

## EFFECT ON THE DURATION OF MECHANICAL VENTILATION OF IDENTIFYING PATIENTS CAPABLE OF BREATHING SPONTANEOUSLY

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### ABSTRACT

**Background** Prompt recognition of the reversal of respiratory failure may permit earlier discontinuation of mechanical ventilation, without harm to the patient.

**Methods** We conducted a randomized, controlled trial in 300 adult patients receiving mechanical ventilation in medical and coronary intensive care units. In the intervention group, patients underwent daily screening of respiratory function by physicians, respiratory therapists, and nurses to identify those possibly capable of breathing spontaneously; successful tests were followed by two-hour trials of spontaneous breathing in those who met the criteria. Physicians were notified when their patients successfully completed the trials of spontaneous breathing. The control subjects had daily screening but no other interventions. In both groups, all clinical decisions, including the decision to discontinue mechanical ventilation, were made by the attending physicians.

**Results** Although the 149 patients randomly assigned to the intervention group had more severe disease, they received mechanical ventilation for a median of 4.5 days, as compared with 6 days in the 151 patients in the control group ( $P=0.003$ ). The median interval between the time a patient met the screening criteria and the discontinuation of mechanical ventilation was one day in the intervention group and three days in the control group ( $P<0.001$ ). Complications — removal of the breathing tube by the patient, reintubation, tracheostomy, and mechanical ventilation for more than 21 days — occurred in 20 percent of the intervention group and 41 percent of the control group ( $P=0.001$ ). The number of days of intensive care and hospital care was similar in the two groups. Total costs for the intensive care unit were lower in the intervention group (median, \$15,740, vs. \$20,890 in the controls;  $P=0.03$ ); hospital costs were lower, though not significantly so (median, \$26,229 and \$29,048, respectively;  $P=0.3$ ).

**Conclusions** Daily screening of the respiratory function of adults receiving mechanical ventilation, followed by trials of spontaneous breathing in appropriate patients and notification of their physicians when the trials were successful, can reduce the duration of mechanical ventilation and the cost of intensive care and is associated with fewer complications than usual care. (N Engl J Med 1996;335:1864-9.)

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FOR over two decades, physicians have attempted to define the best methods of discontinuing mechanical ventilation in patients recovering from respiratory failure. An early study of weaning<sup>1</sup> noted that the clinical decision to discontinue mechanical ventilation is often arbitrary, based on “judgment and experience.” With increasing recognition of the risks and economic consequences of prolonged ventilation, identifying strategies that reduce the duration of mechanical ventilation remains a high priority,<sup>2,3</sup> but no single approach has been established as the best one. Many measures have been proposed to identify patients ready for extubation,<sup>1,4-15</sup> ranging from simple maneuvers, such as counting and measuring breaths,<sup>4</sup> to more complicated methods requiring the insertion of gastrointestinal devices<sup>5,6</sup> or the use of computerized decision-support models.<sup>7</sup> Some investigators have advocated the use of a ventilatory management team,<sup>16</sup> although randomized, controlled trials of this strategy are lacking.

Despite these efforts, there is evidence to suggest that physicians do not discontinue mechanical ventilation expeditiously. Using clinical judgment alone, physicians do not accurately predict whether mechanical ventilation can be discontinued successfully; the positive and negative predictive values of these assessments are only 50 percent and 67 percent, respectively.<sup>17</sup> As many as half of patients who remove their breathing tubes prematurely do not require reintubation within 24 hours.<sup>18,19</sup>

We hypothesized that screening patients daily to identify those who can breathe spontaneously and notifying physicians promptly when patients complete a trial of spontaneous breathing successfully could alter physicians' behavior and promote the earlier discontinuation of mechanical ventilation. We studied whether such a management strategy could alter patients' outcomes.

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## METHODS

### Patients

The study population comprised patients in the medical and coronary adult intensive care units who were admitted to our 806-bed university medical center between June 1995 and February 1996. During the study period, of 323 eligible patients admitted to the study units, 300 patients (151 men and 149 women, 93 percent of the total) were enrolled. The criteria for exclusion were age less than 18 years, lack of informed consent, the existence of an extubation order at the time of the evaluation, and dependence on mechanical ventilation for at least two weeks before enrollment. Twenty-three eligible patients were not enrolled, 15 because informed consent could not be obtained and 8 because they declined to participate.

### Randomization

A computerized randomization scheme determined the patients' group assignments at enrollment. Each assignment was indicated on a data form that was folded and sealed in an opaque envelope and opened only after written informed consent was obtained and the patient was enrolled by a fellow in pulmonary medicine or critical care who was not involved in the patient's routine care.<sup>20</sup> The fellow collected base-line data on demographic and physiologic variables and recorded the patient's group assignment. After the patients were enrolled and randomized, the study protocol was followed; 149 subjects were assigned to the intervention group, and 151 to the control group.

### Study Protocol

The study protocol was approved by the institutional review board of the hospital. The intervention was a strategy of combined management incorporating daily screening of respiratory function, a trial of spontaneous breathing, and notification of the physician of successful results. The patients in the control group received the usual care. All the patients in the intervention group who passed a screening test suggesting that they had recovered from their respiratory failure underwent a trial of spontaneous breathing. If the trial was successful, the patients' physicians were notified orally (at the bedside or by telephone) and the following preprinted message was placed in the patient's chart: "Your patient has successfully completed a 2-hour trial of spontaneous breathing and has an 85 percent chance of successfully staying off mechanical ventilation for 48 hours."

Once this message was delivered, no further intervention was made. Whenever patients failed to meet the criteria of the daily screening test or the trial of spontaneous breathing, they continued to receive morning assessments according to the protocol until their successful extubation or their death. The control subjects were screened daily, but they did not undergo trials of spontaneous breathing, receive prompts, or have any feedback from the study personnel. All decisions about approaches to weaning, the discontinuation of mechanical ventilation, discharge from the intensive care unit, and discharge from the hospital were made by the patients' attending physicians, who were experienced pulmonologists, intensivists, or cardiologists. Neither the mode of ventilation nor the weaning strategy used by the attending physicians was specified.

### Daily Screening

On the basis of two earlier studies, a set of five simple screening criteria was devised.<sup>2,3</sup> All patients enrolled in the study were screened each morning between 6:30 and 7 by the respiratory therapist on the unit. The therapist was not allowed to change the fraction of inspired oxygen or the level of positive end-expiratory pressure. The results of the daily screening were not available to the physicians caring for the study patients. For a patient to pass the screening test, all five criteria had to be met — namely, the ratio of the partial pressure of arterial oxygen to the fraction

of inspired oxygen had to exceed 200; the positive end-expiratory pressure could not exceed 5 cm of water; there had to be an adequate cough during suctioning (that is, the airway reflexes had to be intact); the ratio of the respiratory frequency to the tidal volume could not exceed 105 breaths per minute per liter; and no infusions of vasopressor agents or sedatives could be used (dopamine could be given in doses not exceeding 5  $\mu$ g per kilogram of body weight per minute, and intermittent dosing of sedatives was allowed). To measure the ratio of the respiratory frequency to the tidal volume, a continuous positive airway pressure of 5 cm of water with no mandatory breaths from the ventilator was supplied, and pressure support was removed for one minute (a criterion that differed from the one in the original description of the test<sup>4</sup>). Minute ventilation and respiratory rate were measured by a Puritan-Bennett 7200 or Siemens 900 mechanical ventilator, and tidal volume was obtained by dividing the minute ventilation by the respiratory frequency.

### Trial of Spontaneous Breathing

The patients in the intervention group in whom one screening test was successful underwent a trial of spontaneous breathing later the same morning. In that trial, ventilatory support was removed and the patient was allowed to breathe through either a T-tube circuit or a ventilatory circuit using "flow triggering" (rather than triggering by pressure) and continuous positive airway pressure of 5 cm of water. No change was made in the fraction of inspired oxygen or the level of positive end-expiratory pressure. The trial of spontaneous breathing was initiated and monitored by the respiratory therapist and the nurse caring for the patient, with electrocardiography and pulse oximetry throughout. A fellow in pulmonary medicine or critical care medicine who supervised the study but remained uninvolved in management decisions was always available to assess the condition of any patient who had difficulty during the trial, but this physician was not required to remain in the intensive care unit after the first 5 to 10 minutes. The trial of spontaneous breathing was terminated by the physician if the patient's nurse identified any of the following conditions (determined on the basis of criteria used in previous studies<sup>2,3</sup>): a respiratory rate that exceeded 35 breaths per minute for five minutes or longer, an arterial oxygen saturation below 90 percent, a heart rate that exceeded 140 beats per minute, sustained changes in the heart rate of 20 percent in either direction, a systolic blood pressure greater than 180 mm Hg or less than 90 mm Hg, increased anxiety, and diaphoresis. A trial was considered to have been successful when the patient could breathe without mechanical ventilation for two hours.

### Outcomes

The following primary outcomes were defined a priori: the overall duration of mechanical ventilation, the length of time from a successful screening test to the discontinuation of mechanical ventilation, and the length of stay in the intensive care unit. The secondary outcomes were the frequency of complications (reintubation, removal of the breathing tube by the patient, tracheostomy, and mechanical ventilation for more than 21 days); the cost of respiratory care, intensive care, and overall hospitalization; the length of hospitalization; and death.

### Statistical Analysis

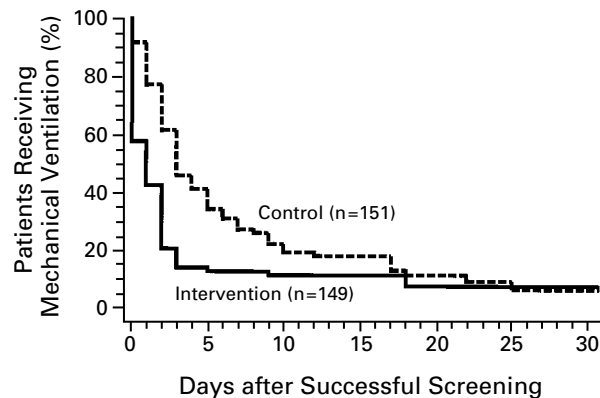
An intention-to-treat analysis was performed in which proportions and rates were compared by the chi-square test when the sample was large (for example, in the analysis of mortality) or by Fisher's exact test when fewer than five subjects were involved (for example, in the analysis of certain complication rates and demographic variables).<sup>21</sup> The Mann-Whitney U test was used to analyze lengths of stay and other continuous variables that were not normally distributed, and two-tailed t-tests were used to compare age and other variables with normal distributions.<sup>21</sup> Kaplan-Meier survival analysis<sup>22</sup> and Cox proportional-hazards analysis<sup>23</sup> were

**TABLE 1.** BASE-LINE CHARACTERISTICS OF THE STUDY PATIENTS.\*

CHARACTERISTIC	INTERVENTION GROUP (N = 149)	CONTROL GROUP (N = 151)
Male sex — no. (%)	67 (45)	84 (56)
Treatment in coronary care unit — no. (%)	33 (22)	29 (19)
Age — yr	61.7±15.8	60.5±15.5
APACHE II score	19.8±6.0	17.9±6.2
Acute-lung-injury score	1.9±0.8	1.7±0.8
Median duration of respiratory failure — days†	3.0	2.0
Mode of ventilation — no. of patients (%)		
Intermittent mandatory ventilation	42 (28)	50 (33)
Pressure-support ventilation	26 (17)	19 (13)
Both	64 (43)	65 (43)
Pressure-control ventilation	3 (2)	5 (3)
Assist-control ventilation	6 (4)	4 (3)
Continuous positive airway pressure	8 (5)	8 (5)
Cause of respiratory failure — no. of patients (%)		
Congestive heart failure	18 (12)	15 (10)
Other heart disease	17 (11)	23 (15)
COPD or asthma exacerbation	23 (15)	22 (15)
Pneumonia	21 (14)	23 (15)
ARDS or multisystem organ failure	23 (15)	19 (13)
Gastrointestinal and liver disease	7 (5)	13 (9)
Cancer or leukemia	7 (5)	9 (6)
Overdose or ketoacidosis	11 (7)	5 (3)
Neurologic emergency	7 (5)	4 (3)
Other	15 (10)	18 (12)

\*Plus-minus values are means ±SD. APACHE II denotes Acute Physiology and Chronic Health Evaluation II, COPD chronic obstructive pulmonary disease, and ARDS acute respiratory distress syndrome.

†Duration of respiratory failure was defined as the number of days between intubation and a successful screening test.



**Figure 1.** Kaplan-Meier Analysis of the Duration of Mechanical Ventilation after a Successful Screening Test.

After adjustment for the severity of illness at base line (as measured by the APACHE II score), age, sex, race, location of the intensive care unit, and duration before enrollment, a Cox proportional-hazards analysis showed that mechanical ventilation was discontinued more rapidly in the intervention group than in the control group (relative risk of successful extubation, 2.13; 95 percent confidence interval, 1.55 to 2.92;  $P < 0.001$ ).

used to assess the effects of the intervention. Cox proportional-hazards modeling was used to assess differences between groups after adjustment for base-line variables, such as the Acute Physiology and Chronic Health Evaluation II (APACHE II) score,<sup>24</sup> the Murray acute-lung-injury score,<sup>25</sup> age, sex, race, the duration of intubation before enrollment, and the type of intensive care unit. When patients died after a screening test was successful but before mechanical ventilation was discontinued, their data were censored in the analysis (12 patients in the intervention group and 16 in the control group). A  $P$  value  $\leq 0.05$  was considered to indicate statistical significance. Severity of illness was described by the APACHE II score<sup>24</sup> and the acute-lung-injury score.<sup>25</sup> The statistical analysis was performed with commercially available computer software (StatView, version 4.51).

### Financial Data

Information on the cost of care was obtained from the hospital. First, the expense ratio (total expenses divided by total gross revenue) was calculated for each department (pharmacy, respiratory therapy, and so forth). Total expenses comprised both direct (salaries, supplies, and other expenses directly attributable to the department) and indirect expenses. The latter (for example, depreciation of buildings and equipment and expenses for water and power) were allocated to the departments on the basis of their estimated use. Second, the expense ratios were multiplied by the charges from each department to the patient. Calculated expenses were then summed to determine the total cost to the hospital for patient care. The expense ratios used in the study were computed with data from the hospital's financial plan for fiscal year 1996. Charges were obtained from the accounting department.

## RESULTS

### Demographic Variables

Demographic information and data on the severity of illness are shown in Table 1. There were 67 men in the intervention group (45 percent) and 84 men in the control group (56 percent,  $P = 0.07$ ). Patients treated in the medical intensive care unit made up 79 percent of the study population, with the remaining 21 percent treated in the coronary care unit. The patients treated in the two types of units were demographically similar. The mean age of the study participants was 61.1 years; 79 percent were white, 20 percent were black, and 1 percent were Hispanic. The patients in the intervention group were more severely ill than the controls, with higher mean APACHE II scores (19.8 vs. 17.9,  $P = 0.01$ ) and mean acute-lung-injury scores (1.9 vs. 1.7,  $P = 0.04$ ).

The causes of respiratory failure were diverse and were similarly distributed between the groups (Table 1). Heart disease, obstructive lung disease, pneumonia, and acute respiratory distress syndrome accounted for 68 percent of the cases of respiratory failure. At enrollment, a variety of modes of mechanical ventilation were used (Table 1); these did not differ significantly between groups.

### Duration of Mechanical Ventilation

The median duration of mechanical ventilation before a successful screening test was 3.0 days in the intervention group and 2.0 days in the control group ( $P = 0.4$ ). Kaplan-Meier survival analysis (Fig.

**TABLE 2.** COMPARISON OF OUTCOMES BETWEEN STUDY GROUPS.

END POINT	INTERVENTION GROUP (N=149)	CONTROL GROUP (N=151)	P VALUE
	median no. of days (interquartile range)		
Weaning time*	1 (0-2)	3 (2-7)	<0.001
Mechanical ventilation	4.5 (2-9)	6 (3-11)	0.003
Intensive care	8 (4-18)	9 (5-16)	0.17
Hospital care	14 (9-26)	15.5 (6-30)	0.93

\*Weaning time was defined as the number of days from the time the patient had a successful screening test to the discontinuation of mechanical ventilation.

**TABLE 3.** COMPLICATIONS OF RESPIRATORY FAILURE.

COMPLICATION	INTERVENTION GROUP (N=149)	CONTROL GROUP (N=151)	P VALUE
	no. of patients (%)		
Any	30 (20)	62 (41)	0.001
Reintubation within 48 hr	5 (3)	12 (8)	0.08
Any reintubation	6 (4)	15 (10)	0.04
Self-extubation	2 (1)	5 (3)	0.25
Tracheostomy	13 (9)	22 (15)	0.10
Mechanical ventilation for >21 days	9 (6)	20 (13)	0.04

**TABLE 4.** COSTS OF CARE.

CATEGORY	INTERVENTION GROUP (N=149)	CONTROL GROUP (N=151)	P VALUE
	median \$ (interquartile range)		
Intensive care unit			
Respiratory	1,477 (648-3,338)	1,774 (974-3,867)	0.04
Nonrespiratory	13,777 (6,768-29,939)	18,905 (10,362-32,695)	0.03
Both	15,740 (7,873-33,035)	20,890 (11,501-37,570)	0.03
Entire hospitalization	26,229 (13,744-51,786)	29,048 (17,264-57,117)	0.3

1) and Cox proportional-hazards modeling showed that mechanical ventilation was discontinued successfully earlier in the intervention group than in the control group (relative risk of successful extubation, 2.13; 95 percent confidence interval, 1.55 to 2.92;  $P < 0.001$ ). Overall, 113 patients in the intervention group had successful screening tests (76 percent), as compared with 103 patients in the control group (68 percent,  $P = 0.14$ ). Eighty-eight patients in the intervention group had successful trials of spontaneous breathing, and 48 of them (55 percent) were extubated the same day. Forty-eight hours after they had successful screening tests, 65 patients in the intervention group had been successfully removed from mechanical ventilation, as compared with 24 controls. The median duration of mechanical ventilation was 4.5 days in the intervention group and six days in the control group ( $P = 0.003$ ) (Table 2). There were no significant differences between groups in the number of days of intensive care or overall hospitalization (Table 2).

**Complications**

No complications occurred during the screening tests or the trials of spontaneous breathing. The pa-

tients in the intervention group had fewer complications than the controls ( $P = 0.001$ ), including fewer reintubations (6 vs. 15,  $P = 0.04$ ) and fewer patients requiring mechanical ventilation for more than 21 days (9 vs. 20,  $P = 0.04$ ) (Table 3). The relative risk of a complication (as defined in the Methods section) in the intervention group as compared with the control group was 0.49 (95 percent confidence interval, 0.29 to 0.82;  $P = 0.001$ ). Mortality was similar in the two groups. Fifty-six patients in the intervention group died (38 percent), as compared with 60 patients in the control group (40 percent,  $P = 0.63$ ).

**Costs**

The costs of patient care are shown in Table 4. The cost of overall hospitalization did not differ significantly between groups (median in the intervention group, \$26,229; in the control group, \$29,048;  $P = 0.3$ ). The cost of medical care in the intensive care unit, both overall and for either respiratory or nonrespiratory care, considered separately, was lower in the intervention group than in the control group ( $P \leq 0.04$  for all three). The total cost of care in the intensive care unit over the entire study

period was \$3,855,001 in the intervention group and \$4,297,024 in the control group.

### DISCUSSION

Promptly identifying patients who have recovered from respiratory failure and “liberating”<sup>26</sup> them to return to spontaneous breathing are important. A prevalent philosophy with regard to the discontinuation of mechanical ventilation has been that a gradual reduction in mechanical support with the patient assuming a progressive increase in breathing is imperative and is reflected in varying, but ubiquitously applied, forms of “weaning” from mechanical ventilation. Our findings, together with other recent observations,<sup>2,3</sup> suggest that a change in this clinical approach is warranted. We found that notifying physicians about their patients’ successful completion of simple trials of spontaneous breathing shortened by about two days the time between the recovery from respiratory failure (i.e., the time the first screening test was successful) and the successful discontinuation of mechanical ventilation, reducing the median overall duration of mechanical ventilation as compared with its duration in patients who had more gradual weaning with standard care.

Our study investigated and documented that the systematic use of predictors of weaning produces better outcomes than the judgment of the physician alone,<sup>27</sup> and thereby extended the insights of two recent studies.<sup>2,3,28</sup> Esteban and colleagues<sup>2</sup> found that trials of spontaneous breathing were preferable to intermittent mandatory ventilation and pressure-support ventilation, whereas Brochard et al.<sup>3</sup> showed that pressure-support ventilation was superior to the other methods. Despite these contradictory conclusions, these trials showed that strategies of weaning influence the duration of mechanical ventilation; that the criteria used in adjusting the ventilator influence the outcome; and that intermittent mandatory ventilation was the most ineffective method among those studied.

We synthesized an approach that incorporates daily objective screening and two-hour trials of spontaneous breathing with messages to the physician that are designed to facilitate the timely extubation of the patient. Our study population included medical and nonsurgical cardiac patients with severe illness and substantial coexisting conditions, unlike other studies<sup>1-3,7,8,10,12,14,16,17</sup> that focused on a surgical or mixed population or excluded patients with acute coronary disease. No diagnostic subgroup of patients had a higher rate of complications than the others.

Considering that our protocol encouraged the extubation of the patient as soon as recovery was objectively documented, higher rates of reintubation and other complications might have been expected in the intervention group. The rates of reintubation,

mechanical ventilation for more than 21 days, and overall complications were all lower in the intervention group. The reintubation rate (4 percent) was lower than those previously reported (7.3 percent<sup>3</sup> and 17.7 percent<sup>2</sup>), which is important because reintubation predisposes patients to nosocomial pneumonia.<sup>29</sup>

Our protocol was associated with a reduction of about 25 percent in the cost of intensive care in the intervention group. Hospital costs were also lower, but the difference between groups was not significant. However, the study was not designed with adequate power to detect such a difference, and further prospective investigation on a larger scale is warranted.

Our observations also underscore the key role of nonphysician health professionals in providing safe, efficient ventilatory care. During the study, the commitment of time by physicians appeared minimal, since most monitoring was done by respiratory therapists and nurses as part of their standard patient care. Although we did not formally assess the time each participant spent in the study, the daily screening tests and trials of spontaneous breathing generally required only a few additional minutes per patient per day and were incorporated readily into the staff routines. Our trials of spontaneous breathing were performed with either standard T-tube circuits or flow-triggered mechanical ventilation. The latter was a particular convenience that minimized the workload of the respiratory therapists. Personnel expenses are thought to account for more than half the cost of mechanical ventilation.<sup>30</sup> Further definition of the optimal staffing to obtain screening data and conduct breathing trials is necessary, and that staffing would be expected to differ considerably among institutions. Because it requires no special monitoring or respiratory equipment, no additional expenditures, and no laboratory studies, this protocol may be widely applicable in both university and community hospitals.

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