ORIGINAL ARTICLE

Withdrawal of Mechanical Ventilation in Anticipation of Death in the Intensive Care Unit

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ABSTRACT

BACKGROUND

In critically ill patients who are receiving mechanical ventilation, the factors associated with physicians' decisions to withdraw ventilation in anticipation of death are unclear. The objective of this study was to examine the clinical determinants that were associated with the withdrawal of mechanical ventilation.

METHODS

We studied adults who were receiving mechanical ventilation in 15 intensive care units, recording base-line physiological characteristics, daily Multiple Organ Dysfunction Scores, the patient's decision-making ability, the type of life support administered, the use of do-not-resuscitate orders, the physician's prediction of the patient's status, and the physician's perceptions of the patient's preferences about the use of life support. We examined the relation between these factors and withdrawal of mechanical ventilation, using Cox proportional-hazards regression analysis.

RESULTS

Of 851 patients who were receiving mechanical ventilation, 539 (63.3 percent) were successfully weaned, 146 (17.2 percent) died while receiving mechanical ventilation, and 166 (19.5 percent) had mechanical ventilation withdrawn. The need for inotropes or vasopressors was associated with withdrawal of the ventilator (hazard ratio, 1.78; 95 percent confidence interval, 1.20 to 2.66; P=0.004), as were the physician's prediction that the patient's likelihood of survival in the intensive care unit was less than 10 percent (hazard ratio, 3.49; 95 percent confidence interval, 1.39 to 8.79; P=0.002), the physician's prediction that future cognitive function would be severely impaired (hazard ratio, 2.51; 95 percent confidence interval, 1.28 to 4.94; P=0.04), and the physician's perception that the patient did not want life support used (hazard ratio, 4.19; 95 percent confidence interval, 2.57 to 6.81; P<0.001).

CONCLUSIONS

Rather than age or the severity of the illness and organ dysfunction, the strongest determinants of the withdrawal of ventilation in critically ill patients were the physician's perception that the patient preferred not to use life support, the physician's predictions of a low likelihood of survival in the intensive care unit and a high likelihood of poor cognitive function, and the use of inotropes or vasopressors.

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MECHANICAL VENTILATION IS THE most common form of advanced life support in the intensive care unit (ICU). Although most critically ill patients are successfully weaned from mechanical ventilation, some patients die while still receiving it or soon after it has been withdrawn in anticipation of death.[1] Mechanical ventilation is the form of support most frequently withheld or withdrawn in anticipation of death.[2]

Retrospective[3-7] and prospective[8-13] studies have demonstrated that in critically ill patients, death is often preceded by the withdrawal or withholding of life support. Surveys have suggested that the patient's age, the patient's wishes, the severity of illness, the number of underlying chronic disorders, and the past and projected future quality of life[14-16] influence decisions to forgo treatment. In addition, physicians may be more inclined to withdraw interventions that are invasive and expensive,[17] that have recently been instituted,[18] and that are related to their own specialty.[19] Factors influencing decisions to withdraw life support have been investigated in national observational studies.[11-13] We examined the relative influence of base-line and time-dependent factors on the decision to withdraw mechanical ventilation from critically ill patients.

METHODS

We prospectively followed consecutive patients who were at least 18 years old, were receiving mechanical ventilation, and were expected to be in the ICU for at least 72 hours. During an enrollment window of at least three months at each unit, we identified patients admitted to 15 medical–surgical, university-affiliated ICUs (11 in Canada, 2 in the United States, 1 in Sweden, and 1 in Australia).[20] For patients who were admitted twice, we included only the second admission.

We recorded age, sex, diagnostic category at the time of admission to the ICU, the Acute Physiology and Chronic Health Evaluation (APACHE II) score,[21] and the attending physician's estimate of the patient's functional status on admission. Daily, we documented the Multiple Organ Dysfunction Score[22]; the use of mechanical ventilation, inotropes or vasopressors, hemodialysis, and do-not-resuscitate orders; the patient's ability to participate in decisions; and the attending physician's clinical prediction of the likelihood of the patient's survival in the ICU and the hospital, projected functional and cognitive status one month after hospital discharge, and perception of the patient's preferences regarding the use of advanced life support (none, partial, or all means necessary). If physicians were unable to determine the patients' wishes from the patients themselves or a substitute decision maker, they recorded that the patients preferred to receive full advanced life support.

Each day, physicians also documented whether patients were successfully weaned from mechanical ventilation, died while receiving mechanical ventilation, or had mechanical ventilation withdrawn. We defined successful weaning as freedom from the need for mechanical ventilation for the duration of the ICU stay, after successful spontaneous-breathing tests or stepwise discontinuation of mechanical ventilation. We defined withdrawal of mechanical ventilation as the discontinuation of mechanical ventilation in anticipation of death, as reported by the physician. All patients were followed until death or hospital discharge. The institutional review board at each institution approved the protocol and waived the need for informed consent.

We expressed continuous variables as means ±SD or as medians and interquartile ranges if their distribution was skewed. Pearson's chi-square test was used to compare categorical variables among the groups. Student's t-test or Wilcoxon's rank-sum test was used to compare continuous variables among the groups, as appropriate. We used survival analysis to determine the duration of mechanical ventilation and the duration of the stay in the ICU for patients who were successfully weaned, those who died while receiving ventilation, and those who had ventilation withdrawn.[23] All statistical tests were two-tailed.

To examine the determinants of the withdrawal of mechanical ventilation, we first identified a group of patients at risk for death during mechanical ventilation or withdrawal of mechanical ventilation, using the data from 851 patients. We developed a logistic-regression model for which the dependent variable was withdrawal of the ventilator or death during mechanical ventilation as compared with successful weaning from mechanical ventilation. The independent variables included the patient's base-line characteristics: age, sex, APACHE II score, medical status (as compared with surgical status), diagnostic category on admission to the ICU, prior functional status, and ability to participate in decisions. Additional independent variables, which were based on data collected during the patient's first day in the ICU, included the Multiple Organ Dysfunc-

tion Score; the need for inotropes, vasopressors, or dialysis; the physician's prediction of the patient's likelihood of survival in the ICU and the hospital (less than 10 percent, 10 to 40 percent, 41 to 60 percent, or greater than 60 percent); the physician's prediction of the patient's functional and cognitive status one month after hospital discharge (will not leave the hospital, will be severely limited, will be somewhat limited, or will be totally independent); and the physician's perception of the patient's preferences about the use of life support. All the independent variables were included in the multivariate model. Using this model, we identified 300 patients at relatively high risk for withdrawal of the ventilator or death, with a threshold sensitivity of 68.6 percent and a specificity of 83.6 percent, a predicted probability of 0.64, and an area under the receiver-operating-characteristic curve of 0.85. Among these 300 patients, 88 (29.3 percent) were successfully weaned, 105 (35.0 percent) died while receiving mechanical ventilation, and 107 (35.7 percent) had the ventilator withdrawn.

For these 300 patients, we conducted Cox proportional-hazards regression analysis to identify the determinants of physician-initiated withdrawal of the ventilator. Data on patients who were weaned from mechanical ventilation or who died while receiving mechanical ventilation were censored. The independent variables were the same base-line factors used in the logistic model, in addition to the number of chronic diseases. Other daily variables were considered in the week preceding withdrawal of mechanical ventilation or death, including indicators of the severity of illness (Multiple Organ Dysfunction Score, ability to participate in decisions, use of inotropes or vasopressors, and use of hemodialysis), factors based on the physician's clinical judgment (prediction of the likelihood of the patient's survival in the ICU and the hospital — excluding predictions made within 48 hours before the withdrawal of the ventilator, death, or successful weaning, prediction of the patient's functional and cognitive status one month after hospital discharge, and perception of the patient's preferences about the use of life support), and geographic factors (center, city, and country). We analyzed each factor in a univariate model, and we included all factors with P values of less than 0.10 in a multivariate regression, using backward stepwise elimination. We also tested for two-way interactions and tested the in-

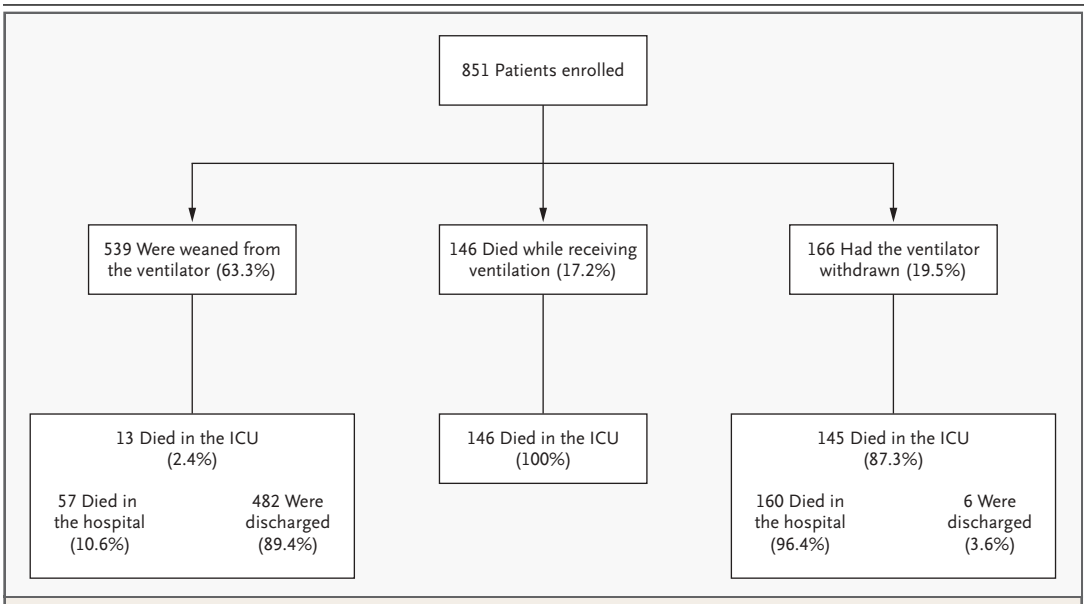

Figure 1. Outcomes among Patients Receiving Mechanical Ventilation Who Were Expected to Remain in the Intensive Care Unit (ICU) for at Least 72 Hours.

Of 851 enrolled patients, 539 were weaned from the ventilator. Of 146 patients who died while receiving mechanical ventilation and 166 who had mechanical ventilation withdrawn, 53 and 72 patients had inotropes or vasopressors withdrawn, respectively (P<0.001), and 8 and 18 patients underwent withdrawal of dialysis, respectively (P=0.01). The number of patients who died in the hospital includes the number who died in the ICU.

teraction of each variable in the final model with time. We calculated the hazard ratios and 95 percent confidence intervals for patients who had mechanical ventilation withdrawn as compared with patients who died while receiving mechanical ventilation. The results are adjusted for the center.

RESULTS

We included in the analysis 851 patients who were receiving mechanical ventilation; their mean (±SD) age was 61.2±17.6 years, and the mean APACHE II score was 21.7±8.6. No eligible patients were excluded. The diagnostic categories on admission to the ICU were as follows: pulmonary disease in 215 patients (25.3 percent), cardiovascular disease in 109 (12.8 percent), gastrointestinal disease in 132 (15.5 percent), central nervous system disease in 130 (15.3 percent), cardiopulmonary arrest in 87 (10.2 percent), sepsis in 65 (7.6 percent), and other categories in 113 (13.3 percent). The majority of patients (679, or 79.8 percent) were unable to participate in decision making during the first 24 hours.

Of these 851 patients, 539 (63.3 percent) were successfully weaned, 146 (17.2 percent) died while receiving mechanical ventilation, and 166 (19.5 percent) had mechanical ventilation withdrawn (Fig. 1). Of the 166 patients who had mechanical ventilation withdrawn, 145 (87.3 percent) died in the ICU and an additional 15 (9.0 percent) died in the hospital, for an overall in-hospital mortality rate of 96.4 percent (160 of 166). Of the 304 patients who died in the ICU, 201 (66.1 percent) died after the withdrawal of one or more of the following: mechanical ventilation, inotropes or vasopressors, or dialysis.

The median duration of the stay in the ICU was nine days for patients who were weaned from mechanical ventilation, six days for those who died while receiving mechanical ventilation, and six days for those who had mechanical ventilation with-

Table 1. Clinical Characteristics of 851 Patients Receiving Mechanical Ventilation in the Intensive Care Unit (ICU), According to the Outcome.*

Characteristic	Weaned from Ventilator (N=539)	Died While Receiving Ventilation (N=146)	Ventilator Withdrawn (N=166)	P Value†
Age — yr	60.4±18.1	60.1±17.7	64.4±15.4	0.02
Female sex — no. (%)	231 (42.9)	60 (41.1)	67 (40.4)	0.90
APACHE II score‡	19.4±8.0	26.5±8.6	25.2±7.6	0.17
Medical admission — no. (%)	362 (67.2)	114 (78.1)	138 (83.1)	0.26
Able to participate in decisions on admission to ICU — no. (%)	123 (22.8)	22 (15.1)	27 (16.3)	0.77
DNR order on admission to ICU — no. (%)	27 (5.0)	20 (13.7)	32 (19.3)	0.19
DNR order during ICU stay — no. (%)§	50 (9.3)	76 (52.1)	166 (100.0)	<0.001
Duration of ICU stay — days				0.75
Median	9	6	6	
Interquartile range	6–16	3–14	3–12	
Receipt of inotropes or vasopressors — no. (%)	240 (44.5)	131 (89.7)	115 (69.3)	<0.001
Inotropes or vasopressors withdrawn — no./total no. (%)	3/240 (1.3)	53/131 (40.5)	72/115 (62.6)	<0.001
Receipt of dialysis — no. (%)	64 (11.9)	32 (21.9)	32 (19.3)	0.56
Dialysis withdrawn — no./total no. (%)	1/64 (1.6)	8/32 (25.0)	18/32 (56.2)	0.01
Died in ICU — no. (%)	13 (2.4)	146 (100.0)	145 (87.3)	<0.001
Died in hospital — no. (%)¶	57 (10.6)	—	160 (96.4)	—

* Plus–minus values are means ±SD. DNR denotes do not resuscitate.
† P values are for the comparison of patients who underwent withdrawal of mechanical ventilation with those who died while receiving mechanical ventilation.
‡ Scores on the Acute Physiology and Chronic Health Evaluation (APACHE II) test range from 0 to 71, with higher scores indicating more severe illness.
§ All 166 patients who underwent ventilator withdrawal ultimately had a DNR order, but 108 (65.1 percent) had a DNR order that was instituted earlier than the decision to withdraw mechanical ventilation.
¶ This category includes patients who died in the ICU and those who survived while they were in the ICU but died before discharge from the hospital.

Table 2. Multivariate Analysis of Base-Line Factors Associated With the Withdrawal of Mechanical Ventilation or Death during Mechanical Ventilation.*

Factor	Odds Ratio (90% CI)	P Value
Patients' characteristics		
Age (per 10-yr increase)	1.07 (0.95–1.21)	0.25
Female sex	1.04 (0.72–1.49)	0.85
APACHE II score (per 5-point increase)	1.23 (1.09–1.39)	<0.001
Medical (vs. surgical) status	1.62 (0.99–2.66)	0.05
Diagnostic category on admission		0.62
Cardiovascular disease	1.63 (0.69–3.83)	
Pulmonary disease	1.37 (0.59–3.21)	
Cardiopulmonary arrest	1.09 (0.47–2.52)	
Central nervous system disease	0.95 (0.45–1.99)	
Gastrointestinal disease	1.19 (0.53–2.68)	
Metabolic disease or miscellaneous	1.62 (0.70–3.77)	
Sepsis†	1.00	
Prior functional status		0.01
Poor	0.84 (0.42–1.65)	
Moderate	2.03 (1.28–3.22)	
Good†	1.00	
Unable to participate in decisions	1.0 (0.69–1.78)	0.68
Severity of illness		
Multiple Organ Dysfunction Score (per 5-point increase)	2.46 (1.77–3.44)	<0.001
Use of inotropes or vasopressors	1.42 (0.78–2.57)	0.25
Use of hemodialysis	0.70 (0.19–2.58)	0.59
Physicians' clinical judgments		
Prediction of the likelihood of survival in ICU		<0.001
<10%	4.71 (1.97–11.25)	
10–40%	3.28 (1.78–6.07)	
41–60%	1.65 (0.99–2.76)	
>60%†	1.00	
Prediction of the likelihood of survival in hospital		0.04
<10%	1.61 (0.61–4.27)	
10–40%	1.58 (0.81–3.10)	
41–60%	2.15 (1.28–3.63)	
>60%†	1.00	
Prediction of functional status 1 mo after discharge		0.98
Will not leave hospital	0.71 (0.05–10.04)	
Will be severely limited	0.95 (0.48–1.86)	
Will be somewhat limited	1.03 (0.62–1.72)	
Will be totally independent†	1.00	
Prediction of cognitive function 1 mo after discharge		0.38
Will not leave hospital	4.11 (0.30–57.06)	
Will be severely limited	0.56 (0.23–1.33)	
Will be somewhat limited	0.94 (0.59–1.47)	
Will be totally independent†	1.00	
Perception of patient's preferences about the use of life support‡		0.02
No advanced life support	1.96 (0.78–4.95)	
Partial advanced life support	2.93 (1.30–6.60)	
All advanced life support as necessary†	1.00	

* The dependent variables were withdrawal of ventilation or death during mechanical ventilation. The independent base-line variables that were used to generate this model were recorded within 24 hours after admission to the intensive care unit (ICU), and all were included in the multivariate analysis. The Acute Physiology and Chronic Health Evaluation (APACHE II) score measures the severity of acute and chronic illness on a scale of 0 to 71, with higher scores indicating more severe illness. The Multiple Organ Dysfunction Score reflects the function of six organ systems; scores range from 0 to 24, with higher scores indicating more severe organ dysfunction. CI denotes confidence interval.

† Patients in this category served as the reference group.

‡ Physicians reported their perception that the patient preferred not to receive advanced life support (e.g., no mechanical ventilation, inotropes or vasopressors, or dialysis), preferred to discontinue some types of advanced life support while maintaining others (e.g., continue mechanical ventilation but discontinue dialysis or continue inotropes or vasopressors but discontinue mechanical ventilation), or preferred to receive all types of advanced life support as necessary.

Table 3. Univariate Analysis of Factors Associated with the Withdrawal of Mechanical Ventilation.*

Factor	Hazard Ratio (95% CI)	P Value
Patients' base-line characteristics		
Age (per 10-yr increase)	1.08 (0.95–1.22)	0.23
Female sex	1.06 (0.72–1.56)	0.78
APACHE II score (per 5-point increase)	1.02 (0.91–1.14)	0.78
Medical (vs. surgical) status	1.50 (0.84–2.69)	0.17
Diagnostic category on admission		0.01
Cardiac	0.87 (0.34–2.22)	
Respiratory	1.50 (0.74–3.03)	
Cardiopulmonary arrest	2.18 (1.09–4.34)	
Central nervous system	1.97 (0.95–4.07)	
Gastrointestinal	0.86 (0.39–1.92)	
Metabolic or miscellaneous	0.76 (0.32–1.82)	
Sepsis†	1.00	
Chronic diseases		0.96
≥2	1.07 (0.51–2.27)	
1	1.06 (0.70–1.60)	
0†	1.00	
Prior functional status		0.59
Poor	1.20 (0.63–2.30)	
Moderate	0.85 (0.56–1.31)	
Good†	1.00	
Unable to participate in decisions	0.72 (0.44–1.18)	0.19
Multiple Organ Dysfunction Score (per 5-point increase)	1.00 (0.82–1.22)	0.99
Severity of illness		
Multiple Organ Dysfunction Score (per 5-point increase)	1.08 (0.83–1.40)	0.57
Unable to participate in decisions	2.09 (0.91–4.80)	0.08
Use of inotropes or vasopressors	1.82 (1.23–2.70)	0.003
Use of hemodialysis	0.71 (0.39–1.31)	0.28

drawn (P<0.001). The duration of mechanical ventilation was similar among the three groups (median of 4.5 days among patients who were weaned from ventilation, 5.0 days among those who died while receiving ventilation, and 5.0 days among those who had the ventilator withdrawn; P=0.24).

Table 1 lists the clinical characteristics of patients who were successfully weaned, patients who died while receiving mechanical ventilation, and patients who underwent withdrawal of the ventilator. Patients who underwent withdrawal of mechanical ventilation were significantly older than those who died while receiving mechanical ventilation (64.4 years vs. 60.1 years, P=0.02). Otherwise, the base-line characteristics were similar in the two groups, including the proportion of patients with explicit do-not-resuscitate orders on admission to the ICU (19.3 percent of those in whom mechanical ventilation was withdrawn and 13.7 percent of those who died while receiving mechanical ventilation, P=0.19). Patients who ultimately had the ventilator withdrawn were more likely to have do-not-resuscitate orders established during their stay in the ICU than patients who died while receiving mechanical ventilation (100.0 percent vs. 52.1 percent, respectively; P<0.001) and were less likely to receive inotropes or vasopressors (69.3 percent vs. 89.7 percent, respectively; P<0.001). Among the patients who received inotropes or vasodilators, those who had the ventilator withdrawn were also more likely to have these drugs withdrawn (62.6 percent, vs. 40.5 percent of the patients who died while receiving mechanical ventilation; P<0.001). Patients who had the ventilator withdrawn were no more likely to receive dialysis than were those who died while receiving mechanical ventilation (19.3 percent vs. 21.9 percent, P=0.56), but they were more likely to have dialysis withdrawn (56.2 percent vs. 25.0 percent, P=0.01).

Table 2 shows the results of the logistic model

Table 3. (Continued.)

Factor	Hazard Ratio (95% CI)	P Value
Physicians' clinical judgments		
Prediction of the likelihood of survival in ICU		<0.001
<10%	9.54 (4.10–22.21)	
10–40%	2.02 (0.80–5.06)	
41–60%	0.95 (0.30–2.96)	
>60%†	1.00	
Prediction of the likelihood of survival in hospital		<0.001
<10%	6.29 (3.31–11.97)	
10–40%	1.52 (0.69–3.31)	
41–60%	0.88 (0.35–2.21)	
>60%†	1.00	
Prediction of functional status 1 mo after discharge		<0.001
Will not leave hospital	8.81 (3.54–21.95)	
Will be severely limited	2.80 (1.06–7.42)	
Will be somewhat limited	1.05 (0.38–2.90)	
Will be totally independent†	1.00	
Prediction of cognitive function 1 mo after discharge		<0.001
Will not leave hospital	8.73 (5.02–15.20)	
Will be severely limited	2.55 (1.04–6.21)	
Will be somewhat limited	1.68 (0.85–3.29)	
Will be totally independent†	1.00	
Perception of patient's preferences about the use of life support‡		<0.001
No advanced life support	8.35 (5.44–12.81)	
Partial advanced life support	2.73 (1.56–4.76)	
All advanced life support as necessary†	1.00	

* Hazard ratios are for the comparison of the withdrawal of mechanical ventilation with death during mechanical ventilation and were based on univariate Cox proportional-hazards regression analysis. The Acute Physiology and Chronic Health Evaluation (APACHE II) score measures the severity of acute and chronic illness on a scale of 0 to 71, with higher scores indicating more severe illness. The Multiple Organ Dysfunction Score reflects the function of six organ systems; scores range from 0 to 24, with higher scores indicating more severe organ dysfunction. CI denotes confidence interval, and ICU intensive care unit.

† Patients in this category served as the reference group.

‡ Physicians reported their perception that the patient preferred not to receive advanced life support (e.g., no mechanical ventilation, inotropes or vasopressors, or dialysis), preferred to discontinue some types of advanced life support while maintaining others (e.g., continue mechanical ventilation but discontinue dialysis or continue inotropes or vasopressors but discontinue mechanical ventilation), or preferred to receive all types of advanced life support as necessary.

used to identify 300 patients at risk for the withdrawal of ventilation or death while receiving mechanical ventilation. Using this cohort, we present in Table 3 the univariate analyses showing factors associated with the withdrawal of mechanical ventilation. Among the base-line characteristics, only the diagnostic category on admission was significantly associated with the withdrawal of ventilation in the univariate analysis. We found that several time-dependent factors were associated with the withdrawal of ventilation in the univariate analysis, including the use of inotropes or vasopressors, the physician's prediction of the likelihood of the patient's survival in the ICU and the hospital, the physician's prediction of the patient's future functional and cognitive status, and the physician's perception of the patient's preferences about the use of life support. We found no relation between the withdrawal of ventilation and the center (P=0.26), the city (P=0.91), or the country (P=0.89).

Table 4 shows the independent predictors of the withdrawal of ventilation. We identified no interactions. The first factor that independently predicted the withdrawal of mechanical ventilation was the use of inotropes or vasopressors (hazard ratio, 1.78; 95 percent confidence interval, 1.20 to 2.66; P=0.004). The second factor independently associated with the withdrawal of ventilation was the physician's prediction that the likelihood of the patient's survival in the ICU was less than 10 percent (hazard ratio, 3.49; 95 percent confidence interval, 1.39 to 8.79; P=0.002). The proportion of patients

who had a probability of survival of less than 10 percent was 85.5 percent among those who ultimately had the ventilator withdrawn, as compared with 76.0 percent among those who died while receiving mechanical ventilation (P=0.03). The third factor was the physician's prediction of such severely impaired cognitive function that the patient would not leave the hospital (hazard ratio, 2.51; 95 percent confidence interval, 1.28 to 4.94; P=0.04). The proportion of patients predicted to have this degree of cognitive impairment was 78.9 percent of those who ultimately had the ventilator withdrawn, as compared with 58.9 percent of those who died while receiving mechanical ventilation (P<0.001). Finally, patients who were perceived by their physicians as not wanting life support used were more likely to have the ventilator withdrawn than to die while receiving mechanical ventilation (hazard ratio, 4.19; 95 percent confidence interval, 2.57 to 6.81; P<0.001). Such patients represented 30.1 percent of those who had the ventilator withdrawn and 11.0 percent of those who died while receiving ventilation (P<0.001).

Table 4. Multivariate Analysis of Factors Associated with the Withdrawal of Mechanical Ventilation.*

Independent Factor	Hazard Ratio (95% CI)	P Value
Use of inotropes or vasopressors	1.78 (1.20–2.66)	0.004
Physician's prediction of the likelihood of patient's survival in ICU		0.002
<10%	3.49 (1.39–8.79)	
10–40%	1.60 (0.63–4.04)	
41–60%	0.95 (0.30–2.96)	
>60%†	1.00	
Physician's prediction of patient's cognitive function 1 mo after discharge		0.04
Will not leave hospital	2.51 (1.28–4.94)	
Will be severely limited	1.45 (0.58–3.63)	
Will be somewhat limited	1.36 (0.69–2.69)	
Will be totally independent†	1.00	
Physician's perception of patient's preferences about the use of life support‡		<0.001
No advanced life support	4.19 (2.57–6.81)	
Partial advanced life support	2.02 (1.13–3.60)	
All advanced life support as necessary†	1.00	

* Hazard ratios are for the comparison of the withdrawal of mechanical ventilation with death while receiving mechanical ventilation and are based on multivariate Cox proportional-hazards regression analysis. CI denotes confidence interval, and ICU intensive care unit.

† Patients in this category served as the reference group.

‡ Physicians reported their perception that the patient preferred not to receive advanced life support (e.g., no mechanical ventilation, inotropes or vasopressors, or dialysis), preferred to discontinue some types of advanced life support while maintaining others (e.g., continue mechanical ventilation but discontinue dialysis), or preferred to receive all types of advanced life support as necessary.

DISCUSSION

In this study of patients who were receiving mechanical ventilation and who were expected to be in the ICU for at least 72 hours, 304 patients (35.7 percent) died in the ICU. Approximately half of those who died had mechanical ventilation withdrawn in anticipation of death; however, 6 of the 166 patients who had mechanical ventilation withdrawn because death was thought to be imminent were ultimately discharged from the hospital. We found that patients who had the ventilator withdrawn and those who died while receiving mechanical ventilation had a shorter stay in the ICU than patients who were successfully weaned. In contrast, two decades ago, patients who eventually died in the ICU had a longer stay, with greater use of resources, than those who lived.[24] We hypothesize that our findings reflect a change in practice caused by earlier elicitation of health care directives regarding the use of life support.

In our study, patients who underwent ventilator withdrawal were also more likely than those who died while receiving ventilation to have inotropes or vasopressors and dialysis withdrawn. These results illustrate how for some critically ill patients, the withdrawal of inotropes, vasopressors, or dialysis and a decision to forgo cardiopulmonary resuscitation result in death with the ventilator in place. We found an increase in do-not-resuscitate orders over the course of the stay in the ICU, which may reflect a stepwise approach to the limitation of life support as the patient's prognosis worsens.[25]

Our results are as notable for the associations we did not confirm as for those we did. In a previous survey, Canadian physicians and nurses reported that they would be most likely to withdraw life support from older and sicker patients and those with poor prior physical and cognitive function.[16] In a study of patients during their first 24 hours after admission to the ICU, we found that the likelihood of having a do-not-resuscitate order was strongly related to the patient's age and the severity of illness.[20] In the current study, we anticipated finding similar determinants of ventilator withdrawal, as suggested by research demonstrating that decisions to forgo cardiopulmonary resuscitation precede 60 to 90 percent of deaths in the ICU.[5,7,26,27]

In contrast, we found no independent association between the withdrawal of ventilation and the patient's age, prior functional status, severity of illness, or severity of organ dysfunction. Although measures of the severity of illness that were previously shown to predict survival were not associated with the withdrawal of ventilation in our study, dependency on inotropes or vasopressors as a secondary means of life support and a likelihood of survival in the ICU of less than 10 percent were strongly associated with withdrawal of ventilation.

We found that the physician's perception of the patient's preferences about the use of life support was an independent predictor of the withdrawal of mechanical ventilation. This finding highlights the importance placed on patients' preferences but is less reassuring when one considers that physicians' understanding of the wishes of many patients who are receiving mechanical ventilation derives from family members. Patients' preferences are often unknown or undocumented at the time of the initial decision to administer life support, and if documented, they may be unavailable[28] or may change over time.[29] Moreover, patients' wishes are often at odds with those of family members[30] or physicians' perceptions of those wishes.[31] It remains questionable whether patients' preferences will be optimally represented in crucial life-support decisions in the absence of clear and detailed advance care plans.

Previous research shows that physicians' personal characteristics and experiences[32] may influence their style of decision making,[33,34] the patient–physician relationship,[35] and ultimately, decisions to withdraw treatment.[17-19] These studies and research demonstrating geographic variation in the withdrawal of life support[6,10,11,16] led us to expect that the center, city, and country would influence the probability of the withdrawal of mechanical ventilation. We did not, however, find significant geographic variation.

Our study has several limitations. First, we did not conduct the longitudinal study necessary to validate physicians' predictions of patients' future functional status and cognitive function.[36] We did not ask physicians to justify their predictions of the likelihood of death or future function. Our focus was on the withdrawal of mechanical ventilation rather than the withholding of mechanical ventilation. Our findings may not apply to nonteaching hospitals,[10] community hospitals, or open ICUs.

This study extends our understanding of the process of withdrawal of life support by focusing on mechanical ventilation as the most common form of advanced life support and evaluating factors that distinguish patients who ultimately have the ventilator withdrawn from other critically ill patients for whom this decision may be considered. We estimated the relative importance of a wide range of potential determinants of the withdrawal of ventilation, including base-line and time-dependent characteristics. We also analyzed key clinical judgments made systematically each day by attending physicians. By enrolling a multicenter cohort of consecutive patients and finding that the proportion who had ventilation withdrawn was consistent across many centers, we increased the precision of our results and enhanced the generalizability of our findings to similar university-affiliated centers.

Our results call into question the traditional biomedical model of withdrawal of life support that focuses on the patient's age and physiological determinants such as worsening organ function. The four independent factors associated with the withdrawal of ventilation that we identified were physicians' perceptions of patients' preferences about the use of life support, physicians' predictions of the likelihood of patients' survival in the ICU, physicians' predictions of patients' future cognitive status, and the use of inotropes or vasopressors. Our findings are encouraging in that they suggest that the process of withdrawal of life support is attentive to patients' wishes. Nevertheless, our results may arouse concern in that when the patients themselves are unable to communicate their preferences, their wishes may not be accurately represented by family members or physicians. Subsequent research on care at the end of life in critically ill patients should examine in detail how, when, and by whom patients' preferences are elicited and honored.

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APPENDIX

In addition to the authors, the following investigators participated in the Level of Care Study: *Toronto Hospital, Toronto* — N. Lazar; *London Health Sciences Center, London, Ont., Canada* — D. Leasa, A. Kirby; *Hamilton Health Sciences Center, Hamilton, Ont., Canada* — A. McLellan, S. Puksa; *Royal North Shore Hospital, Sydney, Australia* — M. Fisher; *study coordinators* — L. Buckingham, N. Krolicki; *data-base management* — L. Buckingham; *data entry* — S. Duchesne, S. Reeve, B. Jedrzejowski, L. Raftery.

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