



Brain Death: Diagnosis and Imaging Techniques

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Brain death (BD) is an irreversible cessation of functions of the entire brain, including the brainstem. The diagnosis of BD is made on clinical grounds and neurologic examination. In the United States, clinical criteria set by the American Academy of Neurology (AAN) emphasize 3 specific clinical findings to confirm BD, which include coma, absence of brainstem reflexes and apnea. Ancillary tests are needed when neurologic examination or apnea test cannot be performed. AAN recommended ancillary tests include electroencephalogram, which confirms electrical activity loss; catheter cerebral angiogram, which confirms loss of cerebral blood flow; as well as transcranial Doppler and nuclear scintigraphy. Digital subtraction angiography remains the gold standard for confirmation of lack of cerebral blood flow. On 99m Technetium hexa methyl propylene amine oxime or 99m Technetium-ethylene cysteine diethyl ester (99mTc-ethylene cysteine diethyl ester) Nuclear scintigraphy, lack of intracranial radiotracer uptake, correlates with BD. Although imaging studies like computed tomography angiogram (CTA), MR angiogram, CT perfusion, and MR perfusion are frequently used, they are currently not recommended by AAN. However, they hold tremendous promise in future as imaging tools in the armamentarium of a radiologist investigating BD as adjunct imaging to clinical findings. Imaging markers for BD on CTA include non-opacification of the cortical middle cerebral arteries and internal cerebral veins. On CT perfusion, there is lack of cerebral blood flow and blood volume in brainstem. Residual brain perfusion can occur with reduced intracranial pressure as in decompressive craniectomy, ventricular drainage and multiple skull fractures leading to false-negative results. On magnetic resonance imaging, there can be massive brain edema with herniations, poor gray or white matter differentiation, diffuse diffusion restriction, and nonvisualization of intracranial vessels on MR angiogram. On transcranial Doppler, cerebral circulatory arrest is indicated by flow patterns without forward flow progress, progressing from decrease in diastolic flow to disappearance of diastolic flow to oscillating pattern with retrograde flow in diastole, short systolic spikes, and finally absence of Doppler signal. AAN has included neuroimaging explaining coma as one of their prerequisite to be checked before evaluation for BD. Thus, a radiologist can play a critical role by recognizing the initial extensive hypoxic or ischemic damage to the central nervous system including the brainstem on imaging; guiding a neurologist evaluating a potential BD, as well as ruling out other pitfalls. In many cases, the radiologist is often the first person to appreciate the devastating findings of irreversible brain damage. Three most common mimics of BD are hypothermia, locked-in syndrome, and drug intoxication. By judicious usage of the available ancillary tests, cautiously

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interpreting the findings with awareness of their limitations and pitfalls, a radiologist can provide the support needed to confirm BD.

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Introduction

“Brain death” (BD) is a medicolegal term that labels a person as dead by neurologic criteria. Currently, it is considered as equivalent to death by cardiorespiratory criteria. BD is defined by complete and irreversible cessation of entire brain activity including the brainstem, which maintains the circulatory and respiratory functions. Ever since the term was coined, it has been shrouded with ethical and legal controversies. In the present medical era, where circulatory and respiratory functions can be maintained indefinitely by external life support, declaring someone “brain dead” as being “dead” has profound legal, medical, and social implications. Early recognition of BD is also important to provide closure for the loved ones, prevent unnecessary negative medical interventions and when possible expedite organ transplantation.

History

When defibrillators and respirators came into use in the late 1940s and early 1950s of last century, death appeared reversible and the line between life and death became fuzzy. There was a raging debate as to when to call a comatose person as “dead.” The concept of BD was first described by Mollaret and Goulon in 1959. They described “le coma depasse” of comatose patients supported by mechanical ventilators with absent electroencephalographic recordings, absent intracranial flow, or total brain necrosis at autopsy,¹ basing death by neurologic criteria. In 1963, Schwab defined irreversible death of the nervous system by a triad of following criteria: (1) fixed and dilated pupils, no elicitable reflexes, and no spontaneous movements; (2) apnea; and (3) isoelectric electroencephalography (EEG) and considered such patients as dead.² Paralleling these developments was the field of solid organ transplantation and there was a growing interest in “live donors.” Soon ethical issues concerning organ harvest from live ventilated patients came to light.³ In 1968, an attempt was made by an ad hoc Committee at Harvard to define death and to allow organ harvest that may follow, to be done within a framework. After several deliberations and hesitations, the committee ended up defining the term “Irreversible Coma” or “brain death” as just death of a tissue and hinted it may be considered equal to “death.”⁴ In spite of controversies and skepticism, legal bodies did recognize the new definition.

In 1979, the President’s Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research was organized to bring clarity to the term “brain death” and the involved ethical issues. In 1981, the Commission released a report titled “Defining Death: Medical, Legal, and Ethical Issues in the Determination of Death.”⁵ In conclusion, the commission stated that the “definition is based on general physiological standards rather than medical criteria and tests which change over time due to refinements in knowledge and techniques.” In

the same year, in an attempt to achieve uniform law on “brain death” throughout the nation, the National Conference of Commissioners on Uniform State Laws drafted the landmark “Uniform Determination of Death Act” (UDDA), which was approved by the American Medical Association and American Bar Association.⁶ The act is a nonbinding statute aimed to serve as guide for state lawmakers. The section 1 of the act read as follows: “An individual who has sustained either (1) irreversible cessation of circulatory and respiratory functions or (2) irreversible cessation of all functions of the entire brain, including the brainstem, is dead. A determination of death must be made with accepted medical standards.” Thus for the first time by statute, both death by neurologic criteria and death by cardiovascular criteria were equated to “death” of an individual. However, the UDDA only put forth a legal standard and did not speak of the “accepted medical standards” or neurologic criteria or the diagnostic tests needed for that determination. The UDDA in a broad sense was adopted as such by all states in the United States. But different subclauses were used by different states in their statute stressing on who is qualified to make the determination of death, number of physicians required and relevance to organ donation.⁷

In 1994, the American Academy of Neurology (AAN), led by Eelco Wijdicks attempted to standardize the neurologic criteria and practice parameters for determining BD.⁸ The criteria and parameters were subsequently published the following year and in 2010 they were again updated.⁹

Neurologic Criteria for BD—AAN Practice Parameters

The demonstration of “cessation of all functions of the entire brain, including the brainstem” as outlined in UDDA forms the guiding principle for formulation of the clinical criteria for diagnosing BD. For the most part, BD is a clinical diagnosis with ancillary testing needed only when the clinical criteria are not satisfied. In 1995, the AAN outlined the three cardinal clinical features required for the diagnosis of BD namely coma or unresponsiveness, absence of brainstem reflexes, and apnea (Table 1).⁸ The prerequisites before clinically evaluating for BD and for brainstem reflexes were also outlined. Apnea testing is undertaken after all the brainstem reflexes are negative. In a recent update on BD, AAN published the prerequisites, clinical examination steps and the steps involved in apnea testing in the form of a checklist.⁸ In a situation when clinical examination cannot be fully performed or if apnea test is inconclusive or aborted, AAN recommends one ancillary tests out of cerebral catheter angiogram (CA), hexamethylpropylene amine oxime (HMPAO) Single photon emission computed tomography (SPECT), EEG, and transcranial Doppler (TCD) (Table 2).⁹ Most states in the United States and many countries

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