Factors Related to Delirium of Intensive Care Unit Patients in Korea: A Systematic Review

Nam Young Kim[1], Se Ang Ryu[2], *Yun Hee Kim[2]

1. Department of Nursing, Jungwon University, Goesan, Korea
2. Department of Nursing, Mokpo National University, Muan, Korea

*Corresponding Author: Email: kimyunhee@mokpo.ac.kr

Abstract

Background: The delirium in Intensive Care Units (ICU) patients is a major cause of unplanned extubation, increased length of hospital day. This study aimed to review systematically risk factors associated with the occurrence of delirium among ICU patients in South Korea.

Methods: Data collection was done with domestic literature search databases including KMbase, KoreaMed, KISS, and KisTi and also with hand searching, from February 17 to May 19, 2019. Two researchers independently selected research literatures, and three researchers summarized and identified related variables based on data extraction methods.

Results: Overall, 140 articles were identified, 18 articles met the inclusion criteria for review. According to the results of the methodological quality, one article was found to have a high level of quality, while the remaining 17 articles belonged to the medium level. Those factors were highly associated with delirium by more than 9 out of the 18 selected studies were listed as follows; age, the application of ventilator, APACHE II score, comorbidity, the application of restraint, and educational level. In addition, catheter insertion and the application of artificial airway had significant relevance with the occurrence of delirium.

Conclusion: For management of delirium among ICU patients, it is necessary to eliminate and prevent delirium-associated risk factors, and also to detect and treat the delirium early through regular monitoring using an appropriate screening tool for delirium.

Keywords: Delirium; Intensive care unit; Systematic review

Introduction

In the studies conducted in South Korea turned out to show widely-varying delirium prevalence rates ranging from 22% to 73% (1). Intensive care unit (ICU) patients showed higher delirium prevalence rates than patients in general ward (2). Such increased risks for delirium were reported to be due to frequent invasive procedures in treatment process and immobility accompanied by discomfort, pain and anxiety (3).

When delirium occurs, unplanned extubation and the length of ICU stay showed an increasing tendency. Treating delirium after occurrence may

cause many negative problems such as a higher risk of dementia, increased medical costs, potential cognitive disorder, and an extended application period of ventilator. Therefore, proper measures should be taken to prevent the occurrence, or more active management efforts, including early detection and selection of high risk groups, should be made (4,5).

In the results of the preceding studies relating to delirium-related risk factors, a systematic review and meta-analysis of 33 overseas studies reported that there were many strong grounds to support that age, dementia, hypertension, surgery or trauma experiences before being hospitalized to the ICU, APACHE II score, the application of ventilators, metabolic acidosis, delirium experiences, confusion were risk factors closely associated with the occurrence of delirium (2). The systematic review which integrate the research results relating to risk factors for delirium among ICU patients have been continuously announced in overseas countries. However, those studies announced in South Korea were not included in these overseas literature reviews due to linguistic constraints. Given this reality, it is necessary to conduct a systematic review on the results of studies relating to delirium and to compare these results with those of the overseas systematic review.

In South Korea, there are 334 general hospitals as of Dec, 2016. The general hospitals with less than 500 beds which operate single unit ICUs were numbered at 243 hospitals, or 72.8% of the total. ICU nurses are taking care of patients with all kinds of diseases (6). However, those studies on delirium-related risk factors released in South Korea until recently have been mostly conducted at a single hospital by targeting patients with specific diseases (7-9). Therefore, it might be difficult to apply the previously published research results directly to the hospitals with less than 500 beds, because this might bring about unexpected problems due to a different situation. The strength of evidence of these delirium-associated risk factors confirmed by each study are not strongly supported, because most of these studies were carried out as survey study.

Therefore, we aimed to identify core factors closely associated with delirium among ICU patients in South Korea by integrating the results of the related studies and by conducting a systematic review on them.

Methods

The inclusion criteria of this review were: 1) patients over 19 yr old hospitalized in the ICUs, 2) studies on risk factors for delirium. The exclusion criteria were: 1) studies on non-ICU patients, 2) dissertations published on academic journals, 3) studies that presented only abstracts, 4) review articles, experimental studies.

Literature search and selection was performed from Feb 17 to May 19, 2019. The literature search was done based on the COSI model suggested by the United States National Library of Medicine (NLM) for a systematic review and by using Korean literature databases which belong to the core, such as KMbase, KoreaMed, KISS and KiSTi. The standard search was done through hand searching by targeting articles published on the Journal of Korean Society of Nursing Science, the Korean Journal of Adult Nursing, the Journal of Korean Society of Clinical Nursing Research, and the Journal of Korean Society of Critical Care Nursing. The literature search was performed independently by two researchers. The keywords such as 'Delirium' and 'Critically-ill patients' were combined with the Boolean operator of 'AND'. In the case of publication forms, both studies published on academic journals and dissertations were all retrieved, but there was no limit to publication years.

EndNote X7.8 was used to exclude duplicated articles among the identified studies. The titles and abstracts were checked in the first round of screening. Based on the data selection criteria, the original texts of the selected articles were identified for content review. The whole process of literature selection was performed independently by two researchers. When their opinions differed from one another, all researchers participated in a plenary meeting to discuss the concerned matter

in accordance with the article selection and exclusion criteria to produce the agreed results. The finally selected articles were summarized independently by three researchers based on data extraction methods.

This study performed qualitative evaluation on the finally selected 18 articles with a qualitative evaluation tool developed by Estabrooks et al (10) and modified and complemented by Cicolini et al (11). The qualitative evaluation in this study was done independently by three researchers, and when their opinions differed from one another, research meetings were held to reach the consensus.

Qualitative synthesis of data was performed using coding book developed by the researchers of this study. After three researchers independently read a total of 18 articles, they included the following general characteristics of study subjects in risk factors: age, sex, sample size, screening tools for delirium, and the prevalence of delirium. The delirium prevalence was calculated as percentage. The risk factors for delirium were classified into sociodemographic factors, patient-related factors, disease-related factors, surgery-related factors, and environment-related factors, based on the prediction model for delirium among ICU patients in South Korea developed by Park (12).

Results

Data selection
After exclusion of the 59 duplicated articles, three researchers reviewed the titles and abstracts of 81 articles. As a result, 68 articles were selected in the first round of screening after excluding 13 not relevant. In the second round, after reviewing the articles in accordance with the selection exclusion criteria, this study excluded two articles conducted on non-ICU patients, as well as another 50 articles which had only abstracts or which were review articles, experimental study and finally selected 18 articles. Among the finally selected 18 articles, 7 of them were dissertations, while 11 of them were published on academic journals (Fig. 1).
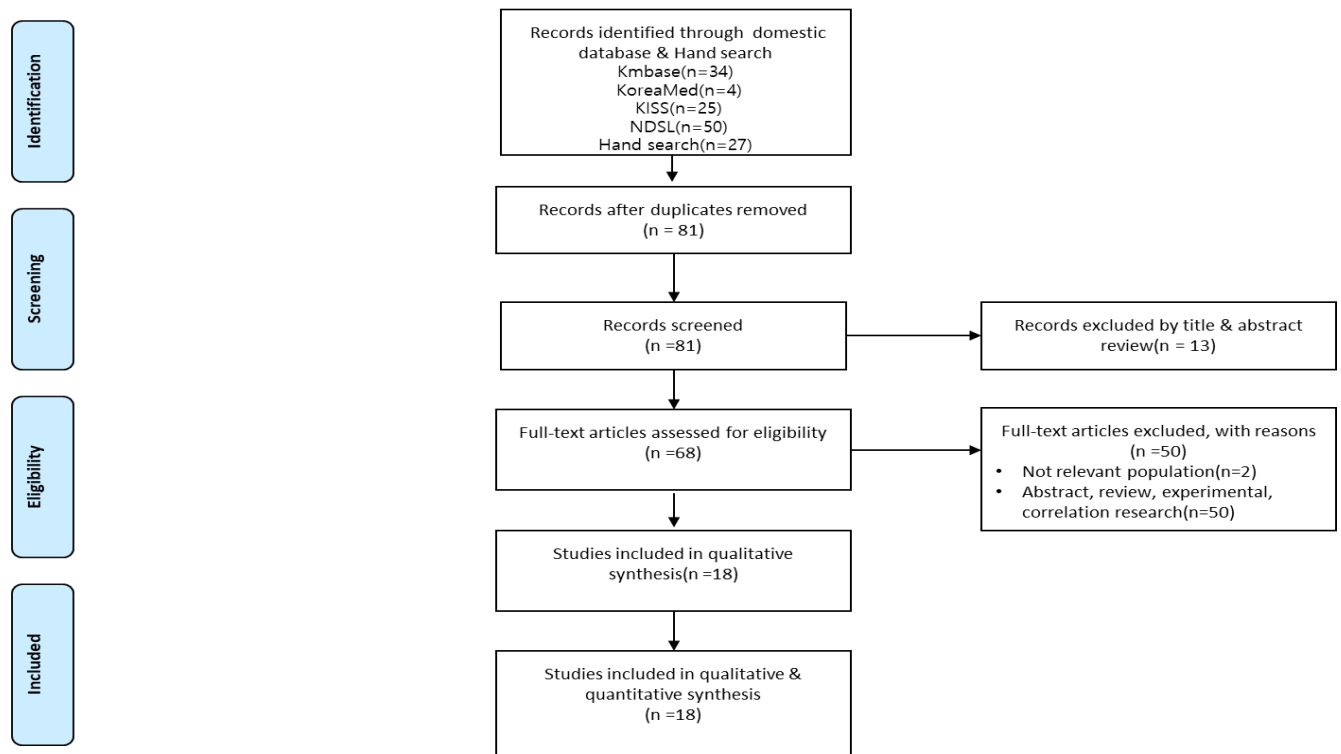
Characteristics of the selected studies

Overall, 18 articles were selected, and all of them were descriptive survey articles. Their publication years were distributed from 2008 to 2019. In the case of sample sizes, the minimum size was 70, while the maximum size was 3,721. The types of ICUs which the researches were conducted, 9 articles belonged to the category of the ICU with a combination of the MICU and the SICU. In the case of survey designs, 14 articles were retrospective studies, while 5 were prospective studies.

The prevalence of delirium among ICU patients showed a wide variation from 11.9% to 80.1%. In the case of screening tools for delirium, the Confusion Assessment Method for the ICU (CAM-ICU) was used by 15 articles, and the Nursing Delirium Screening Scale (Nu-DESC) was used by 2 articles. And the remaining one used the Delirium Observation Scale (DOS). After assessing the selected research literatures with the correlation study quality evaluation tool, the overall quality level of the articles selected for this study was within an acceptable medium level (Table 1).

Significance according to the predictive factor criteria for delirium among ICU patients

This study collected a list of 54 factors in five categories associated with the occurrence of delirium among ICU patients. The demographic-related category consisted of five factors: education level reported by 10 articles, patient-related factors by 17, age by 18, gender by 16, and smoking by 9. The disease-related category consisted of 22 factors; mechanical ventilator reported by 14 articles, APACHE II score by 12, and comorbidity by 11, and hospital day by 9. The surgery-related category consisted of seven factors: operation time reported by 3 articles, operation types by 3, and PCA by 2. The environment-related category consisted of three factors; restraints reported by 12 articles.

There were nine factors reported by more than 9 (50%) out of 18 articles, such as education level, age, gender, smoking, mechanical ventilator,

APACHE II score, comorbidity, hospital day, and restraints. Among them, those factors which showed statistically significant levels of association with the occurrence of delirium included education level, age, APACHE II score, mechanical ventilator, restraints, and comorbidity. Besides, those factors with a low usage frequency but a high statistical significance were listed as follows: use of catheter (7/8, 87.5%), artificial airway (5/5, 100.0%), patient severity score (4/4, 100.0%), infection (3/4, 75.0%), and admission (4/6, 66.7%) (Table 2).

Discussion

Overall, 18 studies were selected for this study, and they showed a wide variation from 11% to 80% in terms of the prevalence of delirium. Similarly, an overseas study which conducted a systematic review of 33 articles also reported a similar variation ranging from 9% to 81% (2). Such difference in the prevalence of delirium can be ascribed to the use of different participants and different screening tools for delirium (13). Especially, a higher prevalence of delirium was reported, when the study participants were elderly patients or when critically-ill patients with surgery experiences had different diseases (14). However, nine out of the 18 articles selected for this study were conducted by including both SICU and MICU, which makes it difficult to identify possible differences in the prevalence of delirium between different types of ICU.

This study used the conceptual framework (12) to conduct a systematic review on 54 factors in five categories which are thought to be associated with the occurrence of delirium. More than nine out of the 18 articles selected for the analysis of this study reported that there were six factors found to have a higher level of association with the occurrence of delirium, such as age, APACHE II score, the application of ventilators, the application of restraints, comorbidity, and education level.

Table 1: Description and summary of the included studies and quality assessment results

Ref. No.	Sample size(n) D^a/N-D^b	S^c	SD^d	Participants D		N-D		Incidence of delirium (%)	Instrument of delirium assessment	Q_h
				Gender (M/F)	Age (M±SD or Median or n)	Gender (M/F)	Age (M±SD or Median or n)			
(1)	133/33	MICU	R^e	83/50	20-44: 17 45-64: 35 ≥65: 81	16/17	20-44: 8 45-64: 8 ≥65: 7	80.12	Nu-DESC	6
(7)	63/358	CSICU	R	NR^f	NR	NR	NR	14.96	Nu-DESC	7
(8)	159/489	CSICU	R	85/74	65.7±11.70	305/184	59.4±12.90	24.54	CAM-ICU	5
(9)	23/170	NICU	P^g	9/14	71.09±12.18	78/92	61.43±13.63	11.92	Korean CAM-ICU	10
(12)	1398/2323	MICU SICU	R	777/621	pre-adolescence: 14 adolescence: 28 adult: 532 old: 824	1348/ 975	pre-adolescence: 15 adolescence: 61 adult: 1125 old: 1122	37.57	DOS	8
(23)	688/2596	MICU SICU	R	395/293	68.43±14.77	1915/1369	58.5±15.59	20.95	CAM-ICU	
(24)	107/48	MICU	R	73/34	65.65±14.08	35/13	58.67±17.90	69.03	CAM-ICU	
(25)	22/77	MICU SICU	R	18/4	76.00	57/20	72.00	22.22	CAM-ICU	
(26)	180/720	MICU SICU	R^e	82/ 98	73.37±11.97	424/296	59.65±15.18	20.00	CAM-ICU	7
(27)	63/51	ICU	P^f	26/ 25	65-74: 27 75-84: 21 ≥85: 3	19/44	65-74: 18 75-84: 23 ≥85: 22	55.26	Korean CAM-ICU	7
(28)	25/45	MICU	P	13/12	≥65: 17 ≤64: 8	23/22	≥65: 20 ≤64: 25	35.71	CAM-ICU	7
(29)	22/77	ICU	P	14/8	≥60: 16 ≤59: 6	44/33	≥60: 42 ≤59: 35	22.22	CAM-ICU	5
(30)	22/88	SICU	P	15/7	66.8±9.60	67/21	60.06±12.10	20.00	CAM-ICU	7
(31)	500/2000	MICU	R	204/296	67.29±15.31	879/1121	59.92±15.37	20.00	CAM-ICU	6
(32)	31/75	ICU	R	20/11	49.7±8.00	59/16	48.4±8.00	29.25	CAM-ICU	5
(33)	46/27	SICU	R	33/13	64.46±9.84	18/9	52.85±15.52	63.01	CAM-ICU	5
(34)	34/91	MICU SICU	R	18/16	71.50	46/45	60.00	27.20	CAM-ICU	6
(35)	107/68	ICU	R	63/44	72.07±13.25	32/36	59.85±17.45	61.14	CAM-ICU	7

[a]D=Delirium, [b]N-D=Non-Delirium, [c]S=Setting, [d]SD=Study design, [e]R=Retrospective survey, [f]P=Prospective survey, [g]Q=Quality

If we look at overseas studies that assessed influential factors for delirium, age (5,15), APACHE II score (5), and comorbidity including hypertension, diabetes, and kidney diseases (2,5,15) were reported to be risk factors for delirium. The results of this study were consistent with those of two systematic reviews that pointed out age and comorbidity as influential factors for delirium among ICU patients.

Table 2: Significance according to the risk factor criteria for delirium among ICU patients

Factors	Variables	n			Significance	Ref. No.
		to-tal	+	-		
Demo-graphic	Education level	10	6	4	+/-/-/+/- /+/+/-/+/+	8/9/12/23/24/25/27/28/31/33
	Marriage	6	2	4	-/+/+/-/-/-	8/12/23/24/28/29
	Religion	6	0	6	-/-/-/-/-/-	8/12/24/28/29/33
	Job	2	2	0	+/+	12/28
	Economical support	1	1	0	+	12
Patient	Age	18	13	5	-/+/+/+/+/+/- /+/+/+/+/-/- /+/+/-/+/+/+	1/7/8/12/23/24/25/26/27/28/29/30/31/32 /33/34/35
	Gender	16	3	13	-/-/+/-/-/+/+/- /-/-/-/-/-/-/-/-	1/7/8/23/24/25/26/27/28/29/30/31/33/34 /35
	Smoking	9	0	9	-/-/-/-/-/-/-/-/-	1/8/12/23/28/30/32
	Drinking	8	1	7	-/-/+/-/-/-/-/-	1/8/12/23/24/28/30/32
	Use of psycho-pharmacology	6	4	2	+/-/+/+/-/++	1/12/23/29/31
Disease	Mechanical ventilator	14	9	5	**+/+/-/+/+/- /+/-/-/+/- /+/+/+**	1/8/9/23/24/25/26/27/28/29/30/31/32/33
	APACHE II[a] score	12	10	2	**+/+/+/+/+/+ /+/-/-/+/+/+**	1/7/9/12/23/25/26/27/28/30/31/35
	Comorbidity	11	6	5	**-/+/-/- /+/+/+/+/-/- /+/+**	7/8/9/12/24/25/28/30/33/34/35
	Hospital day	9	4	**5**	**-/-/-/- /+/+/+/+/-/+**	8/9/12/24/25/29/31/32/34
	Use of catheter	8	7	1	**+/+/+/+/+/+ /-/+**	1/8/12/23/24/27/34
	Admission	6	5	1	**+/+/+/-/+/+**	9/12/23/27/31/35
	Artificial airway	5	5	0	**+/+/+/+/+**	1/12/24/29/35
	Patient severity score	4	4	0	**+/+/+/+**	12/23/25/31
	Infection	4	3	1	**+/+/-/+**	12/23/26/31
Surgery	Operation time	3	2	1	**-/+/+/**	7/12/26
	Operation type	3	1	2	**-/+/-/**	7/12/30
	PCA[b]	2	1	1	**+/-**	12/30
Environ-ment	Restraints	12	10	2	+/+/+/+/- /+/+/+/+/+/+ /+	1/9/12/23/24/25/28/29/30/31/33
	Isolation	4	1	3	**-/+/-/-**	23/12/30/9
	Family visiting	1	1	0	+	12

[a]APACHE II=Acute Physiology and Chronic Health Evaluation II, [b]PCA=Patient controlled analgesia, +=statistically significant, -=not significant

Another systematic review (16) pointed out APACHE Ⅱ score as a factor that affected the occurrence of delirium among ICU patients.

Several systematic reviews explained the grounds to support the association of patients' age with the occurrence of delirium by reporting that an increased psychological stress in the treatment situation of an ICU and age caused hypoxemia and metabolic imbalances, and that patients experienced a lack of neurotransmitters, as they got older (3,15). Therefore, it is considered to be necessary for nurses to consider elderly patients as a potential risk group for delirium and to monitor them intensively for early detection of precursors to prevent the occurrence of delirium.

The result of this study, the application of ventilators affect the occurrence of delirium. The study by Zaal et al (2) pointed out the application of ventilator as an influential factor for delirium. In the United Kingdoms, 55%-69% of those patients who used ventilator developed the occurrence of delirium, and another study released in the United States reported that the prevalence of delirium among patients with ventilator was found to be 80% (17, 18). If a ventilator is applied to a patient with normal LOC admitted to the ICU, the unfamiliar situation of the ICU may cause physical discomfort, as well as emotional and psychological pressure and burden, assumed to lead to an increased risk for delirium among critically-ill patients with ventilator (12). Therefore, if sufficient explanation about the importance of treatments in addition to emotional support and environmental consideration is provided to those patients with ventilator who have normal LOC, it can help to stabilize the patients and contribute to reducing the occurrence of delirium.

The application of restraints was found to affect the occurrence of delirium among critically-ill patients by this study. In South Korea, the restraints are currently applied in order to limit the activity of ICU patients in order to prevent them from pulling off intubation, drainage tubes, and catheters. Although medical staff are aware of the fact that the application of restraints is one of the

risk factors for delirium, they think it is more important to prevent extubation by applying restraints to them (19). However, not only this study but also previous studies pointed out the application of restraints as a risk factor for delirium, and given this, measures need to be devised to minimize the application of restraints to ICU patients.

The results of this study, three out of the four studies which included the delirium on the prior day as a variable reported that delirium on the prior day was not associated with the occurrence of delirium, while five out of the six studies which included the use of sedatives as a variable reported that the use of sedate was associated with the occurrence of delirium. The use of painkillers or sedatives was an influential factor for delirium, and given this, future studies need to be conducted to assess the association of the use of painkillers or sedatives with the occurrence of delirium in South Korea (20).

Seven out of the eight studies that included catheter insertion as a variable reported that catheter insertion was associated with the occurrence of delirium. Catheter insertion affected the occurrence of delirium (5). Although catheters are inserted for treatment of ICU patients, catheter insertion was found to affect the occurrence of delirium among ICU patients. If nurses conduct a regular assessment to find out whether it is good for patients to maintain catheters or remove them when they become unnecessary, they can contribute to reducing the risk for delirium (5).

Three out of the four studies that included infection as a variable reported that infection was associated with the occurrence of delirium. Infection-associated delirium occurred in an early stage of sepsis, and 23% of the patients experienced sepsis developed delirium (21), and another study (22) pointed out infection as a risk factor that affected the occurrence of delirium. However, because the assessment of the association of the above-mentioned risk factors that affected the occurrence of delirium was done based on electronic medical records (EMR) included in this study, it was almost impossible to evaluate the

association of possible risk factors omitted in these EMR with the occurrence of delirium.

Most of the previous studies selected for a systemic review (16), were carried out as prospective studies. In contrast, 13 out of the 18 studies selected for this study were conducted as retrospective studies. a retrospective study might allow the subjective opinion of the medical staff to be involved in the diagnosis for delirium -for instance, the symptom might be diagnosed as delirium by one doctor but as a precursor of dementia by another doctor- and if so, this can bring about several problems. Therefore, further prospective studies need to be actively carried out on delirium-associated risk factors in South Korea.

This study presented meaningful findings from a viewpoint of nursing science. 1) As this study included only those critically-ill patients who developed delirium after admission to the ICUs, the findings are meaningful in that they can clarify what risk factors are actually associated with the occurrence of delirium after admission to the ICUs. 2) As this study considered the peculiar characteristics of the ICUs where intensive monitoring and treatment are provided, if nurses engage in intensive intervention on those delirium-associated risk factors identified by this study, it is possible to prevent the occurrence of delirium.

Conclusion

Factors found to have significant levels of association with the occurrence of delirium by more than 50% of all studies selected for this study included age, the application of ventilators, APACHE II score, comorbidity, the application of restraints, and educational level. In addition, both catheter insertion and the application of artificial airways were found to have a high level of association with the occurrence of delirium. For management of delirium in the ICUs, it is important to remove those risk factors identified by this study and to detect and treat precursor symptoms early through a regular monitoring with an effective screening tool in order to prevent the occurrence of the disease.

Ethical Consideration

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare that there is no conflict of interest.

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