ORIGINAL ARTICLE

EVALUATING THE RISK OF DELIRIUM IN ELDERLY INPATIENTS IN COVID-19 INTENSIVE CARE: A PROSPECTIVE AND OBSERVATIONAL STUDY

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Abstract

Introduction: Delirium is dangerous, often preventable, and associated with a high financial burden and increased morbidity and mortality. This study aimed to evaluate the risk of delirium in elderly inpatients in COVID-19 intensive care units.

Materials and Method: This study used a prospective and observational design. Between July and November 2022, 49 intensive care patients were admitted to a training and research hospital in northeast Turkey. The data were collected using the Patient Information Form, Critical-Care Pain Observation Tool, Ramsay Sedation Scale, and Nursing-Delirium Screening Scale.

Results: The patients' mean age was 76.90±8.29 years. The longer the length of stay in the intensive care unit, the incidence of delirium increased. The incidence of delirium increased in patients aged 70–95 years (p=0.007). Patients with delirium experienced insomnia and agitation and used more sedative drugs (p<0.05). The predictors of early delirium were sedation (β=0.869), agitation (β=-0.582), and diastolic blood pressure (β=0.258). The predictors of delirium were pain (β=-0.599) and sedation (β=0.267).

Conclusion: The study demonstrated that older age, agitation, sedation, pain, and diastolic blood pressure predicted delirium in elderly COVID-19 inpatients. It is necessary to identify and eliminate risk factors to reduce the risk of delirium in elderly patients. Nurses should play an active role in identifying and managing delirium in elderly COVID-19 patients.

Keywords: COVID-19; Delirium; Aged; Intensive Care.

INTRODUCTION

Delirium is a psychiatric disorder defined as acute brain failure that occurs due to reasons such as electrolyte imbalance, a chronic disease, trauma, and polypharmacy (1). It causes symptoms such as agitation, irritability, non-compliance with treatment and aggression, which lead to changes in consciousness such as confusion, lethargy, and stupor in patients. It also causes thought disorders such as delusions, perception disorders such as auditory and visual hallucinations and illusions, and intense emotional reactions such as anger in the patient (2). The diagnosis is often missed due to its subtle clinical manifestation, particularly in the hypoactive type. Delirium is dangerous, often preventable, and is associated with a high financial burden and increased morbidity and mortality.

Some precipitating and predisposing factors are important in the development of delirium. Evaluating and recording these factors before delirium develops and applying preventive interventions to patients at risk of delirium can contribute to the problem's solution (3). Predisposing factors for delirium are age, low mini-mental state assessment, being male, mood disorders, some chronic diseases, severity of the disease, nutritional disorders, visual and auditory diseases, and alcohol use. Precipitating factors are contaminations, drugs, dehydration, electrolytic disturbances, bladder catheters, surgical procedures, and hospitalization (4,5).

Delirium is an important indicator of mortality in adult COVID-19 patients and increases the risk of death in elderly patients. Delirium is also associated with prolonged hospital stays, intensive care unit admissions, and ventilator use (6). Delirium prolongs patient's stay in intensive care unit, and it causes death in elderly COVID-19 patients (7). For patients older than 65 years, the commonness, frequency, and death rates of delirium in COVID-19 patients were 28.2%, 25.2%, and 48.4%, respectively (8). Therefore, defining the risk of delirium in COVID-19 patients is important for the patient's survival and quality of life. The present study was conducted to evaluate the risk of delirium in elderly inpatients in COVID-19 intensive care units.

MATERIALS AND METHOD

Study design

This study was conducted as a prospective and observational study.

Sample and setting

The study population included patients older than 65 years old who were hospitalized in the COVID-19 intensive care unit of a tertiary hospital between July and November 2022. As a result of the power analysis, with an effect size of 0.502, the power of the study was accepted as 80%, type 1 error was accepted as 5%, and the required sample size for the study was determined as 12 individuals (9). The sample included 49 intensive care patients who met the inclusion criteria. Inclusion criteria include (a) being 65 years old and older, (b) being conscious, and (c) obtaining verbal and written consent. Exclusion criteria include (a) taking propofol, (b) taking opioids, and (c) using neuromuscular blockers.

Instruments

Data were collected using the Patient Information Form, Critical-Care Pain Observation Tool (CPOT), Ramsay Sedation Scale (RSS), and Nursing-Delirium Screening Scale (Nu-DESC). Assessments were performed on the first, third, fifth, and seventh days.

Patient information form

Patient Information Form includes variables to determine the patient's social and demographic characteristics and vital signs which consisted of 20 questions, including age, gender, number of

days in the intensive care unit, the status of being connected to a mechanical ventilator, systolic blood pressure, diastolic blood pressure, respiratory rate, pulse rate, white blood cell (WBC), oxygen saturation (SpO_2), insomnia, agitation, sedation, neuromuscular blocker, propofol, opioid treatment, mortality, frailty index, length of intensive care unit stay, and length of hospitalization.

Critical-care pain observation tool (CPOT)

The tool was developed by Gelinas et al. (10). The Turkish validity and reliability study was conducted by Gündoğan et al. (9), and the Cronbach's α value was found to be 0.87–0.99. The scale is divided into four subsections and each section is evaluated between 0 and 2 points, and the total score varies between 0 and 8. Intensive care patients who score above two on the scale are defined as painful. In this study, Cronbach's α values on the scale were 0.89, 0.87, 0.86, and 0.92 on the first, third, fifth, and seventh days, respectively.

Ramsay sedation scale (RSS)

The RSS was a six-point Likert type scale and assessed the sedation level developed by Ramsay et al. (11). In the scale evaluation, score starts from 1: anxious, uneasy and restless and continues until score 6: no response. An increase in the score indicates an increase in the level of sedation.

Nursing-delirium screening scale (Nu-DESC)

The scale was developed by Gaudreau et al. (12). The Turkish validity and reliability study was conducted by Karataş and Samancıoglu-Baglama (13), and Cronbach's α value was found to be 0.74. A score between 0 and 2 is given for each item, and 10 points can be obtained from the scale. According to reports, the threshold value for delirium is 2. In this study, Cronbach's α values of the scale were 0.87, 0.89, 0.88, and 0.90 on the first, third, fifth, and seventh days, respectively.

Delirium diagnosis was made by an anesthesiologist and two psychiatric nurses using Nu-DESC. According to the Nu-DESC, patients with a scale mean score of two or more (≥ 2) were considered to have delirium.

The Clinical Frailty Scale (CFS)

The CFS is a straightforward and accessible tool that can be used to quickly and simply assess frailty (14). The CFS consisted of seven levels: One level = Very Fit = People who are vigorous, active, energetic, exercises regularly, is in the fittest group for her age. Two level = Fit = Previously known as well: People who have no intense disease symptoms but are less fit than level 1. Three level = Managing Well = People whose medical problems are well controlled. Four level = Living with Very Mild Frailty = A common complaint is being "slowed-up" and being tired during the day. Five level = Living with Mild Frailty = These people usually need help in higher-order instrumental activities of daily living. Six level = Living with Moderate Frailty = They need help with all outside activities and with keeping house. Seven level = Living with Severe Frailty = People who are characterized by progressive dependence in personal activities of daily living.

Statistical analysis

The data obtained from the study were analyzed in SPSS 24 package program (IBM SPSS, New York, USA). Descriptive statistics, such as percentages, arithmetic mean, and standard deviation, were used to analyze social and demographic characteristics. The suitability of the sample for normal distribution was evaluated using the Kolmogorov–Smirnov test. Pearson Chi-Square and Fisher's Exact Test were used to compare demographic variables and physiological parameters of patients with and without delirium. The significance level (p) was considered 0.05.

The effect of independent variables (systolic blood pressure, diastolic blood pressure, respiratory rate, pulse rate, WBC, SpO_2, CPOT, and RSS) on the dependent variable (Nu-DESC) was studied using multiple linear regression analysis. This analysis was performed on Day 7 measurements. First, it was evaluated whether the six conditions for the analysis were met. The dependent variable is a continuous variable. All variables have a normal distribution. Skewness and kurtosis values range from −1 and +1. The correlation coefficient between independent variables is less than 0.80. It shows that there is no multicollinearity between independent variables. In the table of residual statistics, standard residual minimum and maximum values are between -3.29 and +3.29. The maximum value in the Cook's Distance row is less than 1.000. It shows that there are no outliers in the observed data. According to the histogram, the errors in the forecasts are normally distributed. The scatter plot shows that there is a linear relationship between the variables. As a result, it was determined that all six conditions for multiple linear regression analysis were met.

Ethical considerations

Ethics committee approval was obtained from Aksaray University Clinical Research Ethics Committee (date: 23.06.2022, Decision No: 2022/12-04). The patients participating in the study and their relatives were informed about the study, and data were collected by explaining that personal information would be kept confidential. Written and verbal consent were obtained from the patients.

RESULTS

Delirium, mortality, frailty index, and hospitalization statistics

According to the Nu-DESC scoring, 36.7% of the patients showed delirium symptoms on the first day, 40.8% on the second day, and 49.0% on the fifth and seventh days (Table 1). The 90-day mortality rate of elderly patients with COVID-19 was 38.8%. The length of intensive care unit stay in patients was 20.55±22.36. The length of hospitalization was 23.36±22.87. The average frailty index was 5.70±1.60.

Table 1. Delirium, mortality, frailty index, and hospitalization statistics (n=49)

	n	%
Day 1 delirium (≥2)		
Yes	18	36.7
No	31	63.3
Day 3 delirium (≥2)		
Yes	20	40.8
No	29	59.2
Day 5 delirium (≥2)		
Yes	24	49.0
No	25	51.0
Day 7 delirium (≥2)		
Yes	24	49.0
No	25	51.0
90-day mortality		
Yes	19	38.8
No	30	61.2
	Mean	**SD***
Length of intensive care unit stay	20.55	22.36
Length of hospitalization	23.36	22.87
Frailty index	5.70	1.60

*SD=Standard Deviation

Sample characteristics

The mean age of the elderly intensive care unit patients who participated in the study was 76.90 ± 8.29 (minimum of 65 and maximum of 95). Of the patients with delirium, 70.8% were between 76 and 95 years old, and 32.0% of the patients with no delirium were between 76 and 95 years old (p = 0.007) (Table 2). Of the patients with delirium, 54.2% were male, and 60.0% of the patients with no delirium were male ($p > 0.05$).

Table 2. Descriptive characteristics of patients with and without delirium (n=49)

Characteristics	Delirium (+)		Delirium (-)		test value*	p value
	n	%	n	%		
Age						
65-75 years	7	29.2	17	68.0	7.389	0.007
76-95 years	17	70.8	8	32.0		
Gender						
Female	11	45.8	10	40.0	0.170	0.680
Male	13	54.2	15	60.0		

*Pearson Chi-Square

Table 3. Physiological variables of patients with and without delirium (n=49)

Variables	Delirium (+)		Delirium (-)		test value*	p value
	n	%	n	%		
Respiration						
Spontaneous	18	75.0	23	92.0	2.590	0.138
CPAP	6	25.0	2	8.0		
Insomnia						
Yes	18	75.0	4	16.0	17.229	p<0.01
No	6	25.0	21	84.0		
Agitation						
Yes	16	66.7	0	0.0	24.747	p<0.01
No	8	33.3	25	100.0		
Sedation						
No	7	29.2	23	92.0	20.855	p<0.01
Seroquel	10	41.7	2	8.0		
Dexmedetomidine+Seroquel	2	8.3	0	0.0		
Dexmedetomidine	5	20.8	0	0.0		
	Mean	SD	Mean	SD	test value**	p value
Systolic blood pressure	121.79	20.45	121.12	19.30	0.118	0.906
Diastolic blood pressure	68.00	9.15	65.40	9.78	0.959	0.342
Respiratory rate	22.45	5.23	20.48	4.57	1.410	0.165
Pulse rate	93.83	18.51	84.00	10.79	1.949	0.057
WBC	11.89	6.79	10.67	4.55	0.741	0.462
SpO_2	95.16	4.28	95.24	2.20	0.076	0.940

*Fisher's Exact Test; ** Independent samples test, CPAP: Continuous Positive Airway Pressure, Seroquel: Quetiapine, WBC: White Blood Cell, SpO_2: Oxygen Saturation

Table 4. Predictors of the delirium in elderly patients with COVID-19

	B (95% CI for B)	SE	β	t	*p*
Day one (R = 0.896, R2 = 0.803, F= 13.709, p < 0.01)					
SBP	-0.001 (-0.023-0.021)	0.011	-0.012	-0.127	0.899
DBP	0.052 (0.013-0.091)	0.019	0.258	2.704	0.010
Respiratory rate	-0.077 (-0.160-0.005)	0.041	-0.176	-1.904	0.065
Pulse rate	0.015 (-0.005-0.035)	0.010	0.141	1.537	0.133
WBC	0.005 (-0.048-0.058)	0.026	0.015	0.190	0.851
SpO2	0.060 (-0.058-0.178)	0.058	0.104	1.030	0.310
Insomnia	-0.267 (-1.199-0.665)	0.460	-0.051	-0.580	0.565
Agitation	-4.342 (-6.205-2.479)	0.919	-0.582	-4.722	0.000
Sedation	0.552 (-1.278-2.382)	0.903	0.059	0.611	0.545
CPOT	-0.634 (-1.760-0.492)	0.556	-0.121	-1.141	0.261
RSS	2.433 (1.896-2.969)	0.265	0.869	9.188	0.000
Day three (R = 0.807, R2 = 0.651, F= 6.274, p < 0.01)					
SBP	-0.014 (-0.052-0.023)	0.019	-0.096	-0.770	0.446
DBP	0.044 (-0.019-0.106)	0.031	0.155	1.415	0.165
Respiratory rate	0.102 (-0.020-0.225)	0.060	0.208	1.692	0.099
Pulse rate	-0.017 (-0.050-0.015)	0.016	-0.131	-1.077	0.289
WBC	0.008 (-0.112-0.128)	0.059	0.016	0.139	0.890
SpO2	0.090 (-0.136-0.315)	0.111	0.097	0.805	0.426
Insomnia	-0.247 (-1.590-1.095)	0.663	-0.044	-0.373	0.711
Agitation	-4.304 (-6.605-2.004)	1.136	-0.661	-3.791	0.001
Sedation	0.492 (-0.532-1.515)	0.505	0.166	0.974	0.337
CPOT	-0.849 (-2.823-1.125)	0.974	-0.134	-0.871	0.389
RSS	1.974 (1.094-2.853)	0.434	0.612	4.546	0.000
Day five (R = 0.757, R2 = 0.573, F= 4.508, p < 0.01)					
SBP	-0.011 (-0.047-0.024)	0.018	-0.096	-0.648	0.521
DBP	0.010 (-0.068-0.088)	0.038	0.033	0.262	0.795
Respiratory rate	0.094 (-0.028-0.215)	0.060	0.189	1.561	0.127
Pulse rate	-0.001 (-0.040-0.037)	0.019	-0.008	-0.057	0.955
WBC	0.011 (-0.153-0.176)	0.081	0.022	0.139	0.890
SpO2	0.038 (-0.240-0.316)	0.137	0.037	0.275	0.785
Insomnia	-0.841 (-2.569-0.888)	0.853	-0.145	-0.986	0.331
Agitation	-3.113 (-6.228-0.003)	1.538	-0.513	-2.024	0.050
Sedation	0.509 (-0.898-1.916)	0.694	0.160	0.733	0.468
CPOT	-1.190 (-3.794-1.414)	1.285	-0.193	-0.926	0.360
RSS	1.461 (0.409-2.513)	0.519	0.407	2.813	0.008

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	B (95% CI for B)	SE	β	t	*p*
Day seven (R = 0.828, R2 = 0.686, F= 7.332, p < 0.01)					
SBP	0.008 (-0.025-0.042)	0.016	0.055	0.502	0.618
DBP	0.049 (-0.018-0.115)	0.033	0.155	1.481	0.147
Respiratory rate	0.044 (-0.093-0.180)	0.067	0.073	0.648	0.521
Pulse rate	0.019 (-0.014-0.052)	0.016	0.117	1.184	0.244
WBC	-0.080 (-0.192-0.032)	0.055	-0.153	-1.439	0.159
SpO2	0.170 (-0.045-0.386)	0.106	0.191	1.603	0.118
Insomnia	-1.051 (-2.801-0.699)	0.864	-0.177	-1.217	0.231
Agitation	-0.035 (-2.117-2.047)	1.028	-0.006	-0.034	0.973
Sedation	0.766 (-0.177-1.710)	0.466	0.250	1.645	0.108
CPOT	-3.711 (-5.942-1.481)	1.101	-0.599	-3.371	0.002
RSS	0.824 (0.093-1.555)	0.361	0.267	2.284	0.028

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, WBC: White Blood Cell, SpO2: Oxygen Saturation, CPOT: Critical-Care Pain Observation Tool, RSS: Ramsay Sedation Scale, B: Unstandardized coefficient, SE: Standard Error, β: Standardized coefficient, CI: Confidence Interval

Physiological variables

The difference between the insomnia and agitation frequencies and the sedative drug use of patients with and without delirium was at the level of statistical significance ($p < 0.01$). The difference between spontaneous breathing, mean systolic and diastolic blood pressures, respiratory and pulse rates, WBC, and SpO_2 levels of the patients with and without delirium was similar between groups ($p > 0.05$) (Table 3).

Predictors of delirium

In the multiple regression model, independent variables (systolic blood pressure, diastolic blood pressure, respiratory rate, pulse rate, WBC, SpO2, insomnia, agitation, sedation, CPOT, and RSS measures) explained approximately 80% of the variance for delirium in elderly inpatients on Day 1 ($p<0.01$). Delirium was predicted by RSS (β=0.869), agitation (β=-0.582), and diastolic blood pressure (β=0.258, Table 4). Independent variables explained approximately 65% of the variance for delirium in elderly inpatients on Day 3 ($p<0.01$). Delirium was predicted by agitation (β=-0.661) and RSS (β=0.612, Table 4). In the evaluation on the third day, delirium was associated with agitation and sedation. Independent variables explained approximately 57% of the variance for delirium in elderly inpatients on Day 5 ($p<0.01$). Delirium was predicted by agitation (β=-0.513) and RSS (β=0.407, Table 4). In the evaluation performed on the fifth day, delirium was associated with agitation and sedation. Independent variables explained approximately 69% of the variance for delirium in elderly inpatients on Day 7 ($p<0.01$). The most important predictors of delirium on the seventh day were CPOT (β=-0.599) and RSS (β=0.267, Table 4). In the last evaluation, delirium was associated with pain and sedation.

The effects of mortality, frailty index, and hospitalization on delirium

The mortality, frailty index, and hospitalization statistics explained 5% of the variance for delirium in elderly inpatients ($p > 0.05$) (Table 5). The 90-day

Table 5. The effects of mortality, frailty index, length of intensive care unit stay, and length of hospitalization statistics on delirium.

	B (95% CI for B)	SE	β	t	*p*
Model 1 (R = 0.543, R2 = 0.295, F= 11.727, p = 0.002)					
Frailty index	0.987 (0.396-1.577)	0.288	0.543	3.425	0.002
Model 2 (R = 0.221, R2 = 0.049, F= 2.404, p = 0.128)					
90-day mortality	-1.335 (-3.067-0.397)	0.861	-0.221	-1.550	0.128
Model 3 (R = 0.221, R2 = 0.049, F= 2.404, p = 0.128)					
Frailty index	0.988 (-0.358-1.618)	0.307	0.544	3.223	0.003
Length of intensive care unit stay	0.038 (-0.117-0.194)	0.076	0.295	0.509	0.615
Length of hospitalization	-0.035 (-0.182-0.113)	0.072	-0.280	-0.480	0.635

B: Unstandardized coefficient, SE: Standard Error, β: Standardized coefficient, CI: Confidence Interval

mortality, length of intensive care unit stay, and length of hospitalization were not associated with delirium ($p > 0.05$). But the frailty index was the most important predictor of delirium and it explained approximately 30% of the variance for delirium in elderly inpatients with COVID-19 ($p = 0.002$).

DISCUSSION

This study aimed to evaluate the risk of delirium in elderly inpatients in COVID-19 intensive care units. We demonstrated that the risk of delirium increased from Days 1 to 7 in elderly patients with COVID-19. Early risk factors for delirium in elderly patients with COVID-19 were sedation, agitation, and diastolic blood pressure. Late risk factors of delirium were sedation, agitation, and pain.

In this study, one of the early and late risk factors of delirium was sedation. In a study of COVID-19 patients, 86.4% of those with delirium had evidence of excessive sedation. In addition, the use of high doses of sedation was associated with the frequency of delirium in these patients, increased deaths in intensive care, and prolonged length of stay in intensive care (15). Another study on COVID-19 patients found a relationship between the proportion of days with delirium symptoms and the level of sedation (16). The use of sedative drugs, particularly sedative-hypnotics and anticholinergic agents, has been associated with the development of delirium in intensive care unit patients (17). Delirium in intensive care patients may be related to sedative use. Sedative-induced delirium is associated with high mortality and prolonged hospitalization (18). In our study, an increase in delirium level may have increased the use of sedatives and, therefore, the level of sedation.

Agitation was one of the most important predictors of early and late delirium in the present study. During COVID-19 infection, delirium and psychomotor agitation were associated conditions that occurred in intensive care patients (19). The hyperactive type of delirium was most common in patients with COVID-19. It causes agitation, which is difficult to control and increases with age. Patients with COVID-19 were more agitated than patients with influenza (20). Our study sample consisted of elderly patients with COVID-19. Agitation is an important predictor of delirium in elderly patients with COVID-19. Therefore, agitation in elderly needs to be well evaluated and managed to prevent delirium in intensive care units.

Another important risk factor for early delirium in this study was diastolic blood pressure. Most

studies of elderly patients with COVID-19 had not found blood pressure to be a risk factor (8–9, 21). The blood pressure values in elderly COVID-19 patients with and without delirium did not differ (8). The incidence of hypertension in adult COVID-19 patients with and without cognitive impairment did not differ (9). Further studies should be conducted to evaluate the effects of systolic and blood pressure in elderly patients with COVID-19. In this study, diastolic blood pressure in the early period was an important risk factor for delirium. In future studies, whether patients are using drugs for blood pressure should also be evaluated.

In this study, the pain was one of the most important predictors of last delirium in elderly patients with COVID-19. The high incidence of delirium in COVID-19 patients was associated with some factors, such as fear, anxiety, insomnia, and pain. Most patients in intensive care units experience pain during treatment and care interventions such as respiratory interventions, invasive strategies, nursing interventions, and trauma (22). One symptom of the novel coronavirus (SARS-CoV-2) is pain. After exposure to SARS-CoV-2, patients with COVID-19 experienced varying degrees of headache, muscle and/or joint pain, sore throat, chest pain, and abdominal pain. The virus affects the nervous system, digestive system, and cardiovascular system due to infection (19). This study also showed that pain is a significant risk factor for elderly COVID-19 patients. Therefore, pain assessment and management should be performed correctly in these patients to reduce or eliminate the risk of delirium.

The frailty index was one of the most important predictors of last delirium in elderly patients with COVID-19. The 90-day mortality, length of intensive care unit stays, and length of hospitalization were not associated with delirium. In one study, delirium was associated with frailty index, length of hospital stay, and 30-day mortality (23). In another study, the frailty index and clinical frailty scale were able to predict an acute delirium episode in patients in intensive care (24). In another study, it was reported that elderly patients with a high frailty index had a high risk of delirium, long hospital stays, and high hospital mortality (25). Therefore, frailty index is important in terms of delirium in elderly patients with COVID-19 in intensive care.

Limitations

This study has some limitations. In the context of risk factors affecting delirium, the scope of the questionnaire can be expanded, and different scales can be used in future studies. The study was conducted in a single center. Therefore, the results of the study cannot be generalized to all elderly patients with COVID-19. Conducting similar and subsequent meta-analysis studies may contribute to forming an opinion on this subject.

CONCLUSION

We suggested that the longer a patient stays in the intensive care unit, the higher the risk of developing delirium regarding COVID-19 patients hospitalized in ICU. The patient's pain, sedation, insomnia, and agitation levels were found to be important risk factors for delirium. Agitation and diastolic blood pressure were the most important predictors of early delirium. The incidence of delirium increases with age.

Delirium is a significant health concern for elderly patients with COVID-19, increasing the length of hospital stay and mortality. To reduce the risk of delirium in elderly patients, it is necessary to identify and eliminate risk factors. Nurses who provide uninterrupted care to patients have a great responsibility. Nurses should take active responsibility in identifying and managing the pain of elderly patients with COVID-19, assessing sedation levels and physiological parameters, such as diastolic blood pressure, agitation, pain, and insomnia, planning appropriate nursing

interventions, and providing medical treatment. Additionally, frailty indexes of elderly patients in intensive care should be evaluated and studies should be conducted to reduce the fragility of patients.

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