Intra/International Variability in the Determination of Death by Neurologic Criteria

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One might think that a medical determination of death by neurologic criteria would not be subject to variability in any regard, because it is a medical and legal determination of death that has been utilized for many decades, both in the United States and throughout the world. However, as with many things in medicine and law, there is both intra- and international variability across a number of domains including the concept of death by neurologic criteria; laws on declaration of death by neurologic criteria; the required credentials for the clinical examiner; the technique to perform the clinical evaluation and apnea testing; the indications for, and selection of, ancillary testing; determination of death by neurologic criteria in children; and communication, documentation, discontinuation of organ support and organ donation after the determination. This variability raises concerns about the accuracy and validity of determinations of death by neurologic criteria, which could be detrimental to the medical field and the public's trust in this core medical determination. In this chapter, we analyze different types of variability in the determination of death by neurologic criteria and explain the steps that are being taken to reduce variability.

1 The Concept of Death by Neurologic Criteria

As described elsewhere in this book, there are two ways to conceptualize death by neurologic criteria: (1) the whole-brain criterion and (2) the brainstem criterion. The United States, and most other countries, utilize the whole-brain criterion, which defines death by neurologic criteria as the irreversible loss of all functions of the entire brain, including the brainstem, and implies that both infratentorial and supratentorial structures are affected. The United Kingdom and many Commonwealth

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countries, on the other hand, use the brainstem criterion, in which irreversible loss of all brainstem functions is sufficient for death by neurologic criteria [1].

In clinical practice, both criteria embrace a three-step approach to the determination: first, establishing a cause for the catastrophic brain injury and determining that the injury is permanent; second, excluding confounders and reversible causes for the neurologic state; and third, confirming the patient is comatose and has absence of all brainstem reflexes and breathing capacity using apnea testing. Because most injuries to the brain that lead to death by neurologic criteria are supratentorial and progress to involve loss of function infratentorially, there is usually no practical difference between these ways to conceptualize death by neurologic criteria [2]. However, questions arise when considering how death should be determined using the whole-brain criterion in patients with a primary injury to the posterior fossa, as they may have persistent brain circulation and/or electrical activity in supratentorial structures. Varelas et al. elucidated this concern by reporting cases of patients with primary posterior fossa injury that satisfied the clinical standards for death by neurologic criteria, but had supratentorial brain circulation but later developed secondary brain edema and hydrocephalus, and ultimately were determined dead using the whole-brain criterion [3]. However, it is unclear whether this is always the case. The potential for reversibility of the condition should give clinicians great pause when considering determination of death by neurologic criteria in a patient who has suffered a primary brainstem or other posterior fossa insult.

2 Laws on Death by Neurologic Criteria in the United States

In 1968, an ad hoc committee at Harvard Medical School introduced the first medical standard for death by neurologic criteria [4]. The committee believed that statutory changes to acknowledge death by neurologic criteria as legal death were not needed unless there was controversy within the medical community about the adoption of neurologic criteria to declare death. A decade later, due to social and legal consequences of this new criterion for death, President Carter tasked the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research to evaluate the definition of death. Through a process involving the American Bar Association, the American Medical Association, the National Conference of Commissioners on Uniform State Laws, and several religious officials, the Commission created the Uniform Determination of Death Act (UDDA) [5]. The UDDA codified determination of death in the setting of "irreversible cessation of function of the entire brain, including the brainstem," according to "acceptable medical standards."

Since the creation of the UDDA, all 50 states have incorporated death by neurologic criteria into their judicial or statutory definitions. However, only 36 states adopted the complete language of the UDDA into their statutes [6] and there are inconsistencies in a number of areas across the country.

One area of variability is in both the use and interpretation of the phrase "acceptable medical standards." This was exemplified by a Nevada Supreme Court ruling in 2015, prompting the State of Nevada to revise their UDDA to stipulate that the determination of death by neurologic criteria should be based on the 2010 standards for determination of death by neurologic criteria in adults published by the American Academy of Neurology (AAN) and the 2011 standards for determination of death by neurologic criteria in pediatric patients written by the Society of Critical Care Medicine, American Academy of Pediatrics, and the Child Neurology Society (SCCM/AAP/CNS), or subsequent standards [7–9].

A second area of variability in laws about death determination is in the management of objections to death by neurologic criteria. The state of New Jersey allows family objection to determination of death by neurologic criteria based on religious or moral grounds [10]. California and New York law allow "reasonable accommodation" of religious and moral objections to determination of death by neurologic criteria, while Illinois indicates that a patient's religious beliefs must be taken into account for documentation of time of death [11]. The AAN issued a position statement in 2019 regarding accommodation, which provides a framework for states and hospitals to develop a formal stance on management of objections, which are arising more and more in recent years [12–14].

International variability in the content of laws on the declaration of death by neurologic criteria is discussed elsewhere in this book.

3 Variability in Institutional Standards on Determination of Death by Neurologic Criteria in Adults in the United States

Variation exists in the United States because each hospital is responsible for developing policies for determination of death by neurologic criteria. In a 2008 study comparing standards for determination of death by neurologic criteria among the top 50 neurology and neurosurgery programs in the United States (according to US News and World Report) against the 1995 AAN standards for determination of death by neurologic criteria in adults, variability was measured according to five domains: number and qualifications of examiners, prerequisites for determination, clinical examination, apnea testing, and ancillary testing [15]. The authors found that in 71% of standards, multiple evaluations were required, and distinct and separate clinicians were required to conduct repeat testing in 44% of standards. Eighty-nine percent of standards noted a minimum temperature for the evaluation, but this varied from 32 to 36 °C. For the clinical evaluation, the lowest concordance with the AAN standard was for evaluating the absence of pain above the foramen magnum (42%) and the absence of spontaneous respirations prior to initiating apnea testing (27%). Guidance regarding apnea testing also demonstrated relatively poor concordance with the AAN standard, with only 66% of standards specifying the need for arterial blood gas

sampling prior to testing, 39% requiring a specific $PaCO_2$ level prior to testing, and 76% requiring preoxygenation. Finally, guidance regarding specific circumstances to pursue ancillary testing was included in only 66% of standards.

In a 2015 follow-up study of the "top 50" neuroscience centers in the United States, the authors assessed the same five domains as in 2008 to determine whether improvements had been made since the interval update to the AAN standard in 2010 [16]. Seventy-six percent of institutions had updated their standards on determination of death by neurologic criteria by that time. Ninety-four percent of institutional standards required the absence of hypothermia (compared to 89% previously). Compliance in the specifics of the clinical evaluation also improved, with the absence of pain above the foramen magnum required in 53% (from 42%), absence of a jaw jerk reflex in 24% (from 18%), and absence of spontaneous respirations in 47% (from 27%). The most significant improvements were related to apnea testing and ancillary testing. Fifty-three percent of standards that required two evaluations stipulated that there was a need for a waiting period between them.

In 2016, an expanded analysis was done of the standards on death by neurologic criteria from 492 individual hospital or system systems in the United States [17]. The areas of greatest difference from the AAN standard included prerequisites for death by neurologic criteria testing, clinical examination of the lower brainstem, apnea testing, and ancillary testing. Exclusion of hypotension and hypothermia prior to the evaluation was specified in only 56% and 79% of standards, respectively. Only 83% of standards required identification of the cause of the patient's neurologic state before the evaluation. Although the 2010 AAN standard noted that ancillary testing is only necessary for death by neurologic criteria determination when clinical and apnea testing cannot be safely or fully completed and interpreted, ancillary testing was mandated in 7% of standards [7]. Clear guidance for ancillary testing indications, timing, and performance were described in only 64% of standards.

4 Variability in Institutional Standards on Determination of Death by Neurologic Criteria in Children in the United States

There is also variability between pediatric institutional standards for determination of death by neurologic criteria throughout the United States as discussed in detail elsewhere in this book. In a recent study, death by neurologic criteria standards were obtained from pediatric institutions in the United States via organ procurement organizations [1]. The standards were assessed with respect to general procedures, prerequisites, clinical examination, apnea testing, and ancillary testing, similar to the adult studies discussed above.

Of the 118 standards developed or revised after 2011, 97% required identification of the mechanism of irreversible brain injury and 67% required an observation period after the brain injury before death by neurologic criteria evaluation. The majority of standards required prerequisites consistent with the pediatric standards published by the SCCM/AAP/CNS such as the absence of hypotension (94%), hypothermia (97%), and metabolic derangements (92%). In respect to the clinical examination, 91% required a lack of responsiveness, 93% no response to noxious stimuli, and 99% the loss of brainstem reflexes. Eighty-four percent of standards required two apnea tests, in accordance with the SCCM/AAP/CNS standards. $PaCO_2$ targets were consistent with the SCCM/AAP/CNS standards in 64% of institutional standards. Fifteen percent of pediatric standards required ancillary testing for all patients, and 15% allowed ancillary studies that are not validated in the pediatric population.

5 Variability in National Standards on Determination of Death by Neurologic Criteria around the World

A subsequent study by Lewis et al. reviewed standards for determination of death by neurologic criteria around the world [18]. Of the 197 countries in the world, contact was made with representatives from 136 countries (69% of the world); representatives from 83 of these countries indicated that they had a national standard for death by neurologic criteria (42% of the world). Notable findings included that 18% of standards referred to "brainstem death"; different rules for multiple age groups was common; the number of examiners was usually 2 (93%), with multiple different areas of expertise specified; and there was variability for the prerequisites, clinical evaluation, apnea testing, and ancillary testing, similar to the aforementioned findings in the studies from the United States. Most international standards (82%) required a known etiology of the neurologic catastrophe, but only 30% required brain imaging. Wide variability and insufficiencies existed in stipulated examination requirements; for example, only 82% of standards stipulated the need for absence of the gag reflex, 79% the cough reflex, and 74% the oculocephalic reflex. Ninety-one percent of standards provided guidance for apnea testing, but most (76%) provided a target for the final $PaCO_2$, ranging from 50 to 60 mmHg. A surprisingly high percentage (28%) of standards required ancillary testing for determination of death by neurologic criteria, with most mentioning EEG (71%), but also digital subtraction angiography in 59% and transcranial doppler ultrasound in 55%. Additionally, instructions on performance and interpretation of ancillary testing are also variable and at times inconsistent, which could cause an error in declaration of death by neurologic criteria [19].

Table 1 reviews the variability in the medical standards for determination of death by neurologic criteria in the United States [17], Europe [20], Asia [21], and Latin America [22].

Table 1 Comparison of standards in the United States [17], Europe [20], Asia [21], and Latin America [22] on determination of death by neurologic criteria

Criteria	Component	United States (492 hospitals) (%)	Europe (28 countries) (%)	Asia (24 countries) (%)	Latin America (15 countries) (%)
Number of exams required	One exam	13	18	14[a]	37[a]
	Two or more exams	87	82	86[a]	63[a]
Prerequisites for clinical exam	Established cause	83	96	88	73
	Absence of hypotension	56	64	37	40
	Absence of hypothermia	79	96	25	40
	Absence of electrolyte/acid–base/endocrine disturbance	71	54	71	67
	Absence of muscle relaxants/paralytics	94	100	63	60
Specifics of clinical exam	Absence of pupillary reflex	93	96	87	87
	Absence of corneal reflex	90	100	83	80
	Absence of oculocephalic reflex	88	96	79	60
	Absence of oculovestibular reflex	89	96	87	80
	Absence of gag reflex	87	79	79	67
	Absence of cough reflex	79	100	75	67
Specifics of apnea testing	Apnea testing is required	97	100	87	87
	Preoxygenation specified	79	NA	79	53
	Arterial blood gas prior to testing	66	82	54	53
	Target $PaCO_2$ or pH specified	84	86	79	67
	Suspension of test with hemodynamic instability	63	71	47	47
Requirement for ancillary testing	Required in all patients	7	50	21	13
	Inability to complete clinical evaluation	51	61	47	38
	Inconclusive apnea test	48	50	47	46
	Presence of drugs that could depress the central nervous system	32	57	21	38

NA data not available

[a] Only 53% of Latin American protocols and 58% of Asian protocols specified the number of exams

6 Qualifications for the Examiner

Given the importance of determinations of death, one might think that both the law and medical standards would be prescriptive about who can perform the evaluation. However, this is not routinely the case. In the United States, for example, only Florida and Virginia require a clinician with expertise in the field of critical care or neuroscience to make a determination of death by neurologic criteria [6].

Surveys and reviews of standards have demonstrated variability in the level of experience and specialization of the recommended examiner(s) (including neurology, neurosurgery, critical care, or simply a "licensed physician") [23].

Although there is clearly value in having trainees and others learn the entire detailed process of determination of death by neurologic criteria from beginning to end, this must be done with strict and direct supervision by a physician with appropriate expertise. The examiner needs to have experience in both the determination of death by neurologic criteria and in the recognition of potential pitfalls [24]. For example, a neurologist with a primarily outpatient practice may be uncomfortable performing a determination of death by neurologic criteria every few years when called upon to do so, whereas a medical or surgical intensivist who is doing coma examinations in the intensive care setting every day has appropriate comfort and expertise in completing the evaluation, particularly as pertains to performance of the apnea test, which could lead to hemodynamic compromise.

7 Communication, Documentation, Discontinuation of Organ Support and Organ Donation

In addition to variability in the evaluation for death by neurologic criteria, there is variability in communication and documentation about death by neurologic criteria, as well as discontinuation of organ support and organ donation following determination of death by neurologic criteria. In the aforementioned international study of national standards on determination of death by neurologic criteria, 50 countries (64%) did not specifically address communication with a patient's family before or after determination of death by neurologic criteria [18]. On the other hand, nine countries (12%) required physicians to inform families before discontinuation of organ support. In 45 countries (58%), the specifics of the time of death were defined in the standard: time of death was the time of completion of the clinical exam in 30 countries, the time of interpretation of ancillary testing in four countries, the time of performing ancillary testing in one country, and other protocols listed a variety of other times. Interestingly, no standards in this study designated the time of arterial blood gas sampling or resulting as the time of death.

The standards from 36 countries (46%) included guidance on discontinuation of organ support after determination of death by neurologic criteria. Five countries allowed "immediate discontinuation" of organ support after determination of death by neurologic criteria. Five countries counseled consideration of a patient's religious beliefs when planning the time to discontinue organ support, five to consider

the family's objection to discontinuation of organ support, three recommended waiting for a "reasonably respectful period" before discontinuing organ support, two to consider a patient's "moral beliefs," and one with specific guidance surrounding death by neurologic criteria in pregnancy.

Thirty-four countries' standards for determination of death by neurologic criteria mentioned organ donation, of which 19 provided specific guidance.

8 Rectifying Variability

8.1 Intranational (the United States)

At the time of this writing, the AAN is leading an effort to combine guidance for determination of death by neurologic criteria for adults and children, as many of the practices and procedures are shared. Of course, there are notable differences, such as norms for blood pressure based on age, as well changes in cranial physiology before and after closure of fontanelles and sutures, and thus there will be essential "carve out" sections to deal with these issues in particular. However, the hope of such a combined document is to harmonize practice wherever possible, thus reducing confusion and inconsistent practice, hopefully leading to a highly stringent process. It remains to be seen how this will impact institutional standards.

In an attempt to rectify the legal variability in death determination in the United States, a Drafting Committee has been convened by the Uniform Law Commission to revise the UDDA [25]. However, it remains unclear what language the new version will contain, how and whether it will be implemented state by state, and whether the revised UDDA will improve variability.

8.2 International

The World Brain Death Project (WBDP), an international consensus statement on death by neurologic criteria, was published in 2020 [26]. Prior to this, there was no global consensus regarding death by neurologic criteria determination. The WBDP provides specific and detailed guidance for clinical and apnea testing ("Minimum Clinical Determination of Brain Death/Death by Neurologic Criteria") and ancillary testing ("Beyond Minimum Clinical Determination of Brain Death/Death by Neurologic Criteria"), including unapproved tests such as computed tomographic angiography. It remains to be seen whether countries around the world will ensure their standards are consistent with the guidance in the WBDP.

As determination of death by neurologic criteria requires consistency and accuracy, it is important to recognize the multiple ways to ensure examiners have proper training and expertise. Options include simulation courses, online training experiences, and national courses, such as those offered by the AAN and the Neurocritical Care Society [27–29]. Some institutions have established brain death "champions," a core group of practitioners who are well-versed in death by neurologic criteria

determination and potential pitfalls, and who do the bulk of determinations for the sake of consistency and practice excellence.

9 Conclusions

Although there is variability in the determination of death by neurologic criteria, both in the United States and worldwide, much work has been done to reduce unevenness and to harmonize standards and practice. We emphasize that much of the research that has been performed to date has evaluated *standards* at the hospital and national levels, but very few have looked at the bedside *practice* of determination of death by neurologic criteria, which may be better (or worse) than that stipulated in standards. Although some variability in practice is likely acceptable—for example, there can be some nuance to evaluation technique—it is necessary to adhere to core minimum standards so that there are no erroneous determinations of death by neurologic criteria. This is truly one of the few areas in medicine where there is no room for error; if there is any doubt as to whether a patient is dead or not, clinicians must err on the conservative side, *not* declaring death until there is irrefutable and consistent evidence to support the determination. Efforts to reduce variability should continue in earnest, ensuring not only stringent, consistent standards at the institutional, national, and international levels but also sound practice at the bedside. These efforts will help to maintain the public's trust in the process, leading to fewer legal challenges and strife for families dealing with the tragic loss of a loved one.

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