



Two-year outcomes of patients with prolonged disorders of consciousness: a prospective cohort study in Russian Federation

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Background: Epidemiological data on prolonged disorders of consciousness (pDOC) are not available due to lack of research in this field. The objective of this pioneering prospective cohort study in the Russian Federation was to collect the data on the survival and the level of consciousness of patients with pDOC, as well as to search for prognostic markers of survival and improvement of the level of consciousness on long-terms outcomes (up to 24 months).

Methods: All patients (n=184) had pDOC and were admitted to the Federal Research and Clinical Center of Intensive Care Medicine and Rehabilitology. We assessed the neurological status and acquired follow-up diagnosis as well. Out of total patients: anoxic brain injury (ABI) (n=52), vascular lesions (VL) (n=50), traumatic brain injury (TBI) (n=74), and other causes (n=8). Changes in patients' vital and conscious status were recorded in four-time slices: 3, 6, 12, and 24 months after the event that led to pDOC.

Results: The survival rate is less than 30%, and the rate of recovery in terms of consciousness is 21%, which are both low, though do not differ significantly from existing data for this category of patients. Unprofessional home care may have a role to play in the declined long-term survival rate. We still do not have reliable prognostic markers among demographical and clinical indices; however, younger age can be considered the only significant predictor of survival and positive dynamics in the level of consciousness.

Conclusions: We expect that our research will help to personalize and help the patient and families with the appropriate clinical as well as social measures.

Keywords: Rehabilitation; minimally conscious state (MCS); prolonged disorders of consciousness (pDOC); vegetative state (VS); medical care

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Introduction

Epidemiological transition from coma to different forms of the prolonged disorders of consciousness (pDOC) are observed in developed countries because of high survival rate in severe acquired brain injury cases caused by trauma, vascular lesions (VL), respiratory or cardiac arrest, and metabolic disorders (1-3). Intentional behavior is absent with no sign of purposeful response to external stimuli, speech understanding, and maintenance of attention during irregular alternating states of sleep and wakefulness in patients with vegetative state (VS) or unresponsive wakefulness syndrome (UWS) (1). They do not control functions of the pelvic organs and have partially or entirely intact stem and spinal reflexes. Minimally conscious state (MCS) is a clinical state, accompanied by severe impairment of consciousness with minimal and unreliable signs of intentional behavior (4). Patients in MCS either can fix their gaze on a significant object and exhibit emotional responses such as smiling or crying to stimuli that are meaningful to them in case of MCS- form, or even follow basic instructions and produce simple answer like yes/no with gestures in MCS+ form. According to the duration, transient disorder of consciousness lasts less than 1 month, and prolonged is beyond this, however, no clear timeframe to regaining consciousness is established, and spontaneous recovery can occur within the first year and even, in some cases, later (5-7). pDOC develop in 1–14% of traumatic brain injury (TBI) patients, and 12% in non-traumatic injuries (8).

Prevalence of pDOC in the world varies around 0.5–6 cases per 100,000 population (9,10), the number of new cases constitutes 2.5 per 100,000 population per year and tend to increase (11). Even though the number of pDOC patients is commonly not significant, the presence of some specific characteristics requires serious attention to this category. Among these features is the total inability to manifest the rehabilitation process based on their self-awareness and desires, the impossibility of socializing them, and the high caregivers' burden for relatives. Tetraplegia, often associated with severe brain injury, leads to absolute immobilization of pDOC patients, leading to infectious complications and multi-organ failure. The balancing act of maintaining pDOC patients between chronic and acute conditions require close monitoring and special measures from the healthcare system in order to organize rehabilitation that is possible and expedient for them. Along with it, their life expectancy can be big enough to pose a

severe problem for households and thus the economy as the whole: generally, it has been estimated as 2–5 years (12), though some findings have suggested more than 10 years of living in this condition (13,14). Such qualities of these patients justify placing them into a separate category in the International Classification of Diseases (ICD).

However, it requires scrupulous data gathering on the number of pDOC patients worldwide, their mortality, changes in the level of consciousness, comorbidity, and other factors. Demographic, clinical, and follow-up data of pDOC patients can contribute to the development of special healthcare measures aimed at mitigating caregivers' burden, rational choice of the vector of care between rehabilitative and palliative medicine, organizing seamless and effective rehabilitation process both in hospital and in the post-discharge state, and also shed light on ethical dilemmas of medical necessity and humanistic views on the pDOC condition. Clinical history of the patients can aid to predict the survival, cognitive outcomes, rehabilitation plan and help to provide correct information to the patient's relatives and care givers. Apart from the instrumental diagnostics and electrophysiological methods demographical data with follow ups also play a major role in solving this task.

In Russian Federation, no statistical data on pDOC patients are currently available. No separate register for these group of patients exist other than their functional states. Though medical insurance provides for the possibility of individual rehabilitation programs, the patient's relatives can receive technical means of rehabilitation, medical therapy, and social assistance. However, due to the limited scope of the assistance, the quality of the care is not high, and provided care for pDOC is not always effective both from an economic and medical point of view.

Our cohort longitudinal study was the first of a kind in Russia, performed on a relatively large group of patients with pDOC, where we collected data on the survival and dynamics of the level of consciousness of patients admitted for treatment and rehabilitation at the Federal Research and Clinical Center for Intensive Care Medicine and Rehabilitation. In addition, we analyzed the markers for survival and positive change in the level of consciousness and thereby indirectly assessed the effectiveness and feasibility of adjusting healthcare and social support measures for this category of patients. We present the following article in accordance with the STROBE reporting checklist (available at <https://apm.amegroups.com/article/view/10.21037/apm-22-403/rc>).

Methods

Participants

Our study involved 184 pDOC patients admitted to the Federal Research and Clinical Center of Intensive Care Medicine and Rehabilitology in Moscow from January 2016 to January 2020. The core competence of the Center is early rehabilitation in intensive care units for patients outside the acute period of the disease. Thus, by the end of the data gathering period, all the patients had more than 2 years post-injury. The common aetiologies comprised TBI, anoxic brain injury (ABI), VL, and to a lesser extent, severe inflammatory diseases of the central nervous system, neurodegenerative diseases, neoplasms.

During treatment and rehabilitation at the center, patients received drug therapy—neuroprotective and GABAergic (with benzodiazepines and Z-drugs) to increase sleep consolidation. To reduce spasticity, in addition to central muscle relaxants, drugs of the dopaminergic medication was used, such as dopamine receptor agonists and dopamine precursors. Despite some data on the effectiveness of dopaminergic medication in DOC treatment (15), we did not use it systematically due to class IV evidence for this therapy. For this reason, we also did not divide patients into groups depending on the drug therapy in our study. Non-drug therapy included multimodal sensory stimulation of the most intact afferent analyzers, transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS). Patients also receive sessions with a speech therapist and neuropsychologist. In order to prevent somatic complications and post-intensive care syndrome, patients were prescribed with symptomatic therapy, mobilization measures (verticalization), massage, and physiotherapy in the amount available to them.

Exclusion criteria comprised previous TBI, age over 80 years, as well as left-hemisphere ischemic strokes due to the problem of differential diagnosis of total aphasia, agnosia, and apraxia from MCS-. We used prospective study design and assessed consciousness level at the time of admission and discharge. Subsequently, we gathered follow-up data on complications and mortality at 3, 6, 12, and 24 months after patients were being discharged respectively.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and approved by the Ethics Committee of the Federal State Budgetary Institution of the Federal Research and Clinical Center of Intensive Care Medicine and Rehabilitology (No. 08/19/22). Informed consent was obtained from all participants or from

their parents or next of kin involved in the study.

Assessment of the level of consciousness and follow-up data collection

To confirm the diagnosis of VS/UWS and MCS+ two independent neurologists used the Coma Recovery Scale-Revised (CRS-R) scale (in Russian). We checked for electrolytic, metabolic, infectious, and other disorders that could affect consciousness and awareness level during the assessment. CRS-R scale was assessed every week during hospital stay. In addition, we interviewed the medical staffs to determine the fluctuating characteristics in the consciousness's level. In cases where neurologists disagreed the level of consciousness, a general consensus on the degree of consciousness was made based on other instrumental methods of diagnosis such as electroencephalogram (EEG), polysomnography (PSG), magnetic resonance imaging (MRI), functional MRI, positron emission tomography (PET). Computed tomography (CT) or MRI scans or both were made to exclude brainstem lesions. Among patients with brainstem lesions may be patients with locked-in syndrome, which can be difficult to clinically identify, and in order to obtain a clean sample of patients with DOC, we decided to exclude them.

Changes in patients' vital and conscious status were recorded in four-time slices: 3, 6, 12, and 24 months after the event that led to pDOC. The first 12 months of recovery after the incident is given more priority. After the discharge, if a patient was alive, the assessment of consciousness was held via telecommunications with relatives (caregivers) and patients themselves if the latter was possible. In addition, neurologists held videoconferences to assess the patient in 70% of cases. In the remaining 30% of cases, the vital status and level of consciousness were assessed by relatives' indications. Finally, when the patient died, the date of death was taken into account.

Considering all possible limitations of remote diagnostics, we decided to check the cognitive function of the patients using one major feature, i.e., communicative skills. We included "non-communicating" patients in VS/UWS and MCS- who could not make any viable communication, where as "communicating" patients by any means consolidated patients in MCS+. Patients were included in "non-communicating" group if there was only single episode of self-awareness or dubious communication registered by the relatives or care giver because family members generally tend to exaggerate the level of

Table 1 Demographical and clinical data of patients at study entry

Indicators	Value				
	Total (M/F)	VS/UWS	MCS–	MCS+	Median CRS-R score [range]
Age (years), mean \pm SD, median [range]	46.49 \pm 15.96, 45 [32, 60]				
Sex (M/F)	109/75				
Aetiology					
ABI	52 (25/27)	39	12	1	6 [4, 10]
TBI	74 (54/20)	33	23	18	7 [6, 11]
VL	50 (25/25)	36	8	6	7.5 [5, 10]
Other	8 (5/3)	4	4	0	7 [5, 8.5]
Total by level of consciousness	184	112	47	25	7 [5, 10]

M, male; F, female; VS/UWS, vegetative state/unresponsive wakefulness syndrome; MCS, minimally conscious state; CRS-R, Coma Recovery Scale-Revised; SD, standard deviation; ABI, anoxic brain injury; TBI, traumatic brain injury; VL, vascular lesions.

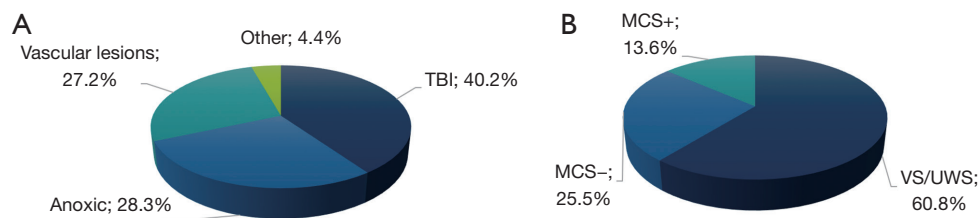


Figure 1 Aetiologies for disorders of consciousness (A) and percentage distribution of VS/UWS and MCS (B) of participants at study entry. TBI, traumatic brain injury; MCS, minimally conscious state; VS/UWS, vegetative state/unresponsive wakefulness syndrome.

communication of their DOC relative, and in cases when they are not sure, it is highly possible that they considered random signs as a significant trait. Possible survival outcomes were considered to be “alive” or “dead” at the control point.

Study size of 184 participants was defined by the number of pDOC patients in our Centre that satisfy eligibility criteria and are fully accessible for data-gathering and follow-up study.

Statistical analysis

Data were analyzed using the program STATISTICA 10 (StatSoft Inc., USA).

Quantitative data were presented as a mean and a standard deviation for normally distributed data. Nonnormally distributed data were described as median value and interquartile interval. We used absolute values and percentage for nominal values. All data presented in *Table 1*, age was only a factor that was found to be normally

distributed after the Kolmogorov-Smirnov test. Hence, we used nonparametric tests for inferential statistics. We calculated Spearman’s rank correlation between different variables. A P value <0.05 was considered statistically significant. We used a logistic regression model for all our patients to determine the correlation between prognosis factors at baseline and at 24 months post injury. Possible predictors like gender, age, aetiology, and the level of consciousness were considered independent variables, and the outcome was the dependent variable. For the analysis of survival, a Kaplan-Meier estimator was used.

Results

Demographical and clinical data

Demographical and clinical data of the patients participating in the study are summarized in *Table 1*.

At study entry in a group of 184 people confirmed eligible, TBI predominates by aetiology (40.2%) (*Figure 1*).

Table 2 Mortality within 2 years after brain injury according to the level of consciousness

Level of consciousness	At 3 months	At 6 months	At 12 months	At 24 months
Total (n=132)	19	49	104	132
VS/UWS (n=90)	14	34	73	90
MCS- (n=29)	3	9	24	29
MCS+ (n=13)	2	6	7	13

VS/UWS, vegetative state/unresponsive wakefulness syndrome; MCS, minimally conscious state.

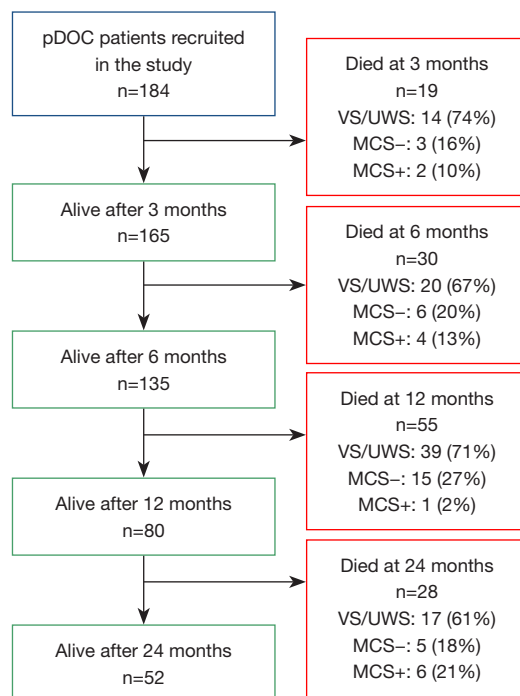


Figure 2 Flow diagram and mortality according to the initial level of consciousness. pDOC, prolonged disorders of consciousness; VS/UWS, vegetative state/unresponsive wakefulness syndrome; MCS, minimally conscious state.

The second most cause for pDOC in our cohort is ABI (28.3%). The consequences of VL account for 27.2%, other causes, such as consequences of degenerative, inflammatory, and neoplastic diseases—for 4.4% of the total number of patients. According to the level of consciousness, 60.8% were patients in the VS/UWS, 25.5% in MCS- and 13.6% in MCS+.

Mortality within 2 years after brain injury

All 184 participants were followed through the study

protocol for 24 months.

Within a year of the event, the mortality was 56.52% (104 people) of the total number of study participants (see *Table 2*). In the first 3 months, 19 people died (10.33% of the total number of study participants). Out of 19 people, 14 (73.7%) were in VS/UWS, 3 (15.8%) were in MCS-, and 2 (10.52%) were in MCS+. After first point of control, only 165 patients survived. By the second control point (6 months after the brain injury), a total of 49 patients died (26.6%), of which 34 people were VS/UWS, 9 patients MCS-, 6 patients MCS+. 116 patients entered the next stage of the study. So, at the third control point (12 months after the brain injury) 55 people were found deceased and 61 patients survived the first year after the event.

During the second year after the event, 28 patients died, i.e., total death at the control point corresponding to 24 months post-injury amounted to 71.7% of the total number of study participants. We used flow diagram (*Figure 2*) to represent all the data on mortality at each control point.

In the non-communicating group of patients, which originally consisted of 159 patients, 119 died at the last control point (24 months after brain damage), 90.15% of all deaths, and 64.64% of the total number of study participants. On the other hand, the group of communicating patients included 25 patients. Seven patients died during the first year, and 6 more died during the second year. Thus, 24 months after brain injury, the lethality of communicating patients was 13 patients (9.85% of all deaths and 7.07% of the total study participants). However, the statistically significant correlation between 24-month survival and initial level of consciousness is very weak ($r_s=0.245$, $P<0.05$).

Mortality and aetiology of pDOC is summarized in *Table 3* and *Figure 3*.

Mortality among TBI patients at the 24 months reference point post-injury constituted 62.16%, ABI patients 78.84%, and VL patients 80%. Among the small group with infectious and neoplasms, lethality amounted

Table 3 Mortality within 2 years after brain injury according to aetiology of pDOC

Aetiology	At 3 months	At 6 months	At 12 months	At 24 months
Total (n=184)	19	49	104	132
TBI (n=74)	2	8	32	46
Anoxia (n=52)	8	17	36	41
VL (n=50)	7	22	34	40
Other (n=8)	2	2	2	5

pDOC, prolonged disorders of consciousness; TBI, traumatic brain injury; VL, vascular lesions.

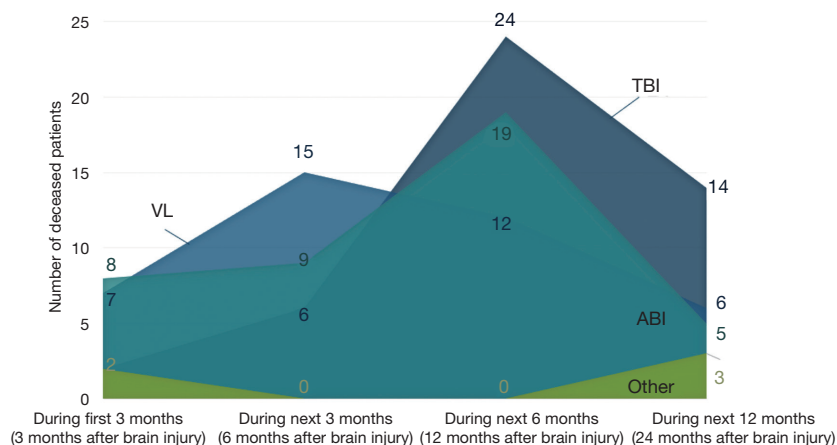


Figure 3 Mortality according to aetiology. Y-axis represents the number of deceased patients. VL, vascular lesions; TBI, traumatic brain injury; ABI, acquired brain injury.

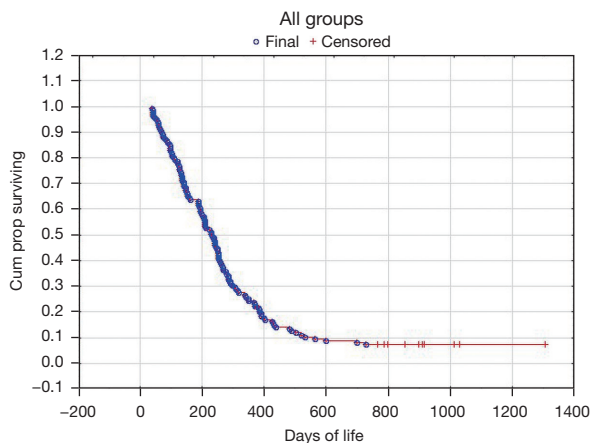


Figure 4 Kaplan-Meier plots of survival function.

to 62.5%. Even though lethality among patients with traumatic aetiology is somewhat less than among other etiologies, the correlation between traumatic injury and the 2-year outcome is weak ($r_s=0.174$, $P<0.05$).

We found no other statistically significant correlations.

We used the Kaplan-Meier estimator to estimate the survival rate (Figure 4) during 24 months after the brain injury and discharge from the hospital for the cohort under consideration. It can easily be seen, that the highest percentage of death occurs during the first year post-injury.

Dynamics in the level of consciousness

During the first year post-injury, 63 patients showed

Table 4 Dynamics in the level of consciousness in 2 years after brain injury according to the initial level of consciousness

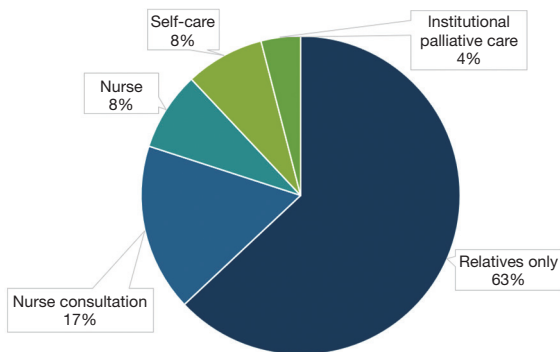
Level of consciousness	Substantial improvement of consciousness during the first year	Substantial improvement of consciousness during the second year	Deterioration of consciousness during the first year	Deterioration of consciousness during the second year	No change of consciousness during the first year	No change of consciousness during the second year
Total	33	6	1	0	60	45
VS/UWS	14	2	0	0	33	19
MCS-	19	4	1	0	12	14
MCS+	0	0	0	0	15	12

VS/UWS, vegetative state/unresponsive wakefulness syndrome; MCS, minimally conscious state.

Table 5 Dynamics in the level of consciousness in 2 years after brain injury according to the aetiology

Aetiology	Communication at study entry	Communication at 1-year post-injury	Communication at 2-year post-injury
Total	24	34	30
TBI	17 out of 74 (23.0%)	24 out of 42 (57.1%)	20 out of 28 (71.4%)
VL	6 out of 50 (12.0%)	5 out of 16 (31.3%)	6 out of 10 (60.0%)
Anoxia	1 out of 52 (1.9%)	4 out of 16 (25.0%)	2 out of 11 (18.2%)
Other	0 out of 8 (0.0%)	1 out of 6 (16.7%)	2 out of 3 (66.7%)

TBI, traumatic brain injury; VL, vascular lesions.

**Figure 5** Structure of care in the cohort.

an increase in the level of consciousness. In 33 cases (17.93%) there was substantial improvement in the level of consciousness, i.e., with the transition from the non-communicating group to the communicating group. During the second year after the injury, the level of consciousness of only 6 more patients substantially improved. Consciousness level deteriorated in a single patient. Thus, irrespective of survival, within 2 years after brain damage, 39 patients (21.20%) substantially increased the level of consciousness during 2 years post-injury (see *Table 4*).

Data on the dynamics of the level of consciousness in connection with the aetiology of the disease are summarized in *Table 5*.

The number of communicating patients 2 years post-injury was relatively higher for traumatic injury. Nevertheless, the correlation between these factors is weak: $r_s=0.245$, $P<0.05$.

We found no other statistically significant correlations.

Place of residence

Only 4% of our pDOC patients had been admitted to care centers (see *Figure 5*). In 63.4% of cases, primary caregivers were relatives, who generally had no help from sitters. On the other hand, 17% had an opportunity to consult the nurse, and 8% used the services of a visiting nurse.

Predictors of survival and recovery of consciousness

Among possible predictors of the outcome of pDOC we tested the following factors:

- (I) Level of consciousness at the discharge;
- (II) Traumatic aetiology;

Table 6 Logistic regression model for survival for all etiologies together

Possible predictor	β	P	OR (95% CI)
Age	-0.042*	<0.001*	0.96 (0.93–0.98)*
Gender	0.114	0.761	1.12 (0.53–2.35)
Level of consciousness at the discharge	0.426	0.079	1.53 (0.95–2.46)
Traumatic aetiology	-0.235	0.584	0.79 (0.33–1.84)

*, indicates statistically significant result. OR, odds ratio; CI, confidence interval.

Table 7 Logistic regression model for the improvement of the level of consciousness

Possible predictor	β	P	OR (95% CI)
Age	-0.039	<0.05*	0.96 (0.92–0.99)*
Gender	-0.482	0.306	0.62 (0.24–1.56)
Traumatic aetiology	0.660	0.190	1.93 (0.71–5.21)

*, indicates statistically significant result. OR, odds ratio; CI, confidence interval.

(III) Gender and age of patients.

In order to construct logistic regression models, we considered the following parameters: gender: 0 male, 1 female; aetiology: 0 non-TBI, 1 TBI; consciousness: 0 VS/UWS, 1 MCS-, 2 MCS+, 3 conscious; outcomes: 0 died, 1 survived; 0 no substantial improvement in consciousness level, 1 consciousness level improved substantially (with the transition of the patient from non-communicating to communicating group).

For regression analysis of survival, we divided all patients into four groups according to aetiology. The analysis provided 3 significant final models: for all groups together (likelihood ratio: $\chi^2=29.357$, $P<0.001$), ABI (likelihood ratio: $\chi^2=12.678$, $P<0.05$), and VL (likelihood ratio: $\chi^2=26.358$, $P<0.001$). TBI model did not show statistical significance (likelihood ratio: $\chi^2=15.228$, $P=0.185$). In all etiologies, younger age predicted 2-year survival. And no other factors were significant (see *Table 6*).

For ABI survival model only age was indicated as a predictor with $\beta=-0.083$ at $P<0.05$. However, in VL model gender ($\beta=5.729$ at $P<0.05$) and higher level of consciousness at the discharge ($\beta=3.684$ at $P<0.05$) were significantly associated with survival rate.

Regression analysis concerning the improvement of the level of consciousness also provided a final significant model (likelihood ratio: $\chi^2=16.881$, $P<0.001$; see *Table 7*). However, in this case no predictors of the improvement were found: age, gender, and traumatic aetiology were not associated with improvement. Level of consciousness was

not considered here in order to avoid the degeneracy.

Discussion

The objective of this study was to obtain data and find the prognostic markers on the survival and the dynamics of the level of consciousness in patients with pDOC for the first time in the Russian Federation. Epidemiological data that were collected as a result of this study show the following.

The sample comprised 184 patients with severe acquired brain injuries in VS/UWS or MCS and represents demographic data. Traumatic aetiology is prevalent prevalence among all etiologies in our cohort, which is consistent with the data of other large studies (16). In addition, TBI patients are on average younger than patients of other etiologies, confirmed by other studies (17,18). The more significant number of males population in TBI group is because they might be more involved in activities, which can cause trauma (19).

In the sample under consideration, 2-year mortality was 71.7% out of the total number of study participants. This result indicates a low survival rate in the cohort, even lower than in pioneer works of Higashi *et al.* (20) and Nakase-Richardson *et al.* (21), though we must note that the latter author considered only TBI patients, and none had ABI patients among their participants. In similar work, Baricich *et al.* (22) observed a 40% survival rate in VS/UWS patients (16). Some of their study participants underwent a long-term recovery brain injury program. However, our

cohort mainly lived at home and did not receive professional care and rehabilitation. This fact can contribute to a lower level of survival. We can therefore generalize that survival of patients at home is worse than in specialized care facilities, and in those countries where such care is not available, measures should be taken to increase life expectancy, increase the chance for cognitive recovery, and lesser caregiver's burdens for relatives. We propose organization of statistical accounting of pDOC patients, possibly by means of central registry, increasing in the number of specialized nursing facilities and rehabilitation programs for pDOC patients, which will let us redraw a trajectory between active rehabilitation and palliative care, improve discharge strategies and provide support for patients and their relatives irrespective of venue.

In the Netherlands, among the cohort of 31 VS/UWS patients, 50% of deaths were preceded by a physician's decision to discontinue of artificial nutrition and hydration (ANH) (23). In Russia discontinuation of life-sustaining treatment is illegal, we continue to treat patients until death is declared. Patients receive full-fledged therapy, regardless of neurological potential, which is considered inappropriate in some countries, where these patients are excluded from the study. Thus, in our case, the most severe patients were included in the study. This fact could also affect the result.

The low recovery rate of consciousness at a 2-year follow-up was circa 22% of the total number of patients may seem small. However, we must note that we divided patients into two groups based on their communication ability and did not consider the improvements inside groups. Thus, we understand significant improvement in the level of consciousness as a transition from non-communicating to communicating. At a first glance, this limits our scientific research, but it must be noted that from the practical point of providing care, rehabilitation, and defining supporting measures only the significant improvement in the level of consciousness has a real impact on the definition of a rehabilitation route and its rehabilitation prognosis. In this perspective, differential diagnosis between VS and MCS- cannot be extremely necessary.

We consider age as a predictive factor both in terms of survival and the increase in the level of consciousness. Several studies have also identified it as a predictor of favorable clinical outcomes in pDOC patients (18,24-26). The search for other markers is mostly inconclusive. Luauté *et al.* (27) showed that patients with a higher level of consciousness (MCS+) demonstrate better survival rate and possessed greater rehabilitation potential. However,

in recent papers of Estraneo *et al.* (28,29) on long-term survival of pDOC patients over 3 years, higher level of consciousness was not considered a predictor of survival. Higher CRS-R score and female gender were identified as predictors of recovery of consciousness during the first 12 months after the injury (17). Unfortunately, in our study, we could not confirm this conclusion. Thus, the search for reliable predictors of survival can be considered one of the urgent current tasks in this area of neurology.

One of the main limitations of the study is the remote method for identification of the level of consciousness after discharge from the hospital. This method, implemented on the basis of a survey of patients' relatives, does not exclude errors in the differential diagnosis of pDOC. First, we abandoned assessment using scales to minimize erroneous results because direct contact with the patient was difficult for the whole investigative period. Second, the study's relatively short duration substantially limits the results, but the authors continue to observe and communicate with the participants. Third, our study did not consider patients' comorbidities, so collecting them can significantly contribute to the research, and authors will see it as a further task. Also, the definition of hospital mortality was not included in the objectives of the study. Our center provides high-tech medical care, a large number of personnel are involved, and thus our unique conditions are not reproducible nowadays, not only in the home settings, but also in other institutions.

Conclusions

Our research showed that the survival rate and the recovery rate of consciousness are both low, though not significantly different from existing data.

The reliable prognostic markers among demographical and clinical indices are hard to obtain; however, younger age can be considered the only significant predictor of a favorable outcome in terms of survival and the recovery rate of consciousness—further more extensive studies with a solid methodology is required to identify other predictors.

We did not find statistically significant correlations between changes in the level of consciousness and survival. This raises a serious question for the medical community about preventing the formation of a functional deficit in such patients, since an increase in the level of consciousness itself does not reduce somatic risks. Even if the brain might have time to recover, but a patient's body cannot wait longer, we need special attention such as special care and

complex rehabilitation measures to reduce sequelae of the immobilization syndrome in all subgroups of the pDOC.

Based on the consistency of our data and global studies, the correct use of statistical methods, and the relatively large number of participants for this category of patients (pDOC), we assume that the sample obtained can be considered representative, and the results can be extended to the general population.

We dare to hope that the data we have obtained on survival and recovery of consciousness will help determine the optimal route for the medical and social rehabilitation of patients with pDOC, and formulate adequate support measures for the patients and their relatives.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://apm.amegroups.com/article/view/10.21037/apm-22-403/rc>

Data Sharing Statement: Available at <https://apm.amegroups.com/article/view/10.21037/apm-22-403/dss>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://apm.amegroups.com/article/view/10.21037/apm-22-403/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and approved by the Ethics Committee of the Federal State Budgetary Institution of the Federal Research and Clinical Center of Intensive Care Medicine and Rehabilitology (No. 08/19/22). Informed consent was obtained from all participants or from their parents or next of kin involved in the study.

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