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Five-Year Risk of Mechanical Ventilation in Community-Dwelling Adults: The Framingham-Intermountain Anticipating Life Support Study

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Abstract

Objectives—To develop a quantitative tool for identifying outpatients most likely to require life support with mechanical ventilation within 5 years.

Design—Retrospective cohort study.

Setting—Framingham Heart Study (FHS) 1991 to 2009 and Intermountain Healthcare clinics 2008 to 2013.

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Participants—FHS participants (n=3,666; mean age 74; 58% female) in a derivation cohort and Intermountain Healthcare outpatients aged 65 and older (n=88,302; mean age 73, 57% female) in an external validation cohort.

Measurements—Information on demographic characteristics and comorbidities collected during FHS examinations to derive a 5-year risk score for receiving mechanical ventilation in an intensive care unit, with external validation using administrative data from outpatients seen at Intermountain Healthcare. A sensitivity analysis investigating model performance for a composite outcome of mechanical ventilation or death was performed.

Results—Eighty (2%) FHS participants were mechanically ventilated within 5 years after a FHS examination. Age, sex, diabetes mellitus, hypertension, atrial fibrillation, alcohol use, chronic pulmonary disease, and hospitalization within the prior year predicted need for mechanical ventilation within 5 years (c-statistic=0.74, 95% confidence interval (CI)=0.68–0.80). One thousand seven hundred twenty-five (2%) Intermountain Healthcare outpatients underwent mechanical ventilation. The validation model c-statistic was 0.67 (95% CI=0.66–0.68). Approximately 1% of individuals identified as low risk and 5% to 12% identified as high risk required mechanical ventilation within 5 years. Sensitivity analysis demonstrated a c-statistic of 0.75 (95% CI=0.75–0.75) for risk prediction of a composite outcome of mechanical ventilation or death.

Conclusion—A simple risk score using clinical examination data or administrative data may be used to predict 5-year risk of mechanical ventilation or death. Further study is necessary to determine whether use of a risk score enhances advance care planning or improves quality of care of older adults.

Keywords

advance care planning; end-of-life care; mechanical ventilation

Mechanical ventilation during critical illness represents an event of significant short-and long-term consequence. Individuals requiring mechanical ventilation have approximately 30% hospital mortality, a substantial risk of near-term death.(1) Older adults who survive hospitalization requiring mechanical ventilation experience a doubling of prehospitalization disability measurements,(2) with approximately 60% requiring discharge to skilled care facilities(3) and 70% dying within 12 months.(2) During mechanical ventilation, people often lose the ability to participate actively in shared decision-making and suffer further threats to self-determination if their wishes are not known before they are placed on a ventilator.

Although prognostic tools that predict mortality in community-dwelling outpatients have been developed,(4) quantitative models that predict the need for life-support treatments such as mechanical ventilation are not readily available. Identifying risk of mechanical ventilation may have practical advantages over models intended to predict mortality alone. For example, many people do not want prognostic information delivered in the form of life expectancy estimates,(5) and individuals at high risk of mechanical ventilation may seek to expedite planning for the likelihood of disability, need for surrogate decision-making, and communication of preferences that may accompany mechanical ventilation during critical

illness. Such foreknowledge could also support efforts to educate people and their families about the challenges associated with critical illness in ways that might improve resilience during recovery from critical illness.(6) Thus, the current study sought to derive and validate a model to predict 5-year risk of mechanical ventilation during critical illness in a cohort of community-dwelling individuals and outpatients aged 65 and older.

METHODS

Derivation Cohort

The Framingham Heart Study (FHS) provides an opportunity to study robust risk profiles in a community-dwelling cohort.(7–10) FHS participants in the Original and Offspring Cohorts aged 65 and older were linked to Centers for Medicare and Medicaid Services (CMS) administrative data. Data collected at Original Cohort study examinations from 1985 to 2009 and Offspring Cohort examinations from 1987 to 2008 were used.

FHS participants undergo standardized assessments and examinations with a study physician approximately every 2 years (Original Cohort) or every 4 to 8 years (Offspring Cohort). Information was collected on age, blood pressure, body mass index, alcohol and tobacco use, and comorbidity at each FHS standardized examination. Comorbidities included previous diagnosis of diabetes mellitus, hypertension, atrial fibrillation or flutter, cancer (excluding nonmelanomatous skin cancer), heart failure, myocardial infarction, and stroke as defined using validated FHS protocols (Supplemental Appendix eTable1). Because spirometry data were available for fewer than 50% of the cohort and are not widely available in the general population, the FHS Clinical Diagnostic Impression of chronic lung disease (e.g., chronic bronchitis or emphysema) as determined by the physician examiner at each FHS examination was used as a measure of chronic pulmonary disease. Information was collected on overnight hospitalization in the year before the FHS examination from Medicare files. Missing covariates were carried forward from prior examinations.

Validation Cohort

Administrative data from Intermountain Healthcare were used to identify a cohort of individuals aged 65 and older with an outpatient visit to an Intermountain clinic during 2008. Intermountain Healthcare is a nonprofit healthcare system based in Salt Lake City, Utah, covering 22 hospitals and more than 1,100 primary care physicians at more than 185 clinics in Utah and southeastern Idaho. Outpatient visits to radiology or laboratory services or similar visits not associated with a physician (e.g., physical therapy, social work) were excluded. Elements of the derivation model were defined using validated *International Classification of Diseases, Ninth Edition, Clinical Modification* (ICD-9-CM) codes present at the time of the outpatient visit (Supplemental Appendix eTable1).

Outcomes: Derivation and Validation Cohorts

It was desired to identify mechanical ventilation associated with critical illness, so concomitant claims for mechanical ventilation and intensive care unit (ICU) admission were required. For the derivation cohort, ICU stays with mechanical ventilation within 5 years of each FHS visit from 1991 to 2009 were identified. CMS data were used to identify

hospitalizations of each eligible FHS participant with billing identifiers of ICU admission using Revenue Codes 200–209 (ICU) and 210–216 (cardiac care unit), as well as the accurate ($\kappa=0.9$) *ICD-9-CM* codes 96.7x denoting use of mechanical ventilation.(11) In the derivation cohort, Diagnosis-Related Group (DRG) codes were also used to identify the most likely reason (medical vs surgical) for hospitalization with mechanical ventilation in the ICU, and an exploratory analysis was performed for models predicting medical or surgical hospitalizations with mechanical ventilation. For the validation cohort, ICU visits with mechanical ventilation within 5 years of the 2008 outpatient index visit were identified, and an identical coding algorithm on Intermountain electronic medical records was used to capture mechanical ventilation outcomes. The institutional review boards of Boston University Medical Center and Intermountain Healthcare approved all study procedures. Framingham Heart Study participants signed written informed consent.

Statistical Methods

Derivation cohort—Pooled, competing risk and Cox proportional hazards models, with censoring for the competing risk of death, were used in the derivation FHS cohort, a strategy that yielded results similar to Fine-Gray methods.(12) Pooled Cox models account for changes in risk factors at subsequent examinations and approximate results of Cox models with time-varying covariates.(13, 14) Candidate variables (Supplemental Appendix eTable1) for the risk model were selected if they had less than 10% missing data and nominal significance ($p<.20$) in age- and sex-adjusted regression. The candidate variables remaining in the final model were chosen through stepwise selection in a pooled Cox proportional hazards model; final variables were selected with entry and stay criteria $p=.05$. C-statistic was used as a measure of the ability of the model to discriminate between FHS participants who would and would not require mechanical ventilation in an ICU within 5 years, and Nam/D'Agostino chi-square values were used to determine model calibration.(15) An a priori cutoff of c-statistic 0.6 or greater was set for fair model discrimination and a chi-square of less than 20 for adequate calibration in the derivation cohort. Significant multivariable risk predictor integer values based on relative values of the model beta coefficients were assigned to construct the risk score.(16) The final model was internally validated using a five-fold random cross-validation method.(17) Sensitivity analyses stratified on five observation periods were performed. The effect of familial correlation was also verified by including the robust sandwich estimator.(18)

Validation cohort—The FHS model was validated in the Intermountain Healthcare cohort using Cox proportional hazards models with censoring for the competing risk of death predicting mechanical ventilation using two approaches; coefficients for the constituent predictors of the derivation model we fitted, and the predicted probabilities from the validation cohort were used. In a sensitivity analysis to evaluate the potential effect of the competing risk of mortality and test the prediction of the model for mortality outcomes, the c-statistic of the risk score was examined in participants who died or required mechanical ventilation as a composite endpoint.

RESULTS

Derivation Cohort

Of 3,724 FHS participants with available CMS data, 3,666 (6,588 person-examinations, average follow-up 4.3 years) with no missing records were identified and included in the FHS derivation cohort. Characteristics of the derivation cohort (average age 73.7; 58% female) are shown in Table 1, stratified according to mechanical ventilation outcome. Within 5 years of index examinations, 381 (10%) participants had died without receipt of mechanical ventilation, 80 (2.2%) had required mechanical ventilation, and 29 of those 80 (36%) had died within 30 days after receiving mechanical ventilation. Of participants who required mechanical ventilation, 49 (61%) were admitted to an ICU with a medical diagnosis (most commonly with a DRG code for respiratory system diagnosis with ventilator support) and 31 (39%) with a surgical diagnosis (most commonly with a DRG code for major cardiovascular procedure).

Results of age- and sex-adjusted and multivariable-adjusted models for mechanical ventilation are shown in Table 2. Predictors of mechanical ventilation included older age, male sex, diagnosis of diabetes mellitus, hypertension, atrial fibrillation, alcohol use, chronic lung disease, and hospitalization in the year before the FHS examination (c-statistic=0.74, 95% confidence interval (CI)=0.68–0.80; Nam/D'Agostino calibration chi square=3.00, Figure 1A). Comorbidities and hospitalization within the prior year were major contributors to the model (c-statistic for comorbidity model without demographics = 0.70, 95% CI=0.64–0.76) (Supplemental Appendix eTable2].

Subgroup analysis showed that variables differed in predicting surgical hospitalizations requiring mechanical ventilation (diabetes mellitus, alcohol abuse, atrial fibrillation) versus medical hospitalizations requiring mechanical ventilation (hypertension, atrial fibrillation, hospitalization within the prior year) (Supplemental Appendix eTable 3), but neither medical (c-statistic=0.73, 95% CI=0.65–0.80, chi-square=7.8) nor surgical (c-statistic=0.75, 95% CI=0.65–0.85, chi-square=3.9) hospitalization substantively changed model discrimination or calibration in the subgroup analysis. Internal cross-validation of the model also showed performance characteristics similar to that of the development model (c-statistic=0.71, 95% CI=0.64–0.77, chi-square=5.6). The results did not materially change in sensitivity analyses stratifying for observation period (c-statistic=0.76, 95% CI=0.71–0.82) or accounting for familial correlation (Supplemental Appendix eTable 4).

Validation cohort

Demographic characteristics of the validation cohort (N=88,302; average age 73, 57% female) were similar to those of the derivation cohort (Supplemental Appendix eTable 6). During the 5-year follow up, 14,144 (16%) died without receipt of mechanical ventilation, 1,725 (2.0%) reached the mechanical ventilation outcome, and 742 (43% of those mechanically ventilated) died within 30 days of receiving mechanical ventilation. Multivariable effect estimates for the refitted model in the validation cohort are shown in Table 2. The primary validation c-statistic was 0.67 (95% CI=0.66–0.68, calibration chi-square=21.6, Figure 1B) in the model using FHS-identified covariates in the Intermountain

validation data set and 0.66 (95% CI=0.65–0.68) using FHS predicted probabilities in the Intermountain data. The sensitivity analysis investigating the composite outcome of mechanical ventilation or death showed a c-statistic of 0.75 (95% CI=0.75–0.75) for the composite outcome of mechanical ventilation or death.

Risk Score Calculator

The point score calculator is shown in Table 3 (and is available online at <http://www.framinghamheartstudy.org/>). Kaplan-Meier curves demonstrating the probability of remaining free from mechanical ventilation within 5 years for low-risk (score 0–5, n=5,068 person-examinations (77%); 0.9% risk for mechanical ventilation), moderate-risk (score 6–10, n=1,405 person-examinations (21%); 3.4% risk), and high-risk (score >10, n=115 person-examinations (2%); 12.8% risk) scores are shown in Figure 2. The risk of mechanical ventilation was 1.4% (918/65,218) for low-risk, 3.2% (643/20,184) for moderate risk, and 5.7% (164/2,900) for high-risk validation cohort participants. The risk of death or mechanical ventilation in the validation cohort was 13.1% for low-risk, 29.1% for moderate-risk, and 50.7% for high-risk participants.

DISCUSSION

Identifying outpatient risks of mechanical ventilation may facilitate and individualize planning for the disability, loss of decision-making capacity, and high mortality that often accompany mechanical ventilation during critical illness. A novel risk score that provides a quantitative estimate of 5-year risk of requiring mechanical ventilation during critical illness was developed and validated in a community-based cohort and outpatients aged 65 and older. The feasibility of constructing a risk score that predicts the need for mechanical ventilation, using diagnostic information readily available during ambulatory encounters or, automatically, from administrative claims and coding data, was shown.

Although advance care planning should be an ongoing process between individuals and their healthcare providers, only approximately 20% of older adults have discussed advanced directives with their physicians.(19) Commonly cited barriers to advance care planning discussions include lack of time to discuss advance care plans adequately during an already full visit,(20) absence of a clear threshold to start the discussion(21, 22), and people's perceptions that advance care planning is not directly relevant to their personal situation.(23) A risk score that objectively identifies outpatients most likely to require life support over a relevant time horizon may help to overcome some barriers by aligning the depth of discussions with risk and providing guidance customized to expected life course. For example, low-risk individuals (~1% 5-year risk) may be introduced to concepts of advance care planning during a routine visit, whereas higher-risk individuals (5–12% risk) may warrant full appointments devoted to individualizing advance care plans and discussing details of rehabilitation and recovery after critical illness, but further studies are necessary to determine whether a risk score might improve advance care planning.

The FHS score was validated in a cohort using administrative data. Thus, according to recent Institute of Medicine recommendations,(24) this risk score may be automated within electronic medical records to alert physicians to risk of mechanical ventilation. An increase

in the number of outpatients counseled regarding advance directives from 4% to 24% was reported in one single-center study using automated alerts.(25) The a priori criteria used in that study to activate advance care planning included aged 75 and older or aged 50 and older plus the presence of a comorbidity, a qualitative strategy that shared some similarities to the quantitative model used in the current study.

This study has strengths and limitations. A broad community-based cohort was included for derivation and a large outpatient-based sample for validation, and clinical covariates routinely available during a general outpatient visit and well-validated methods were used to ascertain mechanical ventilation outcomes. In addition, the risk score was validated in an external cohort that incorporated a different population and separate clinical definitions of relevant predictors. The validation cohort had modestly less discriminative capacity and calibration than the derivation cohort. In addition to the expected decrease in model statistical performance when tested on an external cohort, specific factors possibly contributing to differences in model performance include lower sensitivity of ICD-9 codes for detecting clinical diagnoses, absence of time-varying covariates in the validation cohort, and differences in alcohol use between the two cohorts. The proposed risk score was developed using community-based participants in the FHS who were Medicare eligible; thus, the findings may not be applicable to people younger than 65 or who differ substantially in other demographic or clinical background from the cohorts studied. For example, the validation and derivation cohorts had low racial and ethnic diversity, which may limit generalizability of the findings. The study sought to achieve a balance between use of covariates readily available from a clinical encounter and model accuracy to identify mechanical ventilation risk in a community-dwelling cohort. Whether other clinical variables not routinely available from FHS clinical examinations (e.g., presence of chronic kidney or liver disease) or more-objective clinical measures (e.g., spirometry data) would improve the accuracy of the risk model should be considered in use of the model and merits further study. ICU stay was used as a surrogate for the presence of critical illness, but use of ICU services varies between hospitals and may represent variable degrees of illness severity, particularly between individuals undergoing and not undergoing surgery.(26) Further iterations of the mechanical ventilation risk score may characterize critical illness differently.(27) Individuals who chose do-not-intubate (DNI) status or other limitations on care were not able to be identified and may have biased the results, although it is likely that individuals with a DNI order had comorbidities but were not provided mechanical ventilation, which it is likely would result in a bias to the null. Thus, missing individuals with a DNI order or comorbidities were unlikely to have falsely elevated model accuracy.

Conclusion

In conclusion, a model was developed and validated that estimates 5-year risk of requiring mechanical ventilation in an ICU. The risk score may be further developed into a clinical tool in the outpatient setting to facilitate ongoing advance care planning between individuals and their healthcare providers. Further study is necessary to determine whether clinical implementation of a mechanical ventilation risk score would improve preparation for critical illness, including advance care planning.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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A

B

Figure 1.

Calibration graph of observed versus expected values for the mechanical ventilation risk score in the (A) derivation cohort (Nam/D'Agostino calibration chi-square = 3.00) and (B) validation cohort (Nam/D'Agostino calibration chi square = 21.6).

Figure 2.

Derivation cohort Kaplan-Meier curves demonstrating the probability of remaining free of mechanical ventilation stratified according to low- (0–5), moderate- (6–10), and high-risk (>10) total point scores. Numbers at risk are presented as participant visits.

Table 1

Pooled Characteristics of the Framingham Heart Study (FHS) Derivation Cohort

Variable	No Mechanical Ventilation, n= 3,586 ^a	Mechanical Ventilation, n=80
Age, mean±SD	74±6.6	76±7.5
Male, %	42	59
Diabetes mellitus, %	15	30
Hypertension, %	68	81
Body mass index, kg/m ² , mean±SD	27.2±5.1	27.9±6.4
Systolic blood pressure, mmHg, mean±SD	137±20	140±23
Diastolic blood pressure, mmHg, mean±SD	72±10	70±12
Smoking, %	7	10
Alcohol, drinks/week, mean±SD	2±4	3±6
Moderate to heavy alcohol use, %	4	11
History of cancer, %	15	19
History of heart failure, %	3	8
History of stroke, %	6	8
History of myocardial infarction, %	7	14
History of atrial fibrillation, %	9	25
History of chronic obstructive pulmonary disease, % ^c	7	15
Hospitalized during past year %	9	20

^aFHS participants (n=3,586) were followed for 6508 participant visits and an average of 4.3 years.

^bFHS physician clinical diagnostic impression of a history of emphysema or chronic bronchitis.

Table 2

Prediction of 5-Year Risk of Mechanical Ventilation: Results of Framingham Heart Study Derivation Models and Intermountain Healthcare Validation Model

Candidate Variable	Derivation Cohort		Validation Cohort
	Age- and Sex-Adjusted Model ^a	Multivariable Model ^b	Multivariable Model ^c
	Hazard Ratio (95% Confidence Interval) P-Value		
Age (per 5 years)	N/A	1.16 (0.99–1.37) .06	1.01 (1.00–1.02) .03
Male	N/A	1.79 (1.14–2.83) .009	1.39 (1.26–1.52) <.001
Diabetes mellitus	2.45 (1.51–3.96) <.001	2.17 (1.33–3.53) .002	1.61 (1.44–1.79) <.001
Hypertension	1.98 (1.13–3.48) .02	1.79 (1.02–3.16) .04	1.20 (1.07–1.33) .001
Body mass index (categorical)	1.23 (0.94–1.61) .14	Nonsignificant	—
Systolic blood pressure (per 1 SD)	1.03 (0.83–1.28) .81	—	—
Diastolic blood pressure (per 1 SD)	0.76 (0.61–0.96) .02	Nonsignificant	—
Smoking	1.65 (0.79–3.46) .18	Nonsignificant	—
Alcohol (per 5 drinks/wk)	1.12 (0.97–1.29) .13	Nonsignificant	—
Moderate to heavy alcohol use	2.82 (1.41–5.66) .004	2.78 (1.38–5.60) .004	1.99 (0.82–4.80) .13
Cancer	1.20 (0.68–2.11) .54	—	—
Heart failure	2.28 (0.98–5.31) .06	Nonsignificant	—
Stroke	1.01 (0.43–2.33) .99	—	—
Myocardial infarction	1.62 (0.84–3.11) .15	Nonsignificant	—
Atrial fibrillation	3.00 (1.77–5.08) <.001	2.33 (1.35–4.01) .002	1.69 (1.48–1.93) <.001
Chronic obstructive pulmonary disease	2.40 (1.30–4.44) .005	2.17 (1.17–4.03) .01	2.22 (1.99–2.48) <.001
Hospitalized in prior 1 year	2.34 (1.34–4.09) .003	1.99 (1.12–3.53) .02	1.62 (1.44–1.83) <.001

^aCandidate variables with $p < .20$ in the age- and sex-adjusted model were included in the derivation cohort multivariable model.

Model C-statistic = ^b0.74, ^c0.67.

N/A=not applicable; —=not tested in multivariable models

Table 3

Calculation of the Risk Score for Requiring Mechanical Ventilation within 5 Years

Risk Factor	Points
Age	
65–74	0
75–84	1
85–94	2
Sex	
Female	0
Male	2
Diabetes mellitus	
No	0
Yes	3
Hypertension	
No	0
Yes	2
Moderate to heavy alcohol use	
No	0
Yes	3
Prevalent atrial fibrillation	
No	0
Yes	3
Hospitalization in prior year	
No	0
Yes	2
Chronic obstructive pulmonary disease	
No	0
Yes	3