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著者	YOSHINO Yasuyo, UNOKI Takeshi, SAKURAMOTO Hideaki, OUCHI Akira, HOSHINO Haruhiko, MATSUISHI Yujiro, MIZUTANI Taro
著者別名	吉野 靖代, 卯野木 健, 櫻本 秀明, 大内 玲, 松石 雄二郎, 水谷 太郎
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Association between intensive care unit delirium and delusional memory after critical care in mechanically ventilated patients

Yasuyo Yoshino¹  | Takeshi Unoki²  | Hideaki Sakuramoto³ | Akira Ouchi⁴ | Haruhiko Hoshino⁴ | Yujiro Matsuishi⁴ | Taro Mizutani⁵

¹Kanto Gakuin University College of Nursing, Yokohama, Japan

²Department of Adult Health Nursing, School of Nursing, Sapporo City University, Sapporo, Japan

³Department of Adult Health Nursing, College of Nursing, Ibaraki Christian University, Hitachi, Japan

⁴Department of Emergency and Critical Care Medicine, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan

⁵Ibaraki Western Medical Center, Ibaraki, Japan

Correspondence

Yasuyo Yoshino, Kanto Gakuin University College of Nursing, 1-50-1 Mutsuurahigashi, Kanazawa-ku, Yokohama 236-8503 Japan. Email: mayyasuyo2010@gmail.com

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Abstract

Aim: To determine the relationship between the delirium of patients with mechanical ventilation during intensive care unit (ICU) stay and delusional memory after ICU discharge.

Design: Prospective cohort study.

Methods: Delirium in adult patients who received mechanical ventilation for more than 24 hr was assessed twice daily using the Confusion Assessment Method for the ICU. Delusional memories were evaluated using the ICU Memory Tool 5–10 days after ICU discharge. The associations between the presence of delirium during the ICU stay and delusional memories were evaluated.

Results: Of 60 enrolled patients, 62% had delirium during their ICU stay, and 68% experienced delusional memories 5–10 days after discharge. Delirium during ICU stay was an independent factor to experience delusional memories following discharge. Preventing delirium during ICU stay might reduce delusional memory. We recommend that patients with delirium during their ICU stay should be carefully followed up after discharge from the ICU.

KEYWORDS

delirium, delusional memory, intensive care unit, mechanical ventilation

1 | INTRODUCTION

Intensive care unit (ICU) survivors often report unreal experiences and delusional memories following an ICU admission (Roberts & Chaboyer, 2004). Delusional memories are often vivid, realistic and frightening (Roberts & Chaboyer, 2004). Previous literature has shown that ICU patients often describe persecutory delusions, where they believe that someone was attempting to harm them (Jones et al., 2001). The prevalence of delusional memories in ICU patients ranges between

26%–73% (Bienvenu et al., 2013; Burry et al., 2015; Granja et al., 2008; Jones et al., 2001, 2003, 2007; Ringdal et al., 2009; Samuelson, Lundberg, & Fridlund, 2006, 2007). Several studies have reported that the presence of delusional memories is associated with symptoms of post-traumatic stress disorder (PTSD) (Bienvenu et al., 2013; Granja et al., 2008; Jones et al., 2003; Weinert & Sprenkle, 2008). Many studies have reported PTSD after ICU discharge (Bienvenu et al., 2013; Jones et al., 2007; Kapfhammer et al., 2004; Samuelson et al., 2007), and a meta-analysis indicated that the prevalence of PTSD-related symptoms associated

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with ICU stay was 19.83% (95% confidence interval [CI] 16.72–23.13) (Rigny et al., 2019). The presence of delusional memory following ICU discharge is important since it may influence the survivors' quality of life (Ringdal et al., 2009). For example, patients believe that they have been kidnapped by someone and that their fate is still under the control of their abductor after they leave the ICU (Hewitt, 2002). It has been noted that they live without realizing it is a delusional memory (Kinoshita & Inoue, 2006). Hallucinations, one form of delusional memory, are the most common unpleasant ICU experiences next to the tracheal tube placement (van de Leur et al., 2004). ICU Patients continue to suffer from these delusional memories after they leave the ICU.

Delirium occurs in 83% of patients who are mechanically ventilated during ICU stay (Ely et al., 2001). Many studies have reported that delirium is associated with mortality and long-term cognitive impairments (Ely et al., 2001, 2004; Girard et al., 2010; Pisani et al., 2009). Since the incidence of delirium is independently predicted by the use of sedatives (Reade & Finfer, 2014), guidelines recommend avoiding the unnecessary use of sedatives in mechanically ventilated patients (Barr et al., 2013).

Previous studies investigating the association between delirium during ICU stay and delusional memories following ICU discharge have been inconsistent. Svenningsen et al. (2014) reported that patients with delirium during ICU stay had decreased recall performance compared with non-delirious patients and were more likely to exhibit delusional memories than those without delirium. By contrast, Burry et al. (2015) found no association between the presence of delirium and delusional memories in mechanically ventilated patients during their ICU stay. However, participants in the latter study were receiving benzodiazepines for sedation (Mehta et al., 2012). Since benzodiazepines are no longer recommended since they increase the risk of delirium and delusional memories (Samuelson et al., 2006), the use of benzodiazepines in the patients of the present study was uncommon.

1.1 | Objectives

We, therefore, aimed to investigate whether delirium was associated with the development of delusional memories following ICU discharge. In particular, we investigated whether delirious patients experiencing hallucinations recall these experiences following discharge and whether they exhibit delusional memories.

2 | METHODS

2.1 | Design and study population

This prospective cohort study was carried out between August 2014–March 2016. Study participants were recruited from a 12-bed medical–surgical ICU at a university hospital in Japan.

Inclusion criteria were (a) above the age of 18; (b) admitted to the ICU; (c) receiving mechanical ventilation; and (d) the duration of the ICU admission was at least 24 hr. Because neurologically related

pathophysiologies possibly affected the memory after discharge, we excluded cardiac arrest and head injury patients. Similarly, psychological illness might affect the results; thus, we excluded patients with a history of suicide attempts, psychological illness and conditions affecting memory and verbal response. Accordingly, the exclusion criteria were (a) cardiac arrest; (b) head injury; (c) intoxication; (d) history of suicide attempts; (e) psychotic illnesses; (f) learning disability; (g) hearing difficulties; (h) speech impediments; (i) did not speak Japanese; (j) were transferred to another hospital; (k) were undergoing mechanical ventilation at discharge; (l) were confused or comatose 10 days from ICU discharge; and (m) deceased in the ICU.

2.2 | Sample size calculation

Logistic regression analysis with delusional memory as the outcome, assuming a 40% prevalence of delusional memory based on previous studies and four covariates (APACHE II, Delirium in the ICU, RASS score and ICU lengths of stay), resulted in a minimum sample size of 50 patients (Vittinghoff & McCulloch, 2007).

2.3 | Ethics

Ethical approval for the study was obtained from the Ethical Review Board of the Tsukuba Clinical Research and Development Organization (H26-078). Written informed consent was obtained from all patients at the time of recovery from a coma or confused status.

2.4 | Procedure

Patient demographics, diagnoses and data needed to calculate the Acute Physiology and Chronic Health Evaluation II (APACHE II) score (Knaus et al., 1985) and the Charlson comorbidity index (Charlson et al., 1987) at the ICU admission were calculated. Illness severity during the ICU stay was assessed using the Sequential Organ Failure Assessment (SOFA) score (Ferreira et al., 2001; Vincent et al., 1998). We recorded the highest SOFA score during the ventilated period. The doses of sedative and/or opioid medications per day were logged throughout the ICU stay.

2.5 | Delirium assessment

Delirium was assessed using the Japanese version of the Confusion Assessment Method for the ICU (CAM-ICU) (Ely et al., 2001; Koga et al., 2015). The CAM-ICU is a tool for the assessment of the presence or absence of the nine clinical features of delirium that can be assessed through simple communication even in patients who are unable to speak, such as those who are being ventilated or who have speech difficulties. The Japanese version of the CAM-ICU has comparable validity and reliability (Koga et al., 2015). Patients were

assessed by trained bedside nurses twice per day routinely. A positive result gained at least once in the screenings was considered as delirium, and the duration of the delirium (total number of days) was recorded. In addition, we evaluated patients as delirious if they had at least one positive CAM-ICU result during their ICU stay.

Depth of sedation and agitation was assessed with the Richmond Agitation-Sedation Scale (RASS). RASS consists of 10 categories (-5 to +4) in total and is well validated (Sessler et al., 2002). A Japanese version has been published (Unoki et al., 2010) and is widely used in Japan. The RASS evaluation was performed 6 times a day by trained bedside nurses routinely from the start of the mechanical ventilation until the patient was discharged from the ICU.

2.6 | Memory assessment

To assess memory during ICU stay, we used the ICU Memory Tool (Jones et al., 2001), that is widely used in the research about memory during ICU stay (Burry et al., 2015; Myhren et al., 2010; Ringdal et al., 2009). The scale is subdivided into subscales, such as factual memories scoring 0–11 (faces, family, alarms, voices, lights, darkness, clock, breathing tube, suctioning, tube in nose and ward

rounds), memories of feelings scoring 0–6 (panic, pain, being uncomfortable, feeling confused, feeling anxious or frightened and feeling down) and delusional memories scoring 0–4 (dreams, nightmares, hallucinations and someone trying to harm them). Previous studies reported that the ICU Memory Tool has good internal consistency for both its total and subscale scores (Jones et al., 2001, 2007; Myhren et al., 2010). A single researcher (YY) visited ICU-discharged patients every 2 days to screen whether the patients were able to complete the self-administered questionnaires. This judgment was conducted based on the CAM-ICU and Glasgow Coma Scale (GCS) scores. If the CAM-ICU results were positive or the GCS score was less than 15, the researcher did not conduct the memory assessment. Patients were interviewed by the researcher using the ICU Memory Tool from days 5–10 following ICU discharge in their room. If the conditions did not guarantee privacy, the interview was conducted in another room to protect the privacy of the patients.

2.7 | Data analysis

Parametric and non-parametric tests were performed based on the results of the Shapiro–Wilk test. The RASS score was calculated as

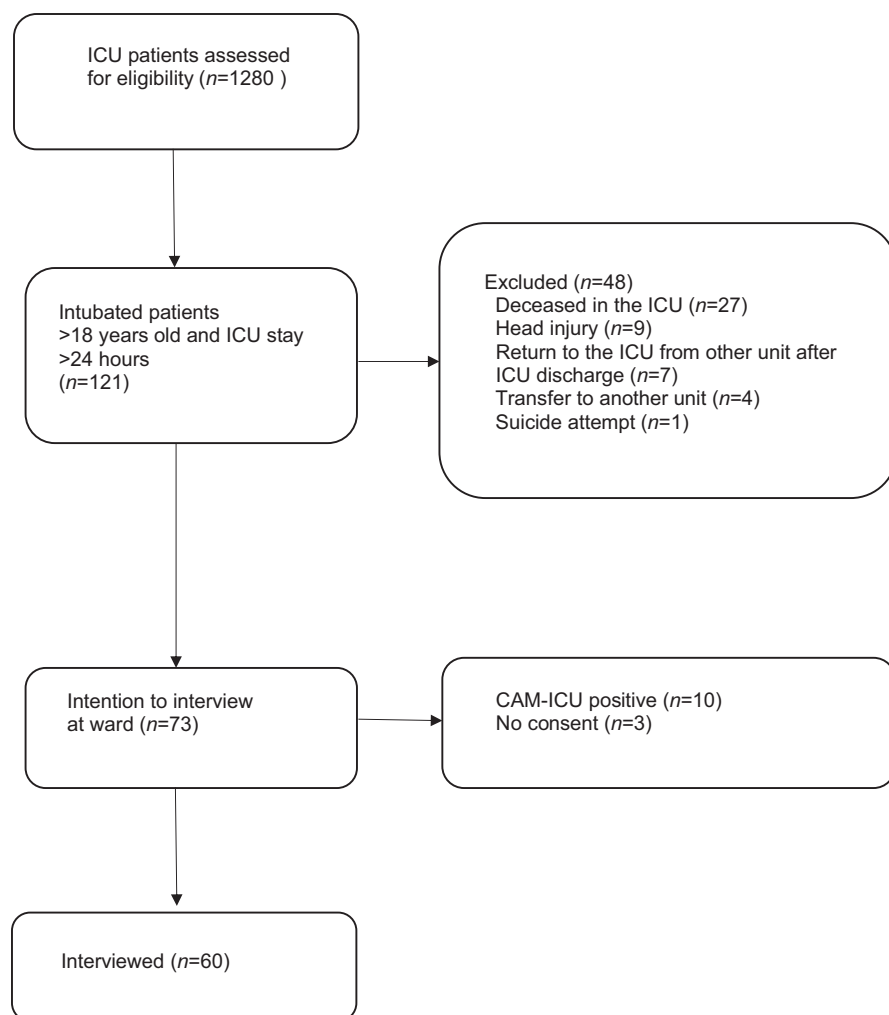


FIGURE 1 Patient recruitment diagram of this study. CAM-ICU, Confusion Assessment Method for the ICU; ICU, intensive care unit

the median of the measurements taken per day during the ventilated period. Dosages of sedatives and/or opioid medications were calculated as the median dose per body weight per day throughout the administration period. Group differences between patients with and without delirium or delusional memories were investigated using the

t test and the Mann–Whitney *U* test. We predefined possible covariates of effect on memory after discharge based on previous studies, and we chose the APACHE II score, Delirium in the ICU, RASS score and ICU length of stay. To adjust these covariates, a logistic regression model was used to evaluate the relationship between the presence of delusional memory determined by the ICU Memory Tool and delirium. Data were computerized and analysed using SPSS 22.0 (IBM Corp., Armonk, NY, USA). Statistical significance was set at $p < .05$.

TABLE 1 Patient baseline demographics ($N = 60$)

	All patients
Age, mean (SD)	62.9 (14.4)
Male, N (%)	39 (65%)
Charlson comorbidity index, median (IQR)	2 (0–3)
APACHE II score, median (IQR)	19 (14–29)
SOFA score, median (IQR)	12 (10–14)
Emergency admission, N (%)	42 (70%)
Admission category	
Cardiac surgery, N (%)	19 (32%)
Gastrointestinal tract surgery, N (%)	13 (22%)
Sepsis, N (%)	11 (18%)
Heart failure, N (%)	4 (6%)
Other, N (%)	13 (22%)
Days in ICU, median (IQR)	9 (6–15)
Days of ventilation, median (IQR)	5 (4–8)
Delirium, N (%)	37 (62%)
Delirium days, median (IQR)	1.5 (0–3)
Coma, N (%)	32 (53%)
Coma days, median (IQR)	1 (0–2)
RASS score for mechanical ventilation, median (IQR)	–2 (–4––1)
Midazolam	
Number of patients receiving midazolam, N (%)	8 (13%)
Amount of midazolam per patient, mg/kg/day, median (IQR)	2.14 (0.4–3.3)
Fentanyl	
Number of patients receiving fentanyl, N (%)	56 (93%)
Amount of fentanyl per patient, $\mu\text{g}/\text{kg}/\text{day}$, median (IQR)	12.2 (9.4–18.2)
Propofol	
Number of patients receiving propofol, N (%)	50 (83%)
Amount of propofol per patient, mg/day, median (IQR)	15.5 (7.2–23.6)
Dexmedetomidine	
Number of patients receiving dexmedetomidine, N (%)	53 (88%)
Amount of dexmedetomidine per patient, $\mu\text{g}/\text{kg}/\text{day}$, median (IQR)	6.5 (3.4–8.3)

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; ICU, intensive care unit; IQR, interquartile range; RASS, Richmond Agitation-Sedation Scale; SD, standard deviation; SOFA, Sequential Organ Failure Assessment.

3 | RESULTS

3.1 | Participants and delirium

Of the 121 mechanically ventilated ICU patients admitted during the study period, 60 patients (50%) were enrolled in the present study (Figure 1). Demographic and admission data are shown in Table 1. The median APACHE II score was 19, and the median duration of mechanical ventilation was 5 days. Overall, 37 patients (62%) screened positive for delirium at least once, and 32 patients (53%) went into a coma during their ICU admission.

3.2 | Delusional memories

Of 60 patients, 41 (68%) had delusional memories. The demographics of patients with and without delusional memories are shown in Table 2. There were no significant differences in the illness severity between the two groups. Patients with delusional memories had a significantly higher prevalence of delirium and a longer duration of delirium during the ICU admission than those without delusional memories. There were no differences between patients reporting delusional memories and those who did not for 1) RASS scores or 2) exposure to opioids, benzodiazepines, dexmedetomidine or propofol. As many as 65% ($N = 24$) of the delirious patients had hallucinations. In addition, delirious patients experienced a greater number of hallucinations relative to non-delirious patients ($p = .01$).

The results of the logistic regression analysis are shown in Table 3. Delirium during ICU stay was independently associated with delusional memory after discharge from ICU (odds ratio, 3.71; 95% CI, 1.038–13.265; $p = .04$). APACHE II score, RASS score and ICU length of stay were not associated with the occurrence of delusional memories.

4 | DISCUSSION

Our findings showed that 68% of patients had delusional memories following ICU discharge. The incidence of delirium during the ICU stay was independently associated with the delusional memories after discharge from the ICU. The odds ratio of having delusional memories was almost four times greater in patients with delirium than in patients without delirium.

	No delusional memory (N = 19)	Delusional memory (N = 41)	p
Age, mean (SD)	62.6 (14.1)	63.0 (14.7)	.94
Male, N (%)	12 (63%)	27 (65%)	1.00
Charlson comorbidity index, median (IQR)	1 (0-2)	2 (0.5-3)	.34
APACHE II score, median (IQR)	19 (13-30)	19 (14.5-29)	.80
SOFA score, median (IQR)	12 (10-13)	12 (10-14)	.30
Emergency admission, N (%)	14 (73%)	28 (68%)	.76
Admission category			
Surgical, N (%)	9 (47%)	30 (73%)	.08
Days in ICU, median (IQR)	7 (6-13)	10 (6.5-16)	.17
Days of ventilation, median (IQR)	5 (4-7)	6 (4-9.5)	.23
Delirium, N (%)	7 (36%)	30 (73%)	.01*
Delirium days, median (IQR)	0 (0-2)	2 (0-4)	.02*
Coma, N (%)	9 (47%)	23 (56%)	.58
Coma days, median (IQR)	0 (0-2)	1 (0-3.5)	.37
RASS score for mechanical ventilation, median (IQR)	-2 (-3-0)	-2 (-4--1)	.28
Midazolam			
Number of patients receiving midazolam, N (%)	1 (5%)	7 (17%)	.41
Amount of midazolam per patient, mg/kg/day, median (IQR)	-	2.5 (1.2-3.3)	.12
Fentanyl			
Number of patients receiving fentanyl, N (%)	19 (100%)	37 (90%)	.29
Amount of fentanyl per patient, µg/kg/day, median (IQR)	12.6 (8.0-22.3)	11.9 (9.4-17.8)	.96
Propofol			
Number of patients receiving propofol, N (%)	16 (84%)	34 (82%)	1.00
Amount of propofol per patient, mg/kg/day, median (IQR)	14.0 (2.7-21.6)	15.5 (8.1-25.9)	.25
Dexmedetomidine			
Number of patients using dexmedetomidine, N (%)	15 (78%)	38 (92%)	.19
Amount of dexmedetomidine per patient, µg/kg/day, median (IQR)	5.0 (2.9-8.1)	6.7 (3.8-8.5)	.44

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; IQR, interquartile range; RASS, Richmond Agitation-Sedation Scale; SD, standard deviation; SOFA, Sequential Organ Failure Assessment.

* $p < .05$.

The prevalence of delusional memories in the present study was consistent with a previous report that 72% of patients, who underwent mechanical ventilation, had delusional memories 3 days following discharge from the ICU (Burry et al., 2015). Similarly, Jones et al. (2001) reported that the prevalence of delusional memories in mechanically ventilated patients 2 weeks after ICU discharge was 72%.

In the present study, delirium during the ICU admission was independently associated with delusional memories following discharge from the ICU. A previous study, although its subjects were patients

TABLE 2 Characteristics of patients with and without delusional memories (N = 60)

with advanced cancer, suggested that patients had painful memories of their experience of delirium (Bruera et al., 2009). In our study, hallucinations were commonly reported in patients with delirium. Patients often reported hallucinations, and persecutory delusions and nightmares. This suggests that many delirious patients may experience hallucinations and may exhibit delusional memories following discharge from the ICU.

Contrary to our findings, a previous study with a larger sample size did not find an association between delusional memories and

TABLE 3 Variables associated with delusional memories in the multivariate analysis (N = 60)

Parameter	Odds ratio	95% Confidence limits	p
APACHE II score	0.98	0.915–1.050	.56
RASS score for mechanical ventilation	0.94	0.645–1.378	.76
Delirium in ICU	3.71	1.038–13.265	.04 [*]
Days in ICU	1.05	0.951–1.169	.31

Note: Logistic regression analysis.

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; ICU, intensive care unit; RASS, Richmond Agitation-Sedation Scale.

* $p < .05$.

delirium experienced during the ICU admission (Burry et al., 2015). These inconsistencies may be explained by several factors, including differences in sedation strategy. The previous study used daily sedation interruption, whereas our study did not. In line with this, Patel et al. (2014) showed that patients with rapidly reversible, sedation-related delirium alone had significantly fewer ventilator, ICU and hospital days compared to patients with persistent delirium. Therefore, although the incidence of delirium in our study is similar to those in previous reports, it is likely that the type of delirium observed in our patients may be different from previous reports. Moreover, the study by Burry et al. (2015) had fewer surgical patients compared with the present investigation, consisting of 13.5% and 65.0% of the study subjects, respectively. In our study, surgical patients received greater quantities of propofol and were more deeply sedated compared with medical patients. The sedative agents used in the study by Burry et al. (2015) were midazolam or lorazepam, whereas dexmedetomidine and propofol were used in the present study in 88% and 83% of the patients, respectively. Only 13% of our patients received midazolam. Given the discrepant findings in the literature, future studies are needed to investigate the association between delirium and delusional memories.

Since ICU nurses have an essential role in the screening for delirium and providing delirium prevention care, it is necessary to consider the potential impact of delirium on the delusional memory after discharge from the ICU. Multicomponent, non-pharmacological interventions are recommended for the prevention of delirium (Devlin et al., 2018). Reorientation, cognitive stimulation, music and the use of clocks are effective to improve cognitive impairment. Reorientation consists of asking and explaining (Colombo et al., 2012). Repeatedly explaining the situation to patients with delirium, helping patients organize their experiences and memories after recovery, and providing ongoing care are crucial to help patients maintain cognitive function.

Our study has several limitations. Firstly, the present study had a relatively small sample size, and the patients were recruited from a single site. However, the sample was heterogeneous since 65% of the patients were receiving mechanical ventilation due to surgical reasons.

Secondly, patients' recall performance may have been influenced by the fact that the interviewer was also involved in their clinical care. Thirdly, although delusional memories can persist, the present study only investigated them from days 5–10 after ICU discharge. Consequently, we may have been unable to measure the incidence of delusional memories manifested after this interview period. Therefore, a longitudinal study using a larger sample size is warranted.

In conclusion, the present study showed that mechanically ventilated patients exhibiting delirium during their ICU admission were likely to experience delusional memories following discharge from the ICU. Prevention of delirium may also help reduce delusional memories. Further prospective studies are needed using larger samples stratified by demographic background.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Participants of this study did not agree for their data to be shared publicly, so supporting data are not available.

ORCID

Yasuyo Yoshino  <https://orcid.org/0000-0001-9201-4570>

Takeshi Unoki  <https://orcid.org/0000-0002-7778-4355>

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