Risk Factors for Delirium at Discharge

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Development and Validation of a Predictive Model

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Background: Persistent delirium at the time of hospital discharge is associated with poor outcomes. The objectives of this study were to develop and validate a predictive model for persistent delirium at hospital discharge.

Methods: This study followed a prospective validation design. For the development cohort, 491 consecutive patients 70 years or older admitted to the hospital without delirium and surviving to discharge were enrolled from the general medical units of an academic teaching hospital. For the validation cohort, 461 comparable subjects were enrolled. Twenty-two candidate risk factors were examined, including 12 baseline factors (present on admission) and 10 precipitating factors (hospital related). The primary outcome was delirium at hospital discharge, measured by the Confusion Assessment Method.

Results: Delirium at discharge was present in 58 patients (11.8%) in the development cohort. Five independent risk factors for delirium at discharge were identified: dementia (odds ratio [OR], 2.3; 95% confidence interval [CI], 1.4-3.7); vision impairment (OR, 2.1; 95% CI, 1.3-3.2); functional impairment (OR, 1.7; 95% CI, 1.2-3.0); high comorbidity (OR, 1.7; 95% CI, 1.1-2.6); and use of physical restraints during delirium (OR, 3.2; 95% CI, 1.9-5.2). A risk stratification system was created by adding 1 point for each factor present. Rates of delirium for the low-risk (0-1 factors), intermediate-risk (2-3 factors), and high-risk (4-5 factors) groups were 4%, 18%, and 63%, respectively ($P<.001$). The corresponding rates in the validation cohort, where 28 patients (6.1%) had delirium at discharge, were 3%, 14%, and 27% ($P<.001$).

Conclusions: A predictive model based on 5 risk factors has been successfully validated for prediction of delirium at discharge in hospitalized older patients. At least 4 of these risk factors are amenable to intervention strategies.

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DELIRIUM REPRESENTS A common, serious, and potentially preventable problem for older persons.[1] Previous work has emphasized its transient nature; however, recent studies document that up to 50% of delirium persists until hospital discharge and often for months beyond.[2-8] Persistent delirium has been associated with worse long-term cognitive and functional outcomes than resolved delirium.[6,9] Delirium may be more persistent in persons with underlying dementia.[4,6,8,10] Moreover, several precipitating factors for delirium may not be completely reversible (eg, those resulting in neuronal injury).[11] Many experts believe that persistent delirium may directly contribute to dementia.[11-13] Thus, understanding factors that lead to persistent delirium will help to clarify the pathways by which delirium may lead to long-lasting cognitive sequelae.

Patients discharged with delirium represent a particularly high-risk group. Hospital discharge has been recognized as a high-risk transition period.[14,15] In previous studies, 49% of older patients experienced at least 1 medical error during transitions from the hospital,[16,17] and 13% to 25% had serious complications.[18] Delirium is reported in only 3% to 16% of documented cases at discharge,[19-21] and unrecognized delirium is associated with high mortality. Patients with delirium at discharge from the emergency department[22] had a 7-fold increased mortality risk, with the highest risk in the unrecognized delirium group. Delirium at discharge was also associated with a 2.6-fold increased risk of death or nursing home placement.[23] Finally, delirium that persisted beyond discharge from acute care was asso-

ciated with rehospitalization, prolonged institutionalization, and death.[24]

Our research group has previously examined predisposing factors (at admission)[25] and precipitating factors (during hospitalization)[26] for delirium. Our goal in the present study is to extend this work to examine persistence factors leading to delirium that persists until discharge. This work appears justified given that hospital discharge represents a transition to a less supervised environment, that delirium at discharge is associated with high morbidity and mortality, and that new interventions may be necessary to improve the transition period.

Specific objectives of the present study were to (1) identify risk factors for delirium at discharge, including baseline vulnerability factors and hospital-related factors; (2) develop a predictive model for delirium at discharge in an initial cohort; and (3) validate the model in an independent cohort. Our hypotheses were that baseline factors (eg, comorbidity) and precipitating factors (eg, iatrogenic events) would be associated with a higher risk of delirium at discharge. We further hypothesized that risk factors would differ between those contributing to delirium that resolves vs those contributing to persistent delirium. Our goals were to develop a predictive model that would help to identify patients at high risk for delirium at discharge for enrollment in intervention programs and to target appropriate interventions toward the identified risk factors for delirium at discharge.

METHODS

The study followed a prospective validation design. The predictive model was first developed in an initial cohort, then externally validated in a separate validation cohort.[27,28]

MODEL DEVELOPMENT

Study Sample

Potential participants were patients aged 70 years or older who were consecutively admitted to 6 general medicine units (nonintensive care) at Yale New Haven Hospital with no evidence of delirium. The sample of 525 patients has been described in detail previously.[29,30] Of the 525 patients, 34 died during hospitalization and were excluded, yielding a final sample of 491 participants.

Study Procedures

Experienced clinical interviewers, who were blinded to the study hypotheses, conducted structured interviews with the patients and their nurses from admission until discharge. The baseline evaluation completed within 48 hours of admission included demographic information and the Mini-Mental State Examination[31]; Digit Span Test[32]; Confusion Assessment Method (CAM) rating[33]; activities of daily living (ADL)[34] and instrumental ADL[35] screening referent to the 2 weeks prior to hospitalization; the Jaeger[36] test for vision and whisper test for hearing[37]; and the Geriatric Depression Scale (GDS).[38] Trained abstractors reviewed hospital records for diagnoses, laboratory results, medications, length of stay, and discharge destination; they also determined the APACHE II score (Acute Physiology and Chronic Health Evaluation II)[39,40] and Charlson Comorbidity Index.[41] A family member was interviewed to rate the modified Blessed Dementia Rating Scale.[42,43] Subsequently, patients were evaluated every other day with the Mini-Mental State Examination, Digit Span Test, and CAM, and directly observed for the use of physical restraints and bladder catheters.

Informed consent for study participation was obtained from the patients or, for those with substantial cognitive impairment, from a proxy (closest relative or legal guardian), according to procedures approved by the institutional review board of Yale University School of Medicine.

Outcomes

The primary outcome was delirium at hospital discharge. This was defined as meeting the full validated CAM criteria for delirium[33] during hospitalization, then continuing to meet full or partial CAM criteria at discharge. The full CAM criteria for delirium required the presence of acute onset and fluctuating course, inattention, and either disorganized thinking or altered level of consciousness. These criteria have a sensitivity of 94% to 100% and specificity of 90% to 95% compared with geropsychiatrists' ratings and high interrater reliability.[31] Partial CAM criteria were defined as the presence of any 1 of the full CAM criteria, a definition used previously.[7,23,24,44,45] Resolved delirium was defined as delirium that developed during hospitalization but resolved before discharge. The CAM has been used to measure changes or resolution in delirium symptoms.[9,46-49]

Definition of Variables

We chose cut points based on previous studies, data distributions, and clinical sensibility. Advanced age was defined as 85 years or older, representing the highest quartile in the sample. Male sex has been identified as a risk factor previously.[25,50] The cut point of greater than 1 ADL impairment was chosen as the highest quartile in the sample. Vision impairment was defined as corrected near vision worse than 20/70 OU.[25] A Mini-Mental State Examination score lower than 24 was used as our cut point.[31] Dementia was defined by either a medical record diagnosis or modified Blessed Dementia Rating Scale score of 4 or higher.[42,51] An APACHE II score higher than 16 or nurse rating of "severe" was used to identify high severity of illness.[25] A Charlson score of 4 or higher was chosen as the highest quartile in the sample.[41] A ratio greater than 18 of serum urea nitrogen to creatinine and albumin levels of 3.5 g/dL or lower were our cut points, as used previously.[25,40,51-53] The number of iatrogenic events was defined by standard criteria[26,54,55] and analyzed as a continuous variable, and the cut point of more than 4 events was used, representing the highest quartile. The cut points of more than 3 medications newly added in 1 day and more than 3 psychoactive medications received in 1 day were used, as previously.[26] Delirium-related variables (eg, severity and/or duration) were not included because they could be determined only in delirious patients.

MODEL VALIDATION

Study Sample

This prospective cohort comprised the control arm of the Delirium Prevention Trial, described previously.[23,46] Potential participants were patients 70 years or older who were consecutively admitted to the general medicine service (nonintensive

Table 1. Baseline Patient Characteristics in the 2 Cohorts[a]

Characteristic	Cohort	
	Development[b] (n = 491)	Validation[c] (n = 461)
Age, y[d]	79.1 ± 6.1	80.0 ± 6.5
Men	211 (43)	182 (39)
Education, y	11.3 ± 3.5	11.1 ± 3.7
Married[d]	229 (47)	159 (34)
ADL score (range, 0-7)	0.9 ± 1.8	1.0 ± 1.7
Any impairment	152 (31)	161 (35)
Impairment >1	97 (20)	105 (23)
Vision impairment[d]	189 (38)	107 (23)
MMSE score	23.1 ± 6.3	23.2 ± 4.9
Score <24[d]	187 (39)	210 (46)
Dementia	96 (20)	91 (20)
APACHE II score[d]	14.6 ± 3.5	15.6 ± 4.1
Charlson score[41]	2.7 ± 2.1	2.7 ± 2.2
Score ≥4	140 (29)	136 (30)

Abbreviations: ADL, activities of daily living[34,35]; APACHE II, Acute Physiology and Chronic Health Evaluation II[39,40]; MMSE, Mini-Mental State Examination.[31]

[a] Data are reported as mean ± SD values or number (percentage) of subjects.

[b] In the development cohort, education data were missing for 19 subjects; Mini-Mental State Examination score, 6 subjects; APACHE II score, 5 subjects; and Charlson score, 1 subject.

[c] In the validation cohort, education data were missing for 3 subjects.

[d] $P<.05$, comparing development and validation groups.

care) at Yale New Haven Hospital with no evidence of delirium but who were at intermediate or high baseline delirium risk.[25] We used the entire sample of 469 control patients, which included 426 matched and 43 unmatched patients. We excluded 8 patients who died during hospitalization, yielding a final sample of 461 participants.

Study Procedures

The clinical evaluations, outcomes, and definitions of variables were identical to those used in the development study. The only difference was that delirium assessments were conducted daily. The same research staff conducted the study using the same data-collection instruments, blinded to the study hypotheses.

STATISTICAL ANALYSES

Baseline characteristics of the development and validation cohorts were compared using *t* test statistics for continuous variables or χ^2 statistics for categorical variables.

For bivariable and multivariable analyses, delirium at discharge represented the highest level of a 3-level outcome, which is ordinal and progressive: (1) no delirium; (2) resolved delirium; and (3) delirium at discharge. The ordinal nature is reflected by the increasing disease severity across categories; the progressive nature is demonstrated by the need to pass through each level to arrive at the next. All analyses were conducted using the continuation ratio model, a log-binomial regression model suited to progressive ordinal outcomes.[56-59] These models allowed us to explore whether risk factors that contribute to delirium that resolves are different from those that contribute to its persistence. Adjusted odds ratios (ORs) and confidence intervals (CIs) were calculated from the parameter estimates and standard errors. For the overall model, the at-risk period for defining risk factors was considered as the delirium interval (ie, the total inclusive days of delirium from first day of a CAM-positive rating until discharge) for the delirium at discharge group, the period from delirium onset to resolution in the resolved delirium group, and the entire hospitalization for the no delirium group.

Initially, bivariable continuation ratio models were conducted, which generated ORs for 3 comparisons—any delirium vs no delirium, delirium at discharge vs resolved delirium, and an overall comparison yielding an overall (combined) OR. For the overall model, an interaction term was included that tested for significant differences between the first 2 comparisons. If the interaction term was not significant, then the overall OR was not significantly different across the 2 comparisons and a single OR was used to describe the likelihood of developing either outcome.

Potential risk factors were narrowed along axes using the following criteria: (1) prevalence of at least 5% for discrete variables; (2) relative risk of 1.3 or higher for delirium at discharge in bivariable analyses (or a statistically significant parameter estimate at $P=.10$ for continuous variables); and (3) clinical relevance. All of the variables measured continuously were considered as continuous variables in the original selection process. In addition, multiple cut points were considered for these variables, selected based on clinical considerations and data distributions. Selection of the final cut point (vs continuous) was based on fulfillment of our a priori selection criteria. For potentially collinear variables, 1 variable was chosen based on its relative risk and clinical relevance. This axis approach to variable reduction has been well described.[25,26,28,60]

Additional analyses were conducted to more fully examine specific hospital-related factors, namely medications and restraints. For these analyses, we conducted nested case-control studies to more fully control for differing exposure periods in the study groups. We constrained the exposure period by matching on delirium duration in the cases and length of stay in nondelirious controls. In addition, we further limited the exposure window to the first 3 days after delirium onset for the 2 delirium groups and 3 consecutive days selected randomly for those without delirium.

The predictive model for delirium created in the development cohort was subsequently tested in the validation cohort. Performance of the predictive model was assessed using the C statistic, approximating the area under a receiver-operating characteristic curve,[61] and ranging from 0.5 (no discrimination above chance) to 1.0 (perfect discrimination). Overall χ^2 and Cochran-Armitage trend tests were used to compare rates of delirium at discharge by risk strata in both cohorts. All analyses were conducted using SAS version 9.1 (SAS Institute, Cary, North Carolina).

RESULTS

Baseline characteristics of the development cohort are summarized in **Table 1**. Of the 491 patients, 106 (21.6%) developed delirium during hospitalization, and median length of stay was 9 days (range, 3-67 days). Of the 58 patients with delirium at discharge (11.8%), median time from admission to delirium onset was 3 days (range, 2-20 days); median duration of delirium in the hospital was 7 days (range, 1-61 days); and median length of stay was 10 days (range, 3-67 days). Of the 48 patients with resolved delirium, median time from admission to delirium onset was 4 days (range, 1-21 days); median duration of delirium in the hospital was 5 days (range, 1-64 days); and median length of stay was 15 days (range, 3-67

Table 2. Potential Risk Factors for Delirium at Discharge in the Development Cohort[a]

Potential Risk Factor	Distribution of Risk Factor[b]			Odds Ratio (95% Confidence Interval)		
	Delirium at Discharge	Resolved Delirium	No Delirium	Overall Model (n = 491)	Any Delirium vs No Delirium (n = 491)	Delirium at Discharge vs Resolved Delirium (n = 106)
Axis 1 Baseline Risk Factors						
Demographics						
Age ≥85 y	22 (37.9)	15 (31.3)	60 (15.6)	2.4 (1.6-3.6)	2.9 (1.8-4.7)	1.3 (0.6-3.0)
Male sex	22 (37.9)	19 (39.6)	170 (44.2)	0.8 (0.6-1.2)	0.8 (0.5-1.2)	0.9 (0.4-2.0)
Education, y	10.5 ± 3.3	10.2 ± 3.9	11.6 ± 3.4	0.9 (0.9-1.0)	0.9 (0.9-1.0)	1.0 (0.9-1.2)
Physical functioning						
ADL impairment >1	26 (44.8)	15 (31.3)	56 (14.5)	3.1 (2.0-4.7)	3.7 (2.3-6.0)	1.8 (0.8-4.0)
Vision impairment	43 (74.1)	26 (54.2)	120 (31.2)	3.6 (2.5-5.4)	4.1 (2.6-6.5)	2.4 (1.1-5.5)
Cognitive functioning						
MMSE score <24	41 (74.5)	30 (63.8)	116 (30.3)	4.1 (2.7-6.1)[c]	5.3 (3.3-8.5)	1.7 (0.7-3.9)
Dementia, by diagnosis or mBDRS score ≥4	34 (58.6)	14 (29.2)	48 (12.5)	5.1 (3.3-7.7)	5.8 (3.6-9.5)	3.4 (1.5-7.8)
Biomedical						
APACHE II score >16 or nurse rating of severe	23 (39.7)	16 (33.3)	96 (24.9)	1.6 (1.1-2.4)	1.8 (1.1-2.8)	1.3 (0.6-2.9)
Charlson score[41] ≥4	25 (43.1)	16 (33.3)	99 (25.7)	1.7 (1.2-2.6)	1.8 (1.2-2.9)	1.5 (0.7-3.4)
SUN-Cr ratio ≥18	39 (67.2)	23 (48.9)	182 (47.3)	1.7 (1.2-2.5)	1.6 (1.0-2.5)	2.1 (1.0-4.7)
Albumin ≤3.5 g/dL	19 (32.8)	17 (35.4)	69 (17.9)	1.8 (1.2-2.8)[c]	2.4 (1.5-3.8)	0.9 (0.4-2.0)
Axis 2 Hospital-Related Factors[d]						
Immobilization						
Restraint use	30 (51.7)	12 (25.0)	33 (8.6)	5.7 (3.6-8.9)	7.0 (4.1-11.9)	3.2 (1.4-7.4)
Catheter use	30 (51.7)	24 (50.0)	110 (28.6)	2.1 (1.4-3.1)	2.6 (1.7-4.0)	1.1 (0.5-2.3)
Iatrogenic events (range, 0-24)	2.6 ± 2.9	3 ± 2.8	1.2 ± 1.6	1.2 (1.1-1.3)[c]	1.4 (1.2-1.5)	1.0 (0.8-1.1)
Any	46 (79.3)	41 (85.4)	218 (56.6)	2.5 (1.6-3.9)[c]	3.5 (2.1-6.0)	0.7 (0.2-1.8)
>4	14 (24.1)	17 (35.4)	33 (8.6)	2.4 (1.5-3.9)[c]	4.4 (2.5-7.6)	0.6 (0.2-1.3)
Intercurrent illness						
New diagnoses	2.7 ± 1.7	3.0 ± 1.8	2.1 ± 1.5	1.2 (1.1-1.3)[c]	1.3 (1.1-1.5)	0.9 (0.7-1.1)
Any new diagnosis	52 (89.7)	46 (95.8)	339 (88.1)	1.2 (0.6-2.4)	1.7 (0.8-3.6)	0.4 (0.1-2.0)
Hospital medications						
>3 Added in 1 day	35 (60.3)	35 (72.9)	203 (52.7)	1.3 (0.9-2.0)[c]	1.7 (1.1-2.7)	0.6 (0.2-1.3)
Total new medications	2.8 ± 2.9	4.0 ± 3.6	2.8 ± 2.3	1.0 (0.9-1.1)[c]	1.1 (1.0-1.2)	0.9 (0.8-1.0)
>3 Psychoactive medications in 1 day	11 (19.0)	16 (33.3)	115 (29.9)	0.7 (0.5-1.1)	0.8 (0.5-1.3)	0.5 (0.2-1.1)

Abbreviations: ADL, activities of daily living[34,35]; APACHE II, Acute Physiology and Chronic Health Evaluation II[39,40]; CAM, Confusion Assessment Method[33]; mBDRS, modified Blessed Dementia Rating Scale[42,43]; MMSE, Mini-Mental State Examination[31]; SUN-Cr, serum urea nitrogen–creatinine.

[a] Education data were missing for 19 subjects; baseline MMSE score lower than 24 data missing for 6 subjects; serum urea nitrogen–creatinine ratio missing for 1 subject.

[b] Data are reported as mean ± SD values or number (percentage) of subjects.

[c] For these analyses, an interaction term indicated a significant difference between the 2 comparisons (any delirium vs no delirium and delirium at discharge vs resolved delirium). None of these variables was included in the final model.

[d] For the overall model, the at-risk period for defining risk factors was considered the delirium interval (ie, the inclusive days of delirium from the first day of CAM-positive rating until discharge) for the delirium at discharge group, the period from delirium onset to resolution in the resolved delirium group, and the entire hospitalization for the no delirium group.

days). Hospital mortality rates in the 3 groups were 22% in delirium at discharge, 17% in delirium resolved, and 2% in no delirium groups.

DEVELOPMENT OF THE PREDICTIVE MODEL

The 22 candidate risk factor variables considered for the predictive model are listed in **Table 2**, including 12 baseline (admission) and 10 precipitating (hospital-related) factors. Using the a priori selection criteria, these variables were narrowed along the 2 axes. Five independent factors were selected for inclusion in the final predictive model (**Table 3**): dementia, vision impairment, ADL impairment, high comorbidity, and restraint use during delirium. These factors were entered into a single model to provide an overall estimate of the independent contribution of each variable to the persistence of delirium until discharge. The nested case-control analyses of medications and restraints did not yield any additional variables for the model.

PERFORMANCE OF THE PREDICTIVE MODEL

Development Cohort

In the development cohort, the final predictive model generated a C statistic of 0.80, indicating good prediction above chance.[61] A risk stratification system was created by assigning 1 point to each of the final risk factors. Three risk groups were created: a low-risk group (0-1 factors), intermediate-risk group (2-3 factors), and high-risk group (4-5 factors). Rates of delirium at discharge increased from 4% to 18% to 63% in the low-, intermediate-, and high-risk groups, respectively (χ^2=87.64 for trend, $P<.001$),

with a corresponding risk gradient extending from 1.0 (reference) to 4.4 to 15.3 (**Table 4**).

Validation Cohort

Of the 461 patients in the validation cohort, 63 developed delirium during hospitalization (13.7%), and median length of stay was 6 days (range, 3-60 days). Of the 28 patients with delirium that persisted to discharge (6.1%), median time from admission to delirium onset was 5 days (range, 2-52 days); median duration of delirium in the hospital was 7 days (range, 1-26 days); and median length of stay was 12 days (range, 4-53 days). Of the 35 patients with resolved delirium, median time from admission to delirium onset was 4 days (range, 2-10 days); median duration of delirium in the hospital was 2 days (range, 1-31 days); and median length of stay was 10 days (range, 3-60 days). Although the development and validation cohorts were comparable in many baseline characteristics, the validation cohort was significantly older, had more cognitive impairment and higher illness severity, and was less likely to be married or visually impaired (Table 1).

In the validation cohort, the predictive model yielded a C statistic of 0.75. Applying the risk stratification system (Table 4), we found that the rates of delirium at discharge increased from 3% to 14% to 27% in low-, intermediate-, and high-risk groups, respectively (χ^2=28.77 for trend, $P<.001$), representing a 10-fold increased risk of delirium at discharge between the low- and high-risk groups.

Table 3. Independent Risk Factors for Delirium at Discharge in 491 Subjects

Risk Factor	Adjusted OR (95% CI)[a]
Dementia, by diagnosis or mBDRS ≥4 (n=96)	2.3 (1.4-3.7)
Vision impairment (n=189)	2.1 (1.3-3.2)
ADL impairment >1 (n=97)	1.7 (1.2-3.0)
Charlson score[41] ≥4 (n=140)	1.7 (1.1-2.6)
Restraint use during delirium (n=75)	3.2 (1.9-5.2)

Abbreviations: ADL, activities of daily living[34,35]; CI, confidence interval; mBDRS, modified Blessed Dementia Rating Scale[42,43]; OR, odds ratio.
[a]Adjusted ORs derived from overall multivariable continuation ratio model analysis.

Clinical Outcomes Related to Delirium at Discharge

The predictive validity of the risk stratification system was evaluated for prediction of death or nursing home placement during 1-year follow-up (**Table 5**). The hierarchical outcome of either death or nursing home placement was chosen since the combination avoids inferential errors that arise because patients who die can no longer be institutionalized.[62] In addition, a previous study demonstrated that delirium at discharge was associated with increased rates of this hierarchical outcome.[23] In the development cohort, the rate of death or nursing home placement increased from 23% to 57% to 77% in the low-, intermediate-, and high-risk groups, respectively, for a 3.4-fold increase overall (χ^2=62.1 for trend, $P<.001$). In the validation cohort, the corresponding rates increased from 15% to 39% to 64%, for a 4.4-fold increase overall (χ^2=42.1 for trend, $P<.001$).

COMMENT

We developed and successfully validated, in a separate, clinically distinct sample, a predictive model for delirium persisting to hospital discharge based on 5 independent risk factors: dementia, vision impairment, functional impairment, high comorbidity, and use of physical restraints during delirium. Four of these factors were baseline factors, a finding that highlights the predominance of vulnerability or impaired cognitive reserve contributing to delirium at discharge and reinforces the importance of preventive approaches. Physical restraint use during delirium was the only hospital-related factor to emerge as a significant predictor. The association of physical restraint use with persistent delirium is not surprising, given the documented association of restraint use with incident delirium[26] and its numerous adverse effects, including increased agitation, immobility, functional decline, incontinence, pressure ulcers, asphyxiation, and cardiac arrest.[63-65] The present findings—that physical restraints may prolong delirium and worsen clinical outcomes—strongly indicate that physical restraints should not be used for older persons with delirium. While the prevalence of restraint use decreased over time between the 2 study cohorts—from 15% in the development cohort to 2% in the validation cohort—the association of restraint use with persistent delirium remained strong in both. Recent reports indicate an average rate of restraint

Table 4. Performance of the Predictive Model in the 2 Cohorts

Risk Group (Risk Factors, No.)	Cohort			
	Development		Validation	
	Delirium at Discharge[a]	RR (95% CI)	Delirium at Discharge[a]	RR (95% CI)
Low (0-1)	13/319 (4.1)[b]	1 [Reference]	9/338 (2.7)[c]	1 [Reference]
Intermediate (2-3)	25/140 (17.9)[b]	4.4 (2.3-8.3)	16/112 (14.3)[c]	5.4 (2.4-11.8)
High (4-5)	20/32 (62.5)[b]	15.3 (8.4-27.8)	3/11 (27.3)[c]	10.2 (3.2-32.7)

Abbreviations: CI, confidence interval; RR, relative risk.
[a]Data are reported as number of applicable subjects/total number of subjects in the group (percentage).
[b]χ^2=87.64 for trend, $P<.001$.
[c]χ^2=28.77 for trend, $P<.001$.

Table 5. Risk of Death or Nursing Home Placement During 1-Year Follow-up in the 2 Cohorts

Risk Group (Risk Factors, No.)	Development Cohort (n = 411)		Validation Cohort (n = 461)	
	Subjects[a]	RR (95% CI)	Subjects[a]	RR (95% CI)
Low (0-1)	59/256 (23.0)[b]	1 [Reference]	49/338 (14.5)[c]	1 [Reference]
Intermediate (2-3)	70/124 (56.5)[b]	2.4 (1.6-3.2)	44/112 (39.3)[c]	2.7 (1.9-3.8)
High (4-5)	24/31 (77.4)[b]	3.4 (2.5-4.5)	7/11 (63.6)[c]	4.4 (2.6-7.4)

Abbreviations: CI, confidence interval; RR, relative risk.
[a] Data are reported as number of applicable subjects/total number of subjects in the group (percentage).
[b] χ^2=62.10 for trend, $P<.001$.
[c] χ^2=42.10 for trend, $P<.001$.

use of approximately 5% across 40 geographically diverse acute care hospitals and no change in restraint rates between 1998 and 2005.[66-68] Moreover, currently, there are concerns about a potential resurgence of restraint use in acute care facilities attributable to nursing shortages, budgetary cutbacks, and decreased availability of alternatives such as sitters.

Previous studies have focused on outcomes related to persistent delirium.[3-9] Only 1 study to our knowledge has examined risk factors for delirium persistence[8] in patients with delirium entering a post–acute care setting. Thus, our study is unique, to our knowledge, in evaluating risk factors for persistence in patients with incident delirium and for separately examining risk factors for delirium onset and persistence.

In contrast to our a priori hypothesis, we did not discover different risk factors contributing to delirium that resolves vs persistent delirium. Baseline risk factors were qualitatively similar but differed in their magnitudes of association. Somewhat stronger relative risks were demonstrated for delirium that resolves than for persistent delirium. For hospital-related factors other than physical restraints, many factors were predictive of delirium that resolves but did not predict persistent delirium.

The analyses of the hospital-related factors presented many challenges, including differing exposure periods between delirium and nondelirium groups, multiple potential factors (eg, diagnoses or medications) that were too varied to examine individually, and limited power. Thus, important associations may have been overlooked. Moreover, the protective ORs demonstrated for some factors such as iatrogenic events raises the possibility that these factors, while precipitating delirium, might also heighten the recognition of delirium and thus lead to its treatment and diminished persistence. Future studies will be needed to confirm this possibility.

Strengths of this study include the frequent, systematic assessment for delirium using a validated instrument and the prospective collection of detailed risk-factor information. The validation of the predictive model in an independent cohort is another important strength. The 2 cohorts demonstrated significant differences in baseline characteristics and delirium rates; therefore, the finding that the predictive model works well in both cohorts lends support for its robustness and generalizability.[27] Finally, the demonstration of the predictive validity of the model for the clinically relevant outcome of death or nursing home placement is another noteworthy strength.

Several caveats deserve comment. The numbers of patients with delirium at discharge were relatively low, limiting our power to examine a large number of potential factors in our model. While the axis approach we chose is well accepted, we recognize that alternative approaches may have been used for variable reduction. In addition, methodologic constraints and small sample sizes limited our ability to examine many hospital-related factors. The differing at-risk periods across the study groups, which included the entire hospitalization period for the no delirium group, may have tended to bias the results against finding a significant association in hospital-related factors. The shift in the magnitude of the ORs between any delirium and persistent delirium is most likely due to measurement issues (such as the difficulty in matching the at-risk periods). Finally, despite the validation of our predictive model in 1 independent sample, future studies will be needed to verify its usefulness in other populations.

Identifying risk factors is the critical first step in developing effective preventive strategies. Four of the identified risk factors are amenable to intervention.[46] Persistent delirium in patients with dementia may respond to orientation procedures and therapeutic activities.[46] Vision impairment may be improved with adaptive devices, magnifying lenses, and improved lighting. Functional impairment may respond to exercise and mobility interventions. Avoidance of physical restraints in delirious patients may help to prevent persistence. Finally, the model identifies patients at intermediate to high risk for persistent delirium who would be appropriate candidates for intervention strategies. Given the high prevalence and poor outcomes of persistent delirium in the older population, this study paves the way for targeted intervention trials to address this important problem.

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