Ethical, palliative, and policy considerations in disorders of consciousness

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Abstract

This essay complements the scientific and practice scope of the American Academy of Neurology Guideline on Disorders of Consciousness by providing a discussion of the ethical, palliative, and policy aspects of the management of this group of patients. We endorse the renaming of "permanent" vegetative state to "chronic" vegetative state given the increased frequency of reports of late improvements but suggest that further refinement of this class of patients is necessary to distinguish late recoveries from patients who were misdiagnosed or in cognitive-motor dissociation. Additional nosologic clarity and prognostic refinement is necessary to preclude overestimation of low probability events. We argue that the new descriptor "unaware wakefulness syndrome" is no clearer than "vegetative state" in expressing the mismatch between apparent behavioral unawareness when patients have covert consciousness or cognitive motor dissociation. We advocate routine universal pain precautions as an important element of neuropalliative care for these patients given the risk of covert consciousness. In medical decision-making, we endorse the use of advance directives and the importance of clear and understandable communication with surrogates. We show the value of incorporating a learning health care system so as to promote therapeutic innovation. We support the Guideline's high standard for rehabilitation for these patients but note that those systems of care are neither widely available nor affordable. Finally, we applaud the Guideline authors for this outstanding exemplar of engaged scholarship in the service of a frequently neglected group of brain-injured patients.

Introduction

For a patient population long marginalized by an uninterested health care system,¹ Practice Guideline: Disorders of Consciousness² is a landmark publication. Through the rigorous application of evidence-based criteria to the available literature, the Guideline demonstrates that patients with disorders of consciousness (DoC) comprise a population at risk, vulnerable to misdiagnosis and to medical mismanagement that can negatively affect their access to ongoing care, rehabilitation, and pain and symptom management. To address this problem, the Guideline affirmatively calls for the provision of skilled care by knowledgeable practitioners—a standard of care that is currently unavailable to most patients except those few who are lucky enough to gain admission to the small number of elite specialized rehabilitation centers. By articulating this aspirational standard of care and laying bare the deficits of current practices, the Guideline provides a useful metric by which society should work to meet its normative obligations to patients with severe brain injury.

In this commentary, we address the ethical, palliative, and policy aspects of the Guideline. When the Guideline was first envisioned, these topics were intended to constitute a companion report, but that effort was abandoned to prioritize an analytical review of the literature. While we understand the reasons for this choice, a full consideration of the Guideline is incomplete without addressing the broader ethical implications for patient care and institutional reform. We address this gap here to lay the foundation for a subsequent multisociety consensus

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Glossary

CMD = cognitive-motor dissociation; DoC = disorders of consciousness; MCS = minimally conscious state; MSTF = Multi-Society Task Force on PVS; VS = vegetative state.

statement on the ethical and policy considerations for the care of patients with disorders of consciousness.

Diagnostic nomenclature, ethics, and ideology

It is a welcome relief to codify and not revisit the category of the minimally conscious state (MCS),³ whose designation dramatically enriched the research and clinical landscape by giving a name to a cohort of patients who previously had been grouped within the vegetative state (VS) and whose diagnosis remains confused with it. The Guideline adds a level of refinement by introducing the term chronic vegetative state to replace permanent vegetative state, which the Multi-Society Task Force on PVS (MSTF)⁴ had codified as a prognostic refinement of the term persistent vegetative state, coined earlier by Jennett and Plum.⁵

This new term represents a justified refinement in our thinking. Nonetheless, we comment upon how changes in the nomenclature of the VS may be received in the bioethics community and in society at large given the etymologic origins of the term vegetative state⁶ and the place that the VS has played within American jurisprudence in the evolution of the right to refuse life-sustaining treatment.⁷ Based on Dr. Plum's testimony, Judge Hughes found that there was no state interest to "compel Karen (Quinlan) to endure the unendurable only to vegetate a few more measurable months with no realistic possibility of returning to any semblance of cognitive or sapient life."8 The futility of the VS became the moral and legal warrant to remove Quinlan's respirator. Thereafter, the VS was linked to the right to die and to the culture wars that later played out in the public debates over removing the feeding tubes of VS patients Nancy Cruzan⁹ and Teresa Schiavo. 10-12

Now based on evidence of late improvements from the VS as well as a reanalysis of the small sample size that led the MSTF to overestimate its permanence, the Guideline acknowledges that perhaps 20% of vegetative patients will evolve into MCS, far outside of the MSTF temporal prognostic boundaries. This reassessment has led the Guideline authors to redesignate this group as the chronic VS.

While this redesignation seems warranted on clinical and epidemiologic grounds, it will create repercussions beyond the house of medicine given that the right to refuse life-sustaining treatment initially was predicated upon the irreversibility of the VS.¹³ With the change from "permanent" to "chronic" VS, we can imagine commentators revisiting

contentious cases like Schiavo. If 20% of VS patients have late improvements, how certain can we be that patients like Schiavo might not have improved? When argued from an ideologic stance, objective evidence about etiology of injury or autopsy data will do little to assuage skeptics. Of course, this is not a reason to eschew improved diagnostic schemata, but this issue may be an unintended consequence that the medical profession will need to address and mitigate.

To that end, we urge additional prognostic refinement clarifying which vegetative patients might make late improvements. This clarity would help minimize the conceptual vulnerability of too broad a category in which 80% of patients will remain permanently vegetative. To this end, we envision several additional nosologic distinctions, each with its own ethical valence. ^{14,15}

The first group is patients who were simply misdiagnosed, a common situation given the known high prevalence of diagnostic errors. 16 To minimize diagnostic error, neurologists should perform a thorough neurologic examination specifically targeting evidence of awareness, such as by employing the Coma Recovery Scale-Revised. 17 A second group is those who underwent a state change from appearing behaviorally vegetative to being overtly minimally conscious after treatment with a drug (such as zolpidem)¹⁸ or neurostimulation (with deep brain stimulation, transcranial magnetic stimulation, or vagal nerve stimulation). ^{19–21} These patients might be better understood as MCS patients with largely intact neural networks that had been underactivated, leading to a vegetative appearance until they were stimulated. A third category is patients with cognitive-motor dissociation (CMD) in whom the behavioral examination was dissociated from detected volitional responsiveness.²² Patients in this group span a range of functional statuses from MCS to those with complete awareness in the locked-in syndrome.²³ A fourth group is those patients who underwent late structural changes recreating network responses necessary for consciousness.^{24,25} Further complicating this framework, patients in this fourth group could either manifest behavioral evidence of consciousness or evolve to CMD.

Given the relationship of permanence to the right to refuse life-sustaining therapy, we emphasize that only patients in the fourth category have true late improvements. The others had been mistakenly classified as vegetative because of misdiagnosis, absence of pharmacologic or electrical stimulation, or CMD. Contrasting the delayed diagnosis of MCS or CMD against late improvement beyond the VS can help temper societal expectations about miracle recoveries for the vast

majority of vegetative patients who will never regain consciousness.

Covert consciousness and the unresponsive wakefulness syndrome

In an effort to counter false-negative bedside examinations that fail to identify covert consciousness, the Guideline calls for the use of ancillary multimodal evaluation with neuroimaging and electrophysiologic testing. The authors' willingness to turn to measures whose test characteristics have not been determined fully speaks to the ethical importance of avoiding type II error: failing to identify consciousness when it is present. While nonbehavioral assessment is less sensitive than the highly validated Coma Recovery Scale-Revised, 17 we fully endorse the use of ancillary assessment tools when doubt remains about the diagnosis. Nonbehavioral assessment may be more specific and identify patients whose consciousness might otherwise lack detection.²⁶ Given that consciousness is an irreducible component of personhood, the use of these additional modalities contributes to respect for persons, a central tenet of the Belmont Report.²⁷

Given the importance placed upon the detection of covert consciousness, we were puzzled by the Guideline's adoption of the behavioral term unresponsive wakefulness syndrome. This term, accepted in Europe to replace VS, is a bedside description that obscures nonobserved biological differences underwriting consciousness. As we recognize the clinical and ethical significance of covert consciousness, the endorsement of this descriptive category seems regressive because it fails to connote the underlying pathophysiology, just as does the term VS. Functional neuroimaging demonstrating covert consciousness in some patients showed that the behavioral "phenotype" of unresponsive wakefulness may not always correlate with the underlying "genotype." This diagnostic error is analogous to that of persisting in the belief that all the generations of colored peas in Mendel's garden remained the same after his discovery of a theory of inheritance.²⁸ As Jennett and Plum⁵ were careful to note in their initial description of the VS, "It seems that there is wakefulness without awareness." Presciently, they admitted the possibility that what they observed behaviorally might not correlate perfectly with the underlying neurologic state, a possibility that also later was acknowledged by the MSTF. 4(p 1501)

Pain management and neuropalliative care

Given the high prevalence of diagnostic errors in distinguishing conscious from unconscious patients, the recommendation about pain management could be strengthened. The Guideline rightly acknowledges the difficulty of assessing pain and suffering and rightly warns that "clinicians should be cautious in making definitive conclusions about pain and suffering in

individuals with DoC." While we agree that available assessment methods (both behavioral and neuroimaging) may not conclusively identify a capacity to experience or perceive pain, we should not allow this limitation to compromise the basic human right to pain relief.^{29,30}

When confronted by diagnostic uncertainty, we need to ask ourselves what type of error is more consequential. Would we rather overdiagnose covert consciousness (and the correlative ability to perceive pain) when it was not present or fail to detect it when it was present?³¹ The consequences of such a diagnostic omission would be to mistake patients who are conscious as insensate and believe that analgesia is unnecessary or unjustified. When in doubt, is it not preferable to presume covert consciousness in order to assure the prevention of pain and suffering?

This call for neuropalliative care³² for patients with DoC may lead to its application to some patients who may not benefit because they are vegetative and insensate. Nonetheless we advocate establishing a lower threshold for pain and symptom management because these patients are at risk for the undertreatment of pain. Moreover, patients in MCS and who have CMD may be unable to give voice to their distress, heightening their vulnerability. Their dilated pupils should not be windows on their tortured souls. For these reasons, we invoke a precautionary principle and recommend universal pain precautions as a prevailing norm for these patients. This standard of care would require the application of pain management and analgesia as is provided to all other patients.

In addition to optimizing symptom management, proper neuropalliative care encompasses skilled communication with patients and their surrogates to enhance medical decisions and the provision of family support. These interventions are essential, particularly during the acute phase of the DoC, just as neurorehabilitation is essential following the acute phase.

Prognostication and family conversations

We applaud the Guideline recommendations for talking with families about prognosis, avoiding categorically dire predictions, and sharing data about the likelihood of recovery and the prospects of functional independence for patients who survive to 1 month. This is a critical corrective to the cited data indicating that DoC hospital mortality for patients with traumatic brain injury was 31.7% with the decision to withdraw lifesustaining therapy accounting for 70.2% of these deaths.³³ These data point to the need to develop discursive techniques to help clinicians more effectively translate aggregate statistical data into care decisions for individual patients.³⁴ This is a complex task and the admonition to engage in conversations with families will not necessarily translate into effective strategies to work with surrogate decision-makers. These conversations are challenging for all families, particularly when an

injury was sudden and unexpected in a previously healthy person. 1,35

We agree with the importance of incorporating the patient's previously expressed wishes when they are known but we also note the inconsistency of the recommendation to complete an advance directive because patients who had the capacity to do so would not need a designated surrogate. Physicians should elicit and discuss the patient's known preferences for living in VS or MCS with the patient's lawful surrogate decision-maker, clarifying the difference in these states and the estimated probabilities of outcomes.

Finally, we note the omission of engaging the recovering patient in conversations about care. While these patients may not regain the status of legal competency to direct their care, as they regain their agency, their voice needs to be incorporated into decisions about their future. This input becomes especially important given the harmful effect of the disability paradox—the ironic mismatch between how healthy observers and disabled patients rate the patient's own quality of life—which engenders unjustifiably negative clinician attitudes that can compromise care. Family members should be educated that many patients possess a remarkable capacity to successfully accommodate to their disability once they have completed a course of neurorehabilitation.

Syndromic prognosis is categorically limited because prognosis depends more upon the underlying pathophysiology, extent and location of lesions, age, duration, comorbidities, and other factors than on membership in a diagnostic syndrome. Moreover, syndromic prognosis is discontinuous: once a patient improves from the VS to the MCS, the patient's prognosis changes to become that of the MCS. This plausible hypothesis requires empirical validation.

Methodology and clinical practice

We applaud the Guideline authors for their methodologic rigor. They excluded studies with fewer than 20 subjects/patients and categorized data based on evidence class. These standards have produced a rigorous set of conclusions about the strength of the available data. Nonetheless, this analytic approach generates its own costs by excluding certain preliminary proof-of-principle diagnostic methods and promising emerging therapies. Because extant trials were limited to small numbers, the inclusion criteria therefore excluded emerging neuromodulation strategies that may hold promise. While we seek to avoid conflating unproven methods with those from a firmer evidence base, neither do we want to perpetuate therapeutic nihilism that too often informs perceptions about DoC by systematically discounting emerging neuroscience.

The stringency of the Guideline analytic approach is evident in the report's assessment of amantadine, which concludes that it "probably hastens functional recovery," even though the cited study was a randomized controlled trial, and a Class I study, published in a preeminent medical journal.³⁸ Thus, while we support the Guideline analytic choice, we question if it should be the sole evidentiary standard for a nascent field struggling for legitimacy.³⁹ No doubt, much of prevailing clinical practice in both neurology and internal medicine would not achieve the exacting standards employed in the Guideline.

An alternate to the Guideline's strict dichotomization of research vs therapy would be to view the evolution of new diagnostic methods and therapies as part of what has been called a learning health care system, as advanced by the Institute of Medicine (now the National Academy of Medicine). Central to this framework is the development of a process of knowledge generation and dissemination "in which evidence is both applied and developed as a natural product of the care process." This approach would catalyze translational efforts between discovery and clinical care, and create an iterative process that could accelerate advancements in this field.

Access and systems of care

In a methodologic aside addressing the challenge of power calculations, the authors make the Guideline's most important point: there has been a worrisome decrease in the number of DoC patients enrolled in rehabilitation. This fact, of course, limits the power of outcomes research but more importantly speaks to the decrease in access to care to quality neurorehabilitation that has afflicted this population over the last decade. 42 Hence the paradox: the Guideline appropriately recommends that "clinicians should be vigilant to the medical complications that commonly occur during the first few months after injury among patients with DoC and thus should utilize a systematic approach to facilitate prevention, early identification, and treatment." But the infrastructure necessary to provide such timely and informed care does not exist and its availability is eroding because of the aforementioned demographics. So despite the demonstrated utility and need for specialized care, currently it is neither accessible nor affordable.

The societal neglect of the DoC population is a breach of the bioethical principle of nonabandonment of patients. Where else in medicine would a diagnostic error rate of over 40% be tolerated? Now that the Guideline has stipulated benchmarks for practice, practitioners and institutions need to meet this standard of care, and payers must ensure that these services are covered. It is acceptable neither to plead ignorance of these conditions nor to assert that nothing can be done to help ameliorate the burden of severe brain injury. Given the utility of greater specialized care in diagnosis, treatment, and rehabilitation, and the equal importance of avoiding medical complications that can impede recovery, our society must provide the infrastructure and resources needed to offer quality care.

Final words

The Guideline authors should be congratulated for their multiyear, interdisciplinary, and multisociety effort to address the health needs of DoC patients, some of our society's most vulnerable and underserved. Their effort is a model of engaged scholarship and collaboration in the service of the common good. If its recommendations are heeded, the Guideline will be viewed as a historic work that helped transform the care of patients with DoC and deepened society's appreciation of the ethical mandate to work towards this laudable goal.

Author contributions

J.J.F.: first draft of manuscript. J.J.F. and J.L.B.: study concept and design, acquisition of data, analysis and interpretation, critical revisions of the manuscript for important intellectual content.

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