

POST-INTENSIVE CARE SYNDROME

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Dynamics of post-intensive care syndrome development in a multidisciplinary hospital ICU: a prospective cohort study

A.E. Rudnik^{1,3}, G.V. Sobetova^{2,3}, N.S. Nagaev¹,
E.N. Rudnik^{1,2}, A.V. Kulikov², A.A. Belkin^{1,2,*}

¹ *Clinical of the Institute of Brain, Berezovskiy, Russia*

² *Ural State Medical University, Yekaterinburg, Russia*

³ *Central City Clinical Hospital No. 1, Yekaterinburg, Russia*

Abstract

INTRODUCTION: Post-Intensive Care Syndrome (PICS) results from multiple factors during an Intensive Care Unit (ICU) stay. PICS symptoms can manifest within the first 48 hours and may exacerbate the patient's condition, prolonging the ICU stay. With increasing ICU survival rates, PICS has become a significant concern as it can lead to chronic critical illness. The lack of sufficient understanding of PICS dynamics and contributing factors limits effective prevention. **OBJECTIVE:** To investigate the influence of clinical, demographic indicators and intensive care parameters on the dynamics of Post-Intensive Care Syndrome development in ICU patients using the PICS index. **MATERIALS AND METHODS:** A descriptive, prospective, non-comparative cohort study included 80 patients. The severity of PICS was assessed at different time points during the ICU stay using the PICS index. A correlation analysis was performed between the PICS index and factors influencing patient severity. **RESULTS:** All patients developed PICS signs after 48 hours in the ICU, with 16.25 % exhibiting severe PICS by day 14. The PICS index correlated positively with length of stay ($r = 0.60$), duration of mechanical ventilation ($r = 0.45$), and duration of sedation ($r = 0.47$). Sedation depth correlated inversely with the index ($r = -0.31$). Demographic variables and comorbidities showed no significant association with the severity of PICS. **CONCLUSIONS:** Measurement of the PICS index revealed that all patients demonstrated signs of PICS after 48 hours in the ICU, with the severity peaking around day 14. The development of PICS was associated with the duration of hospitalization, mechanical ventilation, and the duration and depth of sedation. Demographic indicators, the initial severity of

СИНДРОМ ПОСЛЕДСТВИЙ ИНТЕНСИВНОЙ ТЕРАПИИ

Динамика развития синдрома последствий интенсивной терапии в ОРИТ многопрофильного стационара: проспективное когортное исследование

А.Е. Рудник^{1,3}, Г.В. Соболева^{2,3}, Н.С. Нагаев¹,
Е.Н. Рудник^{1,2}, А.В. Куликов², А.А. Белкин^{1,2,*}

¹ *ООО «Клиника Института Мозга», Березовский, Россия*

² *ФГБОУ ВО «Уральский государственный медицинский университет» Минздрава России, Екатеринбург, Россия*

³ *ГБУЗ СО «Центральная городская клиническая больница № 1 город Екатеринбург», Екатеринбург, Россия*

Реферат

АКТУАЛЬНОСТЬ: Синдром последствий интенсивной терапии (ПИТС) — следствие комплексного воздействия факторов, возникающих при лечении в отделении реанимации и интенсивной терапии (ОРИТ). Его симптомы, проявляясь в первые 48 ч, усугубляют состояние пациента и увеличивают сроки госпитализации. Рост выживаемости в ОРИТ актуализирует проблему ПИТС, который может являться причиной развития хронического критического состояния. Отсутствие достаточных данных о динамике развития ПИТС и способствующих ему факторах ограничивает возможности его профилактики. **ЦЕЛЬ ИССЛЕДОВАНИЯ:** Определить влияние клиничко-демографических показателей и параметров интенсивной терапии на динамику развития ПИТС у пациентов ОРИТ с использованием ПИТС-индекса. **МАТЕРИАЛЫ И МЕТОДЫ:** В описательное проспективное несравнительное когортное исследование было включено 80 пациентов. Проведена оценка тяжести ПИТС в различные сроки пребывания в ОРИТ с использованием ПИТС-индекса. Выполнен корреляционный анализ ПИТС-индекса с факторами, влияющими на тяжесть состояния пациента. **РЕЗУЛЬТАТЫ:** У всех пациентов после 48 ч в ОРИТ регистрировались признаки ПИТС, а к 14-м суткам у 16.25 % отмечалась тяжелая форма. Выявлена корреляция ПИТС-индекса с длительностью госпитализации ($r = 0,60$), искусственной вентиляцией легких (ИВЛ) ($r = 0,45$) и седации ($r = 0,47$). Глубина седации была обратно пропорциональна индексу ($r = -0,31$). Демографические показатели и коморбидность на выраженность ПИТС не влияли. **Выводы:** При измерении

the condition, and the level of comorbidity did not affect the PICS index value. Post-Intensive Care Syndrome contributes to prolonged hospitalization.

KEYWORDS: post-intensive care syndrome, intensive care unit, chronic critical illness, intensive care

* *For correspondence:* Andrey A. Belkin — MD, Professor of the Department of Anesthesiology-Intensive Care, Nervous Disease, Medical Rehabilitation of Ural State Medical University, Director of the Clinical Institute of the Brain, Berezovsky, Russia; e-mail: belkin@neuro-ural.ru

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ПИТС-индекса оказалось, что все пациенты через 48 ч пребывания в ОРИТ демонстрируют признаки ПИТС, выраженность которых достигает максимума к 14-м суткам. Развитию синдрома способствуют длительность госпитализации, ИВЛ, а также продолжительность и глубина седации. Демографические показатели, исходная степень тяжести состояния и уровень коморбидности не влияют на величину ПИТС-индекса. ПИТС приводит к увеличению сроков госпитализации.

КЛЮЧЕВЫЕ СЛОВА: синдром последствий интенсивной терапии, отделение реанимации и интенсивной терапии, хроническое критическое состояние, интенсивная терапия

* *Для корреспонденции:* Белкин Андрей Августович — д-р мед. наук, профессор кафедр анестезиологии-реаниматологии, нервных болезней, медицинской реабилитации ФГБОУ ВО «Уральский государственный медицинский университет» Минздрава России, директор Клинического Института Мозга, Бerezовский, Россия; e-mail: belkin@neuro-ural.ru

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Introduction

Post-intensive care syndrome (PICS) is a complex of physical, psychological, and cognitive impairments that occur in patients as a result of prolonged stay in the intensive care unit (ICU) [1, 2]. For the vast majority of patients, remaining in the ICU for more than 48 hours is accompanied by the development of undesirable, ICU-acquired disorders that limit functional capacity [2]. Such manifestations as chronic infection, paroxysmal sympathetic hyperactivity, depression and physical weakness, dysphagia, and nutritional deficiency substantially reduce the quality of life after the intensive care stage and, in some cases, lead to persistent disability [3]. One year after critical illness, signs of PICS may persist in 20–40 % of patients discharged from the ICU [3]. Half of all patients remain unable to work for 12 months and depend on external assistance [1, 2], and one-

third develop long-term disability [4]. This underscores the high social significance of PICS and the need for effective preventive and rehabilitative strategies [2, 4, 5].

Increasing survival rates in ICUs make the problem of PICS even more relevant [6, 7], as it may contribute to the development of chronic critical illness [8, 9].

A lack of sufficient understanding of the timing, trajectory, and contributing factors of PICS limits effective prevention [10].

Objective

To determine the impact of clinical and demographic characteristics and intensive care parameters on the incidence and progression of PICS in patients of a polyvalent ICU using the PICS index.

Research hypothesis

Regardless of the etiology of the acute condition, after 48 hours in the ICU, patients develop a complex of functional impairments (PICS), the severity of which is directly proportional to the length of stay in the ICU.

Materials and methods

Study design: monocentric, descriptive, prospective, non-comparative cohort study.

The study included patients admitted to the general ICU of the State Budgetary Healthcare Institution “Central City Clinical Hospital No. 1, Yekaterinburg” from December 31, 2023 to December 31, 2024. The study was approved by the local ethics committee of LLC “Brain Institute Clinic” (Protocol No. 005–1/1128 dated November 28, 2023).

Inclusion criteria:

- patients whose condition required an ICU stay longer than 48 hours;
- age between 18 and 90 years.

Exclusion criteria:

- stage IV oncologic disease;
- age under 18 years;
- patient refusal to participate;
- incurable (terminal) patients.

Withdrawal criteria: ICU stay less than 48 hours.

To assess the severity of PICS, the PICS-index scale was used, which includes 14 indicators grouped into four domains: infectious-trophic complications, autonomic-metabolic disorders, emotional-cognitive impairments, and neuromuscular dysfunctions [2].

Statistical analysis

The sample size was not pre-calculated and was determined by a one-year enrollment period. Data are presented as mean with standard deviation, median with interquartile range, or number with percentage. The *t*-test was used for continuous variables, the Mann-Whitney *U*-test for ordinal variables, and the χ^2 test (Fisher’s exact test when appropriate) for nominal variables. Given the exploratory nature of the study, sample sizes were not selected a priori. All analyses were performed using Stata version 17.0 (StataCorp, College Station, Texas, USA). All statistical tests were two-sided with significance defined as $p < 0.05$. Missing data were excluded.

Data were summarized in a cross-reference table. Microsoft Excel version 16.0.10384.20023 was used for data processing.

Cohort characteristics

Cohort characteristics are presented in Table 1.

The cohort included 80 patients: 46 men and 34 women, aged 22 to 86 years; mean age 60.6 ± 17.84 years. The mean duration of total hospitalization was 21.43 ± 9.29 days, and the mean ICU stay was 12.15 ± 6.58 days. At admission, comorbidity burden was assessed using the Charlson Comorbidity Index; the mean score was 3.58 ± 2.01 .

The severity of illness was evaluated using the Sequential Organ Failure Assessment (SOFA) score: 4.44 ± 2.04 , and the Acute Physiology and Chronic Health Evaluation II (APACHE II) score: 16.25 ± 4.55 , reflecting the degree of organ dysfunction and overall severity of illness.

Table 1. Characteristics of the cohort

Parameter (n = 80)	Mean	Median
PICS max*	5.11 ± 1.60	5 (4.0; 6.125)
Quantity (M/F)	46/34	—
Age, years*	60.58 ± 17.84	64 (47; 76)
BMI (kg/m ²)	28.07 ± 5.05	28.3 (24.27; 31.7)
Charlson Comorbidity Index*	3.58 ± 2.01	4 (2; 5)
Duration of mechanical lung ventilation (days)*	6.23 ± 6.44	4 (1.75; 8)
ICU stay (days)*	12.15 ± 6.58 (4; 35)	10 (7;16)
Total days of hospitalization (days)*	21.43 ± 9.29	20 (15;28)
Duration of sedation (days)*	2.64 ± 2.51	2 (0;4)
Depth of sedation RASS*	-1.50 ± 1.84 (-4; 2)	-1 (-3; 0)
SOFA scale evaluation, Day 1 in ICU*	4.44 ± 2.04 (0; 11)	4 (3; 5)
APACHE II scale evaluation, Day 1 in ICU*	16.25 ± 4.55 (4; 25)	16 (13;19)

* All indicators are presented in the following format: mean value ± standard deviation, with the minimum and maximum values indicated, as well as the median for a more accurate description of the data distribution.

The parameters of intensive care included the duration of mechanical ventilation and the duration and depth of sedation assessed by the Richmond Agitation-Sedation Scale (RASS).

At admission, patients did not exhibit signs of PICS.

In the cohort, surgical patients predominated (Table 2). These included individuals with gastrointestinal bleeding, gallstone disease, acute pancreatitis, peptic ulcer disease of the stomach and duodenum, acute intestinal obstruction, and soft tissue cellulitis (38.8 %). Fewer patients presented with cerebrovascular diseases (intracranial hemorrhage, ischemic stroke) — 31.3 %. Patients with inflammatory diseases of the kidneys and urinary tract accounted for 8.8 %. The cohort also included therapeutic patients with respiratory tract infections (acute pneumonia, chronic obstructive pulmonary disease) — 17.5 %, as well as cardiology patients with ischemic heart diseases and pulmonary embolism (3.8 %). A total of 32 patients (40 %) underwent surgery for urgent abdominal or soft-tissue surgical pathology.

A leading intensive care syndrome was identified in all patients (Figure 1).

In this group, patients with sepsis predominated (44 %), followed by those with cerebral insufficiency (31 %), respiratory distress due to respiratory diseases (18 %), non-cardiogenic shock (6 %), and cardiogenic shock (1 %) (Figure 1).

Results

Manifestations of PICS were recorded on Day 3 in all patients admitted to the ICU (Figure 2). Severity grading was determined by the total score according to the described scale: a score of up to 4 corresponded to mild severity; 4–6 points indicated moderate severity; and a score above 6 was classified as severe PICS [2].

It was found that on Day 3, 59 patients exhibited mild PICS, 19 had moderate severity, and 2 had severe PICS. By Day 7 after admission to the ICU, according to the PICS index, 26 patients had mild PICS, 47 had moderate PICS, and 5 had severe PICS. On Day 14, the highest number of patients with severe PICS was recorded (13 patients), along with 25 patients with moderate severity and 34 with mild severity. By the end of hospitalization, 46 patients had a PICS index value not exceeding 3.5 points, corresponding to mild severity, while moderate severity was identified in 15 patients. It should be noted that by the time of discharge, 4 patients still demonstrated severe residual impairments acquired during their stay in the ICU, with a PICS index of 6 or higher. These patients met the criteria for chronic critical illness [8] and required further rehabilitation and additional care.

An analysis was conducted of the prevalence of the PICS domains [2, 8] and the intragroup domain structure among patients with various life-threatening conditions on Days 3, 7, and 14 after ICU admission, as well as on the day

Table 2. Nosological structure of the cohort ($n = 80$)

ICD code	Diagnosis	Number of patients
I61.2	Nontraumatic intracerebral hemorrhage	6
I63.3	Cerebral infarction (stroke)	19
I20.8	Ischemic heart diseases	1
I26.0	Pulmonary embolism	2
J18.9	Acute pneumonia	12
J44.1	Chronic obstructive pulmonary disease	2
K92.2	Gastrointestinal hemorrhage*	5
K80.1	Calculus of the gallbladder	6
K85.9	Acute pancreatitis	10
K25.2	Acute gastric ulcer	2
K26.1	Acute duodenal ulcer	2
N10	Acute pyelonephritis	7
L03.1	Soft tissue cellulitis and acute lymphangitis	3
K56.6	Acute intestinal obstruction	3

of discharge. The obtained results (Table 3) show that all patients, regardless of the leading intensive care syndrome, exhibited manifestations across different domains at all stages of hospitalization.

Regardless of the leading intensive care syndrome, a general trend was observed: all patients demonstrated signs of at least one domain on Day 3. By Days 7–14, the number of domain manifestations reached its maximum for each intensive care syndrome. By the end of hospitalization, these values decreased across the entire cohort.

Already by Day 3 of ICU stay, all patients exhibited symptoms of various PICS domains (Figure 3), with the largest proportion represented by infectious-inflammatory symptoms (31.27 %). By Day 7, the domain of autonomic-metabolic symptoms had progressed, accounting for 46.3 %

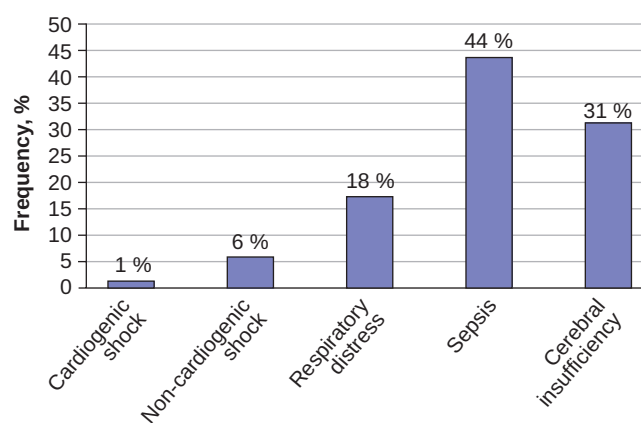


Fig. 1. Distribution of patients by intensive care syndromes

Table 3. Frequency of PICS signs/symptoms in the domain structure by syndrome

Intensive care syndromes	PICS domain	Day 3 (n = 80)	Day 7 (n = 78)	Day 14 (n = 72)	End of Hospitalization (n = 65)
N of symptoms					
Cardiogenic shock	Infectious-inflammatory	0	0	0	0
	Vegetative-metabolic	3	1	3	2
	Neuromuscular	0	1	0	0
	Emotional-cognitive	0	1	1	1
	Mean N of symptoms per patient	3 ¹ (3 ² ; n = 1 ³)	3 ¹ (3 ² ; n = 1 ³)	4 ¹ (4 ² ; n = 1 ³)	3 ¹ (3 ² ; n = 1 ³)
Non-cardiogenic shock	Infectious-inflammatory	3	3	0	0
	Vegetative-metabolic	2	2	3	3
	Neuromuscular	2	2	0	0
	Emotional-cognitive	0	0	2	2
	Mean N of symptoms per patient	3.5 ¹ (7 ² ; n = 2 ³)	7 ¹ (7 ² ; n = 1 ³)	5 ¹ (5 ² ; n = 1 ³)	5 ¹ (5 ² ; n = 1 ³)
Respiratory distress	Infectious-inflammatory	15	19	6	0
	Vegetative-metabolic	31	37	31	29
	Neuromuscular	10	17	17	7
	Emotional-cognitive	7	14	20	19
	Mean N of symptoms per patient	4.5 ¹ (63 ² ; n = 14 ³)	6.2 ¹ (87 ² ; n = 14 ³)	5.7 ¹ (74 ² ; n = 13 ³)	4.2 ¹ (55 ² ; n = 13 ³)
Sepsis	Infectious-inflammatory	60	55	33	9
	Vegetative-metabolic	91	126	101	79
	Neuromuscular	22	35	26	14
	Emotional-cognitive	32	43	50	43
	Mean N of symptoms per patient	5.4 ^{*1} (205 ² ; n = 38 ³)	6.82 ¹ (259 ² ; n = 38 ³)	6.0 ¹ (210 ² ; n = 35 ³)	4.14 ¹ (145 ² ; n = 35 ³)
Cerebral insufficiency without mechanical lung ventilation	Infectious-inflammatory	23	30	28	15
	Vegetative-metabolic	31	42	44	33
	Neuromuscular	10	17	28	18
	Emotional-cognitive	9	13	18	16
	Mean N of symptoms per patient	4.56 ¹ (73 ² ; n = 16 ³)	6.38 ¹ (102 ² ; n = 16 ³)	7.38 ¹ (118 ² ; n = 16 ³)	6.83 ¹ (82 ² ; n = 12 ³)
Cerebral insufficiency with mechanical lung ventilation	Infectious-inflammatory	15	14	13	4
	Vegetative-metabolic	14	18	16	5
	Neuromuscular	5	15	12	4
	Emotional-cognitive	4	5	5	3
	Mean N of symptoms per patient	4.22 ¹ (38 ² ; n = 9 ³)	6.5 ¹ (52 ² ; n = 8 ³)	7.67 ¹ (46 ² ; n = 6 ³)	5.33 ¹ (16 ² ; n = 3 ³)

Note:
¹ Average number of features per 1 patient.
² Total number of features.
³ Number of patients.

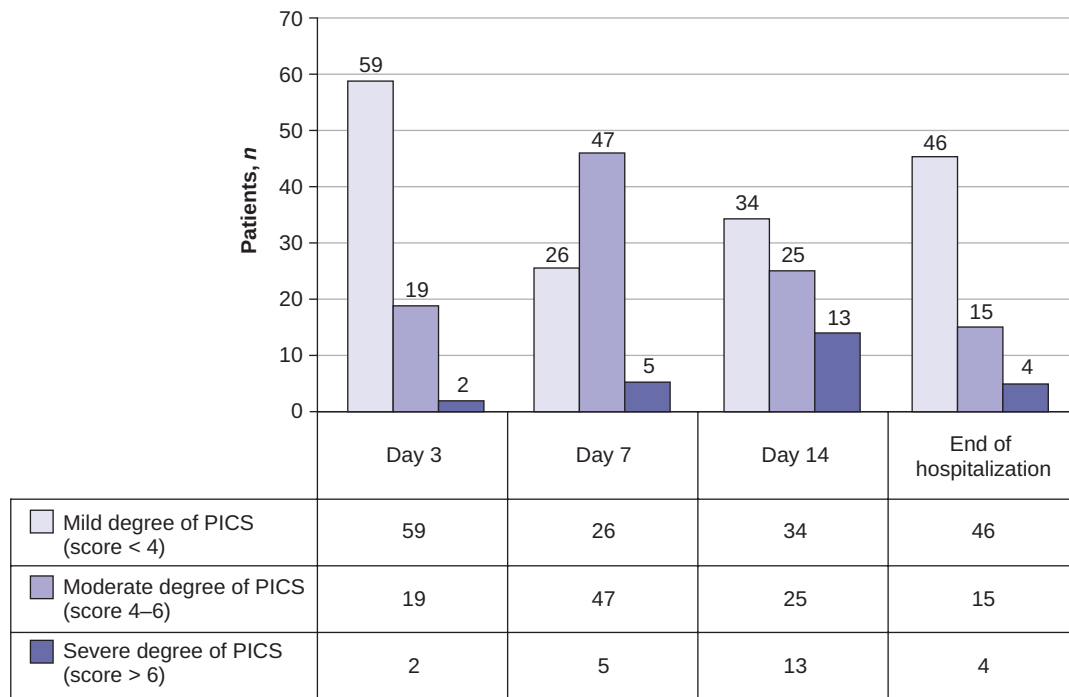


Fig. 2. Distribution of PICS by severity during ICU hospitalization

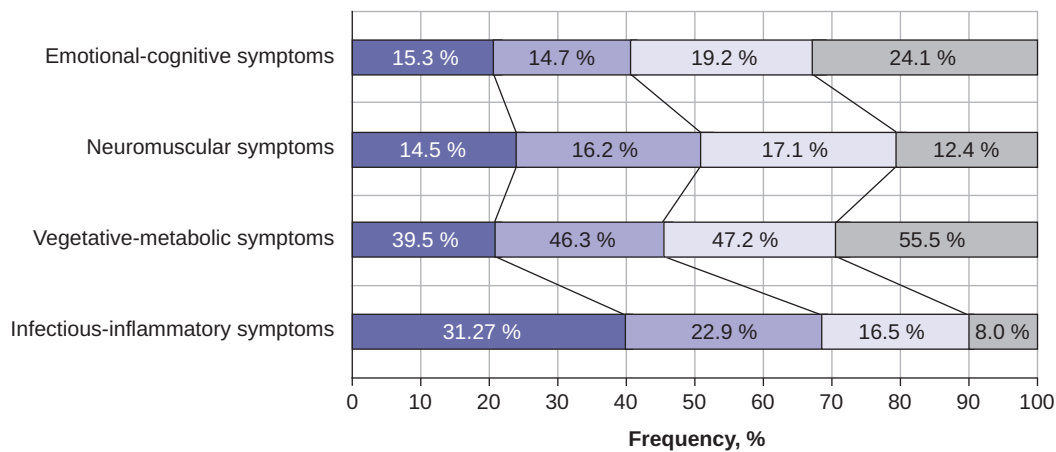


Fig. 3. Dynamics of the development of PICS domains during hospitalization

Time of hospitalization	Type of violations, %			
	Infectious-inflammatory symptoms	Vegetative-metabolic symptoms	Neuromuscular symptoms	Emotional-cognitive symptoms
Day 3	31.27	39.5	14.5	15.3
Day 7	22.9	46.3	16.2	14.7
Day 14	16.5	47.2	17.1	19.2
End of hospitalization	8.0	55.5	12.4	24.1

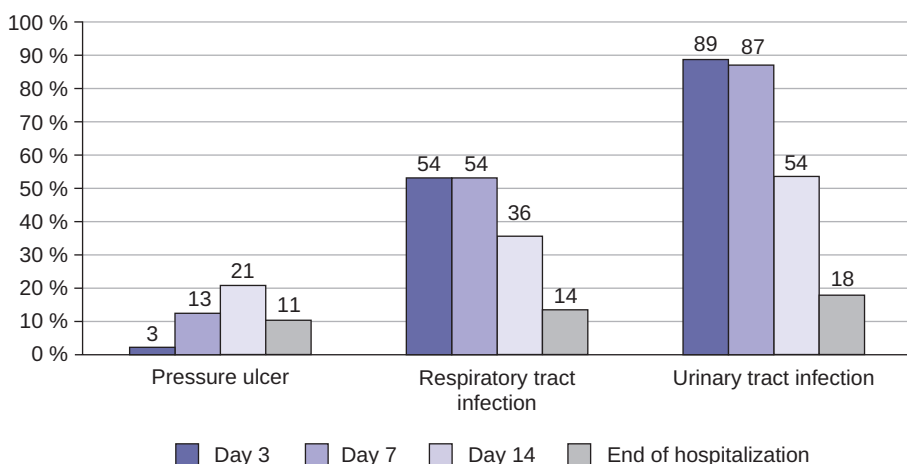


Fig. 4. Dynamics of the development of infectious and trophic disorders

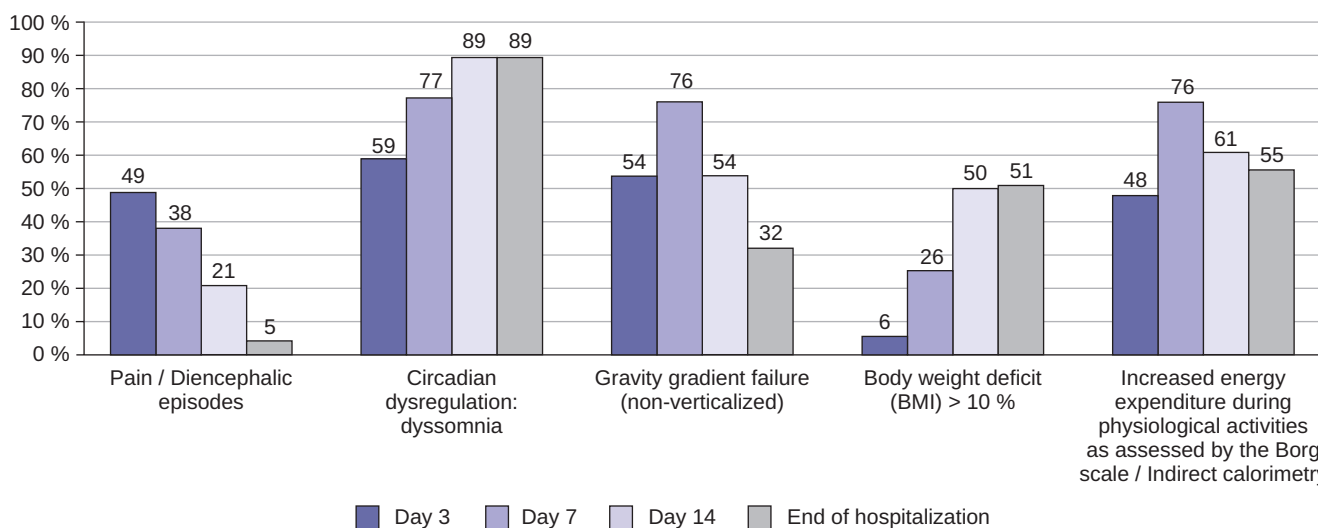


Fig. 5. Dynamics of the vegetative-metabolic domain development

of all PICS symptoms, and these symptoms persisted until the end of hospitalization (55.5 %). By Day 14, neuromuscular symptoms reached their peak (17.1 %) and then declined by the end of hospitalization (12.4 %); however, autonomic-metabolic symptoms remained predominant (55.5 %). From the moment of ICU admission, emotional-cognitive symptoms continued to increase throughout hospitalization and accounted for 24.1 % of all manifestations by the time of discharge.

The analysis of the infectious-trophic domain (Figure 4) showed that on Days 3 and 7, urinary tract infections predominated (89 % and 87 %, respectively). Their frequency decreased to 54 % by Day 14 and persisted in 18 % of treated patients by the time of discharge. Respiratory tract infections in patients with a tracheostomy cannula or endotracheal tube accounted for 54 % on both Days 3 and 7, depending on the timing of restoration of tracheo-esophageal integrity. Manifestations of this domain gradually regressed by Day 14 to 36 %, while 14 % of discharged

patients remained long-term cannula carriers. From Day 3 after ICU admission, the number of patients with pressure ulcers increased from 3 % to 21 %, and 11 % of patients at the time of discharge required ongoing anti-decubitus care at home.

The analysis of the autonomic-metabolic disturbances (Figure 5) revealed that by Day 3, 49 % of patients exhibited signs of pain or paroxysmal sympathetic hyperactivity, which gradually regressed but persisted in 5 % of discharged patients. Orthostatic insufficiency was present in 54 % of patients after 48 hours in the ICU and reached its peak by Day 7 (76 %) from ICU admission, decreasing to 54 % by Day 14 and remaining in 32 % of discharged patients by the end of hospitalization. The most common symptom of the autonomic-metabolic domain was insomnia, which increased from 59 % to 89 % by the end of hospitalization. On Day 3, 48 % of patients experienced increased energy expenditure. By Day 7, 76 % of patients clearly showed signs of low tolerance even to routine daily activities, and 55 %

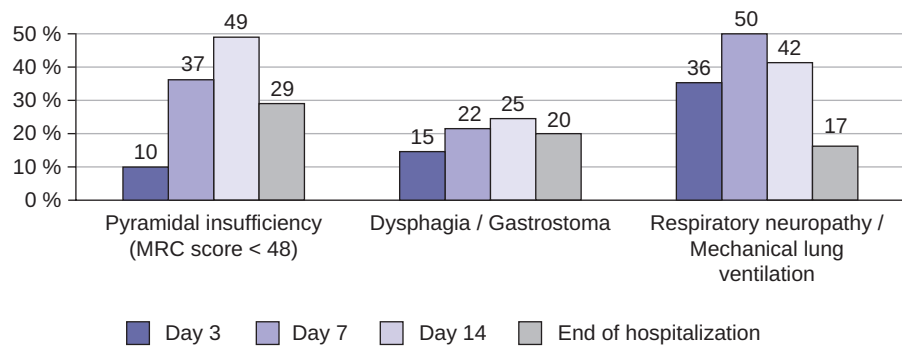


Fig. 6. Dynamics of neuromuscular disorders

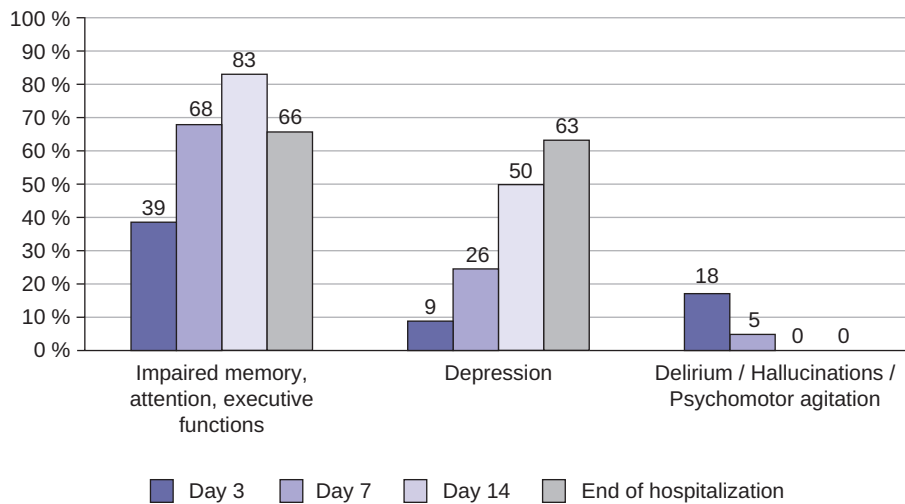


Fig. 7. Dynamics of the development of the domain of emotional and cognitive disorder

experienced rapid fatigue at discharge. During ICU hospitalization, patients exhibited significant nutritional deficiency; in 51 % of survivors transferred to specialty wards, body mass deficit exceeded 10 %.

Signs of pyramidal insufficiency (Figure 6) were observed as early as Day 3 (10 %) and peaked at 49 % by Day 14 from ICU admission, with 29 % of patients being discharged with these impairments. Respiratory neuropathy was present in 36 % of patients on Day 3, reaching its maximum (50 %) by Day 7 and persisting in 17 % of patients by the end of hospitalization. Due to the placement of a nasogastric tube, 15 % of patients experienced disuse dysphagia. By Day 14, signs of disuse dysphagia were detected in 25 % of ICU patients, and 20 % were discharged with a nasogastric tube or gastrostomy.

The study of emotional-cognitive disorders (Figure 7) showed that 18 % of patients experienced delirium on Day 3, decreasing to 5 % by Day 7. By the end of hospitalization, hallucinations and psychomotor agitation had completely regressed. Memory and attention impairments were observed in 39 % of ICU patients on Day 3, increasing to 83 % by Day 14, and were still present in 66 % at discharge. During hospitalization, patients also experienced depres-

sion, affecting 9 % on Day 3 and rising to 63 % by the end of inpatient treatment.

Analyzing changes in PICS severity in surviving patients using APACHE II and SOFA scores (Figure 8), it was found that by Day 14 of ICU stay, organ dysfunction and systemic inflammation had regressed, while the PICS index value increased (0→4.6), which impacted the clinical condition.

By the end of hospitalization, a decrease in patient severity was observed according to the SOFA (4.44→0.83) and APACHE II (16.25→5.5) scores, which was associated with the resolution of organ dysfunction. A reduction in the PICS index was also noted (4.6→3.6), reflecting the regression of short-term manifestations of PICS; however, the acquired long-term domains persisted, contributing significantly to the patients' dependence on external assistance after discharge.

Within the framework of the conducted statistical analysis, the impact of several clinical-demographic and intensive therapy parameters on the maximum PICS index value was evaluated in patients receiving treatment in the ICU (Figure 9).

The presented graphs (Figure 9) show the distribution of correlations between the PICS index and key clin-

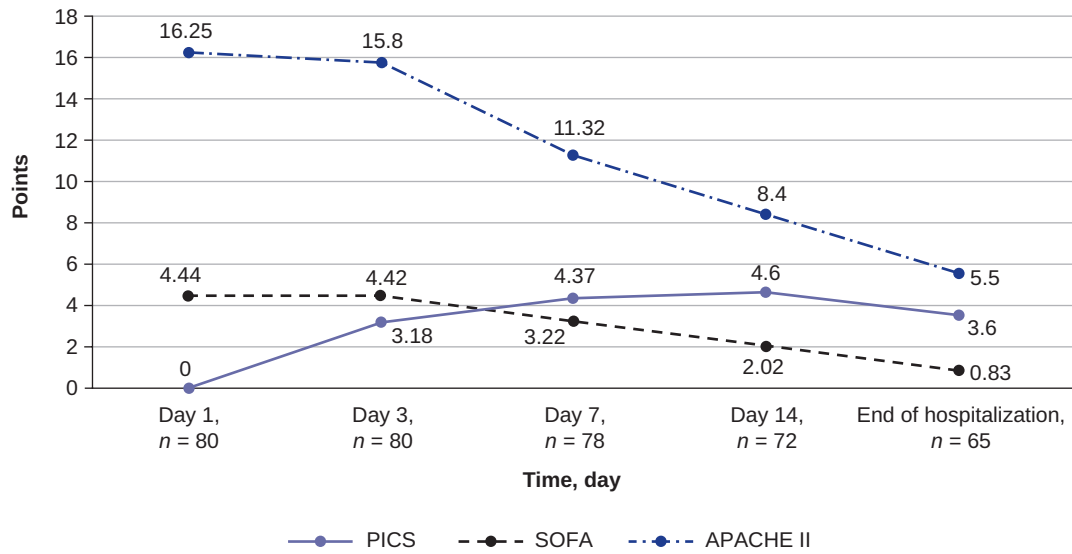


Fig. 8. Dynamics of the severity of the condition according to the SOFA (Sequential Organ Failure Assessment), APACHE II (Acute Physiology and Chronic Health Evaluation II), and PICS indices

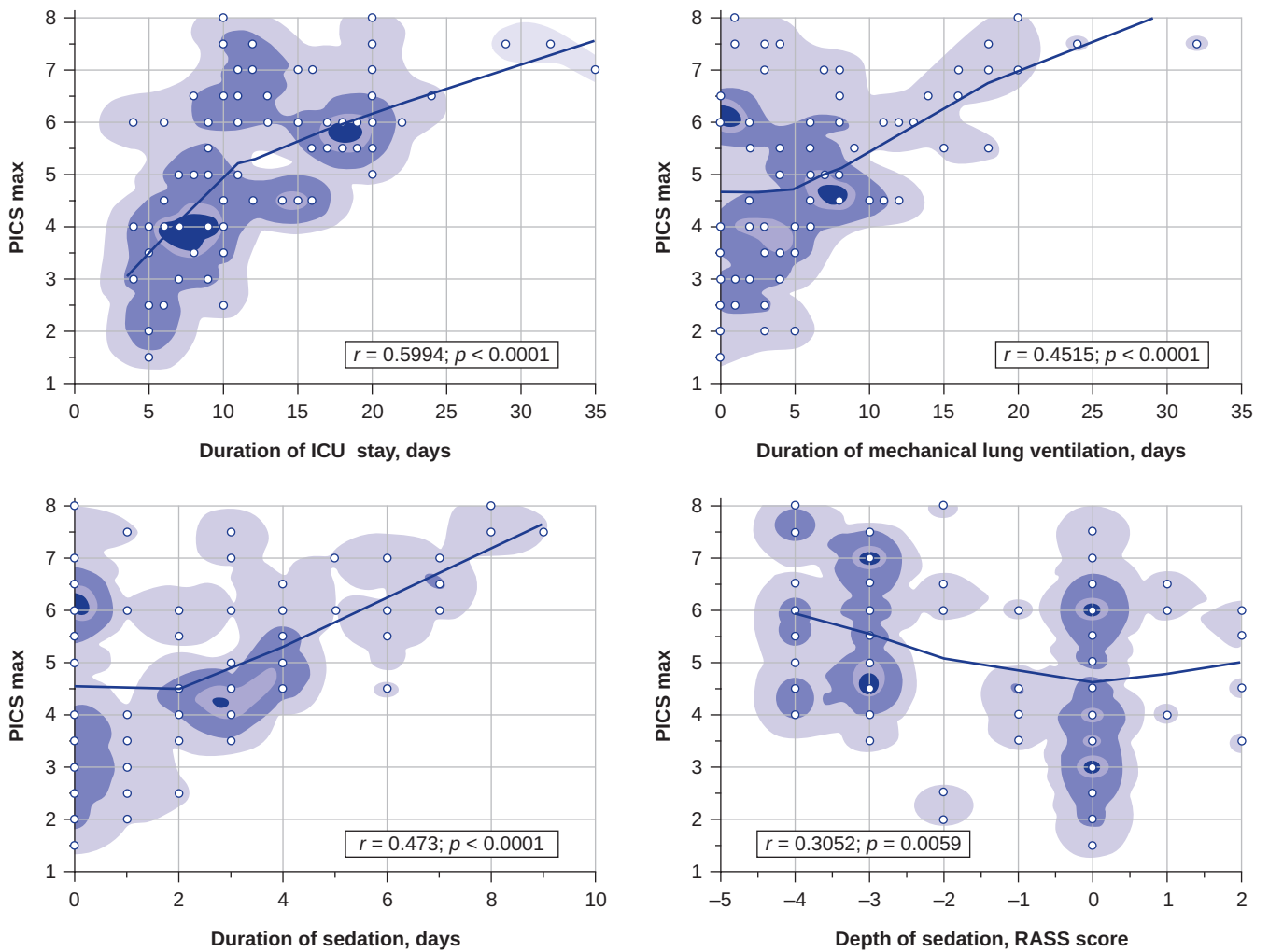


Fig. 9. Correlation of the PICS index with the duration of stay in the ICU, the duration of mechanical ventilation, and the duration and depth of sedation

ical variables (duration of ICU stay, duration of mechanical ventilation, duration and depth of sedation) in patients who survived a critical condition ($n = 80$). The diagrams were constructed using scatter plots overlaid with a heatmap to visualize the density and strength of correlations.

Descriptive statistics demonstrated a wide range of values for both the PICS index and the duration of intensive therapy. Pairwise correlation analysis (Table 3) revealed the most significant associations with PICS index levels for:

- Duration of ICU stay ($r = 0.60$; $p < 0.0001$);
- Duration of sedation ($r = 0.47$; $p < 0.00001$);
- Duration of mechanical lung ventilation ($r = 0.45$; $p < 0.0001$);
- Duration of hospitalization ($r = 0.36$; $p = 0.001$);

- Established inverse correlation with the depth of sedation by RASS scale ($r = -0.31$; $p = 0.006$).
- A weak but significant association was noted between patient comorbidity, assessed using the Charlson Comorbidity Index ($r = 0.27$; $p = 0.017$).

A heat map was drawn based on the results of the statistical analysis (Figure 10).

Analysis of the relationships between features showed that clinical and demographic factors such as sex, age, body mass index, and the severity of patients upon ICU admission, assessed using SOFA and APACHE II scales, did not influence the PICS index, with correlation coefficients not exceeding $r = 0.2$. A weak correlation was observed with patient comorbidity, assessed by the Charlson index ($r = 0.27$).

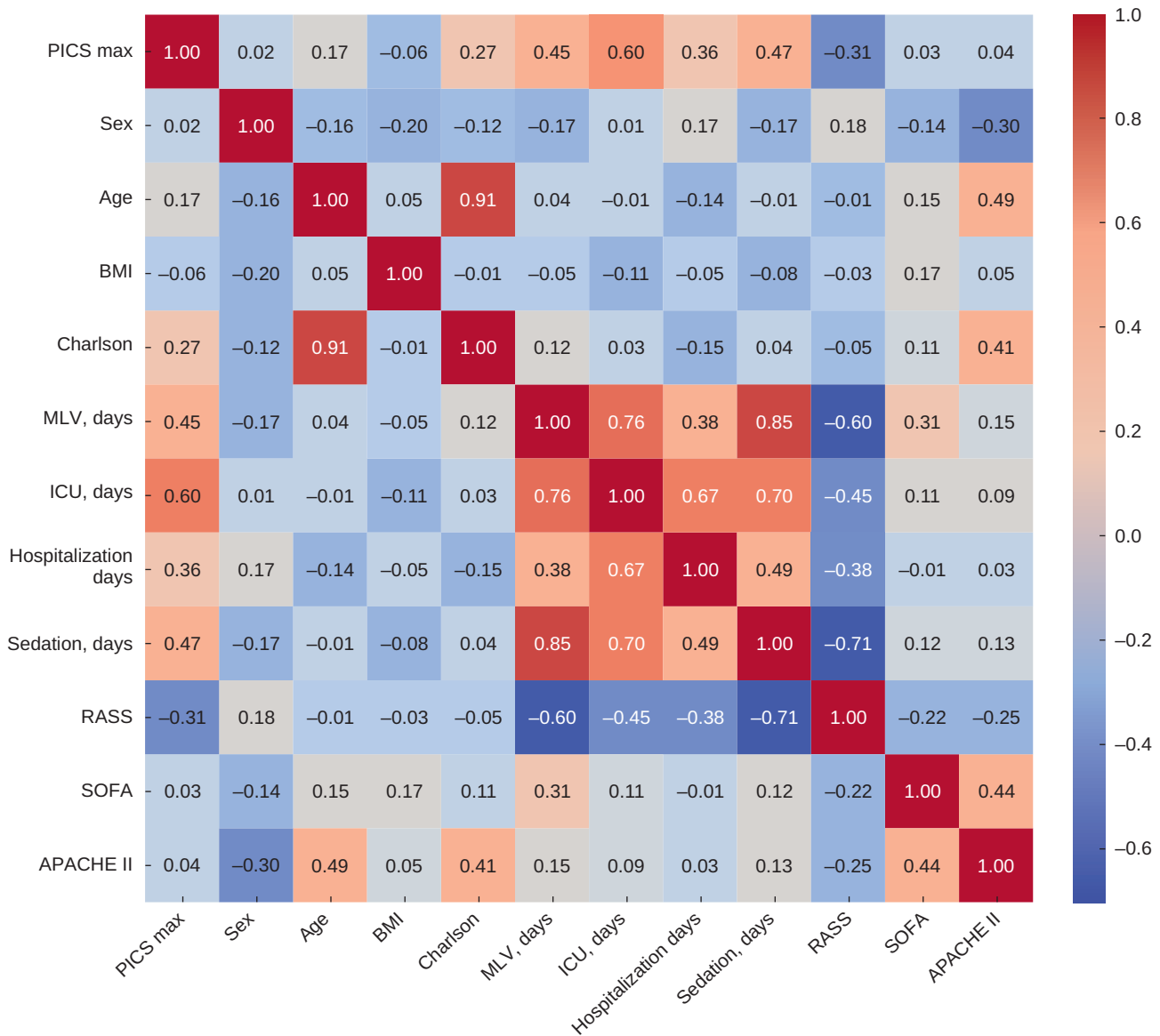


Fig. 10. Heat map of correlations

Discussion

The study confirmed the established understanding that PICS develops within the first 48–72 hours after ICU admission and accompanies critical conditions during the patient's stay, exacerbating the severity of their state and likely contributing to prolonged hospitalization after stabilization [8, 9]. Immobilization, sedation, mechanical ventilation, nutritional deficiencies, circadian rhythm disturbances, and infections are key factors influencing the formation and progression of PICS [4].

Results showed that within 48 hours of ICU admission, signs of PICS were registered in 100 % of patients, with 59 exhibiting mild severity. As ICU stay lengthened, by Day 7, the PICS index reached moderate severity in 47 patients, and 5 patients developed severe PICS.

By Day 14, the number of hospitalized patients with mild PICS increased again to 34, which may be associated with transfer to specialized wards and the elimination of short-term provoking factors. However, moderate and severe PICS persisted in 25 and 13 patients, respectively. By the time of discharge, 46 patients had a PICS index corresponding to mild severity, 15 patients had moderate severity, and 4 survivors exhibited severe PICS, which may indicate the need for further rehabilitation and additional care.

The infectious-trophic domain peaked between Days 3 and 7, regressing by Day 14, corresponding to the duration of mechanical ventilation and the presence of urinary catheters in most patients.

By Day 7, vegetative-metabolic disorders progressed due to prolonged immobilization, reduced gravitational gradient, nutritional deficiencies from hypermetabolism combined with inadequate energy intake, deafferentation, and circadian rhythm disruption. Cognitive impairments, assessed via Hodkinson's Mini-Mental Test, accounted for 46.3 % of all domain features and persisted until discharge (55.5 %).

The neuromuscular domain also peaked by Day 14, with some patients discharged with residual manifestations. Emotional-cognitive disorders steadily increased from ICU admission and required further psychological support post-discharge [11, 12].

Correlation analysis revealed that ICU stay length, duration of mechanical ventilation, and duration/depth of

sedation directly correlated with the PICS index. Strong associations were observed with the ICU length of stay ($r = 0.60$) and mechanical ventilation duration ($r = 0.45$). The PICS index also correlated with sedation duration ($r = 0.47$), while sedation depth per RASS was inversely proportional ($r = -0.31$), indicating that deeper sedation significantly contributes to PICS development.

Correlation analysis demonstrated that higher PICS index values were associated with longer ICU and total hospital stays ($r = 0.60$).

Limitations

This study did not assess the impact of mechanical ventilation types, types of surgical interventions, or anesthesia on PICS severity.

Conclusions

All patients develop PICS manifestations of varying severity after 48 hours in the ICU.

Maximum PICS severity occurs by Day 14 of hospitalization.

PICS development is influenced by ICU stay length, duration of mechanical ventilation, and sedation depth/duration.

Demographic factors and baseline severity do not affect PICS severity.

PICS should be regarded as a side effect of intensive care requiring prevention and subsequent rehabilitation.

The data support the methodological postulate that PICS is not an independent nosological entity but a side effect of intensive therapy and prolonged ICU stay. Future studies may demonstrate possibilities for PICS prevention using early rehabilitation strategies.

Conclusion

The study hypothesis is confirmed. PICS develops in all ICU patients with critical conditions, manifesting clinically after 48 hours of ICU stay, making it an inevitable side effect of intensive therapy.

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Author contribution. All authors according to the ICMJE criteria participated in the development of the concept of the article, obtaining and analyzing factual data, writing and editing the text of the article, checking and approving the text of the article.

Ethics approval. This study was approved by the local Ethical Committee of Clinical Institute of the Brain,

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Author's ORCID:

Rudnik A.E. — 0009-0006-2259-2256

Sobetova G.V. — 0009-0000-8432-9417

Nagaev N.S. — 0009-0007-0561-4879

Rudnik E.N. — 0000-0001-9979-1276

Kulikov A.V. — 0000-0002-7768-4514

Belkin A.A. — 0000-0002-0544-1492

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