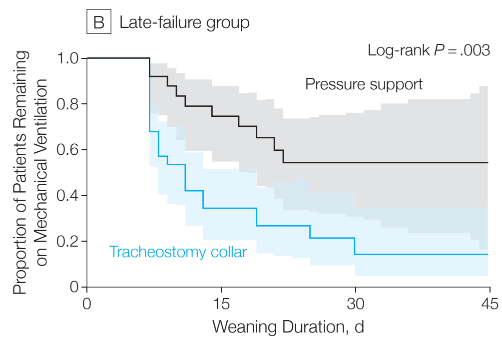
No. of patients at risk				
Pressure support	152	101	45	17
Tracheostomy collar	160	82	37	18

Shaded areas represent 95% CIs.

Figure 3. Proportion of Patients Remaining Ventilator Dependent in the Pressure-Support and Tracheostomy Collar Groups Who Failed the 5-Day Screening



No. of patients at risk				
Pressure support	126	84	38	16
Tracheostomy collar	129	73	34	16



No. of patients at risk				
Pressure support	26	18	8	1
Tracheostomy collar	31	11	3	2

Data are based on the time taken to fail the 5-day screening procedure. Shaded areas represent 95% CIs.

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1 day longer to start the 5-day process of ventilator discontinuation than patients who performed at the fastest possible pace in the pressure-support group. This inequality is not simply theoretical. In reality, 5% of patients in the tracheostomy collar group tolerated 12 hours of unassisted breathing on the first 2 days after randomization. It is likely that these patients could have started the 5-day process of ventilator discontinuation a day earlier.

Pace of Weaning

The faster pace of weaning with tracheostomy collar use may be related to its effect on clinical decision making.[28] During a tracheostomy collar challenge, the amount of respiratory effort is determined solely by the patient. As such, observing a patient breathing through a tracheostomy collar provides the clinician with a clear view of the patient's respiratory capabilities. In contrast, a clinician's ability to judge weanability during pressure support is clouded because the patient is receiving ventilator assistance.[23,29-32] Accordingly, clinicians may accelerate the weaning process more in patients who perform unexpectedly well during a tracheostomy collar challenge than in patients for whom a low level of pressure support is being used.[28] This notion is borne out by the data, which showed that the superiority of tracheostomy collar use over pressure support was evident within the first 10 days (Figure 2). Another contributor to slower weaning with pressure support may have been the predisposition to sleep fragmentation with this mode, which can cause cardiopulmonary abnormalities.[33]

The superior performance of tracheostomy collar use was observed in the late- but not in the early-failure group. Patients who failed the screening procedure within 12 hours (early-failure group) had less endurance and were sicker than patients who took as many as 5 days to fail screening (late-failure group). Accordingly, severity of illness in the early-failure group may have had a greater influence on weaning outcome than did weaning method. Indeed, Cox analysis of the early-failure group showed that weaning time was determined by patient-related factors (age, ventilator duration before randomization, frequency to tidal volume ratio, and maximal inspiratory pressure), and not by weaning method (eTable 4). Because patients in the late-failure group were less sick, the weaning method had a greater likelihood of influencing weaning duration than had the effect of disease. This notion was supported by the Cox model, which showed that the main determinant of weaning duration in the late-failure group was the weaning method: tracheostomy collar achieved successful weaning 3.3 times faster than did pressure support (eTable 5).

Screening Pass Rate

Of 500 enrolled patients, 160 (32%) passed the initial tracheostomy collar challenge. This finding suggests that many patients transferred to the LTACH could have been weaned at the home ICU. One reason that may account for underrecognition of the weanability of such patients is physician mindset.[30] To initiate the steps required for transfer, a physician determines that weaning is not immediately imminent. While awaiting execution of the transfer (which may take 1 or 2 weeks), ICU physicians become less aggressive in the pursuit of ventilator disconnection.

Long-term Mortality

The mortality rate (55%) in our study is lower than that (69%) observed by Kahn et al,[8] who retrospectively analyzed Medicare files of 11 695 ventilated patients transferred from ICUs to LTACHs. Although direct comparisons are not possible because of the lack of severity-of-illness scores in the Medicare data set, patients in this trial may have been less sick than in the national sample. Of note, the Medicare analysis[8] included all patients transferred to LTACHs whereas certain patients were excluded in the present study (Figure 1).

Study Limitations

The nature of weaning techniques made it impossible to mask treatment assignment from clinical staff and research personnel after randomization. To minimize subjectivity on the part of staff, rigid criteria for weaning were used in each study group. After data collection, the 2 groups were coded so that investigators analyzing the data were blinded to the randomized assignment. The study was confined to a single center, which could limit generalizability (external validity) of our findings. A prerequisite for generalizability, however, is sound internal validity.[34] The major obstacle to internal validity is systematic error, which can be more carefully controlled in a single center where selection and patient care is uniform. The study took 10 years to complete. To determine whether the passage of time influenced study outcome, Cox analysis was undertaken with date of randomization of each patient as a covariate. The time covariate was not significant in any of the models (eAppendix, Results). Our study was conducted among patients requiring prolonged mechanical ventilation who received care at a LTACH; the findings do not permit simple extrapolation to patients receiving prolonged ventilation in an ICU.

In conclusion, the time to wean from prolonged ventilation in patients transferred to a LTACH was influenced by the weaning method used: tracheostomy collar use resulted in earlier weaning than did pressure support.

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Author Contributions: Dr Jubran had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Jubran, Duffner, Collins, Lanuza, Hoffman, Tobin.

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