Original Article

Delirium in Internal Medicine Patients Evaluated Using the Thai Confusion Assessment Method for ICU

Methawasin K, MD, MSc[1], Kongsakorn P, MD[1], Kongsakorn N, MD[1], Chonmaitree P, MD[1], Roongsangmanoon W, MD[1], Sangpanich A, MD[1], Lee B, MD[1], Ruchakorn N, MD[1], Charonpongsuntorn C, MD[1], Petborom P, MD[1]

Delirium and fall prevention group of residential medicine

[1] Department of Medicine, Srinakharinwirot University, Ongkharak Campus, Nakhon Nayok, Thailand

Background: Delirium is the condition of an acute confusional state that disturbs both alertness and cognition. The problem is likely to happen with general internal medicine patients admitted in general wards.

Objective: To identify delirium cases in the internal medicine In-Patient Department (IPD) by using the Thai Confusion Assessment Method for intensive care unit (CAM-ICU).

Materials and Methods: The cross-sectional study was conducted between February and December 2018. The Thai version of the CAM-ICU was used as the evaluation form to detect delirium. The patients admitted to the IPD of internal medicine were freely randomized to be volunteers. Demographic data, systemic illnesses, neurology diseases, and current medications were recorded.

Results: Three hundred fifty-six patients, 175 males (49.2%) and 181 females (50.8%), were included in the present study. The mean age was 61.52 years old. The development of acute confusion was significant in patients 50 years old and older ($p<0.001$). Multivariate analysis indicated the significant effect of substance abuse ($p<0.05$), chronic kidney disease ($p<0.05$), cerebrovascular disease ($p<0.05$), benzodiazepine usage ($p<0.05$), alcohol abuse ($p<0.05$), and age 50 years or older ($p<0.001$). Sixty-nine cases met the Thai CAM-ICU criteria for delirium of CAM-ICU, but the interns did not notice this problem ($p<0.001$).

Conclusion: Chronic kidney disease, cerebrovascular disease, substance abuse, benzodiazepine use, alcohol abuse, and age 50 years or older are the factors associated with delirium in the present study. Hypoactive delirium is underdiagnosed by doctors but revealed by using CAM-ICU.

Keywords: Delirium, CAM-ICU, Hypoactive delirium, RASS

Received 14 Jan 2020 | Revised 8 Apr 2020 | Accepted 15 Apr 2020

J Med Assoc Thai 2020;103(7):626-31
Website: http://www.jmatonline.com

Delirium is an acute neurocognitive disorder, which is diagnosed according to guidelines published in the Diagnostic Statistical Manual of Mental Disorders, fifth edition (DSM-V). Clinical manifestations of delirium include disturbances in attention and awareness, the fluctuation of symptoms during the day, and cognitive impairment. To be diagnosed with delirium, patients must not be in a comatose state, have established neurocognitive disorders, have a history of cognitive disorders, or have physical examinations that reveal medical conditions. Toxin exposure, substance abuse, and conditions that include etiologies associated with acute confusion are also excluded from delirium diagnoses. The recent prevalence of delirium in adults and aging patients from Europe and America ranges from 20% to 27%[1,2]. Delirium can result in prolonged hospital stays, increased risks of injury to patients and caregivers, and other complications. However, one systematic review based on the emergency care setting demonstrated poor recognition of this condition among medical workers[3]. Thus, the development of frameworks or algorithms that can promote the recognition of delirium has been recommended[4]. Such a framework

Correspondence to:

Methawasin K.

Division of Neurology, Department of Medicine, Srinakharinwirot University, Ongkharak campus, Nakhon Nayok 26120, Thailand.

Phone: +66-86-8945538, **Fax**: +66-37-395085 ext. 11003

Email: kmmdsresearch@gmail.com

How to cite this article:

Methawasin K, Kongsakorn P, Kongsakorn N, Chonmaitree P, Roongsangmanoon W, Sangpanich A, et al. Delirium in Internal Medicine Patients Evaluated Using the Thai Confusion Assessment Method for ICU. J Med Assoc Thai 2020;103:626-31.

doi.org/10.35755/jmedassocthai.2020.07.11009

should include a multidisciplinary approach that integrates interprofessional communications, patient safety protocols and policies, the implementation of screening tools, and the identification of points of treatment.

In Thailand, the prevalence of delirium in Thai aged patients at admission was 40.4%, while an incidence of delirium during hospital stay was 8.4%. Experienced geriatricians made the diagnosis of delirium in this previous report with using of DSM-IV criteria[5]. However, in Thai general hospitals, internal medicine In-Patient Departments (IPDs) are overcrowded with patients of various severity of illnesses. The workload of medical persons can be a challenging issue for accreditation. A lack of close observation likely leads to the under-recognition of delirium in general medicine wards compared with intensive care units (ICUs), where each nursing unit is responsible to only one patient. The test, which is easy to use and takes minimal time may have the benefit of encouraging more detection of delirium in this situation. The present study aimed to examine the occurrence of delirium in general medicine wards and to identify any factors associated with delirium by using the Thai Confusion Assessment Method-ICU (CAM-ICU). The authors also aimed to disclose an occurrence of missed delirium diagnoses by internal medicine residents. All data from the present study will be used for an educational initiative to create an algorithm designed to promote delirium recognition and care.

Materials and Methods

Settings

The present study was a cross-sectional study conducted between February and December 2018, after receiving an authorized letter of Research with Exemption from the Srinakharinwirot University Ethical Committee (275/60X). Subjects were patients admitted to an internal medicine department. Two general wards, one male IPD and one female IPD, and two private wards of HRH Princess Maha Chakri Sirindhorn Medical Center were the locations for the research. All patients admitted in the ICU and semi-ICU ward were excluded; therefore, critically ill or comatose patients were not included in the present study. There were two first-year residents and one third-year resident responsible for general care and treatment in each ward. The rotation of residency training was every month. Patients to doctor ratio are usually 15:1. An authorized investigator of the present study was the third-year medical resident (Kongsakorn P). He was trained to use Thai CAM-ICU by the neurologist (Methawasin K) before starting the research.

Study population

The inclusion criteria of the present study were age 20 years old, with no previous history of dementia, psychosis, or depression, and stable clinical symptoms, without emergency or life-threatening conditions. The diagnosis of dementia in general medicine patients was classified types and confirmed by neurologists (Methawasin K and Kongsakorn N) according to the definition of the Thai Mental State Examination (TMSE) scales and criteria documented in the clinical practice guideline of dementia 2014[6]. The records of the medical and psychiatric illnesses were available either on paper-based or on computer-based documents. The authors also excluded patients with intubation and ventilator assistant, end-stage diseases with palliative or end of life care, vegetative stage, handicapped, and incapability patients such as blindness, deafness, and autism. The sample size was calculated based on the previously reported delirium prevalence of 30%[7].

Procedure and data collection

Volunteers were selected through a free random survey and after receiving notifications from the first-year residents. A principle investigator initially recorded the resident's diagnosis of delirium, which was based on their knowledge. Thai CAM-ICU was brought to detect delirium for all notified cases and survey cases. Data collection included age, gender, present medical illnesses, underlying diseases (classified by organ systems), neurological conditions including cerebrovascular disease and epilepsy but excluding coexisted dementia and psychiatric conditions, current medications, history of substance abuse, current alcohol use, current cigarette use, injury history, and surgical history. The factor of patients that had two or more underlying diseases referred to patients with any combined existing illnesses such as myocardial ischemia and cerebrovascular disease, chronic obstructive pulmonary disease and hyperlipidemia, and cancer and hypertension. The history of benzodiazepine use included patients with records of taking all types of oral benzodiazepine due to various indications and dosages at least three months before the present study. The alcohol use disorder cases were identified by DSM-V alcohol use disorder[8]. The factor of chronic kidney disease referred to the chronic kidney disease at least stage 3

Table 1. The significant factors associated with delirium

Factors	Delirium n (%)	Non-delirium n (%)	p-value
Sex: male	76 (52.1)	99 (47.1)	0.389
Age ≥50 years old	136 (93.2)	139 (66.2)	<0.001*
Existing medical illness			
Cardiovascular disease	78 (53.4)	113 (53.8)	1.000
Pulmonary disease	25 (17.1)	24 (11.4)	0.159
Gastrointestinal disorder	20 (13.7)	27 (12.9)	0.874
Endocrine disorder	88 (60.3)	105 (50.0)	0.066
Chronic kidney disease	55 (37.7)	35 (16.7)	<0.001*
Hematologic disease	14 (9.6)	18 (8.6)	0.851
Oncology disease	30 (20.5)	41 (19.5)	0.893
Rheumatology disease	23 (15.8)	27 (12.9)	0.443
Patients have ≥2 underlying diseases	70 (47.9)	58 (27.6)	<0.001*
Underlying neurology diseases			
Cerebrovascular disease	21 (14.4)	9 (4.3)	0.001*
Epilepsy	4 (2.7)	1 (0.5)	0.093
Benzodiazepine use	8 (5.5)	1 (0.5)	0.004*
Substance abuse	10 (6.8)	1 (0.5)	0.001*
Alcohol abuse	24 (16.4)	9 (4.3)	<0.001*
Smoking	18 (12.3)	11 (5.2)	0.019*

* Statistical significant

regarding the definition classified by the glomerular infiltration rate. All baseline investigations, such as complete blood count (CBC), blood chemistry analyses, and renal and liver function tests, were recorded. Either computerized tomography (CT) or magnetic resonance imaging (MRI) of the brain was performed on all volunteers with clinical suspicion of neurological disorders. The Thai CAM-ICU was developed and validated in the Thai language by the research team from the Department of Psychiatry, Chiang Mai University[9]. It has two components, the Richmond Agitation-Sedation Scale (RASS), which evaluates alertness, and four questionnaires of acute onset or fluctuating course, inattention, altered level of consciousness, and disorganized thinking. The diagnosis of delirium was to combine the outcomes of these two components. RASS lists the level of sedation from +4 to –5. In reference to the exclusion criteria, the patients with clinically RASS –4 to –5 would not be included in the present research. For RASS –2 and –3, the investigator would try to wake the patients up and estimated the level of consciousness. If patients were still aroused, an investigator considered to go on the test. On the contrary, if patients were found to be RASS –4 and –5 or clinically suspicious to have a critical situation, the investigator excluded them and immediately called the residents or attending staffs. Thai CAM-ICU evaluation was applied once after getting a notification and a survey to document delirium cases during admission. The CAM-ICU outcomes and residents' opinions were recorded to determine the prevalence of missed diagnoses.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics software, version 22 (IBM Corp., Armonk, NY, USA). The chi-squared or Fisher's exact test, Student's t-test, and univariate logistic regression analyses were used to analyze significant factors, at a p-value less than 0.05, with a 95% confidence interval (CI). The multivariate analysis was used to identify significant associated factors. Variables with the significant p-value and p-value less than or equal to 0.100 were included to the multivariate analysis.

Results

Among the 356 internal medicine IPD patients included in the present study, 175 patients (49.2%) were male, and 181 patients (50.8%) were female. Patients ranged in age between 20 and 99 years old, with a mean age of 61.52 years old. One hundred forty-six patients (41%) met the CAM-ICU criteria for delirium, whereas only 79 patients (22.2%) were diagnosed delirium by residents. The mean duration of assessment was 3.5 days after admission. Table 1 shows the demographic data, existing medical illnesses, neurological conditions, and drug or substance use information for patients both with and without delirium, as detected by the Thai CAM-ICU. The most commonly reported form of substance abuse in the present study was the use of fresh Kratom leaves, with a mean daily consumption level of 10 to 20 leaves per person with Kratom abuse. The mean alcohol intake was 130.05 mg/day. Table 2 shows the results of the univariate logistic regression analysis and indicated the significant factors found to be associated with delirium.

The multivariate analyses indicated the significant effects of substance abuse, chronic kidney disease, cerebrovascular disease, benzodiazepine use, alcohol abuse, and age at 50 or older, as described in Table 3.

Sixty-nine cases met the Thai CAM-ICU criteria for delirium; however, residents did not notice delirium among these cases (p<0.001). Figure 1 illustrates the difference in the number of delirium

Table 2. The univariate analysis of factors associated to delirium cases detected by CAM-ICU

Factors	p-value	Crude OR	95% CI
Age ≥50 years old	<0.001*	6.94	3.44 to 14.03
Chronic kidney disease	<0.001*	3.02	1.84 to 4.95
Patients with more than 2 underlying diseases	<0.001*	2.41	1.54 to 3.76
Cerebrovascular disease	0.001*	3.75	1.66 to 8.45
Benzodiazepine use	0.019*	12.11	1.49 to 97.95
Substance abuse	0.010*	15.36	1.94 to 121.40
Alcohol abuse	<0.001*	4.39	1.97 to 9.76
Smoking	0.019*	2.54	1.16 to 5.56

OR=odds ratio; CI=confidence interval

* Statistical significant

Table 3. The multivariate analysis of factors associated with delirium

Factors	p-value	Adjusted OR	95% CI
Chronic kidney disease	0.006*	2.51	1.30 to 4.83
Cerebrovascular disease	0.023*	2.85	1.15 to 7.06
Substance abuse	0.012*	18.93	1.90 to 188.38
Benzodiazepine use	0.034*	10.05	1.18 to 85.17
Alcohol abuse	0.007*	4.27	1.49 to 12.20
Age ≥50 years old	<0.001*	6.79	2.94 to 15.64

OR=odds ratio; CI=confidence interval

* Statistical significant

cases detected by the Thai CAM-ICU compared with the number of cases diagnosed by residents. The outcomes of RASS varied from –3 to 2. Two hundred four patients (57.3%) were in RASS 0. Thirty-seven (10.4%) and 25 (7%) were in RASS 1 and 2, while 31 (8.7%), 57 (16%) and 2 (0.6%) patients were in RASS –1, –2, and –3, respectively. The RASS score of –3 to –1 represented the decreased level of consciousness, which considered to be the hypoactive delirium. This factor influenced the under-detection of the delirium of residents ($p<0.001$).

Discussion

The present study was conducted in the IPD of an internal medicine department of a suburban medical school campus during the development of a fall and injury prevention policy. Falls and injuries occasionally occur in delirious patients and result in severe consequences. Although acute alteration of consciousness is reviewed by either physicians or paramedical workers, alterations

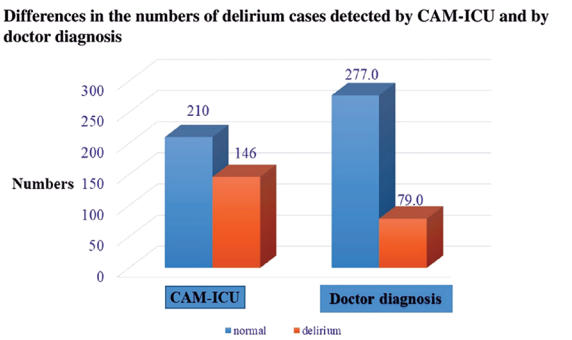

Figure 1. The bar chart illustrated comparison of number differences between delirium cases detected by CAM-ICU and intern's diagnosis.

can go unrecognized or underdiagnosed for many reasons, including fluctuations in clinical symptoms that make physicians reluctant to diagnose delirium, a hypoactive status that mirrors somnolence or depression, and the high workload associated with general wards. Thus, a useful screening tool could help solving this problem. CAM-ICU was first used to assess delirium in an ICU. However, this tool is currently the screening test for delirium available in the Thai language. Although there is a study of using Thai CAM to evaluate delirium in hospitalized patients with good sensitivity and specificity[5], the present research team chose Thai CAM-ICU as a tool for screening. In addition to its excellent sensitivity and specificity[9], this test is easy to administer by either doctors or nurses and is not time-consuming. The RASS provides an ordinary scale, which helps identify an abnormal level of consciousness. The present study confirmed the significantly increased effectiveness of the Thai CAM-ICU for the detection of delirium, especially the hypoactive delirium when compared to resident's diagnosis.

The rate of delirium detection in the present cross-sectional study was slightly higher than the incidence rate reported in the previous studies[7]. This result is not indicative of the prevalence or incidence of delirium for the IPD of the authors' hospital because of the selection bias and randomization. Gender does not appear to affect development of delirium. Renal failure plays a role in delirium due to uremic encephalopathy. Most cases of the cerebrovascular disease involve lacunar infarction. Although this small vessel disease usually has no cortical involvement, delirium can occur when patients experience additional physical stress. This outcome is similar to a previous study that examined the prevalence of delirium in a stroke unit[10].

Interestingly, the most common form of substance abuse identified was Kratom addiction, which affected the occurrence of delirium. The authors' hospital locates in an agricultural area, where population are farmers or orchard workers who wished to increase work tolerance. Smoking demonstrates an effect on the development of delirium during the univariate analysis, but not during the multivariate analysis; however, the alcohol showed a substantial effect on the development of delirium. The alcohol withdrawal syndrome and delirium tremens are both associated with delirium. The alcohol withdrawal effects may explain why the occurrence of delirium in the present study was initially associated with ages over 50 years old. One previous study of delirium among traumatic injury patients found that the age of 55 years or older was a risk factor for delirium tremens[11].

Benzodiazepine use was another factor associated with delirium occurrence. Many published articles have indicated the adverse effects of benzodiazepine as a potent delirium inducer[12-14]. To prevent this problem, neurologists and psychiatrists should orientate new physicians to exercise caution regarding benzodiazepine administration. Age was a substantial factor associated with delirium. Based on the exclusion criteria, none of the elderly patients included in the present study had documented dementia diagnoses. However, these patients may have had undiagnosed dementia or age-related cognitive decline. Other explanations for the high occurrence of delirium in old patients could be an increased susceptibility to underlying diseases, for instance, the coexistent of renal insufficiency and cerebrovascular disease and coronary artery disease, metabolic syndrome, and cerebrovascular disease. Treatments of delirium should be accompanied by the determination and treatment of the underlying etiology, in addition to injury prevention and rehabilitation. Haloperidol is a typical neuroleptic drug that is available at many hospitals and is often used in practice for aggressive behavior control. However, little evidence exists regarding the benefits of this drug. Besides, quetiapine[15], ziprasidone[16,17], and olanzapine[18] have also been shown to have benefits for delirium.

The present study had some limitations. The first was selection bias from a random survey. Although the present study obtained a sufficient sample size to provide significant outcomes following statistical analysis, the rate of delirium detection did not represent the general prevalence of delirium in the internal medicine wards of the present study hospital due to random sampling. Moreover, to achieve the accuracy of estimation, the present study should be conducted as a prospective cohort study with a repeated evaluation regarding the fluctuation of clinical symptoms. For further investigation, the authors aim to use the screening form for delirium, followed by the Thai CAM-ICU, on all patients admitted to the hospital. The authors propose that this way will reveal the true prevalence of delirium. The second limitation was that in some cases, especially among older patients, those with positive Thai CAM-ICU results may have undiagnosed dementia. If the authors consider the clinical criteria outlined by DSM-V, these subjects were not compatible with delirium diagnoses. However, the authors do not have the ability to test and document dementia among all senior citizens. The knowledge retrieved from the present study can be applied to clinical practice by performing cognitive testing with Mini-Mental State Examination (MMSE) in older adults who develop delirium after delirium has been clinically resolved.

Conclusion

Chronic kidney disease, substance abuse, benzodiazepine use, alcohol abuse, and age more than 50 years old were factors associated with delirium in the present study. Hypoactive delirium is underdiagnosed by doctors but can be identified by using the Thai CAM-ICU.

Acknowledgement

The authors would like to acknowledge Sirirat Mueankwan, Master of Nursing Science and the team at Maharaj Nakorn Chiangmai Hospital, Chiang Mai University for allowing us to use the Thai version of the CAM-ICU. In addition, Dr. Suthee Rattanamongkolgul was our statistical consultant.

Funding disclosure

This study was supported by HRH Princess Maha Chakri Sirindhorn Medical Center, Faculty of Medicine, Srinakharinwirot University, Ongkharak, Nakhon Nayok. The research fund contract number is 357/2561.

Conflicts of interest

The authors declare no conflict of interest.

References

1. Ryan DJ, O'Regan NA, Caoimh RÓ, Clare J, O'Connor M, Leonard M, et al. Delirium in an adult acute hospital population: predictors, prevalence and detection. BMJ Open 2013;3:e001772.

2. Whittamore KH, Goldberg SE, Gladman JR, Bradshaw LE, Jones RG, Harwood RH. The diagnosis, prevalence and outcome of delirium in a cohort of older people with mental health problems on general hospital wards. Int J Geriatr Psychiatry 2014;29:32-40.
3. Barron EA, Holmes J. Delirium within the emergency care setting, occurrence and detection: a systematic review. Emerg Med J 2013;30:263-8.
4. Lawlor PG, Davis DHJ, Ansari M, Hosie A, Kanji S, Momoli F, et al. An analytical framework for delirium research in palliative care settings: integrated epidemiologic, clinician-researcher, and knowledge user perspectives. J Pain Symptom Manage 2014;48:159-75.
5. Praditsuwan R, Limmathuroskul D, Assanasen J, Pakdeewongse S, Eiamjinnasuwat W, Sirisuwat A, et al. Prevalence and incidence of delirium in Thai older patients: a study at general medical wards in Siriraj Hospital. J Med Assoc Thai 2012;95 Suppl 2:S245-50.
6. Tantaritthisak T, editor. Clinical practice guidelines: Dementia. Bangkok: Institute of Neurology Department of Medical Services; 2014.
7. Brown TM, Boyle MF. Delirium. BMJ 2002;325:644-7.
8. Grant BF, Goldstein RB, Saha TD, Chou SP, Jung J, Zhang H, et al. Epidemiology of DSM-5 alcohol use disorder: Results from the national epidemiologic survey on alcohol and related conditions III. JAMA Psychiatry 2015;72:757-66.
9. Pipanmekaporn T, Wongpakaran N, Mueankwan S, Dendumrongkul P, Chittawatanarat K, Khongpheng N, et al. Validity and reliability of the Thai version of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). Clin Interv Aging 2014;9:879-85.
10. Nydahl P, Bartoszek G, Binder A, Paschen L, Margraf NG, Witt K, et al. Prevalence for delirium in stroke patients: A prospective controlled study. Brain Behav 2017;7:e00748.
11. Salottolo K, McGuire E, Mains CW, van Doorn EC, Bar-Or D. Occurrence, predictors, and prognosis of alcohol withdrawal syndrome and delirium tremens following traumatic injury. Crit Care Med 2017;45:867-74.
12. Pandharipande PP, Sanders RD, Girard TD, McGrane S, Thompson JL, Shintani AK, et al. Effect of dexmedetomidine versus lorazepam on outcome in patients with sepsis: an a priori-designed analysis of the MENDS randomized controlled trial. Crit Care 2010;14:R38.
13. Riker RR, Shehabi Y, Bokesch PM, Ceraso D, Wisemandle W, Koura F, et al. Dexmedetomidine vs midazolam for sedation of critically ill patients: a randomized trial. JAMA 2009;301:489-99.
14. Zaal IJ, Devlin JW, Hazelbag M, Klein Klouwenberg PM, van der Kooi AW, Ong DS, et al. Benzodiazepine-associated delirium in critically ill adults. Intensive Care Med 2015;41:2130-7.
15. Devlin JW, Roberts RJ, Fong JJ, Skrobik Y, Riker RR, Hill NS, et al. Efficacy and safety of quetiapine in critically ill patients with delirium: a prospective, multicenter, randomized, double-blind, placebo-controlled pilot study. Crit Care Med 2010;38:419-27.
16. Girard TD, Pandharipande PP, Carson SS, Schmidt GA, Wright PE, Canonico AE, et al. Feasibility, efficacy, and safety of antipsychotics for intensive care unit delirium: the MIND randomized, placebo-controlled trial. Crit Care Med 2010;38:428-37.
17. Girard TD, Exline MC, Carson SS, Hough CL, Rock P, Gong MN, et al. Haloperidol and ziprasidone for treatment of delirium in critical illness. N Engl J Med 2018;379:2506-16.
18. Skrobik YK, Bergeron N, Dumont M, Gottfried SB. Olanzapine vs haloperidol: treating delirium in a critical care setting. Intensive Care Med 2004;30:444-9.