Risk Factors for Developing Delirium in Older Patients Admitted to General Medical Wards

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Background: *Delirium in older patients is common and leads to poor clinical outcomes. It is, however, preventable if its risk factors are identified and modified accordingly.*
Objective: *To determine risk factors associated with delirium in hospitalized older patients admitted to general medical wards at Siriraj Hospital.*
Material and Method: *A prospective observational study was conducted at general medical wards, Siriraj Hospital. All consecutive patients aged 70 years or older admitted during study period were assessed and followed until discharge. A diagnosis of delirium was made if patients developed symptoms which fulfilled DSM IV criteria. Information regarding demographic data, co-morbid illnesses, preexisting cognitive status and functional status was collected at admission. Factors associated with delirium were analyzed using logistic regression models.*
Results: *Risk factors associated with developing delirium identified from univariate analysis were female gender, age more than 80 years-old, having 4 or more co-morbidities, azothemia, hyponatremia, presence of infection, severe illness, preexisting dementia, depression, and impaired basic activities of daily living. After adjusted in multivariate analysis; factors those remained statistically significant were preexisting dementia (OR = 5.52, 95% CI = 2.51-12.14), severe illness (OR = 5.18, 95% CI = 2.10-12.76) presence of infection (OR = 2.54, 95% CI = 1.15-5.61) and azothemia (OR = 2.55, 95% CI = 1.20-5.40).*
Conclusion: *Pre-existing dementia and illness severity were strongly associated with developing delirium in older patients in the present study, which is concordant with previous studies. Other factors such as presence of infection and azothemia are modifiable factors that could potentially be important targets, along with other factors identified in the present study, for implementing intervention in order to prevent delirium in this population.*

Keywords: *Delirium, Older patients, Hospitalized, Risk factor*

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Delirium, a clinical syndrome characterized by acute cognitive decline and attention deficit, is a common condition in older people. It usually is caused by multiple medical insults or environmental factors. Occurrence of delirium varies depending upon clinical context and has been reported from 11 to 42% among medical in-patients[1]. Delirium could be a presenting symptom for various serious medical illnesses in older patients and leads to several adverse clinical consequences. Increased in-hospital complications, greater length of hospital stay and higher in-hospital mortality have been shown among hospitalized delirious older patients[1,2]. Moreover, long term complications from delirium, such as persistent cognitive impairment, functional decline and increased post-discharge mortality and institutionalization, are also evident[3-6].

Considering catastrophic sequelae of delirium without promising effective treatment strategy at present, it has been suggested that prevention is the best approach to reduce the occurrence of delirium and its complications in hospitalized older people[2,7]. Successful models for preventing delirium usually stem from identifying risk factors in a particular clinical setting and modify those factors accordingly[8,9].

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Thailand has become an aging society where older patients comprises the majority of hospital admissions and spend significant funds on health care[10]. Delirium will be a growing problem for the health care system in addition to being a frustrating condition for the family. Identifying risk factors for delirium in Thai context is an initial step to be taken in order to create effective preventive strategies for this setting.

The present study, therefore, aims to determine risk factors associated with delirium in hospitalized older patients admitted to general medical wards at Siriraj Hospital, a university hospital in Thailand.

Material and Method

A prospective observational study was conducted at Department of Medicine, Siriraj Hospital, Thailand. All consecutive patients age 70 and older admitted to general medical wards were eligible for the study. Exclusion criteria included patients who were endotracheal intubated at admission, aphasia, comatose or in-cooperative for test administration. All eligible subjects were assessed according to study criteria within 24 hours of admission. Included patients were subsequently followed every 48 hours for eliciting symptoms of delirium until developing delirium or discharge. A diagnosis of delirium was made by geriatricians according to DSM IV criteria[11]. Three geriatricians in the study had excellent agreement for diagnosis delirium with Kappa of 0.88-1.0 (result from pilot study). Initial assessment included a patient interview, a proxy interview and a review of medical record. The patient interview included cognitive assessment using Thai Mental State Examination(a cognitive screening tool assessing six cognitive domains with a total possible score of 30 where the lower scores indicates more impairment)[12]. The rating for illness severity[13] was performed by geriatricians during the first assessment. This rating score was a 9-point ordinal scale rated according to physician's clinical judgment of patients' overall condition. This was performed by having physician's respond to question of 'how sick is the patient now'. The higher score indicates the more severe the patient is. Illness severity was further classified into severe illness for a score of 7 or more. Inter-rater reliability for rating illness severity from this study was high as demonstrated by intraclass correlation of 0.93 (95% CI 0.84-0.97) (result from pilot study). The proxy interview included an assessment of patient's dementia status using Modified IQCODE[14] and assessments of premorbid activity of daily living (ADL), both basic ADL[15]and instrumental ADL[16]. Information regarding demographic data, co-morbid illnesses and functional status was also collected from patient, proxy and medical record. Laboratory results, reasons for admissions were collected at admission while presence of infection was prospectively collect during the admission (prior to delirium, if it occurred). Azothemia was defined when BUN/Cr ratio was more than 20. Dementia was ascertained when patients demonstrate score less than 3.42 on Modified IQ code or preexisting diagnosis. Depression was defined according to depression screening items or preexisting diagnosis. Decreased in ability to perform any of ADLs was classified as impaired ADL. Polypharmacy defined by number of medications taken of 5 or more. Informed consents were obtained from both patient and the proxy. This study was approved by Siriraj Institutional Review Board.

Statistical analysis

Logistic regression models were performed in order to obtain unadjusted and adjusted odd ratios with 95% CI for factors associated with developing delirium. Covariates that were associated ($p < 0.1$) with delirium in univariate analysis were further explored in multivariate logistic model. All statistical analyses were performed using SPSS version 17.0. All reported p-values are two-sided.

Results

Two hundred and twenty five patients were included in the study with mean age of 78 (range 70-97). Around half of them had more than 4 co-morbid illnesses with number of medications taken more than 6 per day. Forty two percent of study population was demented while 60% had impaired basic ADL. Approximately 30 % of patients were rated as having severe illness at the time of admission.

One hundred and ten patients (48.9%) developed delirium during admission, of which 91 (40.4%) of them had delirium at admission. Table 1 showed baseline characteristics of the study population.

Factors associated with developing delirium were shown in Table 2. Female, age more than 80, having four or more co-morbid illnesses, azothemia, hyponatremia, presence of infection, severe illness, dementia, depression and impaired BADLs were associated with delirium in univariate analysis. After adjusted for other covariates, age, gender, number of co-morbid diseases, depression and impaired BADL

Table 1. Baseline characteristic of included population (n = 225)

Characteristic	Total (n = 225)	Not-Delirium (115)	Delirium (110)
Female	111 (49.3)	47 (40.9%)	64 (58.2%)*
Age > 80 yo	68 (30.2%)	25 (21.7%)	43 (39.1%)*
Have 4 or more co-morbid illnesses	109 (48.4%)	47 (40.9%)	62 (56.4%)*
Underlying disease			
DM	92 (40.9%)	47 (49.0%)	45 (40.9%)
HT	151 (67.1%)	74 (64.3%)	77 (70.0%)
Heart failure	24 (10.7%)	12 (10.4%)	12 (10.9%)
COPD	114 (6.2%)	8 (7.0%)	6 (5.5%)
Malignancy	56 (24.9%)	27 (23.5%)	29 (26.4%)
Stroke	26 (11.6%)	10 (8.7%)	16 (14.5%)
Anemia (Hct <30%)	90 (40.0%)	43 (37.4%)	47 (42.7%)
Azothemia	108 (48.2%)	40 (35.1%)	68 (61.8%)*
Hyponatremia		76 (34.1%)	30 (26.5%)
46(41.8%)*			
Presence of infection	94 (42.0%)	30 (26.1%)	64 (58.7%)*
Visual impairment (n = 161)	137 (85.1%)	79 (82.3%)	58 (89.2%)
Hearing impairment (n = 183)	10 (5.5%)	3 (2.9%)	7 (8.9%)
Polypharmacy(n=217)	143 (63.6%)	73 (65.2%)	70 (66.7%)
Benzodiazepine use	32 (14.7%)	19 (17.0%)	13 (12.4%)
Antipsychotic use	19 (8.8%)	4 (3.6%)	15 (14.3%)
Impaired BADL	115 (59.6%)	52 (51.0%)	63 (69.2%)*
Impaired IADL	173 (89.6%)	88 (86.3%)	85 (93.4%)
Dementia	94 (41.8%)	26 (22.6%)	68 (61.8%)*
Depression	26 (12.4%)	9 (8.1%)	17 (17.3%)*
Lack of education	38 (16.9%)	17 (15.5%)	21 (20.8%)
Illness severity			
Mild	26 (11.7%)	22 (19.5%)	4 (3.7%)
Moderate	129 (58.1%)	79 (69.9%)	50 (45.9%)
Severe	67 (29.8%)	12 (10.6%)	55 (40.5%)*

*factors significantly different between delirium and non-delirium groups, $p < 0.05$

Table 2. Results from logistic regression for factors associated with delirium

Variable	Univariate analysis (OR)	Multivariate analysis (Adjusted OR)
Female	2.01 (1.18-3.42)	1.59 (0.74-3.45)
Age more than 80	2.31 (1.29-4.15)	2.15 (0.93-4.96)
Four or more co-morbid	1.87 (1.10-3.17)	1.16 (0.52-2.59)
Azothemia	3.00 (1.74-5.16)	2.55 (1.20-5.40)
Hyponatremia	1.99 (1.13-3.50)	1.63 (0.74-3.56)
Presence of infection	4.03 (2.29-7.09)	2.54 (1.15-5.61)
Severe illness	8.57 (4.23-17.38)	5.18 (2.10-12.76)
Dementia	5.54 (3.10-9.92)	5.52 (2.51-12.14)
Depression	2.38 (1.01-5.62)	1.93 (0.58-6.44)
Impaired BADLs	2.16 (1.20-3.91)	0.69 (0.30-1.59)

showed weaker associations with delirium. Factors those remained significant in multiple logistic regression analysis were preexisting dementia (OR = 5.52,95% CI = 2.51-12.14), severe illness (OR = 5.18, 95% CI = 2.10-

12.76) presence of infection (OR = 2.54, 95% CI = 1.15-5.61) and azothemia (OR = 2.55, 95% CI = 1.20-5.40).

Discussion

The present study identified 4 factors, after adjusted for other covariates, to be associated with developing delirium in older medical in-patients. Dementia, an important risk factor consistently demonstrated in previous studies[17,18] showed the strongest association with delirium in the present study. It has been shown that delirium and dementia shared some features such as decreased cerebral blood flow or cerebral metabolism, cholinergic deficiency and inflammation which might explain the close interrelationship between them[2]. It has also be proposed that delirium and dementia might be a continuum of the cognitive dysfunction[7]. Nevertheless, delirium could be prevented with cognitive enhancement interventions. This has been established among medical in-patient for which demented patients also included[8]. Those interventions would be an interesting area to be studied in the present clinical context with a high proportion of demented patients and high prevalence of delirium.

Severe illness rated by physicians is another important risk factor in the present study. Severe illness has also been identified previously[17,19] and ranked as second most strong risk factor for developing delirium, with a combined OR of 3.8 in a systematic review[18]. Illness severity utilized in the present study has previous been shown to be a reliable predictor for mortality[13] and was rated solely on clinical judgment. It could provide clinician a warning guide for identifying high risk patients who require immediate attention and appropriate interventions.

Association between azothemia and delirium has been reproduced in many studies included in a systematic review[18]. Presence of infection has also been identified as a leading etiology for delirium[7,20]. These two factors are commonly found in older patients, more than 40% of included patients in the present study. They could be important targets for interventions to be implemented, potentially early and more aggressive than conventional fashion. It would be interesting to learn whether an early intervention for these modifiable risk factors would prevent delirium and subsequence adverse outcomes.

Other risk factors identified from univariate analysis also risk factors addressed in previous studies[18]. Although the associations were weaken in the present study, those risk factors remain to be important targets when interventions for preventing delirium are considered. Further study should be conducted using risk factors identified from the present study to create a model for delirium prevention in medical older patients.

The present study was conducted in a university hospital serves as a tertiary center for sicker patients compared to other parts of the country. The generalizibility of the result to other settings where patients are less severe could not be ascertained. Nevertheless, providing that risk factors identified in the present study are in concordant with previous studies conducted in other clinical settings with lower prevalence of delirium and less severely ill patients, the issue of generalizibility might not therefore be a major concern for the present study.

Potential conflicts of interest

None.

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ปัจจัยเสี่ยงต่อการเกิดภาวะสับสนเฉียบพลันในผู้ป่วยสูงอายุที่เข้ารับการรักษาในหอผู้ป่วยอายุรศาสตร์สามัญ

วราลักษณ์ ศรีนนท์ประเสริฐ, สรภพ ภักดีวงศ์, จินตนา อาศนะเสน, วริชา เอี่ยมจิณณสุวัฒน์, อัจฉรา ศิริสุวัฒน์, ดวงสว่าง ลิ้มมธุรสกุล, รุ่งนิรันดร์ ประดิษฐสุวรรณ

ภูมิหลัง: *ภาวะสับสนเฉียบพลัน (delirium) ในผู้สูงอายุเป็นภาวะที่พบได้บ่อยและนำไปสู่ผลลัพธ์ของการรักษาที่ไม่ดี อย่างไรก็ตามภาวะนี้สามารถป้องกันได้ถ้าสามารถค้นหาปัจจัยเสี่ยงที่เกี่ยวข้องและให้การแก้ไขอย่างเหมาะสม*

วัตถุประสงค์: *เพื่อศึกษาปัจจัยเสี่ยงที่มีความสัมพันธ์กับการเกิดภาวะสับสนเฉียบพลันในผู้สูงอายุที่เข้ารับการรักษาเป็นผู้ป่วยในหอผู้ป่วยอายุรศาสตร์ที่โรงพยาบาลศิริราช*

วัสดุและวิธีการ: *ผู้นิพนธ์ได้ทำการศึกษาแบบเก็บข้อมูลไปข้างหน้าในหอผู้ป่วยอายุรศาสตร์ทั่วไป โรงพยาบาลศิริราช โดยผู้ป่วยทุกคนที่มีอายุตั้งแต่ 70 ปีขึ้นไปที่เข้ารับการรักษาเป็นผู้ป่วยใน ในช่วงเวลาที่ศึกษาจะได้รับการประเมินอาการและติดตามจนกว่าจะออกจากโรงพยาบาล การวินิจฉัยภาวะสับสนเฉียบพลัน เป็นไปตามเกณฑ์ตาม DSM IV ข้อมูลพื้นฐานต่าง ๆ ของผู้ป่วย, ข้อมูลโรคประจำตัวของผู้ป่วย ความจำ และความสามารถในการช่วยเหลือตนเอง (functional status) มีการรวบรวมตั้งแต่ตอนเริ่มเข้านอนโรงพยาบาล การวิเคราะห์ข้อมูลเพื่อหาปัจจัยเสี่ยงที่มีความเกี่ยวข้องกับภาวะสับสนเฉียบพลัน ทำโดยการใช้ logistic regression model*

ผลการศึกษา: *ปัจจัยเสี่ยงที่สัมพันธ์กับการเกิดภาวะสับสนเฉียบพลันจาก univariate analysis ได้แก่ เพศหญิง, อายุที่มากกว่า 80 ปี, มีโรคร่วมตั้งแต่ 4 ชนิดขึ้นไป, ภาวะ azotemia, ภาวะโซเดียมในเลือดต่ำ (hyponatremia), การมีภาวะติดเชื้อในร่างกาย,ภาวะการเจ็บป่วยรุนแรง (severe illness), การมีภาวะสมองเสื่อม(preexisting dementia), ภาวะซึมเศร้า และความสามารถในการช่วยเหลือตัวเองลดลง และเมื่อนำปัจจัยดังกล่าวข้างต้นมาวิเคราะห์ต่อใน multivariate analysis พบว่าปัจจัยเสี่ยงที่ยังคงมีนัยสำคัญทางสถิติได้แก่ ภาวะสมองเสื่อม (OR = 5.52, 95% CI = 2.51-12.14), ภาวะการเจ็บป่วยรุนแรง (OR = 5.18, 95% CI = 2.10-12.76) การมีภาวะติดเชื้อในร่างกาย (OR = 2.54, 95% CI = 1.15-5.61) และภาวะ azothemia (OR = 2.55, 95% CI = 1.20-5.40)*

สรุป: *ภาวะสมองเสื่อมและการเจ็บป่วยรุนแรง เป็นปัจจัยที่มีความสัมพันธ์อย่างสูง กับการเกิดภาวะสับสนเฉียบพลันในผู้สูงอายุในการศึกษานี้ ซึ่งสอดคล้องไปกับการศึกษาที่มาก่อนหน้า ปัจจัยอื่นอันได้แก่ การมีภาวะติดเชื้อในร่างกายและภาวะ azothemia อันเป็นปัจจัยที่สามารถให้การแก้ไขได้ อาจเป็นเป้าหมายสำคัญที่ควรนำมาพิจารณาร่วมกับปัจจัยอื่น ๆ ที่ได้จากการศึกษาเพื่อให้การป้องกันการเกิดภาวะสับสนเฉียบพลันในประชากรกลุ่มนี้ต่อไป*