Original Article

Development and Validation of a Delirium Prediction Model for Elderly Patients (DEEP)

Ploylarp Lertvipapath MSc[1], Weerawadee Chandranipapongse MD[1], Suvimol Niyomnaitham MD, PhD[1], Pinpilai Jutasompakorn MD[1], Varalak Srinonprasert MD[2], Titima Wongviriyawong MD[2], Somruedee Chatsiricharoenkul MD[1]

[1] Department of Pharmacology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

[2] Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Background: Delirium is common among hospitalized elderly patients. It is associated with complications and mortality.

Objective: To develop and validate a predictive model for delirium among hospitalized elderly patients.

Materials and Methods: The present study was a single-center, retrospective cohort study performed in 589 patients aged 60 years or older admitted to medical or surgical units at a tertiary hospital in Bangkok, Thailand between 2011 and 2017.

Results: A sample was randomly split (70:30) into the derivation set (n=412; 120 with delirium) and validation set (n=177; 56 with delirium). In the derivation set, multiple logistic regression reveled six potential risk factors, which were older than 75 years, dementia, infection, liver cirrhosis, hypokalemia, and hyponatremia. Hosmer-Lemeshow goodness-of-fit test showed that the model had a good calibration (p=0.27). The model also had a good discrimination ability based on high area under receiver operating characteristic (AUROC) curve of 0.821 (95% CI 0.784 to 0.858). Regression coefficients were used to get a risk score which varied from 0 to 15. The optimal cutoff point of 4.5 or with a higher risk of delirium, gave a sensitivity of 65.8% (95% CI 56.6 to 74.2), a specificity of 82.2% (95% CI 77.3 to 86.4), a positive predictive value of 60.3% (95% CI 53.5 to 66.7), a negative predictive value of 85.4% (95% CI 82.0 to 88.3), and an accuracy of 77.4% (95% CI 73.1 to 81.4). The risk score was then applied to the derivation set resulting in a higher AUROC of 0.855 (95% CI 0.797 to 0.914).

Conclusion: The present study was a simple predictive model that demonstrated good discrimination ability, high specificity, and an excellent negative predictive value. It may permit the use of early preventive intervention to reduce the incidence, severity, and complications of delirium.

Keywords: Delirium; Elderly; Hypokalemia; Hyponatremia; Predictive model

Received 8 November 2021 | Revised 28 January 2022 | Accepted 28 January 2022

J Med Assoc Thai 2022;105(3):180-7

Website: http://www.jmatonline.com

Delirium is a neuropsychiatric syndrome characterized by an acute confusional state affecting attention, cognition, and perception. In elderly patients, the condition is common, serious, costly, under-recognized, and fatal[1,2]. The prevalence of delirium was reported to range from 10% to 31% at admission[3], and from 14% to 56% among elderly, hospitalized, medical patients, depending on the study population and institution[2,4,5]. Among the elderly, the highest rate was observed in intensive care units (19% to 82%)[6], with the incidence reported to be between 12% and 50% in surgical units[7] and 11% to 14% in general medical units[2]. In the United States, hospital stays associated with delirium involved over 2.3 million older people and more than $4 billion in Medicare expenditure[8].

Delirium is associated with complications such as prolonged hospitalization, increased 30-day readmission rate, and high hospitalization costs. These lead to adverse outcomes, such as disability and an elevated mortality rate[1,4]. The condition of delirium is caused by a variety of pathophysiological mechanisms. Evidence suggests that it results from a neurotransmitter imbalance or a dysfunction of the interactions between the cholinergic system and the immune system, involving acetylcholine, dopamine, 5-hydroxytryptamine, norepinephrine, glutamate, and gamma aminobutyric acid[9].

Correspondence to:

Chatsirharoenkul S.

Department of Pharmacology, Faculty of Medicine Siriraj Hospital, Bangkok Noi, Bangkok 10700, Thailand

Phone: +82-9-0990-5119

Email: somruedee.cha@mahidol.ac.th

How to cite this article:

Lertvipapath P, Chandranipapongse W, Niyomnaitham S, Jutasompakorn P, Srinonprasert V, Wongviriyawong T, et al. Development and Validation of a Delirium Prediction Model for Elderly Patients (DEEP). J Med Assoc Thai 2022;105:180-7.

DOI: 10.35755/jmedassocthai.2022.03.13274

The risk factors for delirium include a range of predisposing and pre-existing factors, as well as precipitating factors and acute conditions that directly induce delirium[1]. Moreover, the major risk factors for delirium differ between clinical settings, such as medical units, surgical units, and intensive care units. In hospital medical units, a systematic review and meta-analysis revealed that the most common factors significantly associated with delirium were dementia, old age, comorbid diseases, clinical disease severity, infection, high-risk medication use, urea and electrolyte imbalances, and malnutrition[10]. In surgical units, two additional risk factors were found, the duration of surgery[11] and the perioperative blood transfusion[12].

Delirium is often unrecognized by clinicians[13]. Early recognition may improve its outcomes. In other words, the use of an accurate predictive tool may assist with early detection, inform the level of monitoring, and enable the implementation of preventive measures to reduce the incidence and severity of delirium.

The delirium predictive models that have been published are only suitable for use with specific populations such as surgical or medical patients[14], thereby, limiting their generalizability. A further constraint is that, before they are used in Thailand, the models need to be translated from a foreign language to Thai. Those Thai versions then need to be checked for validity and reliability before being externally validated.

The authors aimed to identify the predictors associated with delirium and to develop a predictive tool for delirium for use with hospitalized elderly patients. The tool should be simple to use and permit delirium to be easily assessed upon admission. Furthermore, it should draw upon data obtained from admission interviews and commonly available hospital laboratory tests.

Materials and Methods

Study design

The present study was a retrospective cohort study undertaken at Siriraj Hospital, a large tertiary university hospital with approximately 2,000 beds, in Bangkok, Thailand. The sample was derived from three cohort studies conducted at the present study center. Two had been performed in medical units with one published work[15], plus one unpublished paper by Wongviriyawong et al, while the third, a published study[16] was conducted in surgical units.

The Institutional Review Board and Ethics Committee of the Faculty of Medicine Siriraj Hospital approved the present study (Si 195/2019). Its procedures adhered to the tenets of the Declaration of Helsinki.

Study population

The eligible participants were patients aged 60 years or older admitted to medical or surgical units. Patients diagnosed with alcohol withdrawal delirium were excluded because it had different pathophysiology from delirium. Moreover, the authors excluded patients with delirium upon admission.

Data collection and outcome assessments

The data had been collected within 24 hours of the admission of a patient to the medical or surgical unit. The delirium cases were confirmed by a geriatrician based on DSM-5 criteria. The time-to-delirium from data collection was under 72 hours. The candidate predictors for delirium consisted of gender, age, status of patients on mechanical ventilation, and systemic-related infections such as urinary tract infection (UTI), lower respiratory tract infection (LRI), cellulitis, sepsis, septic shock, and central nervous infection. For example, the UTI and LRI patients without sepsis will define as infection.

The underlying diseases or conditions included dementia, depression, stroke, hypertension, diabetes mellitus, heart failure, coronary artery disease, advanced cancer, brain cancer, lung cancer, anemia, liver cirrhosis, and chronic obstructive pulmonary disease.

The laboratory candidate risk factors were a BUN/Cr ratio indicating dehydration, chronic kidney disease (CKD) stages 3, 4, and 5[17], hyponatremia with sodium of less than 135 mmol/L, hypernatremia with sodium of more than 145 mmol/L, hypokalemia with potassium of less than 3.5 mmol/L, hypercalcemia with calcium of more than 10 mmol/L, hypoglycemia with glucose of less than 70 mg/dL, hyperglycemia with glucose of more than 126 mg/dL, hypoalbuminemia with albumin of less than 3.5 g/dL, and anemia with hematocrit of less than 30%.

In addition, the presence of polypharmacy, or the use of five or more drugs for one or more conditions before admission, or within one day of admission was regarded as a candidate predictor[18]. The authors also assessed the medications listed.

The primary outcome was the occurrence of incident delirium among hospitalized elderly patients.

Sample size calculation

The sample size required for the derivation

set was estimated by multiple logistic regression analysis, using a rule of thumb of 10 events per variable (EPV)[19]. Sixteen candidate dichotomous predictors associated with delirium were selected from the literature. Thus, 160 patients with delirium were needed. Since the incidence of delirium was about 40%[20], the total sample size for the model development was estimated at 400.

To get 400 patients in the derivation set, the pooled sample from the three cohort studies was randomly split into a derivation set and a validation set with a ratio of 70:30.

Statistical analysis

Data in the derivation set was used to fit the predictive model. All candidate predictors were dichotomized if they were continuous or polytomous variables. Univariable analysis of factors associated with delirium was based on chi-square test, Fisher's exact test and simple logistic regression. Crude odds ratios (ORs) and their 95% confidence intervals (CIs) were presented. Variables with univariable p-value of less than 0.2 were included in a multiple logistic regression analysis. Further consideration for variable selection was made from the literature to reduce the number of predictors. This restriction was intended to facilitate the development of a valid, easily administered, and practical predictive tool for use in a hospital setting. To achieve model parsimony, the backward elimination based on likelihood ratio test was applied. The factors significant in the model at p-value less than 0.5.

The model discrimination ability was assessed by the area under a receiver operating characteristics (AUROC) curve. Calibration was assessed using the Hosmer-Lemeshow goodness-of-fit test by deciles of fitted risk probabilities. The test examined the differences between the observed and expected frequencies of delirium. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated. A risk score was developed using regression coefficients of significant predictors in the predictive model.

The risk score was then applied to data in the validation set to test internal validity. The discrimination ability of the predictive model was reported based on AUROC. The sensitivity, specificity, PPV, and NPV at different cutoff points were also presented.

The statistical analyses were performed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA).

Results

There were 589 patients from three cohorts. Of those, 412 (70%) and 177 (30%) were randomly assigned to the derivation set and the validation set, respectively. The incidence of delirium was 29.1% (120/412) and 31.6% (56/177) for the derivation set and validation set, respectively.

The mean age ± standard deviation (SD) was 77±8 years and 77±10 years for the derivation set and the validation set, respectively. Table 1 details the characteristics of the patients including gender, age, underlying diseases, mechanical ventilation usage, systemic infection, medications, and laboratory findings of both the derivation set and the validation set. Systemic infections involved UTI, LRI, and sepsis. The present study did not find patients with septic shock on central nervous system (CNS) infection.

From the univariable analysis, 22 variables were associated with delirium (all $p<0.2$) (Table 2). Seven variables, including age older than 75 years, dementia, liver cirrhosis, systemic infection, hyponatremia, hypokalemia, and CKD stage 4, were then entered into multiple logistic regression analysis. Backward elimination based on likelihood ratio test resulted in only six predictors in the final model (all $p\leq0.05$) (Table 3). CKD stage 4 was excluded due to p-value of 0.172 (adjusted OR 1.45, 95% CI 0.85 to 2.47). Based on binary logistic regression, the probability of incident delirium occurring in adults aged 60 years or older was as follows:

Prob. (Delirium) = exp(Z) / (1 + exp (Z))

where Z = −2.48 + 0.467*hypokalemia + 0.727*(age older than 75 years) + 0.996*liver cirrhosis + 1.052*hyponatremia + 1.691*infection + 2.071*dementia

and each risk factor was coded as 0 for No and 1 for Yes.

To get the total risk score, each regression coefficient, except the constant, was first divided by the smallest coefficient (0.467) to make the smallest point of 1 and then rounded up (Table 3). The point of each predictor then varied from 1 to 4.5 adding to a total risk score of 0 to 15 as shown below. Higher total risk score indicated a higher probability of delirium.

Risk score = hypokalemia + 1.5*(age older than 75 years) + 2*liver cirrhosis + 2.5*hyponatremia + 3.5*infection + 4.5*dementia

Model performance

The AUROC in the derivation sample was 0.821 (95% CI 0.784 to 0.858). The calibration of the model

Table 1. Characteristics of patients in the model development and validation set

Variables	Model development: n (%)			Model validation: n (%)		
	Total (n=412)	Delirium		Total (n=177)	Delirium	
		No (n=292)	Yes (n=120)		No (n=121)	Yes (n=56)
Sex: female	232 (56.3)	161 (55.1)	71 (59.2)	110 (62.1)	72 (59.5)	38 (67.9)
Age >75 years	119 (28.9)	64 (21.9)	55 (45.8)	55 (31.1)	26 (21.5)	29 (51.8)
Underlying disease						
Dementia	32 (7.8)	9 (3.1)	23 (19.2)	10 (5.6)	2 (1.7)	8 (14.3)
Depression	22 (5.3)	8 (2.7)	14 (11.7)	9 (5.1)	2 (1.7)	7 (12.5)
Stroke	49 (11.9)	27 (9.2)	22 (18.3)	14 (7.9)	7 (5.8)	7 (12.5)
Hypertension	322 (78.2)	226 (77.4)	96 (80.0)	136 (76.8)	93 (76.9)	43 (76.8)
Diabetes mellitus	169 (41)	119 (40.8)	50 (41.7)	67 (37.9)	42 (34.7)	25 (44.6)
CAD	100 (24.3)	65 (22.3)	35 (29.2)	39 (22)	29 (24.0)	10 (17.9)
Heart failure	62 (15.0)	40 (13.7)	22 (18.3)	33 (18.6)	23 (19.0)	10 (17.9)
Advanced cancer	75 (18.2)	60 (20.5)	15 (12.5)	40 (22.6)	27 (22.3)	13 (23.2)
Liver cirrhosis	20 (4.9)	9 (3.1)	11 (9.2)	9 (5.1)	4 (3.3)	5 (8.9)
COPD	28 (6.8)	19 (6.5)	9 (7.5)	6 (3.4)	4 (3.3)	2 (3.6)
Status of patient						
Mechanical ventilator	28 (6.8)	6 (2.1)	22 (18.3)	15 (8.5)	6 (5.0)	9 (16.1)
Systemic infection	120 (29.1)	52 (17.8)	68 (56.7)	54 (30.5)	18 (14.9)	36 (64.3)
UTI	35 (8.5)	9 (3.1)	26 (21.7)	14 (7.9)	4 (3.3)	10 (17.9)
LRI	67 (16.3)	32 (11.0)	35 (29.2)	22 (12.4)	8 (6.6)	14 (25.0)
Sepsis	32 (7.8)	11 (3.8)	21 (17.5)	24 (13.6)	7 (5.8)	17 (30.4)
Medications						
Benzodiazepine	60 (14.6)	45 (15.4)	15 (12.5)	22 (12.4)	15 (12.4)	7 (12.5)
Opioids	39 (9.5)	24 (8.2)	15 (12.5)	11 (6.2)	7 (5.8)	4 (7.1)
Morphine	13 (3.2)	8 (2.7)	5 (4.2)	3 (1.7)	2 (1.7)	1 (1.8)
Tramadol	26 (6.3)	27 (9.2)	9 (7.5)	0 (0.0)	0 (0.0)	0 (0.0)
Anti-HT drug	137 (33.3)	96 (32.9)	41 (34.2)	55 (31.1)	38 (31.4)	17 (30.4)
Beta-blocker	89 (21.6)	63 (21.6)	26 (21.7)	44 (24.9)	31 (25.6)	13 (23.2)
DHP CCBs	66 (16.0)	50 (17.1)	16 (13.3)	16 (9.0)	12 (9.9)	4 (7.1)
Amlodipine	64 (15.5)	49 (16.8)	15 (12.5)	16 (9.0)	12 (9.9)	4 (7.1)
Anticholinergic	39 (9.5)	26 (8.9)	13 (10.8)	16 (9.0)	9 (7.4)	7 (12.5)
Antidepressant	8 (1.9)	5 (1.7)	3 (2.5)	4 (2.3)	4 (3.3)	0 (0.0)
Antipsychotic	14 (3.4)	10 (3.4)	4 (3.3)	9 (5.1)	3 (2.5)	6 (10.7)
Antiparkinson	7 (1.7)	3 (1.0)	4 (3.3)	1 (0.6)	1 (0.8)	0 (0.0)
Antidiabetic	50 (12.1)	39 (13.4)	11 (9.2)	18 (10.2)	11 (9.1)	7 (12.5)
Insulin	22 (5.3)	15 (5.1)	7 (5.8)	9 (5.1)	5 (4.1)	4 (7.1)
Sulfonylurea	30 (7.3)	25 (8.6)	5 (4.2)	11 (6.3)	8 (6.7)	3 (5.4)
Polypharmacy	285 (69.3)	202 (69.2)	83 (69.2)	114 (64.4)	76 (62.8)	38 (67.9)
Laboratory						
CKD < stage 3	209 (50.7)	153 (53.1)	56 (46.7)	93(52.5)	69 (57.0)	24 (42.9)
CKD stage 3*	129 (31.3)	93 (52.4)	36 (30.0)	51 (28.8)	37 (30.6)	14 (25.0)
CKD stage 4*	40 (9.7)	28 (31.8)	12 (10.0)	20 (11.3)	8 (6.6)	12 (21.4)
CKD stage 5*	30 (7.3)	14 (9.6)	16 (13.3)	13 (7.3)	7 (5.8)	6 (10.7)
BUN/Cr ratio >17	193 (46.8)	123 (42.1)	70 (58.3)	85 (48)	53 (43.8)	32 (57.1)
Hypoalbuminemia	131 (31.8)	79 (27.1)	52 (43.3)	59 (33.3)	31 (25.6)	28 (50.0)
Hyponatremia	81 (19.7)	38 (13.0)	43 (35.8)	46 (26)	21 (17.4)	25 (44.6)
Hypokalemia	75 (18.2)	43 (14.7)	32 (26.7)	27 (15.3)	13 (10.7)	14 (25.0)
Hypercalcemia	5 (1.2)	2 (0.7)	3 (2.5)	1 (0.6)	0 (0.0)	1 (1.8)
Hypoglycemia	10 (2.4)	5 (1.7)	5 (4.2)	6 (3.4)	2 (1.7)	4 (7.1)
Hyperglycemia	119 (28.9)	74 (25.3)	45 (37.5)	56 (31.6)	28 (23.1)	28 (50.0)
Anemia	111 (26.4)	69 (23.6)	42 (35)	49 (27.7)	24 (19.8)	25 (44.6)

CAD=coronary artery disease; COPD=chronic obstructive pulmonary disease; UTI=urinary tract infection; LRI=lower respiratory infection; Anti-HT drug= antihypertension drug; DHP CCBs=dihydropyridine calcium channel blockers; CKD=chronic kidney disease; BUN=blood urea nitrogen; Cr=creatinine

* CKD stage 3-5: the calculation of eGFR using the CKD-EPI formula

Table 2. Univariable analysis using logistic regression of delirium

Variable number	Variables	Simple logistic regression	
		p-value	OR (95% CI)
1	Age >75 years	0.001	2.12 (1.35 to 3.33)
2	Dementia	<0.001	7.46 (3.34 to 16.67)
3	Depression	0.001	4.69 (1.91 to 11.5)
4	Stroke	0.011	2.20 (1.2 to 4.05)
5	Coronary artery disease	0.138	1.44 (0.89 to 2.33)
6	Liver cirrhosis	0.009	3.16 (1.28 to 7.84)
7	Mechanical ventilation	<0.001	10.7 (4.22 to 27.16)
8.1	Infection	<0.001	6.04 (3.78 to 9.65)
8.2	Urinary tract infection	<0.001	8.7 (3.94 to 19.22)
8.3	Lower respiratory infection	<0.001	3.35 (1.95 to 5.7)
8.4	Sepsis	<0.001	5.42 (2.52 to 11.64)
9	Opioids	0.18	1.6 (0.81 to 3.16)
10	Antiparkinson	0.12	3.32 (0.73 to 15.07)
11	Sulfonylurea	0.125	0.46 (0.17 to 1.24)
12	BUN/Cr ratio >17	0.004	1.88 (1.22 to 2.9)
13.1	CKD stage 4	0.034	1.78 (1.04 to 3.04)
13.2	CKD stage 5	0.004	3.01 (1.42 to 6.39)
14	Hypoalbuminemia	0.002	2.27 (1.36 to 3.78)
15	Hyponatremia (Na <135 mmol/L)	<0.001	3.68 (2.22 to 6.1)
16	Hypokalemia (K <3.5 mmol/L)	0.006	2.06 (1.22 to 3.45)
17	Anemia (Hct <30 g/dL)	0.027	1.69 (1.06 to 2.68)

OR=odds ratio; CI=confidence interval; BUN=blood urea nitrogen; Cr=creatinine; CKD=chronic kidney disease

resulted in a p-value of 0.27, using the Hosmer-Lemeshow test.

The optimal cutoff point was a score of 4.5 for a substantial risk of delirium. It demonstrated performances for specificity (82.2%) and NPV (85.4%), and performances for sensitivity (65.8%), PPV (60.3%), and accuracy (77.4%) (Table 4).

Table 3. Development of DEEP model to predict delirium

Risk factors	Multiple logistic regression			DEEP model: score
	b	p-value	OR (95% CI)	
Age >75 years	0.727	0.001	2.07 (1.32 to 3.23)	1.5
Dementia	2.071	<0.001	7.94 (3.63 to 17.36)	4.5
Cirrhosis	0.996	0.031	2.71 (1.10 to 6.70)	2
Hyponatremia	1.052	<0.001	2.86 (1.79 to 4.59)	2.5
Infection	1.691	<0.001	5.43 (3.52 to 8.38)	3.5
Hypokalemia	0.467	0.049	1.60 (0.94 to 2.7)	1

OR=odds ratio; CI=confidence interval; DEEP=delirium prediction model for elderly patients

Nagelkerke R^2 (35.1%), overall percentage correct (78.5%)

Model internal validation

Applying risk score to data in the validation set revealed the AUROC of 0.855 (95% CI 0.797 to 0.914). This AUROC was slightly higher than the AUROC of the derivation sample (AUROC 0.821).

Table 5 shows the diagnostic performances of three cutoff points, 4, 4.5, and 5, in the validation set. The sensitivity and specificity for diagnosing delirium at the cutoff point of 4.5 were 69.6% and 87.6%, respectively. The PPV was 69.8%, while NPV was 87.5%.

Discussion

The authors developed a predictive model for the prediction of delirium among elderly patients admitted to medical or surgical units. The model was based on data obtainable from admission interviews and basic laboratory results.

The present study model was termed the "Development and validation of a Delirium prediction modEl for Elderly Patients (DEEP)". The authors

Table 4. Diagnostic performance of different cut-off scores in the derivation set

Cut point	Delirium (n=120)	No (n=292)	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%) (95% CI)	NPV (%) (95% CI)	Accuracy (%) (95% CI)
≥4	80	66	66.7 (57.5 to 75)	77.4 (72.2 to 82.1)	54.8 (48.6 to 60.8)	85 (81.3 to 88)	74.3 (69.8 to 78.4)
≥4.5	79	52	65.8 (56.6 to 74.2)	82.2 (77.3 to 86.4)	60.3 (53.5 to 66.7)	85.4 (82 to 88.3)	77.4 (73.1 to 81.4)
≥5	74	49	61.7 (52.3 to 70.4)	83.2 (78.4 to 87.3)	60.2 (53 to 66.9)	84.1 (80.7 to 87)	76.9 (72.6 to 80.9)

CI=confidence interval; PPV=positive predictive value; NPV=negative predictive value

Table 5. Validity of DEEP model in the model validation set

Cut point	Delirium (n=56)	No (n=121)	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%) (95% CI)	NPV (%) (95% CI)	Accuracy (%) (95% CI)
>4	41	21	73.2 (59.7 to 84.2)	82.6 (74.7 to 88.9)	63.4 (53.3 to 72.6)	88.2 (82.9 to 92.1)	79.9 (73.2 to 85.5)
>4.5	39	15	69.6 (55.9 to 81.2)	87.6 (80.4 to 92.9)	69.8 (58.2 to 79.3)	87.5 (82.4 to 91.3)	82.4 (75.9 to 87.7)
>5	37	14	66.1 (52.2 to 78.2)	88.4 (81.4 to 93.5)	70.1 (58.1 to 79.9)	86.4 (81.4 to 90.2)	81.9 (75.4 to 87.3)

CI=confidence interval; PPV=positive predictive value; NPV=negative predictive value

selected seven candidate predictive variables that had been reported in the literature as having a strong association with delirium. The authors aimed to develop a predictive tool that could rapidly and easily assess delirium upon admission, based on the admission interview and standard blood chemistry findings. The seven candidate predictors were an age older than 75 years, dementia, infection, CKD stage 4, hyponatremia, hypokalemia, and liver cirrhosis.

Furthermore, urinary tract infection, lower respiratory tract infection, sepsis, and CNS infection were combined and recorded as an infection binary categorical variable. There were no patients with septic shock or CNS infection, which are conditions that distinctively cause encephalopathy by themselves.

On the other hand, the events with a low incidence in the derivation sample were not selected. They were stroke, coronary artery disease, malignancy, mechanical ventilation, opioids, anti-Parkinson, sulfonylurea, and hypoalbuminemia. A further reduction in parsimony removed CKD 4, which left the final version of DEEP with six predictors. Each is readily available at admission.

Using the six predictors, the model demonstrated utility and a reasonable predictive value for delirium in patients admitted to a medical or surgical unit. DEEP also confirms the predictive values of factors used in other delirium predictive models reported in the literature such as an age older than 75 years, dementia, infection, and hyponatremia. Conversely, neither hypokalemia nor liver cirrhosis have been previously reported. In the present study, the authors collected data on electrolytes within 24 hours of admission to compare the patients' electrolyte.

DEEP demonstrated good discrimination capacity, which did not diminish upon internal validation. It also exhibited an acceptable calibration, as assessed by the Hosmer-Lemeshow goodness-of-fit test.

The present study findings showed the cutoff point of DEEP at 4.5 had high specificity and high negative predictive value. However, that cutoff point also had moderate sensitivity and moderate positive predictive value. The goal of predictive model is to triage patients upon admission as having a high or low risk of delirium, thereby enabling swift implementation of prevention strategies for high-risk cases. Thus, a high specificity is desirable to avoid incurring unnecessary expenditure on patients at low risk. DEEP has the greatest value in this regard if the result was less than 4.5 points, as evidenced by the high negative predictive values with the derivation and validation samples in the present study. Recent evidence suggests that multicomponent interventions should be utilized to prevent delirium, and that the use of a predictive model as one of those interventions would be cost-effective.

The present study also compared DEEP with other predictive models. One of those was DEMO (DElirium MOdel)[21], whose variables are age and medications. Although both DEEP and DEMO can easily assess delirium, the AUROC for the DEEP derivation sample showed a higher discrimination capacity than that for the DEMO derivation sample. Another delirium prediction model, Delphi (DELirium Prediction based on Hospital Information)[22], has a higher discrimination capacity than DEEP. Nonetheless, the Delphi score was designed specifically for surgical patients. As to DRAS (delirium risk assessment score)[23], it uses similar variables to DEEP, and both tools can be easily applied to medical and surgical patients. A key difference between the two models is that the AUROC for DEEP was higher than that for DRAS.

The present study has important strengths. Firstly, DEEP was developed from three prospective cohort studies set in the medical and surgical units of the same university hospital medical school. Thus, there was a heterogeneous patient population. In addition, DEEP is simple to use, and because it is based on data obtained from admission interviews and blood chemistry results, it provides assessments within hours of admission. Moreover, as the variables in DEEP are normally screened as part of general medical care, the model does not require additional testing or healthcare-personnel resources. In other words, there are no impediments to the early implementation of preventive interventions for delirium. Finally, the simplicity of DEEP allows delirium to be easily assessed by the members of a multidisciplinary hospital team such as physicians, nurses, and pharmacists. This is a major difference from the other predictive models, which require specially trained physicians or nurses.

The current study has limitations. Firstly, a medical chart review method was used to collect the data used to develop the model. However, medical chart reviews have previously been shown to be valid by geriatricians. Moreover, the development and internal validation of DEEP were performed at only one tertiary center. As DEEP has not yet been externally validated elsewhere, its generalizability is limited. The authors found that dementia occurred in only 7% among 390 patients without depression

compared to 23% in 22 patients with depression (Fisher's exact, p=0.021). Therefore, for multivariable analysis with binary logistic regression, either depression or dementia should be one of candidate risk factors.

Finally, the previous history of delirium should be a strong predictor of further delirium. In the future, the authors will study whether previous delirium is strongly predictive of further delirium and develop another predictive model for general geriatric population.

Moreover, DEEP should be used in clinical practice to identify its reliability and to improve the risk factors, and hence the precision of the delirium prediction model.

Conclusion

DEEP performed well in predicting delirium among hospitalized elderly patients in medical and surgical units. The authors identified novel predictors of delirium in the elderly, which were hyponatremia, hypokalemia, and liver cirrhosis. Future studies are required to externally validate DEEP prior to its use in other settings and its application in clinical practice.

What is already known on this topic?

DEEP model is a delirium predictive model in hospitalized elderly patients. The advantage of DEEP model can apply in medical or surgical patients and in different region of the country. DEEP model is simple to use in hospital. Moreover, DEEP model can assess delirium within hours of admission.

What this study adds?

The new delirium predictive model supported the simple variables that are screened in medical care and easily assessed by a multidisciplinary hospital team, which does not require specially trained physicians or nurses.

Acknowledgements

The authors gratefully acknowledge Assistant Professor Dr. Chulaluk Komoltri, DrPH, Research Department, Faculty of Medicine Siriraj Hospital Mahidol University for her assistance with statistical analysis.

Funding disclosure

This research project was supported by the Siriraj Research Fund (grant number [IO] R016231029) and a Chalermphrakiat Grant from the Faculty of Medicine Siriraj Hospital, Mahidol University.

Conflicts of interest

The authors have no conflicts of interest to declare that are relevant to the content of this article.

References

1. Inouye SK. Predisposing and precipitating factors for delirium in hospitalized older patients. Dement Geriatr Cogn Disord 1999;10:393-400.
2. Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. Lancet 2014;383:911-22.
3. Ahmed S, Leurent B, Sampson EL. Risk factors for incident delirium among older people in acute hospital medical units: a systematic review and meta-analysis. Age Ageing 2014;43:326-33.
4. Korevaar JC, van Munster BC, de Rooij SE. Risk factors for delirium in acutely admitted elderly patients: a prospective cohort study. BMC Geriatr 2005;5:6.
5. Khurana V, Gambhir IS, Kishore D. Evaluation of delirium in elderly: a hospital-based study. Geriatr Gerontol Int 2011;11:467-73.
6. McNicoll L, Pisani MA, Zhang Y, Ely EW, Siegel MD, Inouye SK. Delirium in the intensive care unit: occurrence and clinical course in older patients. J Am Geriatr Soc 2003;51:591-8.
7. Chaiwat O, Chanidnuan M, Pancharoen W, Vijitmala K, Danpornprasert P, Toadithep P, et al. Postoperative delirium in critically ill surgical patients: incidence, risk factors, and predictive scores. BMC Anesthesiol 2019;19:39.
8. Agnoletti V, Ansaloni L, Catena F, Chattat R, De Cataldis A, Di Nino G, et al. Postoperative delirium after elective and emergency surgery: analysis and checking of risk factors. A study protocol. BMC Surg 2005;5:12.
9. Hshieh TT, Fong TG, Marcantonio ER, Inouye SK. Cholinergic deficiency hypothesis in delirium: a synthesis of current evidence. J Gerontol A Biol Sci Med Sci 2008;63:764-72.
10. Kim H, Chung S, Joo YH, Lee JS. The major risk factors for delirium in a clinical setting. Neuropsychiatr Dis Treat 2016;12:1787-93.
11. Guo Y, Jia P, Zhang J, Wang X, Jiang H, Jiang W. Prevalence and risk factors of postoperative delirium in elderly hip fracture patients. J Int Med Res 2016;44:317-27.
12. Trabold B, Metterlein T. Postoperative delirium: risk factors, prevention, and treatment. J Cardiothorac Vasc Anesth 2014;28:1352-60.
13. Ruangratsamee S, Assanasen J, Praditsuwan R, Srinonprasert V. Unrecognized delirium is prevalent among older patients admitted to general medical wards and lead to higher mortality rate. J Med Assoc Thai 2016;99:904-12.
14. Jenkins DA, Sperrin M, Martin GP, Peek N. Dynamic models to predict health outcomes: current status and methodological challenges. Diagn Progn Res

2018;2:23.
15. Srinonprasert V, Pakdeewongse S, Assanasen J, Eiamjinnasuwat W, Sirisuwat A, Limmathuroskul D, et al. Risk factors for developing delirium in older patients admitted to general medical wards. J Med Assoc Thai 2011;94 Suppl 1:S99-104.
16. Wongviriyawong T, Sura-Arunsumrit P, Chaiwat O, To-Adithep P, Ramlee R, Srinonprasert V. Diagnosis of postoperative delirium in older adults using the Confusion Assessment Method for the intensive care unit in non-intensive care unit settings: A test modification might improve its diagnostic performance. Geriatr Gerontol Int 2019;19:762-7.
17. Siew ED, Fissell WH, Tripp CM, Blume JD, Wilson MD, Clark AJ, et al. Acute kidney injury as a risk factor for delirium and coma during critical illness. Am J Respir Crit Care Med 2017;195:1597-607.
18. Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. BMC Geriatr 2017;17:230.
19. Hair J, Anderson R, Tatham R, Black W. Multivariate data analysis. 5th ed. New Jersey: Prentice Hall; 1998.
20. Fong TG, Tulebaev SR, Inouye SK. Delirium in elderly adults: diagnosis, prevention and treatment. Nat Rev Neurol 2009;5:210-20.
21. Mestres Gonzalvo C, de Wit H, van Oijen BPC, Deben DS, Hurkens K, Mulder WJ, et al. Validation of an automated delirium prediction model (DElirium MOdel (DEMO)): an observational study. BMJ Open 2017;7:e016654.
22. Kim MY, Park UJ, Kim HT, Cho WH. DELirium prediction based on hospital information (Delphi) in general surgery patients. Medicine (Baltimore) 2016;95:e3072.
23. Vreeswijk R, Kalisvaart I, Maier AB, Kalisvaart KJ. Development and validation of the delirium risk assessment score (DRAS). Eur Geriatr Med 2020;11:307-14.