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SPECIAL REPORT

NEW TAXONOMY FOR PROLONGED DISORDERS OF CONSCIOUSNESS MAY HELP WITH DECISIONS ON WITHDRAWAL OF CLINICALLY ASSISTED NUTRITION AND HYDRATION: A PROPOSED DECISION-MAKING PATHWAY

Liliana DA CONCEIÇÃO TEIXEIRA, OT, MSc[1,2,3], Nuno BARBOSA ROCHA, PhD[2,4] and Rui NUNES, MD, PhD[3,5]
From the [1]Center for Innovative Care and Health Technology (ciTechcare), School of Health Sciences, Polytechnic of Leiria, [2]Centre for Rehabilitation Research, Porto, [3]Faculty of Medicine of the University of Porto, [4]School of Health, Polytechnic of Porto, 5Centro de Investigação e Desenvolvimento sobre Direito e Sociedade (CEDIS) Law & Society Research Center, Nova Lisboa, Portugal

The number of patients surviving severe brain injury is increasing; however, many are left in a prolonged disorder of consciousness. With appropriate treatment, patients with prolonged disorders of consciousness can survive for years. Unless an advance directive exists, the treating clinicians can authorize withdrawal of clinically assisted nutrition and hydration for these patients, based on best interests. The classic terminology used in prolonged disorders of consciousness ranges from coma, vegetative state to minimally conscious state. However, a new group of patients with covert cognition has been identified in the last decade, making it necessary to revise the current taxonomy to better reflect our understanding of these conditions. With the introduction of a less ambiguous terminology, the challenges when it comes to withdrawal of clinically assisted nutrition and hydration of these patients may ease. A decision-making pathway for withdrawal of clinically assisted nutrition and hydration for patients with prolonged disorders of consciousness, based on a new taxonomy is proposed. These decisions should be based primarily on best interests. The adoption of a new classification for impairments of consciousness would clarify and improve how we think about these patients. Moreover, the development of accurate prognostic predictors would be a major step in the decision-making process, as it would influence the beneficent pathway towards the best clinical outcome.

Key words: clinically assisted nutrition and hydration; consciousness; covert cognition; decision-making; minimally conscious state; prolonged disorders of consciousness; vegetative state.

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Correspondence address: Liliana da Conceição Teixeira, School of Health Sciences, Polytechnic of Leiria, Portugal. E-mail: liliana.teixeira@ipleiria.pt

LAY ABSTRACT

The number of patients surviving severe brain injury is increasing; however, many are left in a prolonged disorder of consciousness. With appropriate treatment, these patients can survive for years. Unless a living will exists; the doctors can authorize withdrawal of artificial nutrition and hydration for these patients, based on best interests. There is an urge to revise the current terminology used in prolonged disorders of consciousness (vegetative state and minimally conscious state) to better reflect our understanding of these conditions, which will, in turn, ease the challenges faced when making a decision about withdrawal of artificial nutrition and hydration of these patients. A decision-making pathway based on a new taxonomy is proposed. The importance of reassessment is reinforced to clarify diagnosis and help with prognosis. Adopting a new classification for prolonged disorders of consciousness would clarify how we think about these patients.

It is commonly recognized that, with advances in acute medicine and consequent developments in the management of patients with severe brain injury, there has been significant increase in survival rates. Many patients, however, are left in severely disabled conditions, where there may be an intact brainstem and metabolic function, but no evidence of awareness of self or environment (1). This population fit within the so-called category of prolonged disorders of consciousness (PDOC). PDOC can be used to describe a spectrum of disorders in which consciousness is altered in a transient or permanent way (2). It ranges in the form of a hierarchy, including coma, vegetative state (VS) and minimally conscious state (MCS). Furthermore, it describes any disorder of consciousness that has continued for at least 4 weeks following sudden-onset brain injury (3).

Consciousness is a biological process in which human beings not only are conscious of the passing events of life (awareness of the environment), but also are richly aware of themselves as participants in life (awareness of self) (4). Furthermore, there are 2 components of consciousness: arousal and awareness. Arousal is a state in which an individual's eyes are open, and awareness can be used to described that we are conscious of our surroundings, body's movement, our memories and emotions (5). PDOC affect both arousal level and awareness (6).

The Royal College of Physicians' national clinical guidelines for PDOC (2020) defined VS as a paradoxical state of wakefulness without demonstrated awareness in which there is preserved capacity for spontaneous or stimulus-induced arousal, evidenced

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by sleep-wake cycles and a range of reflexive and spontaneous behaviours (3). There is no evidence of awareness of themselves, others or their environment.

The term MCS was first introduced in 2002. This designation enriched the clinical scene, by giving a name to a cohort of patients who were previously grouped within the VS and whose diagnosis remains confused with it (7). Giacino and colleagues quantified MCS as limited and inconsistent, but clear, evidence of awareness of themselves or their environment (8). Their responses are inconsistent, but reproducible, and above the level of reflexive or spontaneous behaviour, which is indicative of some degree of interaction with the environment (3). Some people with brain damage are blind, or deaf, or unable to move certain parts of their bodies, therefore, what a minimally conscious person can do to demonstrate that they are aware of themselves and their environment will vary. There will be times when they can follow simple commands and times when they cannot; their consciousness is likely to fluctuate. MCS was later subcategorized based on the complexity of the patients' behaviours (9). The term MCS minus is used to describe patients with low-level behavioural responses (i.e. patients who can visual pursuit, localize noxious stimulation or contingent behaviours, such as appropriate smiling or crying to emotional stimuli) and MCS plus is used to describe patients with high-level behavioural responses (i.e. patients who can follow commands, have intelligible verbalizations or non-functional communication). It is important to retain, that, although some MCS patients may follow commands to a certain degree, functional communication is not possible.

This is the classical and generally accepted terminology used to describe PDOC. Whilst the introduction in 2002 of the term MCS was an immense progress to help clinicians to classify a cohort of patients whose criteria did not fit within the VS category; it brought numerous problems. This definition can be considered problematic, as it may carry ambiguity when it comes to the presence of consciousness. Under the current diagnostic criteria, the question arises whether a minimally conscious person is really conscious? Within this classic taxonomy, MCS encompasses a wide and heterogenous set of states that range from unconscious patients with residual islets of cortical activity that translates into overt behaviour, to conscious, but cognitively impaired, patients, who may be self-conscious and able to respond to simple commands, but unable to functionally communicate due to other executive deficits (10). Several authors have reported a need to revise the current taxonomy; as it was devised before the development of techniques such as functional magnetic resonance imaging (fMRI) and electroencephalography (EEG) (10, 11). The new terminology adopted should do justice to the patient's overt and covert consciousness, regardless of whether they demonstrate it behaviourally. It should, therefore, model the relationships between the various behavioural, cognitive and neural capacities of patients (11). Decisions about withdrawal of clinically assisted nutrition and hydration (CANH) should always be made with extreme caution, not only for patients in a MCS, due to its wide spectrum of states, but also for patients in a VS. There is overwhelming evidence that, when patients in a VS are assessed using fMRI, a significant proportion are indeed conscious (12–14). This may be due to the fact that, in some of these patients, motor function is so impaired that behavioural assessments may not reveal awareness, regardless of how thoroughly and carefully they are conducted (13). This covert cognition has recently been named "cognitive motor dissociation". Patients with cognitive motor dissociation, can present behaviourally like VS or low MCS patients, but demonstrate fMRI or electrophysiological evidence of command following (15, 16).

DIAGNOSIS AND PROGNOSIS

Despite the terminology used, patients with PDOC continue to pose problems in terms of their diagnosis, treatment and prognosis (17). Differentiating between the different states of consciousness is often difficult, due to the nature of the changes in both central and peripheral nervous systems (18). Moreover, purposeful, spontaneous and reflexive behaviours can be difficult to differentiate, and subtle signs of consciousness may be missed. This is due, not only to the complexity of this condition, but also to the biological and psychological limitation of what a person can know about the quantity and quality of another person's awareness (19). Nevertheless, establishing a proper diagnosis is of high clinical relevance, as the outcome of a conscious vs unconscious patient is different, not only in terms of care, but also in terms of pharmacological and non-pharmacological interventions, as well as decisions to withdraw CANH.

Serial assessments, already suggested to improve diagnostic accuracy, may also aid with prognosis (20). In addition, age, aetiology and time post-injury have proved to be the most accurate prognostic indicators for patients with PDOC (21, 22). Furthermore, the prognostic uncertainty only aggravates the challenges clinicians face when considering withdrawal of CANH (23). The prognosis for recovery is more homogeneous for VS than for other PDOC, though age and level of awareness may have some predictive value (3). Although very few published papers have addressed the long-term prognosis for recovery in patients with PDOC, it is commonly accepted that the chances in significant improvement diminish over time.

The majority of patients who move out of PDOC do so in the first year after the onset of their illness or injury. Furthermore, after 3 months for an anoxic aetiology and 12 months for a traumatic aetiology of the PDOC, it is known that the functional outcome will not be very different from the functional level to date (24). While it is not known how many patients will emerge after 12 months after injury, most patients in PDOC for this length of time remain severely or totally disabled (22, 25). Recently, a study was conducted with the hopes of using behavioural observations to detect the potential for later emergence from VS (19). The results suggest that the patients who emerged from VS, exhibited a significantly higher number of different behaviours at rest, than those who remained in VS. This should be further explored, as the type of cortical and subcortical behaviours could carry some weight in predicting prognosis for this population.

Some patients may fail to fully recover awareness and, if provided with life-sustaining treatment and adequate medical and nursing care, remain in PDOC for the rest of their lives (26). The critical question is no longer whether the person may emerge, but whether they will recover a quality of life that they themselves would value. Furthermore, awareness or even a functional status improvement, should not necessarily be associated with an improvement in quality of life, unless there is a clear understanding of what "quality of life" means to that person (3).

Finding an accurate prognosis predictor, as well as using a terminology that best defines the reality of these patients, i.e. a terminology that encompasses covert cognition, would be a significant development, since it would help to optimize efficient care management of this population group, would aid in relieving patients' distress, as well as supporting families with their concerns and anxieties, some of them related to withdrawing CANH.

TAXONOMY REFORM

Currently, the assessment of PDOC is clinical, therefore it is based on the patients' behavioural responses. In order to accommodate patients with covert cognition, Naccache proposed a new terminology including functional brain imaging as a source of evidence and based on the type of behavioural responses demonstrated by the patients, introducing the term cortically mediated state (CMS) (10). According to Naccache, this proposal is not to be considered definitive, but rather a sketch of what the next classification should be (10). His new proposal of classification of impairments of consciousness ranges from state 1a – comatose state (source of evidence: behaviour and functional brain imaging); state 1b – comatose state (source of evidence: behaviour); state 2a – VS (source of evidence: behaviour and functional brain imaging); state 2b – VS (source of evidence: behaviour); state 3a – CMS (source of evidence: functional brain imaging); state 3b – CMS (source of evidence: behaviour); state 4a – conscious state (source of evidence: functional brain imaging); and finally state 4b – conscious state (source of evidence: behaviour).

In state 3a, the patients exhibit cortically mediated behaviours on functional brain imaging, but clinically present as VS, with no external evidence of consciousness. In state 3b, the patient presents signs of consciousness by exhibiting cortically mediated behaviours. This new classification fills a significant gap in the field; patients who were assessed as being clinically in VS, but demonstrated signs of consciousness when using functional brain imaging, had no diagnostic category within the current taxonomy; hence their diagnosis continued to be VS. This poses many problems and misunderstandings for some relatives and team members. Moreover, patients that can only localize stimuli, who are currently diagnosed as MCS minus, would, according to this new taxonomy, be classified as CMS (3b – source of evidence: behaviour). Removing the name "consciousness" from the diagnosis of these groups of patients, would help clarify some of the difficulties that relatives sometimes have in comprehending the MCS minus states, most of them leading to a false expectancy of recovery. Ethical and treatment-decision problems that rise from these difficulties would potentially be addressed more easily.

However, it is questioned if the state 4a, proposed by Naccache should still be classified as MCS and 4b as emergence from MCS. As defining it simply as "conscious states" may raise some diagnostic issues, families may not understand that, although it is called a "conscious state", it is still an impairment of consciousness, and ethical problems may also rise when it comes to decision-making about CANH. It is also questioned whether state 4a needs better definition criteria as to the types of behaviours that can be exhibited; and possibly the inclusion of a different sublevel within level 4. Additional studies are required to refine and define these PDOC categories in order to optimize care management and to support families with decisions related to withdrawal of CANH.

CHALLENGES OF WITHDRAWING CLINICALLY ASSISTED NUTRITION AND HYDRATION

CANH is considered one of the 12 categories of rehabilitation interventions for individuals with PDOC (27). The benefit of CANH is to maintain wellbeing through provision of nutrition and hydration, preservation of life, and future improvement in quality of life. Its burdens include ongoing pain or discomfort that the person might experience, frequent replacing of feeding tubes, aspiration, vomiting and hypersensitivity, to name a few (3). Patients with PDOC lack capacity for decision-making and cannot provide consent for a life-ending intervention, such as discontinuing nutrition and hydration, or even to agree to the intervention in the first place (28); unless a living will, or any other form of advance directive exists, namely an Advance Directive Refusing Treatment (ADRT) (29). These patients can survive for years with appropriate treatment. With so many people under these circumstances receiving CANH, which prolongs their life, the questions arise as to when it is potentially not in their best interests, and is their suffering being prolonged by giving them futile treatment? There is no consensus regarding the definition of futile treatment; however it is generally accepted that it can be defined as one that serves no purposes or is ineffective. There are 3 conceptions of futility that are commonly evoked: physiological, quantitative and qualitative (30). Quantitative futility is when the proposed intervention is highly unlikely to achieve the desired outcome. Although CANH in PDOC is not considered quantitatively or physiologically futile, as it serves its purposes of feeding and hydrating the person; it can be considered futile from a quality of life point of view. Qualitative futility is a situation in which, even if the intervention achieves its intended outcome, the outcome or quality of life attained is inherently undesirable (30). Qualitative futility requires judgment about one's quality of life, which are always hard to make in most patients, but even more for PDOC. CANH has enduring side-effects, which must always be outweighed by the promised benefits. If the benefits of CANH do not accrue, the side-effects are not justified, and therefore CANH can be considered futile for that patient. In other cases, continuing treatment could harm patients with PDOC by defeating their interests in not living in these states (1) as CANH is prolonging a life that the person, prior to being in a PDOC, may have not considered worth living.

Withdrawing CANH from a patient in a VS was given court approval for the first time, in England, in 1993 and in 2015 for a patient in MCS (31, 32). In 2018, the requirement to obtain legal sanction for every decision to withdraw CANH from people in PDOC was removed (33). Withdrawal of CANH can be authorized by the treating clinicians, after consulting the relevant people involved and based on the patient's best interests, unless an ADRT exists. Although, the family does not make the ultimate decision and do not carry any responsibility for it, their views are sought by the clinical team, to ascertain what the patient would have wanted.

For patients with no awareness of self or environment, the predominant assumption is that life-prolonging treatment is not in their best interests (34). However, the decision to withdraw CANH from persons with some evidence of consciousness, presents unique ethical challenges for clinicians and relatives, because it leads to the death of a vulnerable person who is not able to express their own opinion (35). Unlike a person who is completely unaware of their circumstances, a person with some degree of consciousness, can potentially have some awareness of their condition and experience distress as a consequence (36). In these cases, an awareness improvement does not mean they are in a better condition; it can mean being in a worse situation with regards to psychological well-being as they may be more aware of their situation and, consequently, their limitations (3). Dealing with these patients is often an enduring task for healthcare professionals. It is not especially relevant if CANH is considered a medical intervention or, on the other hand, only basic support. What is relevant is to determine whether, at least in some circumstances, it is a disproportionate treatment for which the burdens outweigh the benefits.

Patients' wishes are paramount, namely when a written ADRT does exist. Indeed, many patients have a living will precisely for this purpose. Also, having a legal representative with durable power of attorney allows someone close to the patient to respect his/her wishes in accordance with a substituted judgement framework. However, most frequently these patients are in no condition to make such choices per se, and have no advance directive, and therefore healthcare professionals must decide in accordance with accepted ethical standards. In extreme circumstances it would be advisable to ask for a court decision, but, nevertheless, most professionals, as well as patients' families, would prefer a more consensual approach, which leaves aside utilitarian considerations of distributive justice, but is grounded in a strict deontological approach based on the moral duties of healthcare professionals.

The best interests of any patient in PDOC are related to his/her prognosis and to avoid unnecessary harm. Therefore, the development of an accurate prognosis predictor would be a major step towards this goal. Indeed, doing the best for the patient means reaching a delicate balance between the existent clinical evidence (evidence-based medicine), agreed medical best practice (*leges artis*) and the expected outcomes. Usually, this complex mix is accomplished and even optimized by professional know-how and expertise, but, in extreme circumstances, such as in patients demonstrating some, even if minimal awareness, it would be helpful if the decision-making process was indexed to the practical application of the principle of proportionality, meaning that CANH should be proportionate to the goal pursued.

DECISION-MAKING PATHWAY

Physicians have an ethical duty to maximize benefits (beneficence) and to avoid doing harm. This is also an ethical imperative shared by all healthcare professionals. The question is what beneficence means in this context? Although the ethics of resource allocation in healthcare must always be considered, it would be beneficial to have a decision-making pathway that is based primarily on the best interests of the patients, to guide clinicians through this process. Repeated clinical assessment overtime is required, not only for clinical monitoring and treatment planning, but also for best interests decision-making. Reassessment of PDOC should occur at regular intervals (6 and 12 months, and yearly thereafter) to detect any changes in patients' responsiveness (3). Without it, the transition through the PDOC continuum may go unnoticed.

Despite the assessor's experience allied with the best assessment scales that could be used to achieve an accurate diagnosis, there is still this group of patients who are unable to respond behaviourally, but are able to respond mentally to neuroimaging or electrophysiological paradigms (37). Following a decision-making pathway that uses less ambiguous terminology, which is similarly closer to the reality of the patients' responses and includes covert cognition, would also be beneficial when making decisions to withdraw CANH. With this in mind, and following Naccache's proposal, the authors designed a decision-making pathway, with the hopes of describing the steps that need to be taken in order to reach a decision about withdrawal of nutrition and hydration in patients with PDOC.

Replacing the term MCS minus by CMS (or states 3a and 3b), as proposed by Naccache,would improve the way we think about patients with cortically mediated behaviours, but not necessarily conscious, and therefore the way we take care of them; as achieving an accurate diagnosis is critical to direct appropriate rehabilitation and/or decisions about withdrawal of treatment. If a new taxonomy, which is better representative of the patient's reality and our understanding of it is adopted, which encompasses both behavioural and imaging techniques, then for levels 2a to 3b the predominant assumption should be that life-prolonging treatment is not in their best interests. The patients' falling into category 4a, which from our point of view, need better definition criteria, should be analysed on an individual basis. According to Naccache, patients in this category are presumed to have the ability for only a limited range of elementary conscious contents. Hence, if considered by the clinicians and relatives to be in the patient's best interests, withdrawal of CANH can be considered. For these patients the weight of a reliable prognostic predictor is paramount. Having some security about their prognosis, will help with the process. For other cases that fall within the category 4a, where the decisions on best interest remains finely balanced, a court application should be made. Nevertheless, the central feature is that the team must always establish what is in the patient's best interest. Patients in category 4b, which, according to this terminology, are emerging from MCS, have greater degrees of cognitive complexity and are able to functionally communicate, are cases that normally have a better prognosis. Therefore, withdrawal of CANH should not be considered by the team. Fig. 1 illustrates

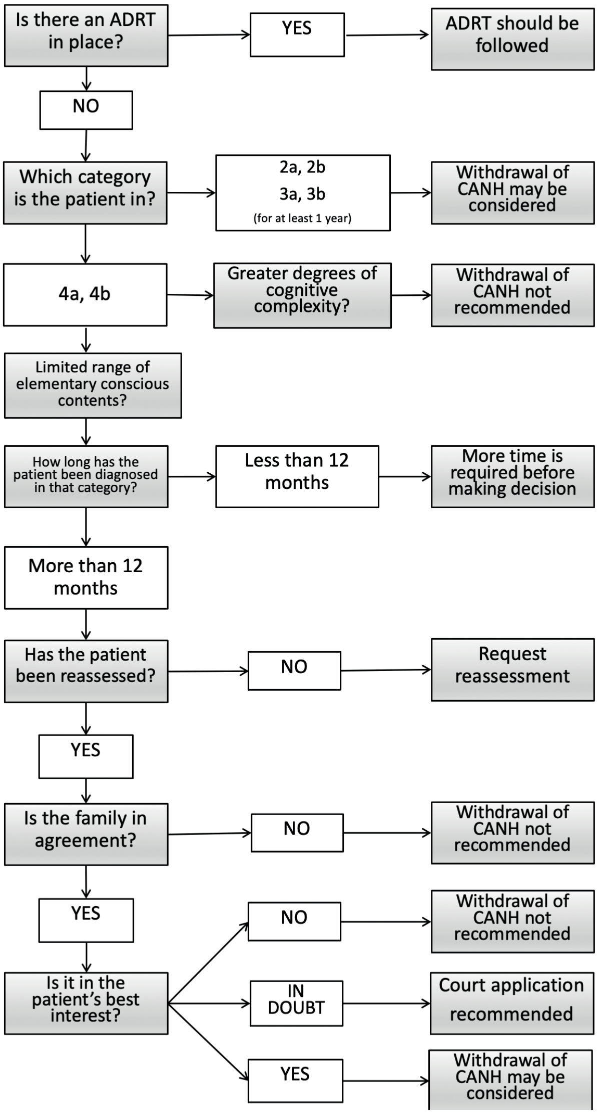

Fig. 1. Diagram to guide clinically assisted nutrition and hydration (CANH) decision-making in patients with prolonged disorders of consciousness (PDOC). ADRT: Advance Directive Refusing Treatment.

a decision-making pathway that will guide clinicians through the process of withdrawing CANH in PDOC.

CONCLUSION

The decision-making process in patients in PDOC, namely the withdrawal of CANH, can be ethically and legally questionable in the absence of an ADRT. Therefore, clinicians must be prepared for legal dispute regarding withholding or withdrawing of life-sustaining treatments. The courts might be the last guarantee that the best interests of the patients are always considered when a person is unable to make choices for themselves. In these cases, the equation between the expected quality of life (and not merely extending life) vs the global suffering of the patient seems to be paramount. The decisions regarding withdrawal of CANH for patients with PDOC should be guided by reliable information on their condition and how the patient wanted to be treated and/or their beliefs about living in such a condition. As best management of PDOC requires a correct diagnosis and prognosis, a new taxonomy is needed.

This decision-making pathway does not try to break any grounds on what is already done by clinicians. However, it is a novelty as it includes a new taxonomy reform proposed by Naccache to support complex decision-making through better representation of the state of the person. Regardless of which terminology is used, as long as it does justice to patients' underlying conscious capacities, it will help clarify some of the misunderstandings around PDOC. The terminology used to define this pathway for withdrawal of CANH is not considered to be a definitive model and needs refining in some levels, but at least tries to evolve into one that uses both behaviour and brain imaging techniques to define consciousness in this complex and vulnerable population. Additional studies are needed to refine and define criteria for those categories; until then, this pathway could support clinicians in complex decision-making. Anything that could assist better understanding of these diagnoses is essential, in order to avoid a false expectancy for recovery, unnecessary prolongation of the patients' lives, and emotional resources, amongst others. A decision-making pathway that guides clinicians through this process may ease some of the struggles related to making such difficult end-of-life decisions. Although it is difficult to predict if CANH would lead to a quality of life that the patient him/herself would value, the existence of predictors of outcome might play a decisive role. It follows that developing a new taxonomy and accurate prognosis predictors should be a priority in the ethical decision-making process. It would have the potential capacity to decisively influence the beneficent pathway towards the best clinical outcome for the individual.

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