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ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

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Sleep Disturbances Associated with Delirium in Conscious Patients in the Intensive Care Unit

Yoğun Bakım Ünitesinde Yatan Bilinci Açık Hastalarda Deliryuma Bağlı Uyku Bozuklukları

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ABSTRACT *Objective:* The primary aim of the study was to analyse the relationship between subjective sleep quality assessed with the Numeric Rating Scale (NRS) and the presence of delirium identified with both the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) and Intensive Care Delirium Screening Checklist (ICDSC). The secondary objective was to analyse the effect of other selected predictors on delirium.
Materials and Methods: The prospective observational study included 126 non-intubated patients staying in the ICU for more than 24 hours. Delirium was assessed simultaneously with both instruments (CAM-ICU and ICDSC) twice daily, and perceived sleep quality (NRS) was evaluated once a day. From 126 patients, 1299 paired questionnaires and 278 NRS records were obtained.
Results: There were 37 (29.4 %) and 40 (31.7 %) patients identified as CAM-ICU positive or having an ICDSC score ≥ 4, respectively. An NRS ≤ 5 was found in 93 patients (73.8 %). A statistically significant relationship between the incidence of delirium (assessed by two instruments) and sleep quality (NRS ≤ 5) was confirmed. CAM-ICU positivity 0.391 [95% CI, 0.36 to 0.421] (p <0.001) and ICDSC positivity 0.463 [95% CI, 0.435 to 0.491] (p <0.001). This relationship strength (assessed using Kendall's Tau) was rated as moderate.
Conclusion: The study suggests a relationship between delirium and subjectively assessed sleep quality. In this respect, sleep disturbances are likely to contribute to the development of delirium, even without valid objective data confirming them as a definite risk factor.
Keywords: intensive care unit, delirium, sleep disturbances, delirium screening tool

ÖZ *Amaç:* Çalışmanın temel amacı, Sayısal Derecelendirme Ölçeği (NRS) ile değerlendirilen subjektif uyku kalitesi ile Yoğun Bakım Ünitesi (CAM-ICU) ve Yoğun Bakım Ünitesi (CAM-ICU) için Karışıklık Değerlendirme Yöntemi ile tanımlanan deliryum varlığı arasındaki ilişkiyi analiz etmektir. Bakım Deliryum Tarama Kontrol Listesi (ICDSC). İkincil amaç ise seçilen diğer belirleyicilerin deliryum üzerindeki etkisini analiz etmekti.
Gereç ve Yöntem: Prospektif gözlemsel çalışmaya yoğun bakım ünitesinde 24 saatten fazla kalan entübe olmayan 126 hasta dahil edildi. Deliryum her iki cihazla (CAM-ICU ve ICDSC) eş zamanlı olarak günde iki kez, algılanan uyku kalitesi (NRS) ise günde bir kez değerlendirildi. 126 hastadan 1299 eşleştirilmiş anket ve 278 NRS kaydı elde edildi.
Bulgular: CAM-ICU pozitif veya ICDSC skoru ≥ 4 olan sırasıyla 37 (%29,4) ve 40 (%31,7) hasta vardı. 93 hastada (%73,8) NRS ≤ 5 bulundu. Deliryum insidansı (iki araçla değerlendirilen) ile uyku kalitesi (NRS ≤ 5) arasında istatistiksel olarak anlamlı bir ilişki doğrulandı. CAM-ICU pozitifliği 0,391 [%95 GA, 0,36 ila 0,421] (p <0,001) ve ICDSC pozitifliği 0,463 [%95 GA, 0,435 ila 0,491] (p <0,001). Bu ilişkinin gücü (Kendall's Tau kullanılarak değerlendirildi) orta düzeyde olarak derecelendirildi.
Sonuç: Çalışma deliryum ile subjektif olarak değerlendirilen uyku kalitesi arasında bir ilişki olduğunu düşündürmektedir. Bu bakımdan, uyku bozukluklarının, kesin bir risk faktörü olduğunu doğrulayan geçerli objektif veriler olmasa bile, deliryum gelişimine katkıda bulunması muhtemeldir.
Anahtar Kelimeler: yoğun bakım ünitesi, deliryum, uyku bozuklukları, deliryum tarama aracı

Introduction

Sleep is vital for physical and mental health. Nowadays, more attention is paid to sleep disturbances in intensive care unit (ICU) patients, as they may potentially contribute to the development of delirium. Studies have shown numerous similarities in the clinical and physiological profiles of patients with delirium and sleep disturbances (1). A study of 29 ICU patients found an association between delirium and severe sleep reduction (2). There is an electrophysiological relationship between sleep architecture changes and delirium, with delirium occurring in patients with rapid eye movement (REM) sleep loss and those with confirmed atypical sleep characterised by electroencephalography (EEG) findings suggesting wakefulness (2–4). A meta-analysis confirmed that preexisting sleep disturbances are likely associated with higher rates of postoperative delirium (OR 5,24; 95% CI: 3,61–7,60; p < 0.001) (5). Even though the link between sleep disturbances and delirium was studied and analysed by many authors (1,6,7), the available literature suggests that there may be a close relationship between delirium, sleep, circadian rhythm, and critical illness; however, no causal pathway has yet been clearly described, and the directionality of the relationship is not understood. The attempts to reduce the incidence of delirium are based on identifying and modifying risk factors. Sleep disturbances are thus one of the potentially suggestible risk factors. To reflect professionals' increasing interest in the recent Society of Critical Care Medicine guidelines on sedation and delirium, the sleep promotion strategy is a fundamental and integral part of delirium prevention and management (8).

Therefore, the present study aimed to investigate the relationship between subjective sleep quality assessed with the Numeric Rating Score (NRS) and the presence of delirium identified with both the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) and the Intensive Care Delirium Screening Checklist (ICDSC). The second endpoint was to analyse the effect of other selected predictors on the occurrence of delirium.

Materials and Methods

Design

A Prospective Observational Study

Patients

Data for the study were collected in the Department of Anaesthesiology and Intensive Care Medicine ICU (5 beds) and multidisciplinary ICU (10 beds) of AGEL Hospital between February 2020 - August 2020. Adult conscious patients who consented to participate and were staying in the ICU for more than 24 hours were included in the study. The following demographic data were collected: age, gender, smoking, alcohol. The following were recorded from the clinical data: operation, length of stay in ICU and overall mortality, type of admission, pain (VAS), sedation (RASS), TISS score, history of mechanical ventilation, restraints, and medication (opioids, benzodiazepines, antipsychotics). The exclusion criteria were a terminal illness, a diagnosis of dementia and an altered consciousness - Glasgow Coma Scale (GCS) score ≤ 12 or deep sedation (Richmond Agitation-Sedation Scale (RASS) score ≤ - 4).

Assessment instruments

Two instruments for diagnosing delirium were used in the study. The ICDSC includes the following eight items: altered level of consciousness, inattention, disorientation, hallucination-delusion, agitation or retardation, inappropriate speech or mood, sleep-wake cycle disturbance and symptom fluctuation. Each positive item scores one point. If the total score is ≥ 4, delirium is diagnosed. Scores of 1–3 indicate subsyndromal delirium (9).

When using the CAM-ICU to diagnose delirium, the first step is to assess the level of sedation with the RASS. (In deeply sedated patients not responding to stimulation, RASS score ≤ -4, the presence of delirium cannot be established.) The second step is an assessment of four key features of delirium: acute change or fluctuating course of mental status (Feature 1), inattention (Feature 2), Altered level of consciousness (Feature 3) and disorganised thinking (Feature 4). Delirium is considered positive when Feature 1 and Feature 2 and either Feature 3 or 4 are present. Otherwise, delirium is excluded (CAM-ICU negative). RASS scores ranging from 0 to –3 are associated with hypoactive delirium. A RASS score of +1 to +4 suggests hyperactive delirium. Mixed delirium is when the patient fluctuates between the two forms (10).

Sleep quality was assessed with the NRS. Patients used this 10-point analogue scale to rate their subjective quality of sleep. All assessments were performed in the morning, between 08.00 AM and noon, when patients were ready for assessment. Nurses asked patients the following question: *Could you rank your sleep of the last night on a scale between 0 (a worst night's sleep) and 10 (a best night's sleep)?*

Good vs. Bad sleep definition

In the study, patients' sleep was classified as either *good* (NRS > 5) or *bad* (NRS ≤ 5) and the sample was divided accordingly. The cut-off was arbitrarily determined based on literature data (16) showing good statistical results, namely a sensitivity of 83%, a specificity of 79%, an area under the receiver operating characteristic curve (AUROC) of 0,81 (95% CI: 0,74–0,87).

Process of translation

The instrument was translated and linguistically validated by the guidelines and standards for the translation and cultural adaptation of patient-reported outcome measures (11).

Data collection

Two assessment instruments (CAM-ICU and ICDSC) were used to detect delirium. Sleep quality was subjectively evaluated with the NRS. Nurses performed delirium screening twice a day, and sleep quality was assessed once a day. On average, the forms took approximately 5 minutes to complete. In total (126 patients), 1299 paired questionnaires and 278 NRS records were obtained.

Ethical aspects

The study, conducted by the Declaration of Helsinki, was approved by the ethics committee of AGEL (no. INT 2019003). Respondents' participation was voluntary and anonymous. The author approved using the Czech version of the CAM-ICU. The ICDSC was translated with the author's permission. The NRS was used as published by Rood et al. (12).

Data analysis

Relationships between pairs of metrics, ordinal or binary variables, were tested using Kendall's τ coefficient. The relationships between a set of explanatory variables (differentiators, predictors) on the one side and predicted (explained, dependent) binary or metric variables on the other were evaluated by multivariate regression with a reduction of dimensionality known as OPLS. This test can cope with the problem of severe multicollinearity (high intercorrelations) in the matrix of explanatory variables, while ordinary multiple regression fails to evaluate such data correctly. The multicollinearity in OPLS is favourable as it enhances the predictivity of the model. In the OPLS models with binary predicted variables, the logarithm of the ratio of the probability of positive outcome to the probability of adverse outcome (logarithm of the likelihood ratio) was chosen as a single dependent variable, so that the predicted probability ranged between 0 and 1. The statistical software SIMCA-P v.12.0 from Umetrics AB (Umeå, Sweden), which was used for OPLS analysis, enabled finding the number of relevant components, the detection of multivariate non-homogeneities, and testing the multivariate normal distribution and homoscedasticity (constant variance).

Results

The study comprised 126 consecutively admitted patients (76 males/ 50 females; 60,3/ 39,7 %) with a median age of 71 (60, 77). Twenty-seven patients (21,4 %) had a positive history of mechanical ventilation, and 38 respondents (30,2 %) underwent surgery. Acute admissions prevailed (81 %). The admission diagnoses varied, with the most frequent being the following International Classification of Diseases (ICD) categories (in descending order): diseases of the respiratory system (ICD J) 17,5 %, diseases of the circulatory (ICD I) and digestive (ICD K) systems 16,7 % each. 18, 3 % of admissions were classified as abnormal clinical findings (ICD R), including frequent ICU syndromes (shock, hypovolemia, sepsis, etc.) without further specification. The most frequently administered drugs related to analgesia, sedation and delirium treatment were opioids (53 patients; 42,1 %), antipsychotics (38 patients, 30,2 %) and benzodiazepines (27 patients, 21, 4%). The median length of stay in the ICU and hospital was six days (from 4 to 9) and 15,5 days (from 9 to 20), respectively. During their stay in the ICU, ten patients (7,9 %) died. The number of deaths throughout the entire hospital stay until discharge (including ICU deaths) was 18 (14,3 %). The median Therapeutic Intervention Scoring System (TISS) score measuring nursing workload was 557 (555, 557), suggesting that mainly conscious, not critically ill, patients were included in the sample.

From the 126 patients, 1299 paired records assessing delirium and 278 records evaluating subjective sleep quality were obtained. According to CAM-ICU assessment, 37 patients were classified as delirium-positive (326 records; 29,4 %) and 89 delirium-negative (973 records; 70 6%). Combining delirium-positivity with RASS, 18 patients showed hyperactive delirium (total of 152 records, 14,3 %), 12 hypoactive delirium (94 records; 9,5 %) and seven mixed forms (80 records, 5,6 %). According to ICDSC, delirium (a score of 4–8) was diagnosed in 40 patients (total

of 346 records; 31,7 %), subsyndromal delirium (a score of 1–3) in 32 patients (381 records; 25,4 %) and 54 patients (572 records; 42,9 %) were delirium-negative. Thirty-three patients (total of 75 records; 26,2 %) reported good sleep (NRS > 5), and 93 patients (203 records; 73,8 %) had lousy sleep (NRS ≤ 5). Based on this rating, the studied population was divided into two subgroups. (Table 1).

Kendall's τ values (using 95% CI), which were used to express the power of the relationships, were interpreted as follows: higher values indicated stronger relationships. In contrast, positive or negative values indicated direct or indirect causality (13). Almost all the following parameters were shown to be statistically significant regarding sleep disturbance ($p < 0.001$) (exceptional alcohol, age, RASS, gender, operation, type of admission, some diagnosis and hospital mortality). The results obtained (ranked by the absolute strength of the first three in the relationship and given with CI) were GCS -0,383 (-0,413 – -0,352), physical restraints 0,243 (0,209 – 0,276), VAS 0,196 (0,161 – 0,23) (Table 2,3).

The association between poor sleep quality (bad sleep, NRS ≤ 5) and delirium assessment (CAM-ICU, ICDSC) scores were studied. The results showed a significant relationship ($p < 0.001$) between sleep disturbances and delirium assessment methods. Kendall's τ was 0,391 (CI 0,36 – 0,421) for CAM-ICU positivity and 0,463 (0,435 – 0,491) for ICDSC positivity, respectively. An important point was that these positive associations (delirium positivity and bad sleep) were rated moderate (13) (Table 4).

To assess variances in the presence of delirium (for each diagnostic tool), advanced statistics were used to select a set of predictors (risk factors) evaluated in the OPLS model. In the OPLS model for multivariate regression, the risk factor with the highest statistical confidence for the CAM-ICU positivity and ICDSC positivity were the first three predictors (according to component loading): (1) GCS followed by (2) physical restraints and (3) VAS. The association of these three predictors were assessed as moderate to strong (14), and prediction is recommended. The rest of the variables and the degree of influence of the monitored variables were evaluated as weak, and thus, they are not suitable for predicting disorders (Table 5,6).

Table 1. Demographic and clinical data (n = 126) and paired observation (1299)

Variables	*n* (%)	median (quartiles)	Paired observation
Men	76 (60.3)		
Mechanical ventilation	27 (21.4)		
Operation	38 (30.2)		
Acute admission	102 (81)		
ICD: A, C, D, E, F	19 (15.1)		
ICD: I	21 (16.7)		
ICD: J	22 (17.5)		
ICD: K	21 (16.7)		
ICD: R	23 (18.3)		
ICD: M, N, S	20 (15.9)		
Opioids	53 (42.1)		
Benzodiazepines	27 (21.4)		
Antipsychotic drugs	38 (30.2)		
CAM ICU +	37 (29.4)		326
Hyperactive form (RASS +1 / +4)	18 (14.3)		152
Hypoactive form (RASS 0 / -3)	12 (9.5)		94
Mix	7 (5.6)		80
CAM ICU -	89 (70.6)		973
ICDSC negative (0)	54 (44.4)		572
Subsyndromal delirium (ICDSC 1-3)	32 (25.4)		381
Delirium (ICDSC 4 – 8)	40 (31.7)		346
NRS >5*	33 (26.1)		75
NRS ≤5 *	93 (73.8)		203
Age		71 (60, 77)	
Length of hospitalization on ICU		6 (4.25, 9)	
Length of hospitalization on hospital		15.5 (9, 20)	
ICU mortality	10 (7.9)		
Hospital mortality (overall include ICU mortality)	18 (14.3)		
TISS		(555, 557)	

*278 overal observation NRS, CAM ICU: Confusion Assesment Method for the Intensive Care Unit, RASS: Richmond Agitation Sedation Scale, ICDSC: Intensive Care Delirium Screening Checklist, ICU: Intensive Care Unit, TISS: Therapeutic Intervention Scoring Systém, NRS: Numeric Rating Score, ICD: International Classification of Diseases

Discussion

In this study, we have made some critical findings. Firstly, although screening questionnaires can help diagnose

Table 2. Relationships between Sleep disturbances and metric indices (n = 278)							
Variable	**n**	**NRS > 5 Good Sleep**		**NRS ≤ 5 Bad sleep**		**Kendall's τ (95% CI)**	**p-value**
	total	**n**	**median(quartiles)**	**n**	**median(quartiles)**		
Alcohol	278	75	1 (1, 1)	203	1 (1, 1)	0.049 (0.0131, 0.0849)	0,066
Age	278	75	71 (60, 78)	203	71 (60.3, 78)	0.0156 (-0.0204, 0.0515)	0,499
Length of_ICU stay	278	75	7 (5, 13)	203	9 (6, 15)	0.136 (0.1, 0.171)	<0.001
Length of hospital stay	278	75	17 (10, 29)	203	20 (14, 31)	0.106 (0.0704, 0.142)	<0.001
GCS	278	75	15 (15, 15)	203	15 (14, 15)	-0.383 (-0.413, -0.352)	<0.001
VAS	278	75	0 (0, 2)	203	1 (0, 3)	0.196 (0.161, 0.23)	<0.001
TISS	278	75	557 (555, 558)	203	557 (555, 557)	-0.13 (-0.165, -0.0944)	<0.001
RASS	278	75	0 (0, 0)	203	0 (0, 1)	0.0561 (0.0202, 0.0919)	0,033

GCS: Glasgow coma scale, VAS: Visual Analog Scale, TISS: Therapeutic Intervention Scoring System, RASS: Richmond Agitation Sedation Scale, NRS: Numeric Rating Score

Table 3. Relationships between Sleep disturbances and binary indices (n = 278)							
Variable	**n**	**NRS > 5 Good sleep**		**NRS ≤ 5 Bad sleep**		**Kendall's τ (95% CI)**	**p-value**
		n	**%**	**n**	**%**		
Mechanical ventilation	278	30	10,7%	55	19,8%	0.234 (0.2, 0.268)	<0.001
Smoking	278	44	15,8%	54	19,4%	0.116 (0.0806, 0.152)	<0.001
Men	278	91	32,8%	81	29,2%	-0.0048 (-0.0407, 0.0312)	0,864
Benzodiazepines	278	11	4,1%	18	6,6%	0.101 (0.0655, 0.137)	<0.001
Opioids	278	28	9,9%	42	15,0%	0.151 (0.116, 0.186)	<0.001
Antipsychotics	278	36	12,8%	44	15,9%	0.103 (0.0672, 0.138)	<0.001
Operation	278	31	11,1%	27	9,7%	0.0213 (-0.0147, 0.0572)	0,444
Type of admission	278	120	43,3%	111	40,1%	0.0377 (0.0017, 0.0736)	0,175
Restraints	278	5	1,9%	25	8,9%	0.243 (0.209, 0.276)	<0.001
ICU mortality	278	10	3,6%	22	7,8%	0.151 (0.115, 0.186)	<0.001
ICD: A	278	5	1,8%	6	2,3%	0.0344 (-0.0016, 0.0704)	0,215
ICD: C	278	10	3,6%	2	0,7%	-0.133 (-0.168, -0.0973)	<0.001
ICD: D	278	3	1,2%	1	0,3%	-0.0684 (-0.104, -0.0325)	0,014
ICD: E	278	2	0,8%	2	0,7%	0.0002 (-0.0358, 0.0362)	0,996
ICD: F	278	3	1,1%	8	2,9%	0.106 (0.0697, 0.141)	<0.001
ICD: I	278	20	7,2%	15	5,3%	-0.0377 (-0.0736, -0.0017)	0,174
ICD: J	278	27	9,7%	35	12,7%	0.101 (0.0654, 0.137)	<0.001
ICD: K	278	25	9,1%	26	9,5%	0.0357 (-0.0003, 0.0716)	0,199
ICD: M	278	0	0,1%	1	0,5%	0.0567 (0.0207, 0.0925)	0,041
ICD: N	278	7	2,5%	6	2,1%	-0.0102 (-0.0461, 0.0259)	0,715
ICD: R	278	28	10,1%	20	7,2%	-0.0529 (-0.0888, -0.017)	0,057
ICD: S	278	15	5,4%	9	3,2%	-0.0635 (-0.0993, -0.0276)	0,022
Hospital mortality	278	23	8,2%	25	9,1%	0.0475 (0.0115, 0.0833)	0,087

NRS: Numeric Rating Score, ICD: International Classification of Diseases

Table 4 . Relationships between Sleep disturbances and delirium parameters (CAM ICU / ICDSC) (n = 278)								
Tool	**Parameters**	**n**	**NRS > 5 Good sleep**		**NRS ≤ 5 bad sleep**		**Kendall's τ (95% CI)**	**p-value**
	Feature_1	278	25	9,0%	82	29,8%	0.471 (0.442, 0.498)	<0.001
	Feature_2	278	15	5,3%	52	18,7%	0.345 (0.313, 0.376)	<0.001
	Feature_3	278	14	5,0%	61	22,1%	0.419 (0.388, 0.448)	<0.001
	Feature_4	278	13	4,8%	53	18,9%	0.36 (0.329, 0.391)	<0.001
CAM ICU	CAM_ICU +	278	13	4,8%	56	20,3%	0.391 (0.36, 0.421)	<0.001
	HYPER	278	5	1,8%	28	9,9%	0.271 (0.238, 0.304)	<0.001
	HYPO	278	4	1,3%	16	5,9%	0.194 (0.159, 0.228)	<0.001
	MIX	278	4	1,5%	13	4,6%	0.142 (0.107, 0.177)	<0.001
	Altered Level of Consciousness	278	13	4,8%	63	22,7%	0.434 (0.404, 0.463)	<0.001
	Inattention	278	14	5,2%	49	17,8%	0.329 (0.296, 0.36)	<0.001
	Disorientation	278	10	3,5%	42	15,2%	0.326 (0.294, 0.358)	<0.001
	Hallucination, delusion	278	4	1,5%	15	5,5%	0.171 (0.136, 0.206)	<0.001
ICDSC	*agitation or retardation*	278	13	4,7%	51	18,3%	0.354 (0.322, 0.385)	<0.001
	Inappropriate speech or mood	278	5	1,8%	31	11,0%	0.295 (0.262, 0.328)	<0.001
	Sleep-wake cycle disturbance	278	0	0,0%	132	47,3%	0.528 (0.501, 0.553)	<0.001
	Symptom Fluctuation	278	20	7,1%	85	30,6%	0.663 (0.643, 0.683)	<0.001
	ICDSC 0 (normal)	278	119	42,9%	15	1,2%	-0.793 (-0.806, -0.78)	<0.001
	ICDSC 1 – 3 (subsyndrome delirium)	278	17	6,1%	64	23,2%	0.413 (0.383, 0.442)	<0.001
	ICDSC 4 – 8 Delirium	278	11	3,8%	63	22,9%	0.463 (0.435, 0.491)	<0.001
CAM ICU: Confusion Assessment Method for the Intensive Care Unit, , ICDSC: Intensive Care Delirium Screening Checklist, NRS: Numeric Rating Score								

delirium quickly (within 2 to 5 minutes), they can detect delirium differently. Unfortunately, the patient's ability to answer the questionnaire is limited in the ICU environment. Secondly, we found that patients who reported poor sleep quality had a higher incidence of delirium, 93 (73.8%) vs. 33 (26.1%). While several validated methods exist for screening, monitoring, and diagnosing sleep in the ICU, each technique has limitations and cannot be used for all patients. This is also one of the reasons why the effects of poor sleep quality and delirium development on patient outcomes are not immediately apparent. Finally, to prevent the growth of delirium, predicting its occurrence based on various indicators is a tendency; however, many of these indicators are not modifiable (e.g. age, TISS, gender).

The incidence of delirium varies considerably depending on the population of patients examined and diagnostic methods. Delirium has been reported in 16–89 % of ICU patients, and its incidence appears to be highest (up to 80 %) in mechanically ventilated patients (14,15). Our reported incidence (29 4 % when assessed with the CAM-ICU and 31 7% with ICDSC, respectively) lies within the lower part of the range, which could be explained by patients' characteristics (majority not very sick and not being actually mechanically ventilated). Delirium includes three motor subtypes – hyperactive, hypoactive, and mixed – which may be associated with different prognoses. In the present study, 14,3 % of cases were hyperactive, 9,5 % hypoactive, and 5,6 % mixed. A meta-analysis of 18 studies showed, on the other hand, different incidences, when the most frequent type was hypoactive (11 %), followed by mixed (7 %) and hyperactive (4 %) (16). Another methodological pitfall of assessing delirium with certain diagnostic instruments is the influence of sedative drugs, which may affect the results, as the positivity may be overrated due to RASS other than 0. A possible solution is to assess consciousness only after pharmacological sedation wears off. Therefore, to assess the persistence of delirium, many ICUs use routine daily sedation disruptions (spontaneous awakening

Table 5. Relationships between CAM-ICU and predictors for the predictive component as evaluated by OPLS model (n = 1299)								
		OPLS model Predictive component				Ordinary multiple regression		
	Variable	Component loading	t-statistics	R[a]		Regression coefficient	t-statistics	
Relevant predictors (matrix **X**)	Day	-0,134	-10,87	-0,193	**	0,056	5,43	**
	Supervision	0,058	2,78	0,083	*	0,004	0,25	
	Mechanical Ventilation	0,108	8,76	0,155	**	-0,010	-1,08	
	Smoking	0,109	10,85	0,156	**	-0,003	-0,30	
	Men	0,026	1,56	0,038		-0,060	-4,08	**
	Alcohol	0,159	24,38	0,228	**	0,061	11,31	**
	Benzodiazepines	0,192	6,68	0,276	**	0,015	0,53	
	Opioids	0,102	4,25	0,147	**	-0,008	-0,42	
	Antipsychotics	0,171	12,91	0,245	**	0,012	1,06	
	Operation	-0,135	-6,78	-0,194	**	-0,143	-10,44	**
	Age	0,051	4,10	0,073	**	0,070	4,51	**
	Restraints	0,458	24,78	0,656	**	0,233	16,86	**
	ICU mortality	0,147	10,02	0,211	**	0,064	3,05	**
	ICD: A	-0,060	-2,33	-0,086	*	-0,006	-0,25	
	ICD: C	-0,104	-7,99	-0,149	**	-0,029	-3,01	**
	ICD: F	0,182	14,53	0,260	**	0,012	0,72	
	ICD: I	0,058	4,84	0,083	**	0,017	2,04	*
	ICD: N	0,025	1,63	0,036		-0,004	-0,39	
	ICD: R	-0,062	-4,02	-0,089	**	0,012	0,53	
	ICD: S	-0,062	-6,28	-0,088	**	-0,008	-1,23	
	Hospital mortality	0,142	9,07	0,204	**	0,016	1,01	
	GCS	-0,648	-36,65	-0,929	**	-0,580	-19,05	**
	VAS	0,280	16,80	0,401	**	0,152	13,18	**
	TISS	-0,036	-2,66	-0,052	*	0,054	2,61	*
	RASS	0,168	10,18	0,241	**	-0,018	-1,74	
(matrix **Y**)	CAM-ICU	1,000	71,65	0,809	**			
Explained variability		65,5% (64,4% after cross-validation)						

[a]*R…Component loadings expressed as a correlation coefficients with predictive component, *p<0.05, **p<0.01,* GCS: Glasgow coma scale, VAS: Visual Analog Scale, TISS: Therapeutic Intervention Scoring System, RASS: Richmond Agitation Sedation Scale, ICD: International Classification of Diseases, CAM ICU: Confusion Assessment Method for the Intensive Care Unit

trials) as a part of standardised protocols for assessing delirium and the need for further sedation (8). The ICDSC diagnosed subsyndromal delirium (10) in 25,4 % of cases. Subsyndromal delirium could be viewed as a pre-delirium – a transition between delirium and normal mental status. It is very frequent in ICU patients, but its actual incidence and impact on the outcome of critically ill patients remain unclear. In a meta-analysis of 6 studies, subsyndromal delirium was found in one-third of critically ill patients, having a limited impact on their outcomes. (17) One of the study's primary goals was to assess the impact of sleep disturbances (for our purposes, classified subjectively as bad sleep, NRS ≤ 5) and their association between studied parameters. The study presumes that sleep disturbances may be a risk factor for delirium and prolonged mechanical ventilation, independently associated with other parameters (ICU deaths, ICU length of stay and hospital length of stay). Our findings are consistent with these hypotheses and

Table 6. Relationships between ICDSC and predictors for the predictive component as evaluated by OPLS model (n = 1299)								
		OPLS model Predictive component				**Ordinary multiple regression**		
	Variable	**Component loading**	**t-statistics**	**R[a]**		**Regression coefficient**	**t-statistics**	
Relevant predictors (matrix **X**)	Day	-0,092	-7,11	-0,136	**	0,039	2,77	*
	Supervision	0,066	2,80	0,098	*	0,027	1,07	
	Mechanical Ventilation	0,179	17,49	0,264	**	0,032	2,24	*
	Smoking	0,086	6,88	0,126	**	0,042	2,38	*
	Men	0,067	4,70	0,100	**	-0,020	-2,63	*
	Alcohol	0,187	15,94	0,276	**	-0,068	-6,51	**
	Benzodiazepines	0,183	5,88	0,270	**	-0,016	-0,66	
	Opioids	0,123	8,22	0,182	**	0,018	1,32	
	Antipsychotics	0,192	15,35	0,284	**	0,024	2,65	*
	Operation	-0,081	-3,61	-0,120	**	-0,115	-9,82	**
	Type of admission	0,046	2,36	0,068	*	0,022	1,72	
	Restraints	0,425	25,43	0,628	**	0,219	16,99	**
	Length of_ICU stay	0,072	4,29	0,106	**	0,037	3,98	**
	ICU mortality	0,183	11,53	0,271	**	0,104	5,38	**
	ICD: A	-0,081	-5,00	-0,119	**	-0,020	-1,11	
	ICD: C	-0,103	-7,61	-0,151	**	-0,018	-2,59	*
	ICD: F	0,195	9,28	0,287	**	0,061	2,91	*
	ICD: K	0,073	3,21	0,108	**	0,065	6,43	**
	ICD: S	-0,080	-3,75	-0,118	**	-0,045	-3,44	**
	Hospital mortality	0,164	16,84	0,242	**	0,023	1,53	
	GCS	-0,632	-70,86	-0,934	**	-0,560	-40,14	**
	VAS	0,273	25,68	0,403	**	0,129	11,03	**
	TISS	-0,095	-28,18	-0,140	**	0,028	2,20	*
	RASS	0,148	10,05	0,218	**	-0,020	-1,54	
(matrix **Y**)	ICDSC	1,000	59,96	0,805	**			
Explained variability		64,8% (63,9% after cross-validation)						

*[a]R…Component loadings expressed as a correlation coefficients with predictive component, *p<0.05, **p<0.01,* GCS: Glasgow coma scale, VAS: Visual Analog Scale, TISS: Therapeutic Intervention Scoring System, RASS: Richmond Agitation Sedation Scale, ICDSC: Intensive Care Delirium Screening Checklist

are similar to data reported by other authors (18,19). Even though our results are based on subjective assessments, which is a substantial limitation, the relationship between delirium and sleep disorders has been confirmed. On the other hand, a contrary data exists. The study by Kamdar et al. (20) has shown no difference between subjectively perceived sleep quality assessed with the Richards-Campbell Sleep Questionnaire (RCSQ) in patients with and without delirium (mean RCSQ 57 vs 58) and no relation between perceived sleep quality and transition to delirium (adjusted OR 1; 95% CI, 0,99-1,00). Interventional studies, however, suggest the opposite. According to Patel et al. (21), the sleep efficiency index has the potential to predict the development of delirium, with patients reporting high sleep efficiency index scores demonstrating a reduced risk of delirium (OR 0,9; 95% CI: 0,84–0,97). Similarly, Van Rompey et al. (22) revealed, using Cox regression, that earplugs lowered the risk of delirium or mild confusion in the ICU by 53 % (HR 0,47; 95% CI 0,27–0,82), with more patients reporting better subjectively assessed sleep quality.

Previous studies that potentially solved the problem are far from providing unambiguous results.

Another issue regarding the sleep-delirium study is the selection of adequate assessment instruments. Many authors have mentioned problems finding suitable techniques for assessing delirium and detecting sleep disorders simultaneously. It seems reasonable to combine an objective instrument with a subjective assessment (23). A possible approach (suitable mainly for non-ICU patients) is an objective assessment of sleep by actigraphy, a monitoring technique based on alterations in motor activity in combination with another subjective method (23). In ICU patients with altered consciousness (lower GCS, sedation), it is the gold standard considered polysomnography, together with a validated subjective questionnaire filled out by nurses (24).

According to reported results, patients with perceived poor sleep quality more often received sedative medication (benzodiazepines, opioids, and antipsychotics). Thus, the optimal approach to analgesia and sedation in ICU patients seems to be a matter of concern. Good clinical practice is well-established, such as using drugs with short half-lives, implementing nurse-driven sedation protocols, including daily awakening trials, limiting deep sedation, minimising the use of muscle relaxants, and monitoring the depth of sedation if necessary (12). Maintenance of normal circadian rhythm, promotion of physiological (good quality) sleep, and prevention of sleep deprivation/ disorders are crucial parts of ICU nursing care and are immediately related to sedation strategy, affecting numerous clinical outcome parameters, including delirium incidence. Recently, the main principle of delirium management has been shifting from treatment to prevention, requiring knowledge of the associated risk factors. According to Ely et al., patients staying in the ICU have ten or more risk factors for delirium onset (25). A meta-analysis by Zaal et al. (26) identified 11 risk factors for delirium supported by solid or moderate levels of evidence. Similarly, Van Rompaey et al. (27) grouped the most important risk factors into four domains, with 13 risk factors being identified as significant. Our findings agree with the abovementioned studies and add more statistical significance to relationships between delirium and its predictors by applying an OPLS model with consistent results. All the findings above related to sleep and delirium are generalisable and applicable to everyday clinical practice in the form of the so-called ABCDE bundle of proper analgesia, sedation, and delirium management. It has been proved that such a bundle of care, including appropriate pain management, light sedation, avoidance of benzodiazepines, early awakening and weaning from mechanical ventilation, routine delirium monitoring and early mobilisation, improves patient outcomes and decreases the delirium incidence by one-third (14).

Study limitations and recommendations.

The study's primary limitations are the size of the sample (number of patients, unicentric design) and the selection of subjective sleep quality instruments. For a complex and comprehensive evaluation, valid, consistent, and objective methods for sleep measurement (actigraphy, polysomnography) must be combined with subjective assessment instruments completed by patients or nurses. The high-quality, multicentric randomised trial could overcome these limitations and increase knowledge of the relationship between sleep disturbances and delirium in ICU patients.

Conclusion

Even though the relationship between sleep disturbances and delirium has not been fully elucidated, many authors assume a bidirectional causal relationship, suggesting that sleep disorders are a risk factor for the development of delirium. The presented study's results are consistent with this hypothesis. Early detection of delirium is fundamental, and choosing appropriate diagnostic tools remains a concern. Modern trends in intensive care reflect this two-way relation between sleep and delirium by respecting sleep-promoting (primarily non-pharmacological) strategies, prevention, and early therapy of delirium as the standard of nursing care. More detailed analysis of this sleep-delirium association is needed for even better and more personalised care in the future, minimising the incidence of delirium and need for sedation on the one hand and maximising ICU patients' sleep quality on the other hand.

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Ethics

Ethics Committee Approval: The study, conducted by the Declaration of Helsinki, was approved by the ethics

committee of AGEL (no. INT 2019003). Respondents' participation was voluntary and anonymous.

Informed Consent: Adult conscious patients who consented to participate and were staying in the ICU for more than 24 hours were included in the study.

Authorship Contributions

Surgical and Medical Practices: H.L., Concept: H.L., P.M., Design: H.L., P.M., K.A., Data Collection and Process: H.L., P.M., Analysis or Interpretation: H.L., K.A., Literature Search: H.L., P.M., Writing: H.L., P.M., K.A.

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