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Original article

Long-term outcomes of prolonged disorders of consciousness: a prospective cohort study in specialized neurorehabilitation

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ABSTRACT

Background: There is limited information on the course of recovery and long-term outcome of people with prolonged disorders of consciousness (PDOC).
Objective: To determine long-term outcomes (mortality, recovery of consciousness, disability, functioning, and independence) in people with PDOC after early intensive neurorehabilitation (EIN) within a novel nationwide PDOC care pathway.
Methods: Prospective cohort study with 2-year follow-up. All people with PDOC admitted to EIN at a single rehabilitation center in the Netherlands were screened for inclusion. Baseline measurements of level of consciousness (CRS-R), disability (DRS), and functioning (FIM) were collected at rehabilitation admission, and follow-up was at 14, 28, 40, 52 and 104 weeks post admission.
Results: Of 129 participants included (mean age 38.1 years, SD 16.4), 33 (26%) patients died, and 80 (62%) regained consciousness within the 2-year follow-up. From them, 56 (43%) regained consciousness during 14 weeks of EIN, 14 (11%) within 6 months after admission, and 10 (8%) between 6- and 24-month follow-up. Mean level of disability and functioning significantly increased over time, with the largest improvement between 14- and 28-week post admission. Amongst responders who regained consciousness, the proportion of participants functioning independently (FIM total score ≥78) increased from 4% (3/78) at 14 weeks to 41% (25/61) at 2-year follow-up.
Conclusions: Improvement of level of consciousness, disability, and functioning in people with PDOC occurs beyond the early stages of specialized neurorehabilitation until 2 years post injury, despite substantial mortality. These results highlight the need for specialized care for people with PDOC during the first 2 years after their injury, which focuses on both functional recovery and personalized decision-making.
Protocol registration number: International Clinical Trial registry Platform (ICTRP) of the World Health Organization (WHO): NL-OMON23779.

Introduction

Acquired brain injury is the leading cause of death and disability in modern neurologic practice [1]. After the first days of coma, some people resume independent breathing and eye opening while showing no or little evidence of awareness of the self or their environment. A distinction is made between the unresponsive wakefulness syndrome (UWS) in people who do not demonstrate signs of awareness [2], and a minimally conscious state (MCS) in people with inconsistent but reproducible intentional behavior (eg, visual pursuit, localization to pain, command-following) [3]. When these conditions persist for over 28 days, they are referred to as prolonged disorders of consciousness (PDOC) [4]. People with these dramatic clinical conditions may evolve towards recovery of full consciousness (functional use of common objects or reliable, basic

Abbreviations: CRS-R, Coma Recovery Scale-Revised; DOCTOR, Disorders of Consciousness, Treatment and Outcome Registry; DRS, Disability Rating Scale; EIN, Early intensive neurorehabilitation; e-MCS, Emergence from minimal conscious state; FIM, Functional Independence Measure; GEE, Generalized Estimating Equations; LOC, Level of consciousness; MCS, Minimally conscious state; NTBI, Non-traumatic brain injury; PDOC, Prolonged disorder of consciousness; PIN, Prolonged Intensive Neurorehabilitation; TBI, Traumatic brain injury; TPI, Time post injury; UWS, Unresponsive wakefulness syndrome

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yes/no communication [3]) or they may remain in PDOC for years [5,6] (Appendix).

Specialized intensive neurorehabilitation has been shown to facilitate the recovery of consciousness [7,8]. People with traumatic brain injury (TBI) (78%) and, less frequently, non-traumatic brain injury (NTBI) (25%) may regain full consciousness [8–10], even beyond the 1st year after their injuries [11–13]. Studies evaluating functional outcomes indicate that, after 1 year post injury, 27–34% of all people with PDOC, mostly in UWS, are able to look after themselves for 8 h a day [14,15], and 19% of all surviving people with PDOC demonstrate employment potential [16]. In 2 studies of people with TBI, derived from 1 database, functional independence ranged from 44 to 69% [17] in surviving people with PDOC at 5 years post event, to 50–75% after 10 years [18]. Functional outcomes in all studies were based on telephone interviews [14–18], which may carry a risk of bias.

Long-term outcome studies are scarce, mortality numbers unclear, and independence has mainly been studied in people with TBI. This hampers appropriate decision-making, especially during the acute phase of care, leading to both over- and undertreatment. Evidence-based understanding of long-term functional recovery in people with PDOC is vital for personalized treatment, from the earliest phases in the ICU to palliative care or chronic care.

In the Netherlands, specialized PDOC care was centralized on a national level in 2019 [19]. This academically embedded chain of care consists of:

- A mobile team of experts, delivering in-hospital diagnostic and therapeutic advice starting in the acute stages;
- Early Intensive Neurorehabilitation (EIN), concentrated in a single specialized rehabilitation center (Libra Rehabilitation & Audiology, Tilburg) and consisting of 14 weeks of intensive multidisciplinary rehabilitation providing up to 25 therapy sessions a week;
- Prolonged Intensive Neurorehabilitation (PIN), for people who remain in PDOC following EIN. PIN is offered by 3 accredited nursing homes, involving approximately 10 therapy sessions a week, for up to 24 months post ictus, and can be shortened if the level of consciousness remains stable for 6 months.

This novel chain of care offers the opportunity to study PDOC on a national scale [20,21]. We have previously published the early outcomes of EIN [8]. The aim of the current study is to evaluate the long-term outcomes in terms of mortality, recovery of consciousness, disability, functioning, and independence of people with PDOC in a prospective cohort study with a 2-year follow-up. Based on the literature, we hypothesized that in a mixed population of TBI and NTBI people, 60% of people with PDOC will regain consciousness within 2 years of follow-up and 50% of PDOC survivors will regain functional independence.

Methods

Study design

The DOCTOR study: Disorders of Consciousness, Treatment and Outcome Registry, is a single-center prospective cohort study with a 2-year follow-up [20].

Regulatory and ethical aspects

The Medical Ethics Committee of Erasmus MC, University Medical Centre Rotterdam declared that the study was not subject to the Dutch Medical Research Involving Human Subjects Act, meaning that ethical approval for the study was waived under the national laws (MEC-2019-0127). Written informed consent was obtained from the legal representatives of all participants, and participants who showed sufficient recovery during the study trajectory were asked for consent for further participation in the study.

Participants

All people with PDOC in the Netherlands admitted to EIN between April 2019 and April 2023 were screened for eligibility.

The admission criteria for EIN were 1) PDOC lasting at least 4 weeks and less than 6 months at admission; 2) medical stability (eg, without mechanical ventilation, no intravenous or intra-arterial lines) as judged by the treating rehabilitation physician; 3) capable of participating in the highly intensive program (ie, premorbid independence in activities of daily living and able to engage in an active daily schedule) and 4) life expectancy should not be limited by comorbidity. Exclusion criteria were coma and uncontrollable epilepsy.

Additional criteria for the study were 1) a minimum age of 16 years at the time of injury and 2) first-time acquired non-progressive brain injury of any etiology.

The sample size depended on the number of people admitted to EIN during the 4 years of inclusion. We estimated that approximately 30 people aged ≥16 years would be admitted each year and that 90% would meet the inclusion criteria and were willing to participate in the study.

A detailed description of the EIN program and specialized PDOC chain of care has been published elsewhere [19,20]. During EIN, people with PDOC receive continuous skilled nursing (24/7) and medical care and a daily maximum of 150 min (5 × 30 min) of interdisciplinary rehabilitation to facilitate recovery of consciousness and prevent complications. The program provides multimodal stimulation, pharmacological treatment, and mobilization therapies (eg, out of bed, physical interventions) to promote body function and reduce complications secondary to inactivity and deconditioning.

Study measurements were performed at EIN admission and discharge, and during follow-up at 28, 40, 52, and 104 weeks after the start of EIN. EIN ended as soon as the person reached consciousness or, if the person did not emerge from PDOC, after a maximum of 14 weeks. Thereafter, people were discharged to regular medical rehabilitation, to their own home, a specialized PDOC nursing home providing PIN, or to another institution, depending on their Level of Consciousness (LOC), functional abilities, and preferences of their families. If people could not immediately be transferred to the next institution after 14 weeks of EIN, therapy intensity was adjusted to that provided in the intended follow-up setting.

Data collection

Demographic characteristics, clinical characteristics, medical history, length of stay in EIN, and data regarding prior hospital admissions were obtained from the medical records. Measurements were performed by specialized staff members during EIN, and on-site by a trained research assistant during follow-up.

Measurement instruments

Level of consciousness

LOC was measured using the Coma Recovery Scale-Revised (CRS-R), a bedside assessment tool for differentiating levels of consciousness (UWS, MCS-, MCS+, and e-MCS) (Appendix) by the observation of responses to various stimuli [22,23]. The assessment comprises 6 hierarchical subscales (auditory, visual, motor, oromotor/verbal, communication, and arousal function) with 23 dichotomously scored items. Total CRS-R score ranges from 0 (worst possible score) to 23 (best possible score).

Level of disability

The Disability Rating Scale (DRS) was used to identify the level of disability.

The DRS is an observational tool assessing residual functional abilities across 4 domains: arousability (3 items), dependence (1 item),

cognitive abilities (3 items), and employability (1 item). The total scores ranges from 0 to 29, indicating no disability (score of 0), mild (score of 1), partial (score of 2−3), moderate (score of 4−6), moderately severe (score of 7−11), severe (score of 12−16), extremely severe (score of 17−21) disability, vegetative state (score of 22−24), and extreme vegetative state (score of 25−29) [24]. The DRS has a minimal clinically important difference (MCID) of 1 in chronic people with TBI [25].

Level of functioning and independence

The Functional Independence Measure (FIM) was used to assess the level of functioning and independence.

The FIM evaluates functional independence through 18 items covering self-care (6 items), mobility (7 items), and cognition (5 items), each rated on a 7-point scale (1 = total assistance, 7 = complete independence) [26]. Total scores range from 18 (lowest level of functioning) to 126 (highest level), with scores ≥78 indicating functional independence [27,28]. The FIM has an MCID of 22, based on data from people after a stroke [29].

The CRS-R, DRS, and FIM were performed at admission and discharge of EIN and during follow-up at 28, 40, 52, and 104 weeks after admission. Once the participant was conscious, CRS-R measurements were discontinued.

Statistics

Descriptive statistics were used to summarize the baseline characteristics. Means and standard deviations (SD) were calculated for interval variables, and medians and interquartile ranges for ordinal variables. Proportions were calculated for nominal variables.

Mortality rate was calculated. Differences in mortality of subgroups based on etiology (TBI versus NTBI) were analyzed using the Chi-square test, and differences in the LOC at admission (UWS, MCS-, and MCS+) were analyzed using the Kruskal-Wallis test.

Proportions of participants regaining consciousness at each time point are presented for the total sample and based on etiology (TBI/NTBI) and LOC at admission. The total sample was divided into 2 subgroups of people regaining consciousness (e-MCS) and those remaining in PDOC during the 2-year follow-up.

Proportions of participants at different disability levels across time points, as measured with the DRS, are presented for the total sample and for the 2 subgroups.

Generalized Estimating Equations (GEE) analyses for linear outcomes were performed to estimate the course of functional recovery over time, as measured with FIM and DRS, and GEE for binary logistic outcomes for the course of regaining independence (yes/no) as measured with the FIM. The exchange structure was used in the GEE model. GEE analysis is a semiparametric method that does not depend largely on the specification of the underlying distribution of the outcomes. As part of this model, a covariance matrix was estimated to represent the within-subject dependencies in repeated measurements, which also takes into account missing data. Assuming that data are missing at random, data imputation is unnecessary in GEE analyses, and all observations of all participants are taken into account, in contrast to complete-case analyses. Total scores at each time point were included as the dependent variable in the GEE model, and time of measurement as the independent variable. In a sensitivity analysis, any mixed model would produce the same results.

Analyses were performed for the overall group, but also for the 2 subgroups separately.

In all analyses, a P-value < 0.05 was considered statistically significant.

Results

Of the 169 people admitted to EIN, 137 were considered eligible for the study, and 129 were enrolled (Fig. 1). During the study, 19 participants or family members withdrew their consent (15%). Participants who were lost to follow-up (secondary withdrawal of consent by participants $n = 4$, or representative $n = 10$, or no contact possible $n = 5$) were younger (mean 27.6 years (SD 11.2), $P = 0.004$) and were more often male (71%, $P = 0.099$), than participants completing follow-up. Accidentally, no appointment could be made with 6 participants at week 28, 5 participants at week 40, 4 participants at week 52 and 2 participants at week 104 due to various logistical reasons (ie, participant was

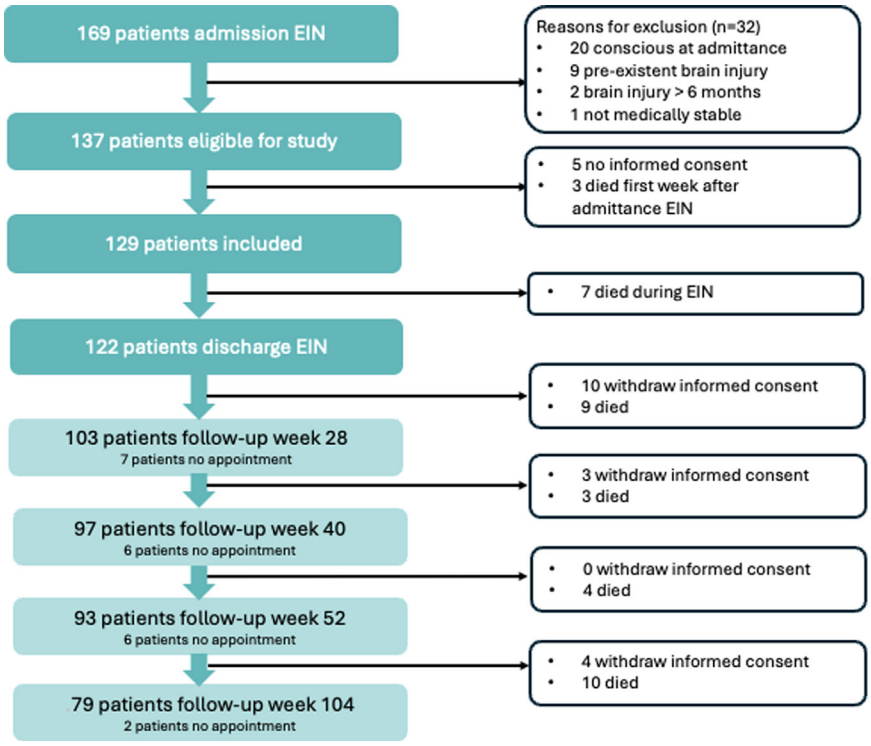

Fig. 1. Flowchart illustrating participant enrolment and follow-up measurements.

Table 1
Baseline demographic and clinical characteristics of the study population.

	Total sample
N (%)	129 (100)
Age (years) mean (SD)	38.1 (16.4)
Sex *n* (%)	
Female	62 (48)
Male	67 (52)
Level of education *n* (%)	
low	14 (11)
middle	52 (41)
high	35 (27)
unknown	28 (21)
Living situation *n* (%)	
alone	23 (18)
with spouse or parents	105 (81)
unknown	1 (1)
Work situation *n* (%)	
Work/study fulltime	89 (69)
Work/study parttime	13 (10)
Voluntary work	1 (1)
None	26 (20)
Level of consciousness[a] *n* (%)	
UWS	48 (37)
MCS-	45 (35)
MCS+	36 (28)
Etiology *n* (%)	
TBI	72 (56)
NTBI	57 (44)
Anoxia	34 (26)
Other	23 (18)
TPI (days) mean (SD) median (IQR)	71.8 (28.8) 65 (53.5;85.5)
Time at ICU (days) mean (SD) median (IQR)	32.8 (22.4) 29 (17.5;43)
Tracheal tube *n* (%)	55 (43)
CRS-R total score mean (SD) median (IQR)[a]	8.7 (4.3) 8 (5.25;12)
DRS total score mean (SD) median (IQR)[b]	23.3 (2.9) 24 (22;25)
LOS EIN center (days) mean (SD) median (IQR)	93.4 (37.6) 99 (66.5;117)
Medication use during study: stimulantia[c] *n* (%)	
Yes	76 (59)
No	53 (41)

[a]1 participant had no CRS-R data at admission to EIN because of agitation and was diagnosed as MCS+ based on clinical judgement.
[b]DRS of 127 participants.
[c]Stimulantia are amantadine, dopamine, zolpidem, methylphenidate.
RS-R, Coma Recovery Scale-Revised; DRS, Disability Rating Scale; EIN, Early Intensive Neurorehabilitation; ICU, Intensive Care Unit; LOS, Length Of Stay; MCS, Minimally Conscious State; NTBI, Non-Traumatic Brain Injury; TBI, Traumatic Brain Injury; TPI, Time Post-Injury; UWS, Unresponsive Wakefulness Syndrome.

admitted to hospital, family had no time, no contact was possible at that time) (Fig. 1).

Demographic and clinical characteristics are shown in Table 1. The mean age of the study population was 38.1 years (SD 16.4), and 52% was male. The etiology of brain injury was TBI in 56% and NTBI in 44%. Mean time post injury (TPI) at EIN admission was 71.8 days (SD 28.8), and mean length of stay in EIN was 93.4 days (SD 37.6).

Mortality

Of the 129 participants, 33 (26%) died during the study, of whom 7 (5%) died during EIN, and 26 (21%) died during follow-up. Fig. 2 shows the percentages of participants who had died at each time point. Mortality was higher in NTBI (38%) than in TBI (24%), however not statistically significant ($P = 0.070$) over 2 years follow-up (Fig. 2B). In addition, mortality was higher among participants in UWS at admission (42%) compared to MCS- (28%) and MCS+ (14%) ($P = 0.040$) (Fig. 2C). Of the 33 deceased participants, 12 (36%) died of medical complications despite ongoing life-sustaining treatment, 10 (30%) died due to severe medical complications following a decision to withhold or withdraw treatment, and 11 (33%) died as a result of their brain injuries after withdrawal of life-sustaining therapy. At time of death 26 (79%) participants were in PDOC, while 7 (21%) participants had emerged from unconsciousness.

LOC during follow-up

Of the total cohort, 56 (43%) participants regained consciousness during EIN, ie, within 14 weeks of specialized treatment (Fig. 2). After EIN discharge, another 24 (19%) participants regained consciousness; 14 (11%) within 28 weeks, 5 (4%) between 28 and 40 weeks, 2 (2%) between 40 and 52 weeks, and 3 (2%) between 52 and 104 weeks. Of the 3 participants who regained consciousness beyond 52 weeks, for 1 participant, prior follow-up measurements were missing due to various reasons. Within 2 years of follow-up, 37 (65%) participants with TBI and 24 (48%) participants with NTBI regained consciousness (Fig. 2B). Of the participants in UWS at admission, 16 (42%) regained consciousness within 2 years, compared to 25 (62%) of those in MCS-, and 20 (78%) of those in MCS+ at admission (Fig. 2C).

Level of disability

Fig. 3 presents the proportion of participants in the different levels of disability measured by the DRS at each moment in time. During 2 years of follow-up, the percentage of participants in severe disability or worse (ie, extremely severe disability, vegetative state, and extreme vegetative state) decreased from 63% to 18%, and the percentage of participants with moderately severe disability or better increased (Fig. 3) to 69% at 2 years. All participants who remained in PDOC at 2 years had severe or worse disability, and recovery to moderately severe disability or better functioning only occurred in participants who had regained consciousness at 2 years (Fig. 4). In participants who remained in PDOC at 2 years, some recovery was observed. The proportion of participants in vegetative state or extreme vegetative state decreased from 76% at discharge from EIN to 12% at 2 years.

Mean total DRS score of the total cohort decreased significantly during follow-up from 23.33 (SD 0.25) at admission to 10.57 (SD 0.55) after 2 years of follow-up, indicating an improvement of functional status (Table 2). The improvement in DRS total score was largest between EIN discharge and 28 weeks (mean difference, MD 4.98; $P < 0.001$). There was also a significant improvement between the 1- and 2-year follow-up measurements (MD 1.23; $P < 0.001$). Both subgroups—participants who regained consciousness and those who remained in PDOC—demonstrated significant improvements, with the most substantial gains occurring between discharge from EIN and 28 weeks, as well as a significant improvement between the 1-year and 2-year follow-up (Table 2).

Level of functioning and independence

Total FIM scores of the total cohort showed the same pattern as total DRS scores. There was an increase in scores over time from 19.40 (SD 0.39) at admission to 62.15 (SD 3.99) at 2 years follow-up, meaning an increase in the level of independence (Table 2). The improvement in FIM scores was largest between discharge EIN and week 28 (MD 19.02; $P < 0.001$). FIM scores also improved significantly between 1- and 2-year follow-up (MD 6.80; $P < 0.001$). No significant change over time was observed in participants who remained in PDOC (Fig. 5).

At discharge, EIN 3 (2%) participants of the initial cohort had a score of 78 or higher on the FIM, corresponding to independent functioning (Table 2). This number increased to 25 (20%) of the initial cohort, representing 41% of responders in the e-MCS subgroup at 2-year follow-up.

At 2-year follow-up, 14 participants (11% of the initial cohort) achieved household independence or were mildly dependent with limited assistance (DRS score 0 to 2), representing 23% of the 61 responders in the e-MCS subgroup. Two (2%) participants (3% of the responders in the e-MCS subgroup) were able to return to work or school, although not at their premorbid level of functioning (DRS score 1). None of the

Fig. 2. Level of Consciousness during follow-up (A, total population; B, subgroups according to etiology; C, subgroups according to Level of Consciousness at admission to EIN).

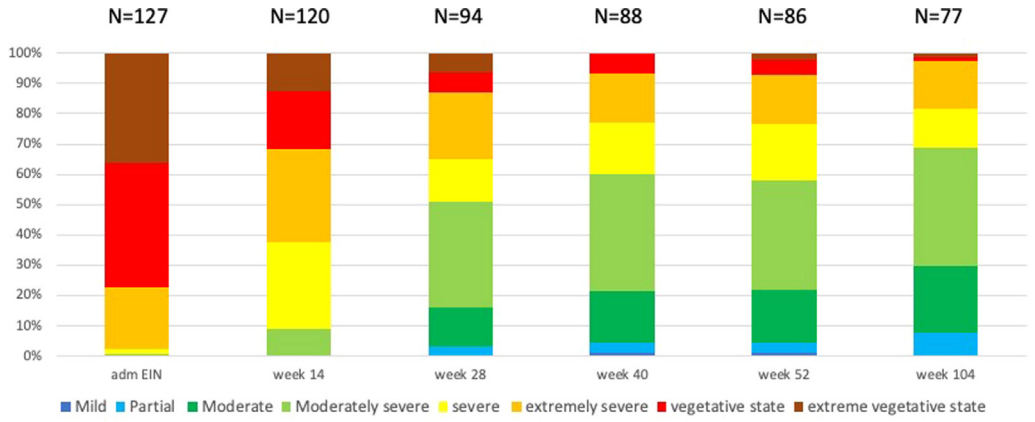

Fig. 3. Level of disability, as measured with the Disability Rating Scale during follow-up of all participants.

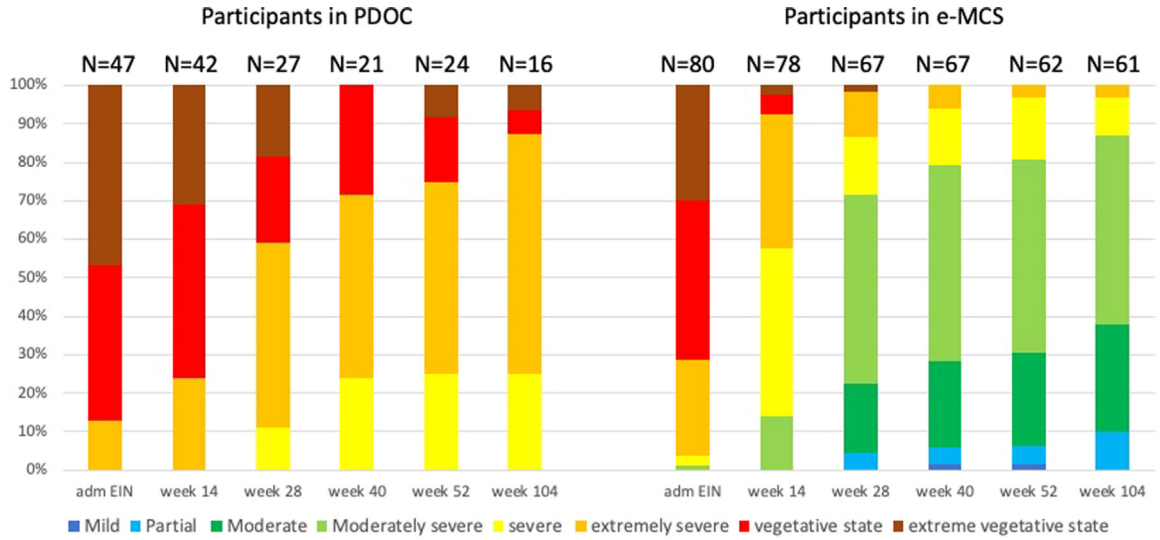

Fig. 4. Level of disability, as measured with the Disability Rating Scale during follow-up organized by subgroups of participants who stayed in Disorder of Consciousness (n = 49) and participants who regained consciousness (n = 80) during 2-year follow-up.

participants returned to their previous occupation or educational program at the 2-year follow-up.

Discussion

This prospective, nationwide cohort study included almost the entire pool of people with PDOC at hospital discharge following severe acquired brain injury. At 2 years follow-up, 47% had regained consciousness, 26% had died, 15% was lost to follow-up, and 12% remained in PDOC.

During 2 years of follow-up, 7 participants regained consciousness and died subsequently, and 12 participants regained consciousness and were lost to follow-up. Thus, across the total group of 129 participants, we found that 62% regained consciousness during the first 2 years of specialized treatment. Recovery of consciousness most frequently occurred during EIN (42% of the original cohort) or within 28 weeks after admission (another 11%). Although rare, emergence to a full conscious state even occurred beyond the 1st year. After 2 years, 20% of the original cohort were independent in activities of daily living according to the FIM, representing 41% of survivors who regained consciousness.

Our finding that people can regain consciousness even after initial treatment (6 months post injury) is consistent with previous research [9,16,30–33]. However, comparing our results with other studies is also challenging due to variations in the presentation of outcomes. Most studies report median time to emergence [30,32] or improvements in specific aspects of LOC, such as command-following [14] or communication ability [31], rather than focusing specifically on the recovery of consciousness as defined in our study.

Only one study is comparable to ours, with our study showing better outcomes. Lopez-Rolon et al. showed that 35% of the people with PDOC emerged to a conscious state after a mean follow-up of 3 years in a single-center study [31]. This difference might be explained by cohort-specific factors, such as the fact that our cohort is relatively young, with higher levels of consciousness at admission and fewer participants with a non-traumatic etiology. These 3 factors—higher age, lower LOC at admission, and non-traumatic etiology—have been shown to be less favorable for regaining consciousness [9,34,35]. A systematic review [9], on the other hand, showed higher recovery rates in people with TBI, which could be explained by the fact that most of the source articles studied survivors only. Still, people with NTBI in our cohort had better outcomes than those reported in the systematic review of Giacino et al. [9].

In the Netherlands, a country with a tradition of open discussion about quality of life in relation to end-of-life decisions, it is a legal option to withhold or withdraw life-sustaining treatment in people with PDOC. In the acute phase, after extensive examination, deliberation, and communication with the person's representatives, medical doctors may withhold or discontinue life-sustaining treatment when the chance of recovery to an outcome the person would find acceptable is considered

Table 2
Independence in functioning at admission and during follow-up: in the total group and in subgroups of participants in Disorder of Consciousness and participants who regained consciousness.

	All participants			e-MCS during follow-up			PDOC during follow-up		
	N	Estimated mean (SE)	*P*-value*	N	Estimated mean (SD)	*P*-value*	N	Estimated mean (SD)	*P*-value*
DRS total score									
Admission EIN	127	23.33 (0.25)		80	22.76 (0.34)		47	24.30 (0.31)	
Discharge EIN	120	18.49 (0.46)	0.000	78	16.03 (0.50)	0.000	42	23.09 (0.36)	<0.001
Week 28	94	13.52 (0.61)	0.000	67	10.28 (0.55)	0.000	27	20.71 (0.55)	<0.001
Week 40	88	11.99 (0.58)	<0.001	67	8.86 (0.47)	<0.001	21	19.50 (0.65)	0.009
Week 52	87	11.80 (0.59)	0.304	62	8.41 (0.44)	0.005	25	19.34 (0.58)	0.811
Week 104	77	10.57 (0.55)	<0.001	61	7.64 (0.43)	0.014	16	17.87 (0.71)	0.016
FIM total score									
Admission EIN	126	19.40 (0.39)		79	19.67 (0.60)		47	18.72 (0.35)	
Discharge EIN	120	28.42 (1.57)	<0.001	78	33.37 (2.18)	<0.001	42	18.41 (0.21)	0.451
Week 28	94	47.25 (3.25)	<0.001	67	58.78 (3.92)	0.000	27	19.93 (0.81)	0.066
Week 40	88	52.62 (3.50)	<0.001	67	65.10 (4.00)	<0.001	21	19.95 (0.49)	0.969
Week 52	86	55.34 (3.65)	0.005	62	69.68 (4.09)	<0.001	24	20.24 (0.48)	0.409
Week 104	77	62.15 (3.99)	<0.001	61	75.58 (4.36)	0.002	16	22.19 (1.07)	0.062
	N	*n* (%)	*P*-value*	N	*n* (%)	*P*-value*	N	*n* (%)	*P*-value*
FIM score ≥78 (independent)									
Admission EIN	126	0 (0)		79	0 (0)		47	0 (0)	
Discharge EIN	120	3 (3)	0.057	78	3 (4)	0.055	42	0 (0)	
Week 28	94	20 (21)	<0.001	67	20 (30)	<0.001	27	0 (0)	
Week 40	86	20 (23)	0.356	67	20 (30)	0.530	21	0 (0)	
Week 52	86	21 (24)	0.313	62	21 (34)	0.192	24	0 (0)	
Week 104	77	25 (32)	0.030	61	25 (41)	0.070	16	0 (0)	
Residence and work/school at 2-years									
	N	*n* (%)		N	*n* (%)		N	*n* (%)	
Residence at 2-years									
	77			61			16		
Home		32 (41)			27 (44)			5 (31)	
Sheltered housing		4 (5)			4 (7)			0 (0)	
Nursing home		36 (47)			26 (43)			10 (63)	
Other		5 (6)			4 (7)			1 (6)	
Work/school at 2-years									
	77			61			16		
Yes		2 (3)			2 (3)			0 (0)	
No		75 (97)			59 (97)			16 (100)	

**P*-value is the difference between the current measurement and the previous measurement time (GEE).
DOC: Disorders of Consciousness, DRS: Disability Rating Scale, EIN: Early Intensive Neurorehabilitation, FIM: Functional Independence Measure, GEE: Generalized Estimating Equations.

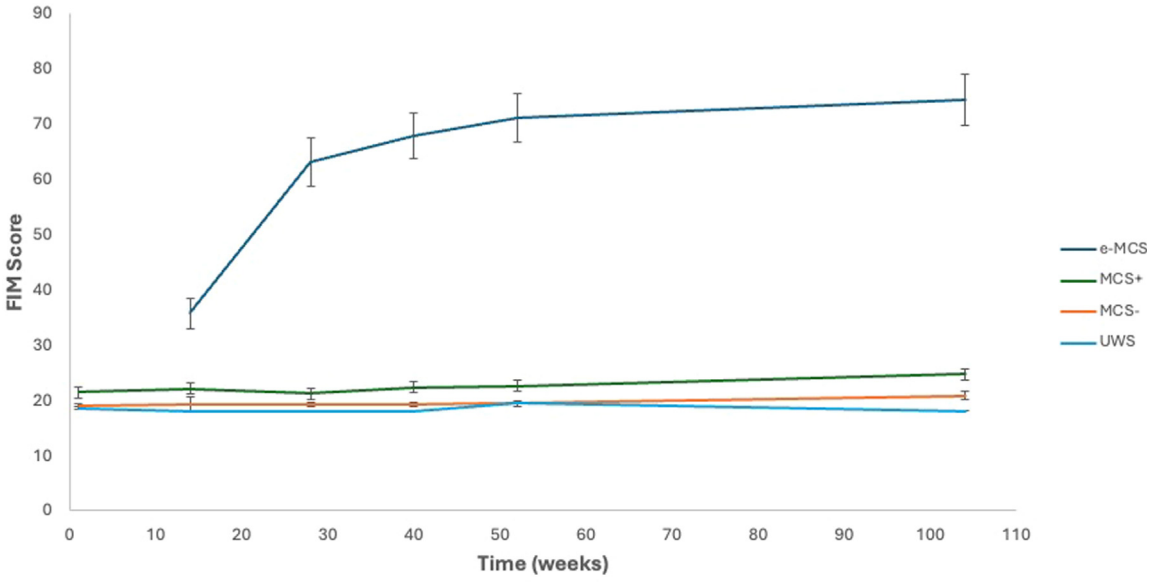

Fig. 5. Mean FIM scores for different levels of consciousness during follow-up.

too small [36]. Because the participants with NTBI in our study were older than the participants with TBI [8], and both age and NTBI are negative prognostic factors, we suspect that only people with NTBI with a relatively good prognosis were referred to EIN.

Our findings indicate that significant improvements in functional outcomes (mean DRS and FIM scores) may occur in the long-term phase, even beyond 1-year post injury. Some studies [16,37] have reported higher levels of functioning than observed in our cohort. In contrast,

another study has reported poorer outcomes [30]. These discrepancies may be attributed to differences in participants' characteristics across studies, including younger age [16,37], etiology (eg, inclusion of only people with TBI [16]), TPI (either shorter TPI [16,37] or longer [30]), and shorter follow-up periods [30].

Most improvement in level of functioning occurred between EIN discharge (on average 6 months post injury) and 28 weeks (ie, 3 months after discharge). Other studies, with 1-year time intervals between measurements, show that the largest gains in functional recovery occur in the 1st year post injury [17,18]. Our results suggest that most of the gain in functional recovery occurs within the first 9 months post injury. This is important for people with PDOC, their families, and healthcare professionals for a better understanding of long-term functional recovery, and it will be helpful for decision-making regarding persons' care.

Although we found statistically significant differences between time points, in clinical practice, it is important to reflect on the clinical relevance of these differences. Between discharge from EIN and 1 year follow-up, we observed a mean improvement of 6.69 points on the DRS, followed by an additional improvement of 1.23 points between the 1- and 2-year follow-ups. Given that the MCID on the DRS is 1 point, these changes represent clinically meaningful improvements. An improvement of a minimum of 1 point on the DRS was achieved for participants who regained consciousness, as well as for those who remained in PDOC during 2 years of follow-up. Regarding the FIM, we found an overall improvement of 26.92 points between discharge and 1 year, and a difference of 6.81 points between 1 and 2 years. The improvement during the first year is greater than the MCID on FIM of 22. Though the improvement between year 1 and 2 follow-up does not reach the level of clinical importance, the percentage of the participants who scored independence on the FIM total score (≥78), in the subgroup of conscious participants, increased from 34% to 41%.

At 2-year follow-up, 18% of surviving participants lived at home without in-house supervision (DRS 0−2). This is in line with Nakase et al. [16], who reported that 19% of all people with TBI lived without in-house supervision. Return to work or school after 2 years at a full level, or close to premorbid level of functioning (DRS score 0 or 1) occurred less frequently (3%) in our study than in other studies. Two studies found return to work/school rates of 10 and 17% [37,38] and another study reported 19% [16], but the latter also considered participants who demonstrated employment potential in sheltered workshop environments (DRS score 2). These differences may be explained by the differences in follow-up time, namely 2 years in our study versus 4 years in others [16,37,38]. Also, previous research in people with TBI has shown that employment rates may increase over time [39].

A major strength of our study is its prospective design with detailed, on-site follow-up assessments, where most previous long-term outcome studies have been retrospective [9,14,30−32,37,38]. Furthermore, outcomes were evaluated at multiple time points within a 2-year period, offering a more detailed perspective on recovery trajectories than previously reported in the literature. The nationwide scale and fully centralized chain of care allowed us to reach virtually all newly diagnosed people with PDOC within this country, with optimal sample representativeness. The exceptionally high participation rate further strengthens the study's validity.

Nevertheless, several limitations should be noted. First, there was a 15% loss to follow-up over the 2-year period. Although relatively low for a study of this duration, it can influence the outcomes because the participants who lost to follow-up in our study were younger and more often male—their data may have shown even better outcomes. Second, because the starting point of our study was EIN admission, TPI at baseline varied between 1 and 6 months. As a result, comparisons with other (retrospective) studies, using TPI as baseline, should be done with this difference in mind. Third, the absence of information on imaging data might limit the depth of clinical relevance for the acute phase. Nonetheless, the study provides valuable information on long-term recovery trajectories when DOC is prolonged in the 1st weeks after brain injury. To enhance clinical relevance, it is advised that future research incorporate variables often used and collected in the acute phase into studies on long-term outcomes, such as imaging findings, and TPI as the baseline. Fourth, some data relevant for this population are missing, such as a clearly defined number of acute coma patients as the preceding condition for admission to EIN, the absence of return to home data (including level of independence), and the absence of a detailed patient-level analysis of stimulant drug exposure. Last, while this study assessed functional outcomes, these do not necessarily reflect quality of life. To evaluate whether recovery from PDOC results in meaningful, fulfilling lives for the people with PDOC and their loved ones, alternative research methods are needed. The TOP-DOC (True Outcomes of PDOC) study [21] addressed these aspects through qualitative interviews.

Conclusion

This study suggests that the majority of people with PDOC regain consciousness during specialized rehabilitation, mostly during the first 14 weeks (during EIN). Although rare, recovery to a conscious state may also occur beyond the 1st year of follow-up. Conscious people may become independent in activities of daily living within 2 years in 41% of responders. The largest improvement in functional status occurred within 3 months after regaining consciousness. Mortality was high (26%), and 63% of deaths followed a decision to withhold or withdraw life-sustaining treatment. Only 12% of participants remained in PDOC at the 2-year follow-up. These results highlight the importance of specialized care for people with PDOC, which focuses both on functional recovery and personalized decision-making, during the first 2 years after their injury.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used Copilot for conventional English grammar and spelling tools. After using this tool, the authors reviewed and edited the content as needed and take(s) full responsibility for the content of the publication.

Author's contribution

All authors contributed to the conception and design of the study. DD and MH contributed to analysis of data. CU and DD contributed to drafting the text or preparing the figures. All authors contributed to the writing process and approved the final version of the manuscript.

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Data availability

Data will be made available on request.

Declaration of competing interest

None.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.rehab.2026.102143.

Appendix

Different levels of consciousness.

References

[1] Maas AI, Stocchetti N, Bullock R. Moderate and severe traumatic brain injury in adults. Lancet Neurol. 2008;7(8):728–41.
[2] Laureys S, Celesia GG, Cohadon F, Lavrijsen J, Leon-Carrion J, Sannita WG, et al. Unresponsive wakefulness syndrome: a new name for the vegetative state or apallic syndrome. BMC Med. 2010;8:68.
[3] Giacino JT, Ashwal S, Childs N, Cranford R, Jennett B, Katz DI, et al. The minimally conscious state: definition and diagnostic criteria. Neurology. 2002;58(3):349–53.
[4] Turner-Stokes L. Prolonged disorders of consciousness: new national clinical guidelines from the Royal College of Physicians, London. Clin Med (Lond). 2014;14(1):4–5.
[5] van Erp WS, Lavrijsen JCM, Vos PE, Bor H, Laureys S, Koopmans RTCM. The Vegetative State: Prevalence, Misdiagnosis, and Treatment Limitations. Journal of the American Medical Directors Association 2015;16(1):85.e9–85.e14.
[6] van Erp WS, Lavrijsen JCM, Vos PE, Laureys S, Koopmans R. Unresponsive wakefulness syndrome: Outcomes from a vicious circle. Ann Neurol. 2020;87(1):12–8.
[7] Giacino JT, Katz DI, Schiff ND, Whyte J, Ashman EJ, Ashwal S, et al. Practice Guideline Update Recommendations Summary: Disorders of Consciousness: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology; the American Congress of Rehabilitation Medicine; and the National Institute on Disability, Independent Living, and Rehabilitation Research. Arch Phys Med Rehabil. 2018;99(9):1699–709.
[8] Driessen DMF, Utens CMA, Ribbers PGM, van Erp WS, Heijenbrok-Kal MH. Short-term outcomes of early intensive neurorehabilitation for prolonged disorders of consciousness: A prospective cohort study. Ann Phys Rehabil Med. 2024;67(5):101838.
[9] Giacino JT, Katz DI, Schiff ND, Whyte J, Ashman EJ, Ashwal S, et al. Comprehensive Systematic Review Update Summary: Disorders of Consciousness. Archives of Physical Medicine and Rehabilitation. 2018;99(9):1710–9.
[10] Faugeras F, Rohaut B, Valente M, Sitt J, Demeret S, Bolgert F, et al. Survival and consciousness recovery are better in the minimally conscious state than in the vegetative state. Brain Inj. 2018;32(1):72–7.
[11] Estraneo A, Moretta P, Loreto V, Lanzillo B, Santoro L, Trojano L. Late recovery after traumatic, anoxic, or hemorrhagic long-lasting vegetative state. Neurology. 2010;75(3):239–45.
[12] Pavlov YG, Spiegelsberger F, Kotchoubey B. Predicting outcome in disorders of consciousness: A mega-analysis. Ann Clin Transl Neurol. 2024;11(6):1465–77.
[13] Magliacano A, De Bellis F, Panico F, Sagliano L, Trojano L, Sandroni C, et al. Long-term clinical evolution of patients with prolonged disorders of consciousness due to severe anoxic brain injury: A meta-analytic study. Eur J Neurol. 2023;30(12):3913–27.
[14] Liu Y, Kang XG, Gao Q, Liu Y, Song CG, Shi XJ, et al. Long-Term Outcomes among Patients with Prolonged Disorders of Consciousness. Brain Sci. 2023;13(2).
[15] Chen WG, Li R, Zhang Y, Hao JH, Du JB, Guo AS, et al. Recovery from prolonged disorders of consciousness: A dual-center prospective cohort study in China. World J Clin Cases. 2020;8(12):2520–9.
[16] Nakase-Richardson R, Whyte J, Giacino JT, Pavawalla S, Barnett SD, Yablon SA, et al. Longitudinal outcome of patients with disordered consciousness in the NIDRR TBI Model Systems Programs. J Neurotrauma. 2012;29(1):59–65.
[17] Whyte J, Nakase-Richardson R, Hammond FM, McNamee S, Giacino JT, Kalmar K, et al. Functional outcomes in traumatic disorders of consciousness: 5-year outcomes from the National Institute on Disability and Rehabilitation Research Traumatic Brain Injury Model Systems. Arch Phys Med Rehabil. 2013;94(10):1855–60.
[18] Hammond FM, Giacino JT, Nakase Richardson R, Sherer M, Zafonte RD, Whyte J, et al. Disorders of Consciousness due to Traumatic Brain Injury: Functional Status Ten Years Post-Injury. J Neurotrauma. 2019;36(7):1136–46.
[19] Bodien Y VRC, Venkatasubba R, Lavrijsen J, Giacino JT, Schnakers C, Laureys S. Book: Coma and Disorders of Consciousness (ed. 3) Chapter: Models and Systems of Care for Patients with Disorders of Consciousness. Coma and Disorders of Consciousness. Models and Systems of Care for Patients with Disorders of Consciousness: Springer; 2023.
[20] Driessen DMF, Utens CMA, Ribbers GM, van Erp WS, Heijenbrok-Kal MH. Outcome registry of early intensive neurorehabilitation in patients with disorders of consciousness: study protocol of a prospective cohort study. BMC Neurol. 2021;21(1):69.
[21] Sharma-Virk M, van Erp WS, Lavrijsen JCM, Koopmans R. Intensive neurorehabilitation for patients with prolonged disorders of consciousness: protocol of a mixed-methods study focusing on outcomes, ethics and impact. BMC Neurol. 2021;21(1):133.
[22] Giacino JT, Kalmar K, Whyte J. The JFK Coma Recovery Scale-Revised: measurement characteristics and diagnostic utility. Arch Phys Med Rehabil. 2004;85(12):2020–9.
[23] Kalmar K, Giacino J. The JFK coma recovery scale—revised. Neuropsychological Rehabilitation 2005;15(3-4):454–60.
[24] Rappaport M, Hall KM, Hopkins K, Belleza T, Cope DN. Disability rating scale for severe head trauma: coma to community. Arch Phys Med Rehabil. 1982;63(3):118–23.
[25] Mattke S, Cramer SC, Wang M, Bettger JP, Cockroft KM, Feng W, et al. Estimating minimal clinically important differences for two scales in patients with chronic traumatic brain injury. Curr Med Res Opin. 2020;36(12):1999–2007.
[26] Hamilton BB, Laughlin JA, Fiedler RC, Granger CV. Interrater reliability of the 7-level functional independence measure (FIM). Scand J Rehabil Med. 1994;26(3):115–9.
[27] Reistetter TA, Graham JE, Deutsch A, Granger CV, Markello S, Ottenbacher KJ. Utility of functional status for classifying community versus institutional discharges after inpatient rehabilitation for stroke. Arch Phys Med Rehabil. 2010;91(3):345–50.
[28] Snider SB, Kowalski RG, Hammond FM, Izzy S, Shih SL, Rovito C, et al. Comparison of Common Outcome Measures for Assessing Independence in Patients Diagnosed with Disorders of Consciousness: A Traumatic Brain Injury Model Systems Study. J Neurotrauma. 2022;39(17-18):1222–30.
[29] Beninato M, Gill-Body KM, Salles S, Stark PC, Black-Schaffer RM, Stein J. Determination of the minimal clinically important difference in the FIM instrument in patients with stroke. Arch Phys Med Rehabil. 2006;87(1):32–9.
[30] Llorens R, Ippoliti C, Navarro MD, Colomer C, Maza A, Goizueta S, et al. Minimally conscious state plus versus minus: Likelihood of emergence and long-term functional independence. Ann Clin Transl Neurol. 2024;11(3):719–28.
[31] Lopez-Rolon A, Vogler J, Howell K, Shock J, Czermak S, Heck S, et al. Severe disorders of consciousness after acquired brain injury: A single-centre long-term follow-up study. NeuroRehabilitation 2017;40(4):509–17.
[32] Lee HY, Park JH, Kim AR, Park M, Kim TW. Neurobehavioral recovery in patients who emerged from prolonged disorder of consciousness: a retrospective study. BMC Neurol. 2020;20(1):198.
[33] Nekrasova J, Kanarskii M, Borisov I, Pradhan P, Roshka S, Musatov D, et al. Two-year outcomes of patients with prolonged disorders of consciousness: a prospective cohort study in Russian Federation. Ann Palliat Med. 2022;11(10):3160–70.
[34] Estraneo A, Fiorenza S, Magliacano A, Formisano R, Mattia D, Grippo A, et al. Multicenter prospective study on predictors of short-term outcome in disorders of consciousness. Neurology. 2020;95(11):e1488–e99.
[35] Xiong Q, Le K, Wang Y, Tang Y, Dong X, Zhong Y, et al. A prediction model of clinical outcomes in prolonged disorders of consciousness: A prospective cohort study. Front Neurosci. 2022;16:1076259.
[36] Niemeyer MJS, Jochems D, Van Ditshuizen JC, de Kanter J, Cremers L, van Hattem M, et al. Clinical outcomes and end-of-life treatment in 596 patients with isolated traumatic brain injury: a retrospective comparison of two Dutch level-I trauma centers. Eur J Trauma Emerg Surg. 2024.
[37] Katz DI, Polyak M, Coughlan D, Nichols M, Roche A. Natural history of recovery from brain injury after prolonged disorders of consciousness: outcome of patients admitted to inpatient rehabilitation with 1–4 year follow-up. Coma Science: Clinical and Ethical Implications. Progress in Brain Research; 2009. p. 73–88.
[38] Nakamura Y, Shiozaki T, Ito H, Nakao S, Ogura H, Oda J. Long-Term Outcomes Over 20 Years in Persons With Persistent Disorders of Consciousness After Traumatic Brain Injury. Neurotrauma Rep. 2023;4(1):805–12.
[39] Forslund MV, Arango-Lasprilla JC, Roe C, Perrin PB, Sigurdardottir S, Andelic N. Multi-level modelling of employment probability trajectories and employment stability at 1, 2 and 5 years after traumatic brain injury. Brain Inj. 2014;28(7):980–6.