A prognostic model for one-year mortality in patients requiring prolonged mechanical ventilation*

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Objective: **A measure that identifies patients who are at high risk of mortality after prolonged ventilation will help physicians communicate prognoses to patients or surrogate decision makers. Our objective was to develop and validate a prognostic model for 1-yr mortality in patients ventilated for 21 days or more.**

Design: **The authors conducted a prospective cohort study.**

Setting: **The study took place at a university-based tertiary care hospital.**

Patients: **Three hundred consecutive medical, surgical, and trauma patients requiring mechanical ventilation for at least 21 days were prospectively enrolled.**

Measurements and Main Results: **Predictive variables were measured on day 21 of ventilation for the first 200 patients and entered into logistic regression models with 1-yr and 3-mo mortality as outcomes. Final models were validated using data from 100 subsequent patients. One-year mortality was 51% in the development set and 58% in the validation set. Independent predictors of mortality included requirement for vasopressors, hemodialysis, platelet count $\leq 150 \times 10^9$/L, and age ≥ 50 yrs. Areas under the receiver operating characteristic curve for the development model and validation model were .82 (SE .03) and .82 (SE .05), respectively. The model had sensitivity of .42 (SE .12) and specificity of .99 (SE .01) for identifying patients who had ≥90% risk of death at 1 yr. Observed mortality was highly consistent with both 3- and 12-mo predicted mortality. These four predictive variables can be used in a simple prognostic score that clearly identifies low-risk patients (no risk factors, 15% mortality) and high-risk patients (three or four risk factors, 97% mortality).**

Conclusions: **Simple clinical variables measured on day 21 of mechanical ventilation can identify patients at highest and lowest risk of death from prolonged ventilation. (Crit Care Med 2008; 36: 2061–2069)**

KEY WORDS: mechanical ventilation; illness severity scores; outcomes; statistical model; critical illness; prognosis

As patient management strategies in the intensive care unit continue to advance, more patients are surviving the early acute phases of critical illness. However, when multiorgan failure fails to resolve or leads to subsequent complications such as critical illness polyneuropathy, prolonged mechanical ventilation (PMV) can result (1, 2). The number of patients requiring PMV has been increasing over the last decade and promises to increase dramatically when members of the baby boomer generation reach advanced age and become particularly susceptible to this complication (3).

Patients requiring PMV consume a disproportionately high amount of healthcare resources both in the intensive care unit and after hospital discharge (4, 5). Their short-term and long-term mortality is high (6), and they experience a very heavy symptom burden for prolonged periods (7, 8). Hospital survivors have a significant degree of functional and cognitive limitations and a high readmission rate (9). Some remain at high risk for death after hospital discharge, but not all. Prolonged hospitalization for patients on PMV who are at high risk of death does not meet current standards of cost-effectiveness (10). Considering the high symptom burden of this population and often poor outcomes, a mortality prediction model that identifies patients on PMV with the highest and lowest risk for death would be useful to inform discussions of prognoses among clinicians and patients or their surrogate decision-makers. Such a model could also standardize illness severity in cohort studies examining outcomes and interventions in this resource-intensive group of patients.

A consensus conference defined PMV as patients requiring invasive mechanical ventilation for at least 21 days after acute illness (1). We conducted a prospective cohort study to develop and validate a mortality prediction model for adult patients meeting this definition. Our intention was to develop a model that would be practical for use in the clinical setting and have very high specificity in patients at highest risk of death.

MATERIALS AND METHODS

Patients

A total of 300 adult patients were prospectively enrolled from University of North Carolina Hospitals, a 640-bed university-based tertiary care medical center with 65 adult intensive care unit beds that can accommodate mechanically ventilated patients. Two hundred patients were consecutively enrolled from November 2001 to January 2004 for the development set of the prognostic model. One hundred patients were consecutively enrolled from February 2004 to June 2005 to form the

***See also p. 2200.**

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model's validation set. Enrollment criteria included requirement of mechanical ventilation after acute illness for at least 21 days after initial intubation. If patients were extubated within that initial 21-day period but needed reintubation, they were enrolled only if the period of spontaneous breathing was ≤72 hrs. Exclusion criteria included age <18 yrs, severe burns, chronic neuromuscular diseases, chronic mechanical ventilation before admission, receipt of >7 days of mechanical ventilation before transfer from a referral center, prisoners, and refusal of consent.

Patients in adult medical and surgical intensive care units were screened on a daily basis. All eligible patients were enrolled for review of existing medical records. We requested permission through primary physicians to approach patients or, as was usually necessary, their surrogates to request consent for interviews and telephone follow-up. If patients or surrogates refused consent to participate, they were excluded from the study, including review of existing data. If a surrogate was not available, follow-up was achieved by review of medical records and the National Death Index. The research protocol was approved by the University of North Carolina Institutional Review Board.

Data Collection

On day 21 of mechanical ventilation, medical records were abstracted for demographic data, diagnoses, comorbidities, and premorbid functional status. Physiological variables were recorded from the first day of intensive care unit admission and from day 21 of mechanical ventilation. Acute Physiology and Chronic Health Evaluation II scores were calculated using data from the first 24 hrs of intensive care unit admission (11). Sequential Organ Failure Assessment scores were calculated using data from the first 24 hrs of intensive care unit admission and from data collected on day 21 of mechanical ventilation (12). The Charlson Index score, a measure of medical comorbidities, was calculated from medical record data based on conditions present at day 21 (13). Premorbid functional status was assessed by the surrogate's perception of whether the patient needed assistance with any activity of daily living (ADL) during the 2 wks before acute illness.

Patients were followed during the rest of their hospitalization for duration of mechanical ventilation, mortality, intensive care unit and hospital disposition, and length of stay. Patients or surrogates who consented to telephone follow up were contacted at 3 mos, 6 mos, and 12 mos from the time of enrollment (day 21 of mechanical ventilation). They were interviewed regarding the patient's vital status, place of residence, number of hospital readmissions, requirement for mechanical ventilation, tracheostomy, feeding tubes, and the patient's functional status. Performance of six basic ADLs was assessed by questionnaires asking how much assistance patients needed with feeding, getting out of bed, walking, dressing, toileting, and bathing (14). A written notification that a phone call was going to be made was mailed 2 wks before the scheduled contact, and multiple telephone calls were attempted until the patient or surrogate was reached. Patients and surrogates were reminded that they had the option of not answering any or all of the questions. For hospital survivors who were enrolled for review of existing data only, and for patients who were lost to telephone follow-up, 1-yr mortality was assessed by review of the National Death Index.

All data collection instruments were pretested using records from ten patients who were not part of the study sample. Revisions were made after clarifications by all investigators. Data on the first ten patients enrolled in the study were collected by both the primary data collector and the principal investigator to ensure concordance. Similar quality checks were conducted on a random sample of 10% of the first 100 patients enrolled. Subjective variables such as primary and secondary diagnoses and comorbidities were made by both the primary data collector and the principal investigator on all patients, and discrepancies were settled together. Interview instruments were pretested on a sample of ten patients and surrogates, and revisions were made accordingly. Telephone interviewers received full instruction from the principal investigator, and mock interviews were conducted until performance was consistent and reproducible. Analysis on the development set model was not begun until follow up on the validation set was completed and the database was closed.

Statistical Analysis

Summary analyses were performed on demographic and physiological variables and expressed as mean ± SD for normally distributed data and median, interquartile range for nonnormal data. Power analyses indicated that a logistic regression model with 200 patients

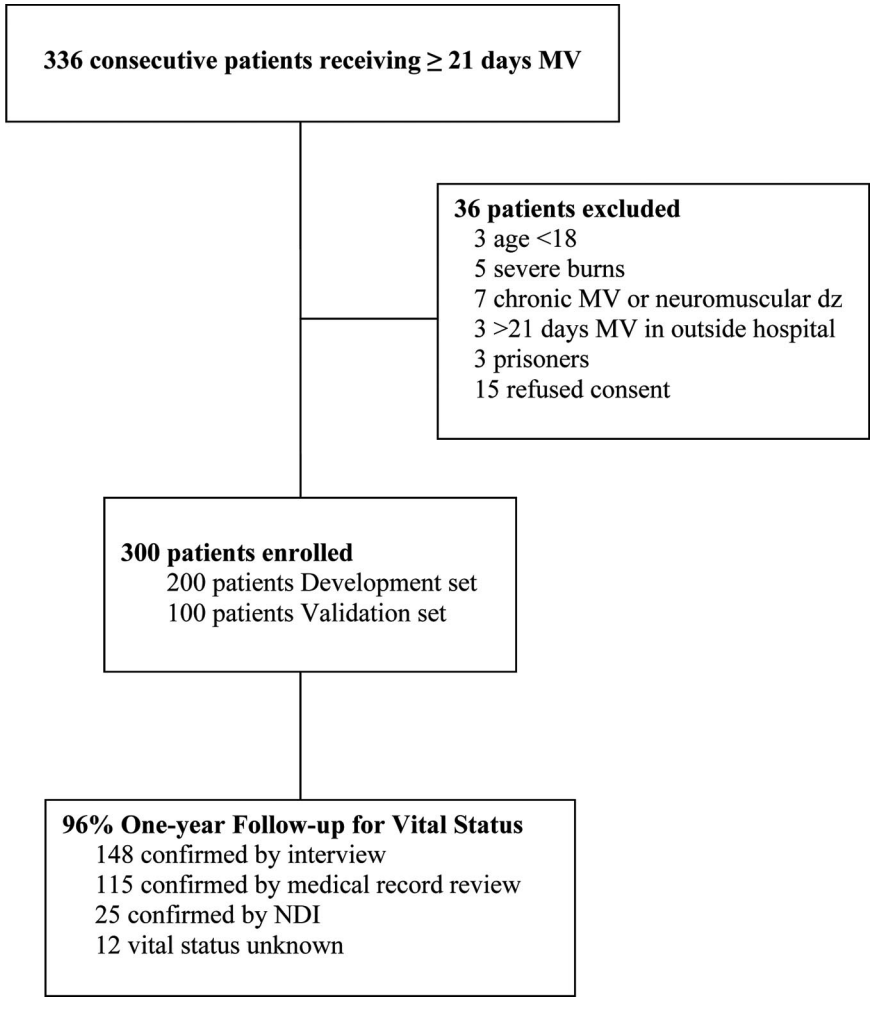

Figure 1. Enrollment and follow-up data. *MV*, mechanical ventilation; *NDI*, National Death Index.

and 130 expected deaths would have sufficient power to include 13 variables. These predictor variables were chosen *a priori* based on clinical judgment and previous studies in different settings (15–18). All were measured on day 21 of mechanical ventilation. The variables included age, premorbid independence in ADL, Pao_2/Fio_2, inability to lift the upper extremity from the bed, requirement for any dose of pressor (dopamine, norepinephrine, phenylephrine), platelet count, requirement for hemodialysis (any patient receiving hemodialysis between days 19 and 22 of mechanical ventilation or any patient with renal failure for whom hemodialysis had been indicated but withheld), and specific comorbidities (severe chronic pulmonary disease, peripheral vascular disease, diabetes mellitus with chronic complication, congestive heart failure). Bivariate analysis of associations between the primary outcome, death at 1 yr, and the preselected predictor variables were performed for descriptive purposes. Potential collinearity was assessed by examining pairwise correlations and measuring variance inflation factors. Collinearity was not found to be an issue in our data and therefore did not affect our modeling strategy.

All variables identified *a priori* as potential predictors were included in a logistic regression model with death at 1 yr as the primary outcome. The maximal model was reduced by the investigators by eliminating variables sequentially and comparing each new model by likelihood ratio tests and by comparing the area under the receiver operating characteristic curve for each new model. Calibration of the model was assessed using Pearson's chi-square goodness-of-fit test (GoF). Odds ratios and 95% confidence intervals associated with each variable in the final model are reported. A similar model was constructed using 3-month mortality (90 days after day 21 of mechanical ventilation) as the primary outcome.

For the validation phase of the study, values for predictive variables measured for the 100 patients in the validation set were entered into logistic regression models using the beta values from the reduced logistic regression model from the 200-patient development phase. Validation of the prediction model was established by comparing the area under the receiver operating characteristic curve, sensitivity, and specificity of the development and validation study models. Calibration of the validation study model was assessed using Pearson's GoF test. Similar analyses were performed using 3-month mortality as the primary outcome.

A clinical prediction rule was adapted from the final prediction model by assigning points to each predictive variable based on regression coefficients from the development model. Performance of this clinical prediction rule was assessed by comparing observed to predicted outcomes for 1-yr and 3-month mortality and by comparison of area under the receiver operating characteristic curve to that of the final model.

Data are presented as mean ± SD or median (interquartile range). Area under receiver operating characteristic curves, sensitivity, and specificity are presented as value (SE). All analyses were performed using Stata 8.0 software (Stata, College Station, TX).

RESULTS

Of 336 consecutive patients who were eligible for the study, 36 were excluded (Fig. 1). Vital status 1 yr after enrollment

Table 1. Patient characteristics

Variable	Development	Validation	*p* Value
	n = 200	n = 100	
Age, mean ± SD	55.7 ± 16.7	55.5 ± 16.6	.92
Age, median (IQR)	58 (42–69)	57 (44–66)	.82
Male, n (%)	120 (60)	49 (49)	.07
Race, n (%)			.31
White	124 (62)	61 (61)	
African American	61 (31)	36 (36)	
Hispanic	9 (5)	1 (1)	
Asian	4 (2)	1 (1)	
Native American	1 (0.5)	1 (1)	
Premorbid status			
Residence, n (%)	n = 181	n = 81	.27
Home	171 (94)	75 (93)	
Assisted living facility	3 (2)	4 (5)	
Skilled nursing facility	7 (4)	2 (2)	
Independent in ADLs, n (%)	n = 175	n = 79	.29
	143 (82)	60 (76)	
APACHE II ICU Admit, mean ± SD	20.6 ± 7.3	25.3 ± 6.8	.0001
SOFA day 1 MV, mean ± SD	9.9 ± 3.4	9.8 ± 2.9	.78
Day 21 measurements			
Advance directives, n (%)			.94
Do-not-resuscitate order	12 (6)	6 (6)	
Advanced power of attorney	9 (5)	6 (6)	
Living will	5 (3)	2 (2)	
None	168 (87)	81 (85)	
Service, n (%)			.20
Medicine	79 (40)	46 (46)	
General surgery/trauma	56 (28)	26 (26)	
Cardiac surgery	20 (10)	5 (5)	
Thoracic surgery	18 (9)	10 (10)	
Neurosurgery	17 (9)	4 (4)	
Transplant surgery	7 (4)	5 (5)	
SOFA day 21 MV, mean ± SD	7.6 ± 3.9	7.7 ± 3.4	.94
Pao_2/Fio_2, mean ± SD	219 ± 95.7	216 ± 110	.82
WBC, mean ± SD	13.3 ± 8.6	11.7 ± 7.1	.10
Platelet count ($\times 10^9$/L), mean ± SD	307 ± 216	243 ± 159	.009
Pressors, n (%)	33 (16)	28 (28)	.02
Hemodialysis, n (%)	49 (25)	32 (32)	.15
Albumin, median (IQR)	2.0 (1.7–2.4)	2.0 (1.8–2.5)	.58
BMI, mean ± SD	30.2 ± 8.2	33.5 ± 11.9	.009
Charlson index score, mean ± SD	2.7 ± 2.2	3.1 ± 2.3	.16
Specific comorbidities, n (%)			
Severe chronic pulmonary disease	22 (11)	14 (14)	.45
Chronic vascular disease	16 (8)	7 (7)	.78
Diabetes with chronic complications	23 (12)	10 (10)	.70
Congestive heart failure	30 (15)	15 (15)	1.0
Upper extremity strength, n (%)			.10
Against gravity	129 (66)	59 (60)	
Withdraw to pain	42 (21)	17 (17)	
No movement	25 (13)	22 (22)	
Lower extremity strength, n (%)			.10
Against gravity	94 (48)	42 (43)	
Withdraw to pain	63 (32)	26 (27)	
No movement	38 (19)	30 (31)	
Tracheostomy, n (%)	167 (84)	77 (77)	.38
Days to tracheostomy, n (%)	17 (12–22)	19 (12–26)	.11

ADLs, activities of daily living; APACHE II, Acute Physiology and Chronic Health Evaluation System; SOFA, Sequential Organ Failure Assessment; WBC, white blood cell count; BMI, body mass index; IQR, interquartile range; MV, mechanical ventilation; ICU, intensive care unit.

Table 2. Outcomes

Variable	Development N = 200	Validation N = 100	*p* Value
Hospital disposition, n (%)			.56
Died	82 (41)	50 (51)	
Long-term acute care	21 (11)	13 (13)	
Rehabilitation	59 (30)	24 (24)	
Skilled nursing facility	15 (8)	5 (5)	
Home with assistance	19 (10)	5 (5)	
Home independent	2 (1)	1 (1)	
If died			
Received CPR at time of death, n (%)	10 (12)	3 (6)	.02
Days DNR to death, median (IQR)	1 (0–3)	2.5 (1–7)	.27
Liberated from MV in hosp, n (%)	106 (53)	43 (43)	.23
Liberated, hospital survivors	n = 118 95 (81)	n = 50 39 (78)	.88
Reintubated, n (%)	14 (8)	14 (14)	.10
Liberated from MV in one year, n (%)	114 (58)	47 (49)	.14
Ventilator days, median (IQR)	35 (26–51)	35 (27–54)	.71
Ventilator days, survivors	39 (29–58)	38 (29–52)	.72
Ventilator days, nonsurvivors	32 (25–45)	35 (25–59)	.29
ICU length of stay, median (IQR)	37 (28–52)	36 (30–54)	.46
Hospital length of stay, median (IQR)	51 (36–72)	50 (37–74)	.91
Mortality, n (%)			
Three months	83 (42)	52 (52)	.08
One Year: known follow-up	n = 175 103 (59)	n = 84 58 (69)	.11
One Year: includes NDI data[a]	n = 200 103 (52)	n = 100 58 (58)	.18

[a]All hospital survivors in the Development set who did not have a record of subsequent death at University of North Carolina survived the year based upon National Death Index (NDI) records. This assumption was made for 12 similar patients in the Validation set; CPR, cardiopulmonary resuscitation; DNR, do-not-resuscitate; MV, mechanical ventilation; IQR, interquartile range; ICU, intensive care unit.

was confirmed by telephone follow up or medical record review in 263 patients and by National Death Index review in 25 patients. One-year mortality was unknown for 12 patients for an overall follow-up rate of 96%.

Patient demographics and outcomes for the development and validation sets are presented in Tables 1 and 2. Intensive care unit admission diagnoses are shown in Appendix 1. The groups were mostly similar, but patients in the validation set had higher admission Acute Physiology and Chronic Health Evaluation II scores and higher hospital and 3-month mortality. Thirty-seven of the patients who survived hospitalization were not confirmed to have died by review of medical records or telephone follow-up. National Death Index records were available for 25 of them. All were noted to have survived the year. The remaining 12 patients for whom National Death Index records were not yet available were counted as survivors based on survival of the 25 patients lost to telephone follow up who did have National Death Index data available.

Results of bivariate analyses are presented for descriptive purposes in Table

Table 3. Bivariate analysis of associations between predetermined predictive variables and one-year mortality in development set

Variable	n	Survived	Died	RR (95% CI)	*p* Value
Age					
≥50 years	128	51 (40)	77 (60)	1.66 (1.19, 2.34)	.001
<50 years	72	46 (64)	26 (36)		
ADLs					
Needs assistance with 1 ADL	32	11 (34)	21 (66)	1.47 (1.07, 2.0)	.03
No assistance needed	143	79 (55)	64 (45)		
Pa_{O_2}/Fi_{O_2}, mean ± SD	181	229 ± 96	208 ± 103	—	.21
Upper extremity strength					
Cannot lift against gravity	61	15 (25)	46 (75)	1.84 (1.44, 2.36)	.0001
Can lift against gravity	137	81 (59)	56 (41)		
Vasopressors					
Required	33	2 (6)	31 (94)	2.18 (1.79, 2.66)	.0001
Not required	165	94 (57)	71 (43)		
Platelets					
$\leq 150 \times 10^9$/L	48	4 (8)	44 (92)	2.41 (1.93, 3.01)	.0001
$>150 \times 10^9$/L	150	93 (62)	77 (38)		
Hemodialysis					
Required	49	10 (20)	39 (80)	1.88 (1.49, 2.37)	.0001
Not required	151	87 (58)	64 (42)		
Chronic pulmonary disease					
Present	22	10 (45)	12 (55)	1.07 (0.71, 1.60)	.76
Absent	178	87 (49)	91 (51)		
Peripheral vascular disease					
Present	16	8 (50)	8 (50)	0.97 (0.58, 1.61)	.90
Absent	184	89 (48)	95 (52)		
Diabetes with chronic complication					
Present	23	7 (30)	16 (70)	1.41 (1.03, 1.93)	.06
Absent	177	90 (51)	87 (49)		
Congestive heart failure					
Present	30	12 (40)	18 (60)	1.20 (0.86, 1.67)	.31
Absent	170	85 (50)	85 (50)		

ADL, activities of daily living; RR, relative risk; CI, confidence interval.

3. All predetermined predictor variables were included in the initial maximal logistic regression model. Requirement of vasopressors, platelets $\leq 150 \times 10^9$/L, age ≥ 50 yrs, requirement of hemodialysis, and upper extremity weakness were independent predictors of death at 1 yr in a reduced model. Clinically, upper extremity weakness was considered difficult to reproduce because the use of sedatives, which strongly affected this measurement, varied significantly between patients. This issue has affected the reliability of other illness severity models (19). Therefore, models with and without this variable were compared. The area under the receiver operating characteristic curve for the final reduced model shown in Table 4 (vasopressors, platelets $\leq 150 \times 10^9$/L, age ≥ 50 yrs, requirement of hemodialysis) was .82 (SE .03). This compares with .84 (SE .02) for the model with the final four variables plus upper extremity weakness and .85 (SE .03) for the maximal model ($p = .46$ for comparison of all three). For the final reduced model, sensitivity for identifying patients at $\geq 50\%$ risk of death was .58 (SE .16), and specificity was .91 (SE .16). Sensitivity for identifying patients at $\geq 90\%$ risk of death was .42 (SE .12), and specificity was .99 (SE .01). The model had good fit based on its nonsignificant GoF test ($\chi^2_{10df} = 6.72$, $p = .75$).

Using values measured in patients from the validation set, the same model had an area under the receiver operating characteristic curve of .82 (SE .05) ($p = .93$ compared with development set) and again demonstrated good fit (GoF $\chi^2_{16df} = 18.31$, $p = .31$). Comparisons of observed to predicted values for development and validation sets are shown in Figure 2. Reliability of the model was very consistent in the validation set. These four variables were also independent predictors of 3-mo mortality in a separate model (GoF $\chi^2_{10df} = 11.39$, $p = .33$) and showed consistent performance in the validation set (GoF $\chi^2_{16df} = 23.99$, $p = .09$) (Table 4).

As a sensitivity analysis, patients in the validation set who were lost to follow up were assumed to have all died (rather survive, as was the case in the development set, confirmed by the National Death Index). The area under the receiver operating characteristic curve for that

Table 4. Model performance

Variable	Three-Month Mortality Development OR (95% CI)	One-Year Mortality Development OR (95% CI)
Vasopressor	4.2 (1.2, 14.2)	8.8 (1.6, 48.4)
Platelets $\leq 150 \times 10^9$/L	7.1 (2.7, 18.6)	14.5 (4.1, 50.8)
Age ≥ 50 years old	3.5 (1.6, 7.8)	5.6 (2.4, 12.9)
Requiring hemodialysis	3.1 (1.3, 7.5)	2.9 (1.1, 7.7)

	Three-Month Mortality		One-Year Mortality	
Model	Development	Validation	Development	Validation
Area under ROC (SE)	0.81 (0.03)	0.79 (0.05)[a]	0.82 (0.03)	0.82 (0.05)[b]
Sensitivity[c] (SE)	0.31 (0.10)	0.32 (0.13)	0.42 (0.12)	0.44 (0.20)
Specificity[c] (SE)	0.97 (0.01)	0.95 (0.02)	0.99 (0.01)	0.95 (0.02)

[a] $p = .75$ for comparison with Development set; [b] $p = .93$ for comparison with Development set; [c] sensitivity and Specificity determined for 90% risk of death. Presented as value (standard error).

CI, confidence interval; OR, odds ratio; ROC, receiver operating characteristic.

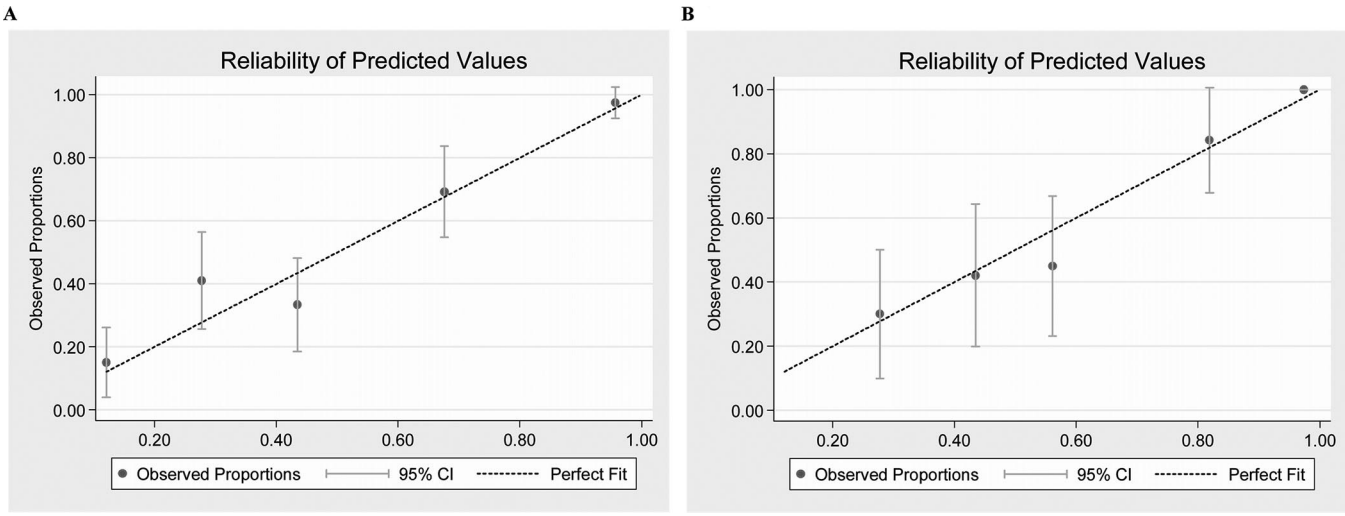

Figure 2. Comparison of observed and predicted 1-yr mortality for patients divided into five equal-sized groups from the Development set (*A*) and Validation set (*B*). *CI*, confidence interval.

Table 5. *Pro*gnosis for *Pro*longed *Vent*ilation (ProVent) score variables measured on Day 21 of mechanical ventilation: Age ≥50 = 1 point Vasopressor = 1 point platelets ≤150 × 10^9/L = 1 point requires hemodialysis = 1 point

	Development Set			Validation Set	
ProVent Score	n (%)	Predicted 1-Year Mortality (95% CI)	Observed 1-Year Mortality	n (%)	Observed 1-Year Mortality
0	41 (21)	0.12 (0.06, 0.21)	0.15	14 (14)	0.14
1	98 (50)	0.44 (0.36, 0.53)	0.42	42 (42)	0.43
2	26 (13)	0.83 (0.71, 0.90)	0.88	21 (21)	0.86
3	22 (11)	0.97 (0.90, 0.99)	0.95	13 (13)	1.0
4	9 (5)	0.99 (0.97, 1.0)	1.0	8 (8)	1.0
	Development Set			Validation Set	
		Predicted 3-Month Mortality 95% (CI)	Observed 3-Month Mortality		Observed 3-Month Mortality
0	41 (21)	0.10 (0.05, 0.17)	0.12	14 (14)	0.07
1	98 (50)	0.32 (0.25, 0.40)	0.29	42 (42)	0.38
2	26 (13)	0.67 (0.55, 0.77)	0.77	21 (22)	0.80
3	22 (11)	0.90 (0.78, 0.95)	0.91	13 (14)	0.85
4	9 (5)	0.97 (0.91, 0.99)	0.89	8 (8)	1.0

CI, confidence interval.

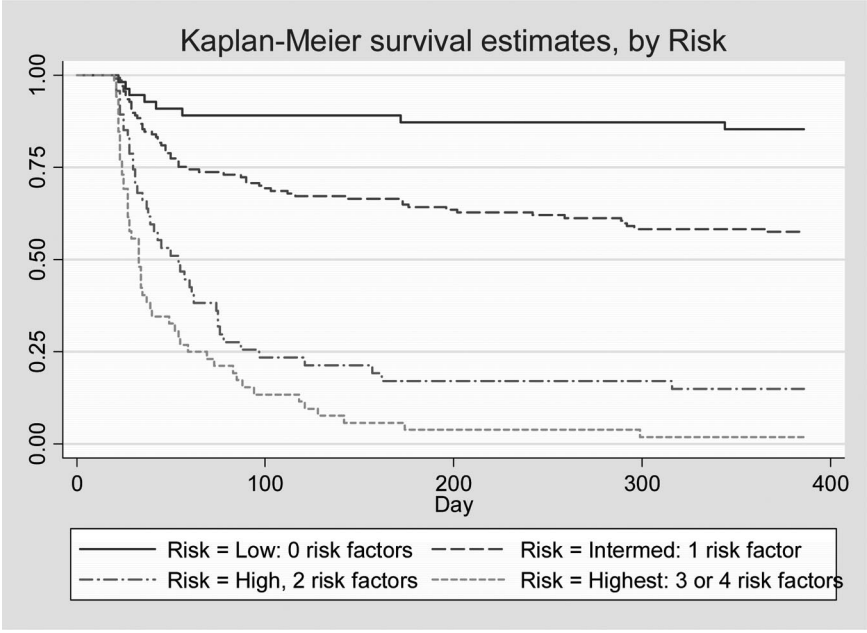

Figure 3. Kaplan-Meier curves by risk group for combined cohort: low = ProVent score 0 (no risk factors), n = 55 (18% of cohort); intermediate = ProVent score 1 (one risk factor), n = 137 (47% of cohort); high = Provent score 2 (two risk factors), n = 47 (16% of cohort); highest = ProVent score 3 or 4 (three or four risk factors), n = 52 (17% of cohort). Day 0 is the time of intubation.

model was .76 (SE .05). Sensitivity was .37 (SE .18) and specificity remained high at .93 (SE .02) for ≥90% likelihood of death.

To create a prognostic scoring system that could ultimately be used by clinicians in daily practice, we assigned points to each of the four predictive variables in proportion to the regression coefficients from the development model. The regression coefficients were of similar magnitude, so we assigned 1 point for each risk factor resulting in a range of scores from 0 to 4. Performance of the 4-point prognostic scoring system (*Pro*gnosis for *Pro*longed *Vent*ilation [ProVent] score) is shown in Table 5. Predicted and observed mortality for patients in the development set and observed mortality for patients in the validation set are included. In the development set, patients with the ProVent score of 0, representing no risk factors (n = 41 [21%]) had a 1-yr mortality of only 15%. Patients with the score of 1, representing one risk factor (n = 98 [50%]), had a 1-yr mortality rate of 42%. Patients with the score of 2, representing two risk factors (n = 26 [13%]), had mortality rate of 77% at 3 mos and 88% at 1 yr. Patients with the three or four risk factors had 3-mo mortality of 90% and 1-yr mortality of 97%. This highest risk group (scores 3 or 4) represents 16% of the development set and 24% of the validation set. The area under the receiver operating characteristic curve for ProVent score for the combined cohort is .82 (SE .03; 95% confidence interval, .75–.88). For patients with ≥50% risk of death, sensitivity is .58 (SE .12) and specificity is .95 (SE .07). For patients with ≥90% risk of death, sensitivity is .32 (SE .20) and specificity is .99 (SE .01). Survival according to ProVent score risk group is shown in Figure 3.

Data on functional status were available for 57% of 1-yr survivors. There were no differences between patients with and without available data for age (p =.4), Sequential Organ Failure Assessment score at day 21 (p = .30), Charlson score (p = .88), or premorbid independence in ADLs (p = .68). Only 24% of survivors were independent in all ADLs after 1 yr. Thirty-nine percent of survivors with ProVent scores of 0 and 18% of survivors with ProVent scores of 1 were independent in all ADLs. None of the patients with ProVent scores of 2 or greater were both alive and independent in all ADLs after 1 yr.

DISCUSSION

This prospective cohort study confirms that four easily measured variables recorded at day 21 of ventilation can identify patients who are both at high risk

and low risk of mortality during prolonged mechanical ventilation. This prognostic model has very high specificity, limiting the possibility of inappropriately poor prognoses. The model performed well during validation in a cohort that was enrolled during a different time period than the development set and that had higher illness severity. Three of the four variables that are independent predictors of mortality—requirement of pressors, requirement of hemodialysis, and platelet count $\leq 150 \times 10^9$/L, reflect ongoing systemic inflammation and multiorgan failure. The other prognostic variable, age 50 or older, likely reflects lower physiological reserve independent of acute organ failure and specific comorbidities. It may also reflect less willingness on the part of older patients or surrogates to endure weeks and months of invasive care when progress does not seem apparent (20).

Much has been written about how patients on PMV require a unique approach to care as a result of differences in physiology (1, 21–23). However, few studies of interventions in this patient population have been published. The ability to standardize illness severity would facilitate the design of cohort studies evaluating interventions to improve process of care and survival. For example, as a result of issues of high costs and limited resources, hospitals are compelled to discharge patients on PMV to various postintensive care unit settings, including respiratory care units, long-term care hospitals (LTCH), or even skilled nursing facilities, for continued weaning and management (24–26). These facilities have been proliferating at a high pace to meet increasing demand (27). Although it is possible that these facilities decrease hospital costs, it is not clear whether outcomes are affected. This prognostic model was developed and validated in a population with relatively limited access to postacute care weaning facilities. Therefore, this model provides an acute care baseline against which outcomes from care in different settings can be compared. Variables for the model are measured before most LTCH transfers occur (25) so illness severity can be standardized before transfer to alternative care settings.

Two prognostic models have been published for patients on PMV managed in LTCH (15, 16), but neither have been validated and only one included long-term follow up. In one study, existing illness severity scores demonstrated poor discrimination and calibration for hospital mortality in patients on PMV at an LTCH. When measured on the day of admission to the LTCH, the area under the receiver operating characteristic curve was <.70 for Acute Physiology and Chronic Health Evaluation II, Simplified Acute Physiology Score II, Mortality Probability Model II, and Logistic Organ Dystunction System (28).

The majority of patients with advanced illnesses do not want to be kept alive on life support when there is little hope for a meaningful recovery (29). Focus group studies involving patients on PMV and their families have revealed that they would benefit from more direct communication with healthcare providers, especially with regard to prognosis (30). Another study of prognostication during physician–family discussions about limiting life support revealed that prognoses for long-term survival were given in only 12% of conferences (31). In the Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatment (SUPPORT) study, of the 1,494 patients who spent more than 14 days in the intensive care unit, fewer than 40% reported that their physicians had talked with them about their prognoses or preferences for life-sustaining treatment (32). The simple prognostic model developed in this study could enhance communication of prognosis to these patients and their surrogates by providing objective estimates of short-term and long-term outcome.

A major strength of this study is the heterogeneous patient population, including medical and surgical patients as well as patients with major trauma. The prognostic model does not require assignment of a specific diagnosis, which is usually difficult in critically ill patients with multiple active processes. Nor does it require assessments of neurologic function, which can be unreliable in patients receiving sedation (19). Selection bias was limited by consecutive and prospective enrollment and a high follow-up rate for mortality.

This study has several important limitations. Differences in management at other centers or communities could result in worse performance of this model in those settings. External validation using multiple tertiary care centers in diverse regions is warranted before clinical or research application of this model is considered (33). Although the study was large enough to have sufficient power to assess the preselected variables in the study protocol, other potential predictors may not have been examined. However, the variables that were studied produced a model that is simple, reproducible, and highly specific.

It is possible that objective prognostic information will not change physician practice. In the SUPPORT trial, an intervention using a sophisticated prognostic model designed to facilitate discussion of prognosis and wishes for aggressive care in acutely ill patients had no significant impact on these outcomes (34). There are several reasons why the prognostic model in this study could have a more significant impact than that of the SUPPORT trial. The prognostic score is simple to understand and can be assessed by the clinician at the bedside within seconds rather than relying on an intermediary with a complicated formula. The prognostic information comes later in the patient's clinical course when extensive efforts have been made on the patient's behalf, yet progress has stalled and reserve is limited. Both clinicians and surrogates may be more likely to accept a change in the course of care when poor outcomes are expected despite weeks of maximal treatment.

The majority of physicians find prognostication to be stressful and difficult, and they feel that they have inadequate training in this area (35). They are particularly concerned about being wrong, especially when withholding or withdrawing life support is a possible outcome of decision making. Variables were selected *a priori* for this model with an aim to identify the patients at highest risk of death. Consequently, the model has very high specificity (.99) for patients with a 90% mortality risk. There is minimal chance of misclassifying a patient as very high risk (false-positive). Measuring specificity at a high mortality risk comes at the expense of lower sensitivity. As many as 58% of patients who ultimately died were not classified in the highest risk group (false-negatives). When prognosticating, however, most clinicians are worried more about giving negative prognoses for patients who would otherwise survive (35), favoring a mortality model with high specificity.

Of course, objective prognostic information will not change physician practice in isolation. Other important factors are necessary to improve patient/family communication about end-

of-life issues (36, 37). Finally, such a scoring system should not be used to replace clinician judgment regarding likely outcomes, but rather to inform those judgments (38).

CONCLUSIONS

Patients receiving PMV who are at the highest risk of death can be identified based on the requirement of either vasopressors or hemodialysis or the presence of platelet counts $\leq 150 \times 10^9$/L or age over 50 yrs. After external validation, a prognostic scoring system using these risk factors could facilitate earlier and more definitive discussions between clinicians and patients or surrogates regarding appropriate goals of care.

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Intensive Care Unit Admitting Diagnosis n = 200	Development Set n = 100	Validation Set
Pulmonary fibrosis	3 (2)	0
Chronic obstructive pulmonary disease	4 (2)	2 (2)
Acute respiratory distress syndrome	10 (5)	5 (5)
Respiratory arrest	3 (2)	5 (5)
Cystic fibrosis	5 (3)	1 (1)
Pneumonia	13 (7)	14 (14)
Sepsis	14 (7)	8 (8)
Congestive heart failure	2 (1)	4 (4)
Myocardial infarction	3 (2)	0
Cardiac arrest	5 (3)	2 (2)
Intracranial hemorrhage, nonoperative	3 (2)	0
Overdose	1 (<1)	2 (2)
Neuromuscular weakness	8 (4)	0
Hepatic failure	1 (<1)	2 (2)
Gastrointestinal hemorrhage	3 (2)	2 (2)
Pancreatitis	6 (3)	1 (1)
Other GI condition	1 (<1)	2 (2)
Hematologic malignancy	2 (1)	0
Other malignancy	1 (<1)	1 (1)
Other medical	4 (2)	1 (1)
Multiple trauma	32 (16)	10 (10)
Head trauma	4 (2)	0
C-spine injury	3 (2)	1 (1)
Coronary artery bypass graft	5 (3)	1 (1)
Heart valve surgery	8 (4)	2 (2)
Thoracic surgery	13 (7)	6 (6)
GI perforation/obstruction	7 (4)	6 (6)
Other GI surgery	6 (3)	7 (7)
Vascular surgery	7 (4)	2 (2)
Surgery for intracranial hemorrhage	8 (4)	2 (2)
Heart transplant	3 (2)	2 (2)
Lung transplant	1 (<1)	1 (1)
Liver transplant	8 (4)	6 (6)
Other surgery	3 (2)	2 (2)

Data presented as n (%). Percentages do not add to 100 due to rounding. Other Medical includes asthma, diabetic ketoacidosis, pulmonary embolus, meningitis, acute renal failure, 1 case each.

GI, gastrointestinal.

A multicenter mortality prediction model for patients receiving prolonged mechanical ventilation*

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Objective: **Significant deficiencies exist in the communication of prognosis for patients requiring prolonged mechanical ventilation after acute illness, in part because of clinician uncertainty about long-term outcomes. We sought to refine a mortality prediction model for patients requiring prolonged ventilation using a multicentered study design.**

Design: **Cohort study.**

Setting: **Five geographically diverse tertiary care medical centers in the United States (California, Colorado, North Carolina, Pennsylvania, and Washington).**

Patients: **Two hundred sixty adult patients who received at least 21 days of mechanical ventilation after acute illness.**

Interventions: **None.**

Measurements and Main Results: **For the probability model, we included age, platelet count, and requirement for vasopressors and/or hemodialysis, each measured on day 21 of mechanical ventilation, in a logistic regression model with 1-yr mortality as the outcome variable. We subsequently modified a simplified prognostic scoring rule (ProVent score) by categorizing the risk variables (age 18–49, 50–64, and ≥65 yrs; platelet count 0–150 and >150; vasopressors; hemodialysis) in another logistic regression model and assigning points to variables according to β coefficient values. Overall mortality at 1 yr was 48%. The area under the curve of the receiver operator characteristic curve for the primary ProVent probability model was 0.79 (95% confidence interval 0.75–0.81), and the *p* value for the Hosmer-Lemeshow goodness-of-fit statistic was .89. The area under the curve for the categorical model was 0.77, and the *p* value for the goodness-of-fit statistic was .34. The area under the curve for the ProVent score was 0.76, and the *p* value for the Hosmer-Lemeshow goodness-of-fit statistic was .60. For the 50 patients with a ProVent score >2, only one patient was able to be discharged directly home, and 1-yr mortality was 86%.**

Conclusion: **The ProVent probability model is a simple and reproducible model that can accurately identify patients requiring prolonged mechanical ventilation who are at high risk of 1-yr mortality. (Crit Care Med 2012; 40:1171–1176)**

Key Words: communication; critical care; mechanical ventilation; multiple organ failure; outcomes; prognosis

Many patients who survive the first few days of critical illness do so with multiple persistent organ failures, ultimately becoming dependent on mechanical ventilation for prolonged periods (1). Up to 10% of patients who develop acute respiratory failure require prolonged mechanical ventilation (PMV) (2). The number of patients receiving PMV has increased in recent years, likely as a result of improvements in acute management and supportive care for critically ill patients (2, 3). As the population ages, it is expected that this number will increase further, because advanced age is a key risk factor for PMV (3, 4). One-yr mortality for patients receiving PMV is high (5–9), and only 11% percent of patients are functionally independent and living at home by 1 yr (9, 10). During the year of their illness, 74% of the patients' days alive are spent in a hospital, postacute care facility, or receiving home health care.

Recent empirical studies have documented serious shortcomings in the process of decision making about life support for patients on PMV. Up to 93% of families and surrogate decision makers do not receive any information about expected long-term survival despite explicit wishes to have this information (11, 12). In one study, 93% of surrogate decision makers had high expectations for survival of patients on PMV compared with only 44% of physicians for the same patients (12). These deficiencies are problematic for two reasons. First, they are a threat to

*See also p. 1357.

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patient-centered care because existing data suggest that patients often prefer treatment focused on palliation in the setting of a poor prognosis (13–15). Second, patients receiving PMV are among the highest consumers of healthcare resources (16) and, from a societal perspective, it is important to ensure that the provision of this very expensive resource is reserved for patients who would choose such treatments after a careful discussion of the risks and benefits.

Although there are likely several reasons for suboptimal discussions about prognosis between physicians and families, one important reason is clinicians' uncertainty about the long-term outcomes of patients on PMV (17–20). This is perhaps not surprising because most intensive care unit (ICU) clinicians have little opportunity to follow patients after they leave the ICU and therefore little opportunity to refine their prognostic abilities regarding long-term outcomes. To address this gap for patients on PMV, the ProVent model was developed and internally validated at a single tertiary care medical center to predict 1-yr mortality for patients receiving at least 21 days of mechanical ventilation after acute illness (5). Using four easily identified clinical variables (age, platelet count, ongoing use of vasopressors, and hemodialysis), the ProVent model had very good discrimination (area under the curve [AUC] of the receiver operator characteristic curve 0.81) and calibration for identifying patients who were at high risk of death after PMV. To establish broader applicability, we sought to refine the ProVent model and provide external validity using data from a heterogeneous group of patients from multiple hospitals across the United States.

MATERIALS AND METHODS

In a retrospective cohort design, patients were enrolled from five tertiary care centers including the University of Washington, University of California at San Francisco, Denver Health Medical Center, the Hospital of the University of Pennsylvania, and Duke University Medical Center. Centers were selected based on geographic distribution and access to a broad range of medical, surgical, and trauma patients requiring PMV. None of the centers had contributed data to the original development model. The research protocol was approved by institutional review boards at each of the five centers as well as the coordinating center at the University of North Carolina.

Patients receiving mechanical ventilation in 2005 for at least 14 days after acute illness, uninterrupted by >48 hrs of unassisted breathing, were followed, and patients who were still receiving mechanical ventilation by day 21 were included in the study. Exclusion criteria included age <18 yrs old; diagnosis of acute or chronic neuromuscular disease such as Guillain-Barré syndrome, muscular dystrophy, or myasthenia gravis; patients sustaining extensive burn injuries; and requirement for chronic mechanical ventilation before acute admission. These inclusion and exclusion criteria are the same criteria used for the original model development. Patients were identified by screening records of mechanical ventilation for all patients admitted to adult medical, neurologic, surgical, cardiac, or trauma ICUs. Either consecutive samples or random samples of patients were enrolled at each center depending on the number of patients who were eligible.

Data were abstracted from medical records by two trained individuals at each site. One abstractor who was blinded to patient outcome determined eligibility and collected data on demographic variables and risk factors. The other abstractor collected data on hospital outcomes. The principal investigator at each site reviewed the first ten charts that were abstracted and a random sample of ten subsequent charts to confirm accuracy of data and identify errors that would prompt review of additional charts and correction.

Descriptive variables included age, admission source, primary ICU service, ICU admission diagnoses, and comorbidities based on a modified Charlson score (21). Race and ethnicity as listed in medical records were abstracted to provide information regarding generalizability. We assessed severity of illness on ICU admission using the Acute Physiology and Chronic Health Evaluation III score (22) determined using the worst values measured within the first 24 hrs of index ICU admission. Because the objective of this study was to provide external validity for the mortality prediction model developed at a single center, we only included the four original predictive variables in the probability model. The four predictor variables collected on day 21 of mechanical ventilation included age, platelet count, and requirement for vasopressors and/or hemodialysis.

Requirement for hemodialysis was defined as provision of any form of renal replacement therapy on or within 48 hrs of day 21 of mechanical ventilation. The primary outcome variable was 1-yr mortality using death dates obtained by linking patient records to the National Death Index or the Washington State Death Database. We also assessed several inhospital outcome variables, including duration of mechanical ventilation, liberation from mechanical ventilation in the hospital defined as unassisted breathing for 7 consecutive days, ICU and hospital length of stay, and hospital mortality. For patients who died during the index hospitalization, records were reviewed for use of mechanical ventilation, vasopressors, and hemodialysis within 72 hrs of death as well as mechanical ventilation, vasopressors, or cardiopulmonary resuscitation on the day of death.

Analysis. Descriptive statistics are presented using mean ± SD for normally distributed continuous variables, median with interquartile range for nonnormally distributed continuous variables, and proportions for categorical variables. To validate the predictive capabilities of the four ProVent predictor variables, we included all variables in a logistic regression model (ProVent probability model) with 1-yr mortality as the outcome variable. We assessed model discrimination using the AUC and model calibration using the Hosmer-Lemeshow goodness-of-fit statistic comparing observed mortality with predicted mortality for each decile of predicted risk. Because a second external cohort was not available, a bootstrap method was used to validate the model by repeating 1000 random samples consisting of 60% of the cohort to provide a 95% confidence interval for the AUC.

After validation of the primary ProVent probability model that used the risk variables as they were measured, we categorized the risk variables and included them in a second logistic regression model. Before initiation of data collection, the investigators elected to modify the cut point for age from the original ProVent score (5). Specifically, two cut points were included for age (age 50 and 65 yrs) rather than one at age 50 yrs to better reflect the higher risk associated with advancing age. Other categorical variables remained the same. We then created a new ProVent score by assigning points to each risk factor according to the β coefficients in the logistic regression model. Long-term survival based on the range of cumulative scores was represented by Kaplan-Meier curves, and the performance of the ProVent score was assessed in a third logistic regression model.

Data were analyzed using SAS software (SAS Institute Inc., Cary, NC). Kaplan-Meier curves were drawn using Stata 8.0 software (Stata, College Station, TX).

RESULTS

A total of 289 patients were enrolled from the five centers. Of those, 260 patients (90%) had complete data for risk variables and were included in analyses. Patient characteristics and outcomes are shown in Table 1. The mean age ± SD of patients was 55 ± 17 yrs, and 41% were female. Patients were diverse

Table 1. Patient characteristics and outcomes

Patient Characteristics	n = 260
Age, yrs, mean ± SD, [range]	55 ± 17 [18–90]
Female, no. (%)	102 (41%)
Race, no. (%)	
Native American or Alaska Native	2 (1%)
Asian or Pacific Islander	16 (6%)
Other nonwhite	10 (4%)
Black	49 (19%)
White	152 (58%)
Unknown or not reported	31 (12%)
Ethnicity, no. (%)	
Hispanic or Latino	7 (3%)
Not Hispanic or Latino	207 (80%)
Unknown or not reported	46 (17%)
Primary intensive care unit service, no. (%)	
Medicine	90 (35%)
Cardiology	7 (3%)
General surgery/trauma	80 (31%)
Cardiac surgery	31 (12%)
Thoracic surgery	8 (3%)
Neurology/neurosurgery	31 (12%)
Transplant surgery	4 (1%)
Other	9 (3%)
Comorbidity score, median (IQR)	1.0 (0–3)
Admission Acute Physiology and Chronic Health Evaluation III score, mean ± SD	83 ± 29
Intensive care unit admission diagnoses, no. (%)	
Cardiovascular	30 (11%)
Pulmonary including pneumonia	42 (16%)
Gastrointestinal	18 (7%)
Neurologic	30 (12%)
Endocrine	2 (1%)
Hematologic or malignancy	8 (3%)
Infection other than pneumonia	20 (8%)
Surgery	45 (17%)
Trauma	65 (25%)
Hospital outcomes	
Duration of MV, median (IQR), days	30 (25–40)
Duration of MV if died in the hospital, median (IQR), days	32 (26–43)
Liberation from MV, no. (%)	134 (52%)
Intensive care unit length of stay, median (IQR), days	34 (28–48)
Hospital length of stay, median (IQR), days	44 (33–70)
Discharge disposition, no. (%)	
Died in the hospital	71 (28%)
Long-term acute hospital	51 (20%)
Rehabilitation facility	58 (22%)
Skilled nursing facility	45 (17%)
Home with assistance	15 (6%)
Home independent	16 (6%)
Other	4 (2%)
One-yr mortality, no. (%)	124 (48%)

IQR, interquartile range; MV, mechanical ventilation.
Some percentages do not add to 100 as a result of rounding.

in diagnosis, admission source, and primary critical care service including medical, surgical, trauma, and neurologic units. Median (interquartile range) duration of mechanical ventilation was 30 (25–40) days, and median ICU and hospital lengths of stay were 34 (28–48) and 44 (33–70) days, respectively. Twenty-eight percent of patients died in the hospital and 12% were discharged home. Of the patients who died in the hospital, 90% were receiving mechanical ventilation and 46% were receiving vasopressors within 72 hrs of death. Only 8% of patients received cardiopulmonary resuscitation at the time of death. Patients who died in the hospital received a median of 32 (26–43) days of mechanical ventilation before death. One-yr mortality for the cohort was 48%. The 29 patients not included in analyses as a result of incomplete data for risk variables were similar in mean age (57 ± 15 yrs), gender (39% female), comorbidity score (median, 1 [0–3]), and 1-yr mortality (48%).

In the ProVent probability logistic regression model (see subsequent equation), each of the four ProVent variables was independently associated with 1-yr mortality, including age (odds ratio 1.04; 95% confidence interval 1.03–1.06) for each additional year of age, platelet count (0.996; 0.994–0.998) for each increase of 1×10^9/L, vasopressors (2.96; 1.03–8.46) relative to no vasopressors, and hemodialysis (2.52; 1.00–6.34) relative to no hemodialysis. Enrollment center was not an independent predictor when included as a model variable. Discrimination as measured by the AUC was 0.79 (95% confidence interval 0.75–0.81). In comparison, the AUC for the Acute Physiology and Chronic Health Evaluation III score measured at ICU admission and 1-yr mortality was 0.63. A comparison of observed vs. predicted mortality for the model is shown in Table 2. The Hosmer-Lemeshow goodness-of-fit statistic was 3.58 with 8 df ($p = .89$).

Using the ProVent probability model, the predicted probability of death within 1 yr can be calculated using the following equation:

$$\text{Prob(death in 1-year}|\text{A,P,V,H)} = \frac{\exp^{(-1.7401+0.0435\text{A}-0.00363\text{P}+1.0835\text{V}+0.925\text{H})}}{1+\exp^{(-1.7401+0.0435\text{A}-0.00363\text{P}+1.0835\text{V}+0.925\text{H})}}$$

where A = person's age (in years); P = platelet count (in 10^9/L units), V = 1 if on vasopressors or = 0 if not, and H = 1 if on hemodialysis or = 0 if not; "exp" is the exponential constant (2.71828). Variables are measured on day 21 of mechanical ventilation. Requirement for hemodialysis is defined as provision of hemodialysis on or within 48 hrs of day 21 of mechanical ventilation.

The second logistic regression model with categorized variables had an AUC of 0.77, and the Hosmer-Lemeshow goodness-of-fit statistic was 5.70 with 5 df ($p = .34$). Point values were assigned according to the β values from the second model as shown in Table 3 to generate the ProVent score. Two points were assigned to age ≥65 yrs, and 1 point was assigned to each of the other risk factors including age 50–64 yrs, platelet count $\leq 150 \times 10^9$/L, and requirement for vasopressors or hemodialysis on day 21 of mechanical ventilation. Scores could range from 0 to 5 points. The third logistic regression model using the cumulative ProVent score had an AUC of 0.76, and the Hosmer-Lemeshow goodness-of-fit statistic was 1.86 with 3 df

Table 2. Calibration of the ProVent probability model

Partition for the Hosmer-Lemeshow Test ($p = .89$)					
		Died in 1 Yr		Alive in 1 Yr	
Group	Total	Observed	Expected	Observed	Expected
1	26	1	1.80	25	24.20
2	26	3	3.91	23	22.09
3	26	8	6.50	18	19.50
4	26	11	9.37	15	16.63
5	26	11	11.54	15	14.46
6	26	15	13.53	11	12.47
7	26	16	15.74	10	10.26
8	26	16	17.72	10	8.28
9	26	18	19.89	8	6.11
10	26	24	23.01	2	2.99

Deciles of expected mortality according to the ProVent probability equation in the equation in "Results." Hosmer-Lemeshow goodness-of-fit statistic 3.58 with 8 df ($p = .89$).

Table 3. Model with categorized risk variables

Categorical Variable	No. (%)	Odds Ratio (95% Confidence Interval)	Beta Value	Points
Age ≥65 yrs	80 (31%)	7.6 (3.8–15.5)	2.03	2
Age 50–64 yrs	88 (34%)	2.0 (1.0–3.9)	0.67	1
Platelets ≤150 × 10^9/L	65 (25%)	1.9 (0.9–3.9)	0.65	1
Vasopressors	35 (13%)	4.4 (1.6–12.6)	1.49	1
Hemodialysis	34 (13%)	2.4 (1.0–6.0)	0.89	1

Table 4. ProVent score and observed 1-yr mortality

ProVent Score	No.	Observed Mortality Percent (95% confidence interval)
0	72	20 (10–29)
1	60	36 (24–48)
2	78	56 (45–68)
3	36	81 (67–94)
4 or 5	14	100 (77–100)

The ProVent score is calculated by summing the point values assigned according to the presence of risk variables listed in Table 3 when measured on day 21 of mechanical ventilation.

($p = .60$). Table 4 and Figure 1 show 1-yr mortality and long-term survival for patients according to their ProVent score. For patients in the highest risk groups (ProVent score >2 points), hospital mortality was 43%, yet only one patient was discharged home, and 1-yr mortality was 86%.

DISCUSSION

In a multicenter cohort study, the primary ProVent probability model accurately predicted risk of 1-yr mortality for patients requiring at least 21 days of mechanical ventilation. The cohort included a racially diverse group of patients from medical, surgical, and neurologic ICUs. The model has good discrimination and excellent calibration for patients at all levels of risk. The ProVent model uses only four variables that are easily measured on day 21 of mechanical ventilation. The model does not require subjective assessments such as the Glasgow Coma Scale that can be affected by sedation practices or primary admission diagnosis, which can be uncertain in patients presenting with multiorgan failure (23). Predicted mortality for patients can be obtained by using the prediction equation provided. Alternatively, the model has been converted to a simple scoring rule (ProVent score) to aid in clinical application at the bedside if a computer or handheld device is not available to complete the probability equation. Less than 15% of patients with ProVent scores >2 were alive after 1 yr. The Model for End-Stage Liver Disease score, which uses three objective variables to predict survival in patients with advanced liver disease, provides a clear example of how simple prediction rules can gain wide general use in the acute care setting for purposes of risk prediction and scarce resource allocation (24, 25).

Prognostication is not straightforward in many clinical conditions. PMV presents unique challenges for long-term prognostication because few inpatient clinicians participating in ICU decision making have experience with patient outcomes beyond hospital discharge. Existing severity of illness measures using variables measured on the day of ICU admission do not perform well in the PMV population as demonstrated in previous analyses (26) and in the current assessment of the Acute Physiology and Chronic Health Evaluation III system in this cohort. Therefore, a model specific to the PMV population is necessary. Published outcome studies provide mean outcomes for large cohorts (5–9) but are not sufficiently tailored to individual patient characteristics to reliably inform clinical prognostication.

This validated prediction model for long-term outcome can: 1) standardize illness severity in observational and interventional studies of chronically critically ill patients; 2) help determine appropriate levels of postacute care (27–29); and 3) increase clinicians' confidence in responding to informational needs of patients, families, and surrogate decision makers (30, 31). It is yet to be determined whether the ProVent models are more accurate than physician estimates of high risk, and like with any prognostic model, the ProVent models are intended to complement the *a priori* assessments of an experienced clinician rather than replacing clinical judgment (32). Given the inherent limitations in translating data on population-level outcomes to individual risk estimates, the use of scoring systems as a sole guide to making decisions about whether to initiate or continue to provide intensive care is inappropriate by current ethical standards (33). However, the data derived from these systems can provide relevant information for decision making, especially when combined with physician estimates of outcome.

Another consideration is whether clinicians will use prognostic information from the ProVent model. The Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatment (34) was a large randomized controlled trial in which physicians were given prognostic estimates for individual patients based on a sophisticated prognostic model. The intervention had no significant impact on the main outcomes, in part because only 20% of physicians disclosed the prognostic information to surrogates.

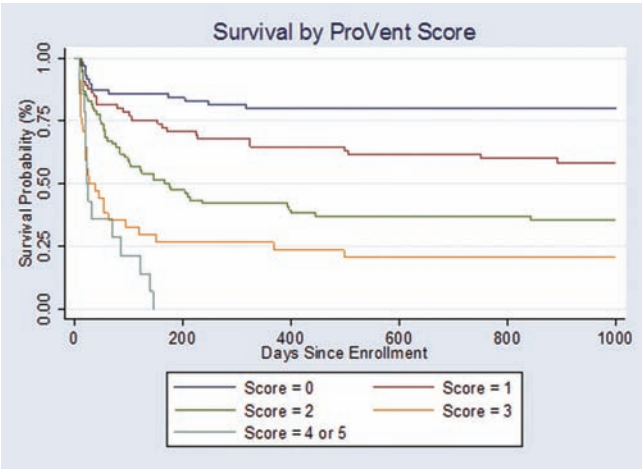

Figure 1. Kaplan-Meier curve of survival for patients by ProVent score.

These data suggest that to meaningfully impact care, the ProVent score may need to be part of a more sophisticated decision support process that is acceptable to clinicians. Examples of decision support interventions that could incorporate ProVent data and may benefit patients on PMV include structured family meetings led by intensivists or palliative care-trained clinicians (35–38) or formal decision support tools that can be shared with patient surrogates in a formal setting (39). Future iterations of the ProVent model should involve measurement of variables before 21 days of mechanical ventilation to aid decision making earlier in the course of ICU care.

Multiple studies have suggested that intensivist perceptions of extremely poor prognosis are associated with less aggressive or invasive care (40–42). Prognoses in the intermediate range may be less likely to impact decision making, but intermediate prognoses are still valuable in the setting of prolonged ventilation and chronic critical illness. For example, patients with a ProVent score of 3 have predicted 1-yr mortality of 81% (95% confidence interval 67–94). Although clinicians and families will not perceive this as hopeless, it is likely to help focus their attention on the patient's desires for prolonged invasive care in the context of lower expectations for survival, a universally high symptom burden (43), and poor expected functional outcomes in long-term survivors (6–8).

Our study has several limitations. Although we refined our model in a geographically diverse population, we conducted our study primarily in large tertiary centers. However, previous literature indicates that large centers take care of the majority of patients requiring PMV as a result of the greater complexity of their patient populations and transfer practices from smaller community hospitals (44). The confidence interval around the AUC and measures of calibration for the primary probability model using the original continuous variables are excellent. However, further validation of the modified scoring rule (ProVent score) in a larger external sample is indicated. The retrospective study design could have introduced bias in ascertainment of data, but patient eligibility and risk variables were easily identified in medical records, and investigators measuring risk variables were blinded to patient outcomes. Our study also did not assess long-term functional status, an important factor in decision making for many patients (41), because the study design did not allow for measurement of those outcomes. Because some patients or surrogates opted not to pursue full life support throughout their entire course, the model likely predicts an interplay of physiological and social factors rather than the bare natural history of disease (15, 45). This is true of all mortality models derived from clinical populations.

CONCLUSION

The ProVent probability model is a simple and reproducible model that can accurately identify patients requiring PMV who are at high risk of 1-yr mortality. When paired with clinical judgment, this model may increase clinicians' ability to discuss the likely outcomes of treatment and to tailor care to achieve patient-centered goals. Future studies should examine similar models using variables measured earlier in the course of prolonged ventilation and outcomes that include long-term functional status.

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