Controversies in defining and determining death in critical care

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Abstract | Circulatory–respiratory or brain tests are widely accepted for definition and determination of death, but have several controversial issues. Both determinations have been stimulated by organ donation, but must be valid independently of this process. Current controversies in brain death include whether the definition is conceptually coherent, whether the whole-brain or brainstem criterion is correct, whether one neurological examination or two should be required, and when to conduct the examination following therapeutic hypothermia. Controversies about the circulatory determination of death include the minimum duration of asystole that is sufficient for death to be declared, and whether the distinction between permanent and irreversible cessation of circulatory functioning is important. In addition, the goal of organ donation raises issues such as the optimal way to time and conduct the request conversation with family members of the patient, and whether the Dead Donor Rule should be abandoned.

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Introduction

Contemporary controversies about brain and circulatory determinations of death in the intensive care unit (ICU) can be informed by studying the historical impact of life-sustaining therapies (LSTs) on the definition of human death.[1] Prior to development of LSTs—particularly tracheal positive-pressure ventilation (TPPV) and cardiopulmonary resuscitation (CPR)—in the 1950s, death was a unitary phenomenon. When illness or injury caused cessation of one of the three 'vital' functions critical to life—circulation, respiration and brain function—both of the others ceased within minutes. This interdependence of vital functions, and the inability of physicians to intervene to restore or support them, made the definition of death straightforward, although its determination was incorrect at times.[2]

The development of LSTs abolished the unitary nature of death, as the new technologies could support or restore individual vital functions while others remained absent.[3] CPR could reverse cardiac arrest and restore circulation, vasopressors could maintain blood pressure in shock, and TPPV could support ventilation in apnoea. These LSTs were valuable interventions when they led to restoration of normal function, but were harmful when they restored circulation and supported ventilation in patients in whom all brain functions had ceased irreversibly. The concept of a brain-based determination of death was proposed, which asserted that the irreversible loss of all clinical brain functions was sufficient grounds to declare death, irrespective of continued technological support of ventilation and circulation.[4]

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Two emerging medical needs stimulated the development of standards of death determination in patients receiving LST: multi-organ transplantation, and the desire to discontinue LST in cases of hopeless brain damage.[1] Organ transplantation technology became successful in the 1960s as patients who were 'brain dead' represented ideal multi-organ donors, because their intact circulation preserved organs. The desire to promote organ donation for transplantation encouraged initial acceptance of the concept of brain death.[5,6] Additionally, physicians saw the need to discontinue meaningless LSTs for those unfortunate patients who had been rescued by CPR and TPPV but whose brain had been destroyed by lack of blood flow. Prevailing laws at the time prohibited physicians from stopping LSTs before the patient was declared dead.[1]

The concept that brain function was necessary for life and that its irreversible cessation was sufficient for death arose independently in several countries. In the late 1950s, French neurologists reported cases of complete cessation of brain function that they called *coma dépassé* (irretrievable coma).[7,8] American scholars systematized the criteria for, and popularized, the misleading term 'brain death' in the 1960s,[9] and British physicians propounded the concept of brainstem death in the 1970s and 1980s.[10,11] By the turn of the 21st century, over 80 countries in the developed and developing world had accepted a brain-based determination of death, and most developed countries enacted this medical practice into public laws.[12] Despite the arguments of scholars who reject brain death on scientific, conceptual or religious grounds, the practice of brain-based death determination continues to increase in prevalence throughout the world.[13]

This Review examines what we mean by the term 'death', and discusses the brain criteria and circulatory–respiratory criteria that can be used to define death. Controversies surrounding the application of these criteria are discussed, and ethical issues arising in the context of organ donation are considered.

Key points

- Death can be determined by circulatory–respiratory or brain tests
- All brain death practices use the whole-brain or brainstem criterion of death
- Controversies about brain death focus on the coherence of the concept, the extent of necessary neuronal damage, and the tests required to prove irreversibility
- Controversies about circulatory death focus on the required duration of asystole before death can be declared, and whether permanent or irreversible cessation should be the standard
- The option of organ donation should be presented to families of deceased patients, but the optimal timing of and approach to the donation request remain unclear

A biophilosophical analysis of death

Initially, the brain-based determination of death was accepted as a medical and legal standard in the absence of a rigorous philosophical justification. Throughout the 1970s, many states in the USA incorporated brain death determinations into their death statutes because of its acceptance by physicians, despite the lack of a compelling rationale.[14] Early attempts to justify the equivalence of brain death and human death were provided by Korein[15] and Pallis,[11] as well as a US President's Commission[16] and my own research group.[3,17] We have refined our original analysis over the past three decades.[18–20] Most scholars in this field, including some who disagree with our conclusions,[21–23] regard our approach as the 'standard' analysis of death. A vigorous debate over the definition of and criterion for death continues within academia but, tellingly, this scholarly dispute has had no effect on the medical practice of bedside death determination.

The analysis of death features four sequential stages: first, the context of death states the conditions for the argument, including the nature of death and words we use to describe it; second, the definition of death makes explicit what we mean in our ordinary use of the word 'death'; third, the criterion of death states the general measureable standard that is both necessary and sufficient for death, and that can be included in a death statute; and fourth, the tests of death are devised by physicians to show that the criterion of death has been fulfilled.[24] Even scholars who maintain that defining death could be an impossible task agree that conceptual clarity about the nature of death must precede creation of tests for its measurement.[25,26]

The context conditions include the view that 'death' is a nontechnical word, the meaning of which has been rendered ambiguous by technology. The goal of philosophical analysis is to make explicit the consensual meaning that is implicit in our common use of the word, not to contrive its redefinition. Death, like life, can be considered a fundamentally biological phenomenon that is not primarily a social contrivance or a religious or cultural custom, although many cultures have rich customs, beliefs, practices and laws surrounding death and dying. 'Alive' and 'dead' are the only two possible states of an organism, so the transition from one state to the other is necessarily instantaneous, although determination of this precise moment may only be possible in retrospect. Death is the event that separates the process of dying from the process of bodily disintegration. The transition from alive to dead is unidirectional because death is irreversible.[19,24]

The most precise definition of death in our technological era is the cessation of the critical functions of the organism as a whole.[19] The organism as a whole refers not to the whole organism (the sum of its parts), but to those behaviours that are greater than the sum of its parts and cannot be reduced to individual parts of the organism.[27] The phenomenon of consciousness is the most exquisite example of a function of the organism as a whole. These behaviours emerge spontaneously from the normally functioning assembled parts of the organism.[28] The concept of the organism as a whole emphasizes the unity and coherent integrity of the organism and the interrelatedness of its parts that, operating in unison, contribute to the overall health of the organism.[29] This concept also posits that life in part of an organism is distinct from life of the organism itself. It is possible, therefore, to technologically maintain the life of parts of an organism—such as cells, tissues and organs—despite the cessation of functioning of the organism as a whole.[19,24] This is the unique condition of the brain-dead patient: the organism as a whole has ceased to function, although many parts of the organism obviously remain alive by technological support.[29]

The dual criteria of death present in many death statutes (including those of the USA) are the irreversible cessation of clinical functioning of the brain, and the irreversible cessation of circulatory and respiratory functioning. Physicians apply the circulatory–respiratory death criterion in most patients who are not receiving TPPV. Physicians reserve the brain death criterion for the few ICU patients with apnoea on TPPV, to whom the circulatory–respiratory criterion cannot be applied. The two criteria of death are not independent. Although few data inform the discussion, the circulatory–respiratory criterion is valid because it leads to fulfilment of the brain criterion: circulatory arrest induces a rapid process in which neurons are progressively destroyed by hypoxaemia and ischaemia.[3]

The brain criterion of death

The brain criterion of death (brain death) is necessary and sufficient for death because the brain enables the critical functions of the organism as a whole, although not all functions of the organism as a whole.[30] Debate continues over the extent of the brain functions that must cease in order to satisfy the definition. Three separate brain death criteria, known as the whole-brain, brainstem and higher-brain formulations, have been defended.[31] The accepted testing standards are shown in Boxes 1, 2 and 3.

Box 1 | The brain criterion of death in adults

Determination of death using the brain criterion involves clinical examination to show irreversibility of the patient's condition and to rule out alternative causes, neurological examination to establish absence of all brain clinical functions, ancillary tests in some cases, and appropriate documentation.[32]

Clinical evaluation to establish preconditions

1. Establish irreversibility and proximate cause
- No CNS-depressing drugs
- No neuromuscular blockade or peripheral paralysis
- Neuroimaging findings document adequate cause and irreversibility

2. Achieve normal physiological parameters
- Normal core temperature
- Normal systolic blood pressure
- No severe acid–base or electrolyte disorder, or endocrinopathy

Neurological examination

1. Coma with no responsiveness
- No spontaneous or evoked movements; muscle flaccidity
- No response to noxious stimuli except spinal reflexes

2. Absent brainstem reflexes
- Pupils unreactive to bright light and darkness
- Corneal reflexes absent
- Vestibulo-ocular reflexes absent
- No facial movements to craniofacial noxious stimuli
- Absent gag reflexes
- Absent cough reflexes to tracheal suctioning

3. Apnoea
- Complete lack of respiratory effort on apnoea test (Box 3)
- Ensure haemodynamic stability, euvolaemia, normotension, no hypoxia, and no history of CO_2-retaining chronic pulmonary disease prior to apnoea testing

Ancillary tests

Ancillary tests are optional but can be used to confirm clinical findings in the following circumstances: the clinical examination including apnoea testing cannot be completed; the examiner is inexperienced; results of the examination are questionable; or a confounding medication effect cannot reasonably be excluded. One of two options can be chosen:

1. Neuroimaging to document absence of intracranial blood flow (preferred) using one of the following:
- Single-photon emission CT
- Transcranial Doppler ultrasound
- Contrast angiography
- Others not validated: radionuclide angiography, magnetic resonance angiography, CT angiography

2. Brain electrical potential recording (all are necessary):
- EEG, brainstem auditory evoked responses and somatosensory evoked responses

Documentation

- Use brain death checklist
- Time of death is the time at which the patient fulfilled all tests, usually after apnoea test

The whole-brain formulation

Death standards in the USA and many other countries employ the whole-brain criterion, which requires that all clinical functions of the brain, including those served by the cerebral hemispheres, diencephalon and brainstem, must have ceased.[32–35] Apnoea, which represents medullary failure, must be present, and all brainstem reflexes such as pupillary light reflexes, corneal reflexes, vestibulo-ocular reflexes, and gag and cough reflexes must be absent, reflecting failure of the midbrain, pons and medulla. Complete unresponsiveness and the deepest possible coma reflect failure of the reticular system in the brainstem and its projections to the thalamus and forebrain. Cerebral hemispheric function is difficult to assess at the bedside, however, once brainstem functioning has ceased. Only clinical brain functions—which, unlike activity of individual neurons, are assessed by bedside neurological examination—must be shown to be absent.[16]

The pathogenesis of brain death following brain illness and injury accounts for the emphasis on assessment of brainstem functioning in the determination of brain death. Diffuse hypoxic–ischaemic neuronal insults during cardiac arrest, massive traumatic brain injury, intracranial haemorrhage, and meningitis each produce marked increases in intracranial pressure, leading to syndromes of transtentorial cerebral herniation, which cause diffuse infarction of the brainstem.[36,37] Once intracranial pressure exceeds mean arterial blood pressure, intracranial circulation ceases, leading to secondary diffuse infarction of cerebral hemispheric neurons that survived the initial brain insult. The whole-brain formulation, therefore, contains a fail-safe mechanism that ensures that the definition encompasses global neuronal damage and loss of all clinical functions.[38]

The brainstem formulation

In the UK, Pallis championed the concept of brainstem death, pointing out that the accepted clinical tests all assessed brainstem function, that the brainstem was responsible for consciousness, breathing and circulatory regulation, and that it conducted nearly all throughput to and from the brain.[11] The whole-brain and brainstem criteria of death are essentially identical, diverging only in the exceedingly rare instance of a massive brainstem infarct or haemorrhage that destroys the midbrain, pons and medulla but spares the cerebral hemispheres.[39,40] In such cases, a patient would be diagnosed as dead according to the brainstem criterion but might not be declared dead under the whole-brain criterion. In a modification of this formulation, Machado emphasized the brainstem basis for brain death as the irreversible loss of both dimensions of human consciousness: wakefulness and awareness.[41]

The higher-brain formulation

The higher-brain formulation was proposed in the 1970s by scholars who argued that because consciousness and cognition are the unique characteristics of humans, irreversible absence of these functions constituted death. According to this formulation, patients in permanent vegetative states with spontaneous breathing should be declared dead, despite the fact that universally they are regarded as alive. The higher-brain formulation fails the context condition of making explicit the ordinary meaning of 'death'. Rather, this formulation is a radical redefinition of death and one that no medical society or country has adopted.[18]

Controversies about brain death

Two lines of criticism

Critics of the brain criterion of death fall into two camps: those who argue that the concept of brain death should be rejected, and those who accept brain death but disagree

with prevailing standards or practices. Most prominent among scholars who argue that the brain criterion of death should be abandoned are Shewmon,[21,26,30,42] Miller[22] and Truog.[22,43]

Shewmon agreed with the definition of death as the cessation of critical functions of the organism as a whole, but argued that only the circulatory criterion—and not the brain criterion—satisfies the definition. He posited that the role of the spinal cord in integrating some functions of the organism as a whole undermined the justification for a brain-based concept of death.[30] Shewmon reported a series of patients diagnosed with brain death whose circulation and visceral organ function were maintained for many months or longer, which showed both that some functions of the organism as a whole persisted after brain destruction and that prolonged 'survival' was counterintuitive to a concept of death.[44] He emphasized the case reported by Repertinger and colleagues of a 4-year-old child who was diagnosed as brain dead after bacterial meningitis and was then supported for 19 years on a ventilator.[45] Shewmon argued that the prolonged duration of successful support in this case was inconsistent with the concept of death.

Miller and Truog claimed that use of a brain criterion of death is an anachronism and a legal fiction that was created decades ago to achieve the goals of organ donation and withdrawal of LSTs, which in contemporary medical practice can be more successfully accomplished by other means.[22] They argued that although we all know that brain-dead patients are not dead, we accept the legal fiction to permit organ donation.

Are two examinations required?

A current practice controversy concerns whether physicians must conduct two sequential examinations to determine brain death, or whether a single examination is sufficient. Prior practice guidelines throughout the world mandated two sequential examinations separated by a time interval that varied as a function of the patient's age, the nature of the brain injury, and the presence of concomitant ancillary tests. A large study of adults with brain death showed that the second examination added nothing to the first, delayed the declaration of death, and reduced organ donation.[46] As a result, the American Academy of Neurology (AAN) revised its long-standing guideline on adult brain death to require only a single examination.[32] One critic questioned the methodology, wondering whether some patients had been excluded from the study after the first examination,[47] but a later smaller series confirmed the findings.[48] The change to a single examination has not been uniformly accepted. One prominent guideline for the determination of brain death in infants and children, published after the AAN guideline update, required two examinations,[33] as do some death statutes in the USA. How many future guidelines will adopt the single-examination rule remains unclear.

Ancillary tests

Another practice controversy surrounds the use of ancillary tests to confirm brain death, such as imaging studies that show absent intracranial blood flow, or electrical recording studies that show absent EEG and evoked potentials.[49] These tests have been performed since the formulation of the definition of brain death. Wijdicks recently argued that because brain death is a clinical diagnosis and ancillary tests can be inaccurate and misleading, such tests should not be used to support determination of brain death.[50] However, ancillary tests remain useful in cases in which clinical tests cannot be performed fully, and to support the diagnosis when inexperienced or careless examiners have performed the brain death examination improperly,[38] particularly in light of the known pitfalls of the examination such as the confounding presence of pre-existing neurological deficits and the unexpected presence of potentially reversible metabolic or toxic factors.[51]

The need for standardization

A survey of brain death protocols in leading neurology departments in the USA disclosed a shocking lack

Box 2 | Brain determination of death in infants and children

Because infants and children usually have a greater capacity to withstand brain injuries and illnesses than do adults, testing to document brain death in young patients requires a more conservative approach with a longer observation period, more than one examiner, and mandatory ancillary testing in specific circumstances.[33]

Requirements

1. Two sequential examinations performed by different examiners
2. Time interval between sequential examinations varies by age:
   - For term newborn (37 weeks gestational age) and up to 30 days old: at least 24 h
   - For 31 days to 18 years of age: at least 12 h
   - Intervals can be shortened with ancillary confirmatory tests

Neurological testing

Same testing as in adults (Boxes 1 and 3) with the following stipulations:

- Two sequential tests with two examiners
- Both apnoea tests can be performed by the same examiner

Ancillary testing

Same testing as in adults (Box 1). Required when:

- Any component of the examination or apnoea testing cannot be completed
- The results of clinical testing are uncertain
- A potentially reversible medication effect may be present

Documentation

- Use brain death checklist
- Time of death is the time at which the patient fulfilled all tests, usually after apnoea test

Box 3 | Apnoea testing

- Ensure haemodynamic stability, euvolaemia, normotension, no hypoxia, and no history of CO_2-retaining chronic pulmonary disease
- Adjust ventilator to achieve partial pressure of CO_2 ($PaCO_2$) = 35–45 mmHg
- Pre-oxygenate with 100% O_2 for >10 min to achieve PaO_2 >200 mmHg and reduce positive end-expiratory pressure to 5 cmH_2O
- Administer passive oxygenation by catheter placement at the carina at 6 l/min or attach T-piece with continuous positive airway pressure at 10 cmH_2O
- Disconnect ventilator and observe until $PaCO_2$ >60 mmHg or 20 mmHg above baseline value (usually takes 8–10 min)
- Abort apnoea test if pulse oxygenation <85% for 30 s or systolic blood pressure <90 mmHg
- Apnoea declared only if no respiratory effort is detected

Box 4 | Circulatory–respiratory determination of death

The medical criterion of death is the permanent absence of breathing and circulation
- Bedside testing depends on the clinical context
- Permanent absence of breathing and circulation cannot be assessed if the patient is receiving ventilatory support, circulatory support or CPR, in which case death must be determined using brain tests
- Organ donors require proof of permanent circulatory absence

For patients with cardiorespiratory arrest for whom no ventilatory support, circulatory support or CPR is planned or administered (for example, terminally ill patients with 'do not resuscitate' orders):
- Document the absence of breathing, heartbeat, circulation and pupillary light reflexes

For ventilator-dependent patients who develop cardiorespiratory arrest after ventilator and/or circulatory support is withdrawn to allow death:
- Without organ donation—document absence of breathing, heartbeat, circulation, and pupillary light reflexes
- In controlled DCDD—await 2–5 min of mechanical asystole to exclude autoresuscitation before declaring death, and prove circulatory absence using intra-arterial pressure monitoring, Doppler ultrasound, or echocardiography

In patients with sudden cardiorespiratory arrest in whom CPR is unsuccessful and is discontinued:
- Without organ donation—document absence of breathing, heartbeat, circulation, and pupillary light reflexes
- In uncontrolled DCDD—await 7–10 min of mechanical asystole to exclude autoresuscitation before declaring death, and prove circulatory absence using intra-arterial pressure monitoring, Doppler ultrasound, or echocardiography

For documentation purposes, the time of death is the time at which the examination concludes

Abbreviations: CPR, cardiopulmonary resuscitation; DCDD, donation after circulatory determination of death.

of standardization,[52] despite availability of the accepted AAN guidelines for over a decade.[32] In one institution, apnoea testing (Box 3), which has been a prerequisite in every published battery of brain death tests since the 1970s was, inexplicably, not required. Other studies have disclosed the inadequacy of documentation of brain death testing.[53] The need for greater uniformity in performing and recording the tests is obvious,[54] and some have advocated for a national standard.[55] Many institutions have developed brain death checklists to ensure that examiners test all appropriate functions and adequately document the test results.[32]

Confounding effects of induced hypothermia

False-positive brain death examinations result from examination inadequacies. Webb and Samuels reported a well-documented case of spontaneous improvement after brain death declaration in a patient who had received therapeutic hypothermia to protect the brain following cardiac arrest.[56] He was rewarmed according to protocol, but just as organ donation was beginning 24 h later, he began to breathe and show corneal and cough reflexes. He improved no further and developed asystole.

This case provoked debate over the mechanism of spontaneous improvement. Some commentators argued reasonably that hypothermia may have slowed the metabolism of depressant or neuromuscular-blocking drugs administered earlier, which continued to exert effects for hours after rewarming.[57] Because of this case, some hospitals have altered their therapeutic hypothermia protocols to require a delay of 24–72 h between rewarming and determination of brain death, to allow resolution of a potentially reversible confounding toxic–metabolic encephalopathy. Brain death guidelines require reversible causes of brain dysfunction, including therapeutically induced hypothermia, to be excluded.[32]

Opposition from family members

Family member opposition to brain death usually results from emotional inability to accept the finality and hopelessness of the diagnosis, particularly when the patient is a previously healthy young person with a traumatic brain injury. For many family members, the counter-intuitive nature of death declaration in a person with intact heartbeat and circulation and the desperate hope for recovery makes acceptance of the physician's pronouncement difficult.[58,59] Medical and nursing personnel may compound the problem by using misleading terms, such as 'life support' to refer to TPPV, and 'irreversible coma'.[60] Thoughtful guidelines have been developed to negotiate and compassionately resolve this conflict.[61,62] Inviting family members to observe the patient's complete unresponsiveness during the brain death examination has been advocated as a solution,[63] but is difficult to manage in practice.[64]

Opposition on religious grounds

Religious opposition to brain death is an uncommon issue in most communities.[13] Protestantism uniformly accepts brain death as human death. Roman Catholicism endorsed the practice in a statement made by Pope John Paul II in 2000,[65] which was reaffirmed in 2006 by the Pontifical Academy of Sciences.[66] The situation in Judaism is more complex: Reform, Conservative and many Orthodox rabbis accept the concept of brain death[67] but ultra-Orthodox rabbis do not.[68] Islam is similarly complex, with general acceptance of brain death but variation among denominations and among Islamic countries.[69] Hindu India accepts brain death,[70] as does Shinto-Buddhist Japan with some conditions,[71] but China does not. Family members may erroneously cite their religion's objection to extubation or organ donation because they are unaware of the actual teachings. Guidelines are available for managing cases of religious exception to brain death.[72]

The circulatory criterion of death

Determination of death using the circulatory–respiratory criterion is straightforward for most deaths in which respiratory and circulatory support is not administered (Box 4). Use of this determination in the ICU has become controversial, however, owing to increasing use of protocols for organ donation after the circulatory determination of death (DCDD), formerly called non-heart-beating organ donation or donation after cardiac death.[73] As with organ donation after brain death, the advent of DCDD has stimulated greater medical exactitude in death determination.

The contentious issue in these protocols is determination of the necessary duration of circulatory cessation. In a 'controlled' DCDD protocol, family members of a

severely brain-damaged (but not brain-dead) ventilator-dependent ICU patient decide to withdraw LSTs to allow the patient to die, and request that the patient becomes an organ donor after death, often to follow the patient's wishes. The DCDD protocol coordinates withdrawal of LST with the rapid removal of organs following death determination.[74] In an 'uncontrolled' DCDD protocol, practiced in some European countries, patients with unanticipated cardiac arrest who cannot be resuscitated serve as organ donors.[75]

Identification of the moment of death is necessary because the Dead Donor Rule prohibits transplantation of vital organs until after the donor has been declared dead, so that the donation does not kill the donor.[76] Transplant surgeons wish to remove the organs as quickly as possible after death to minimize warm ischaemic time and, thereby, yield healthier organs for transplantation.

Agreement on the exact moment of death remains surprisingly controversial. Since the earliest practice of DCDD, some critics have claimed that the organ donor was not truly dead at the moment death was declared.[77] In the pioneering University of Pittsburgh protocol of the early 1990s, donor patients were declared dead after 2 min of asystole and apnoea.[78] Critics argued that because some patients with 'do not resuscitate' (DNR) orders nevertheless remained able to be resuscitated at the moment they were declared dead, they did not satisfy the statute of death, which requires the irreversible cessation of circulation.[79]

The duration of asystole that is required before death can be determined varies widely among protocols.[35] Medical societies and expert groups have issued guidelines stipulating for how long the donor patient must have apnoea and asystole to be declared dead. The Ethics Committee of the Society of Critical Care Medicine[80] and the National Conference on Donation after Cardiac Death[81] both require 2–5 min, whereas the US Institute of Medicine[82] and the Canadian Council for Donation and Transplantation[83] require 5 min, and some European countries stipulate 10 min.[84] In an experimental neonatal DCDD heart transplantation protocol at Denver Children's Hospital, the hospital ethics committee controversially approved the ad hoc reduction of the required interval of asystole from 2 min to 75 s.[85]

Mechanical versus electrical systole

Attendees at a large US DCDD consensus conference in 2005 agreed that asystole in the context of circulatory death determination requires mechanical but not electrical asystole.[81] Because the circulatory criterion addresses blood flow, the absence of circulation—not of cardiac electrical activity—is the relevant criterion. Thus, pulseless electrical activity (PEA) during cardiac arrest[86] is fully compatible with the circulatory criterion of death. Electrical asystole, although sufficient to warrant declaration of death, is unnecessary.[81]

Autoresuscitation

Autoresuscitation initially referred to the spontaneous return of heartbeat after asystole. Early reports did not distinguish between autoresuscitation leading to PEA and autoresuscitation leading to restored circulation.[87] Later, it became clear that because the death standard was cessation of circulation and not of cardiac electrical activity, true autoresuscitation required the spontaneous return of circulation.[88]

The incidence of autoresuscitation is an empirical question, and current data are limited. A recent series of 73 cases of controlled DCDD showed no cases of autoresuscitation.[89] In the largest review of all published cases of autoresuscitation, Hornby and colleagues found cases of PEA reported up to 65 s after asystole but no cases of restored circulation after withdrawing LSTs. By contrast, they found many cases of autoresuscitation leading to restored circulation after failed CPR, up to an interval of 7 min after asystole began.[88] Autoresuscitation can occur many minutes following unsuccessful CPR owing to delayed effects of administered medications or to the 'auto-positive end-expiratory pressure' phenomenon of reversible PEA resulting from dynamic lung hyperinflation.[90]

These findings support the prevailing practice of death determination in controlled DCDD, but the occurrence of autoresuscitation after unsuccessful CPR reduces the accuracy of death determination in uncontrolled DCDD. The requirement to wait until after the period in which autoresuscitation can occur could jeopardize organ health in uncontrolled DCDD protocols. Autoresuscitation, therefore, represents a major impediment to uncontrolled DCDD but only a minor one to controlled DCDD.[91]

Circulatory-criterion controversies

Permanent versus irreversible cessation

Distinguishing between permanent and irreversible cessation of circulation helps to answer the question of whether, in controlled DCDD, the patient is dead at the moment of death declaration. Permanent cessation of a function means that the lost function will not be restored because it will neither recover spontaneously nor will medical attempts be made to restore it. By contrast, irreversible cessation of a function means that the lost function cannot possibly be restored even if medical attempts are made. Many death statutes use the term 'irreversible cessation of circulation', although medical standards for death declaration have always relied on permanent cessation of circulation.[92]

Following cessation of circulation and breathing in the context of controlled DCDD, the patient can be declared dead after the period during which autoresuscitation could occur, as the DNR order precludes resuscitative attempts. As for terminally ill patients with DNR orders who are not organ donors, once circulation and respiration have ceased permanently, the declaration of death need not be delayed until circulatory–respiratory failure can be shown to be irreversible. Although consensus has not been reached about the importance of this distinction,[93,94] an expert panel on death determination recruited by the US department that funds experimental organ transplantation protocols endorsed the distinction

as the conceptual basis for prevailing practices of declaring death in DCDD donors.[95] The unresolved empirical issue is determination of the exact time during which autoresuscitation can occur. Confidence limits will improve as more cases are studied.

Organ preservation technologies

Another controversy related to the circulatory criterion of death surrounds what types of organ preservation interventions can be performed on the DCDD donor following death determination. Some transplant surgeons have used extracorporeal membrane oxygenation (ECMO) on DCDD donors following death determination to preserve organ function prior to donation.[96,97] The expert panel mentioned above criticized this practice on the grounds that, by re-establishing blood flow to the brain, ECMO retroactively negates the prior death determination because the cessation of circulation is not permanent, and ECMO circulation might allow the brain to continue to function.[93] Other transplant surgeons amended the ECMO protocol to include inflation of a balloon catheter in the thoracic aorta to restrict the ECMO perfusion circuit to abdominal–pelvic organs and block perfusion to the thorax and head.[98] The expert panel acknowledged that this modification eliminated the problem of retroactive invalidation of the prior death determination but criticized it on ethical and legal grounds.[95]

Recent analyses of death determination

The most recent comprehensive re-examination of the definition of death was published in 2008 by the US President's Council on Bioethics.[99] The Council reaffirmed that brain-dead patients were truly dead, and that public laws supporting the practice of brain death determination should be maintained. However, the Council rejected the standard rationale for equating brain death with human death—namely, the loss of the organism's capacity for integration—and replaced it with cessation of the capacity to perform the essential work of a living organism. A prominent critic of the integration rationale subsequently argued that the Council's new explanation contained the same flaw as the one it replaced.[42] The Council also endorsed DCDD and the importance of maintaining the Dead Donor Rule.

An international research group supported by the Canadian Blood Services is currently working in collaboration with the WHO to produce international guidelines on the determination of death. The group met in Geneva in 2010 and Montreal in 2012. To date, they have produced a framework for discussing medical and scientific aspects of death determination, as well as clinical standards, definitions and a research agenda. Next, they will grade evidence to confirm the clinical standards and to develop strategies to implement the guidelines globally.[100]

Death and organ donation

ICU patients declared dead by either brain or circulatory criteria are potential organ donors. Because the demand for organs to transplant far exceeds the supply of donor organs,[101] many countries have developed programmes that aim to increase the donor organ supply. Governmental and professional organizations support the laudable goal of increasing organ donation because of its obvious life-saving benefits to the organ recipients. Donation also confers benefits to family members of the deceased patient by giving profound meaning to a tragic death, through knowledge that the loved one has contributed to the life and health of others.[102]

Several scholars have expressed concern that the way in which the organ donation programmes are implemented may unintentionally harm end-of-life care.[103–105] Once organ donation becomes a goal, medical and nursing staff might consider—or be perceived to consider—the dying patient as a means to the end of organ donation.[106] This problem is more serious in DCDD than in organ donation after brain death, because organ donation discussions with family members in DCDD always occur before death is declared. Some ICU physicians expressed concern that awareness that their patients could serve as organ donors may subconsciously influence their treatment of patients while they are alive.[107] Two recent surveys of the opinions of critical care physicians and nurses about DCDD have confirmed the existence of these concerns.[108,109]

In the USA, the regulations of the Centers for Medicare and Medicaid Services require hospitals to notify the local organ procurement organization (OPO) "of individuals whose death is imminent or who have died in the hospital," to allow a 'designated requestor' (usually an OPO representative) to present the option of donation to the family and obtain consent.[105] Several studies have shown that OPO representatives, because of their knowledge and training, are more successful than are physicians and nurses in securing family consent.[110] Furthermore, most OPOs lack a policy whereby physicians can obtain consent.[111]

Some OPOs adopt a 'presumptive approach strategy' to organ donation that frames the consent discussion in a leading way.[112] Defenders of this consent technique cite the concept of dual advocacy, in which the interests of the donor family and of patients awaiting transplantation are simultaneously valued because of the presumption that "given the opportunity, most people will chose to help others."[113] One instance in which the dual advocacy concept becomes strained is in the decision to maintain TPPV and other LSTs in an unsalvageable patient with massive brain injury solely for the purpose of declaring brain death to permit organ donation.[114]

Another controversy in deceased organ donation is whether the Dead Donor Rule is necessary. This rule is an informal but widely accepted requirement that the organ donor must first be declared dead so that donation does not cause the death of the donor.[76] The organ transplantation community uniformly supports this rule as a condition necessary to maintain public confidence in physicians and the transplantation enterprise. Miller and Truog[22] called for abandonment of the rule, however, arguing that the present or prior consent of the dying patient, who is beyond harm, or of the lawful surrogate

validly consenting on behalf of the patient, should be sufficient to allow donation before death is declared. The benefits and drawbacks of adopting this approach have been debated,[93,115] but most scholars endorse retention of the Dead Donor Rule.

Conclusions and future directions

Death determination in the ICU using circulatory–respiratory or brain tests are well-established practices with rigorous conceptual foundations, and are not contrived to facilitate organ donation. Controversies about practical issues of death determination can be resolved by reasoned arguments citing physiology and public policy, leading to consensus among practitioners. International consensus remains an important goal, but is challenged by differences in culture, religion, accepted practices, and laws. Conceptual disagreements over the definition of death will not be resolved in the foreseeable future, but might not impede development of consensus on practices of death determination. Controversies about organ donation may be mitigated by optimizing conversations among family members, physicians and organ donation personnel to reassure family members and physicians that the dual goals of excellent end-of-life care and organ donation need not conflict.

Review criteria

The PubMed MEDLINE database was searched for articles published between 2000 and 2012, using the keywords: "definition of death", "brain death", "donation after cardiac death", and "ethics/organ transplantation". Full-length articles published in or translated into English were retrieved. Reference lists of review articles, and selected articles and books from the author's collection, were consulted.

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