Organ Donation: Circulatory Death, Brain Death, and the Eureka Effect*

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Over the past 50 years, the success of solid organ and tissue transplantation has made great strides in the care of individuals who suffer from organ and tissue failure. The advancements in medical and pharmaceutical care for patients undergoing transplant and an increase in the availability of living organ donors have all worked together to increase the available organs for donation. However, the need for organs continues to be far greater than available organs. According to U.S. Department of Health and Human Services, someone is added to the national transplant waiting list every 10 minutes and on average, "22 people die each day while waiting for a transplant" (1).

Because the number of people who are waiting for organ transplants is far greater than the rate of organ donation, medical professionals, especially in the ICU settings, must continue to capture potential organ donors as clinically indicated. Critical care professionals must manage not only anxious patients and family members during stressful situations but also often have to work through "difficult end-of-life decisions, identifying when to call the Organ Procurement Organization, caring for brain-dead patients, managing a potential DCD candidate" (2) within institutional and standard of care guidelines, all in the hopes of increasing organ donation for transplantation (3).

In this issue of *Critical Care Medicine*, Broderick et al (4) describe their study concern that donation after circulatory death (DCD) may come at the expense of less donation after brain death (DBD) in the United Kingdom. The authors present their study that compares organ donation in people after circulatory death with organ donation in people after brain death in the United Kingdom. The definitions of both DCD and DBD in the United States are similar to those in the United Kingdom. DCD is often a "planned withdrawal of ventilator and organ-perfusion support in the case of catastrophic illness" (5) and allows the patient and/or family to donate when death by neurologic criteria will not be met (6). The planned withdrawal of the ventilator may be done in the ICU setting or in the operating room setting with institution protocol guidelines to be followed regarding organ harvest procedure. DBD refers to brain death, now termed "death by neurologic criteria" in the United States with the definition established in 1978 in the Uniform Death Act and approved federally in 1980 as the U.S. Uniform Determination of Death Act, which allowed brain death to become a legal standard (7). This act defines death as "irreversible cessation of circulatory and respiratory functions (1) or cessation of all functions of the entire brain (2), including the brain stem (8).

Broderick et al (4) reviewed 257 patient records who were referred and assessed as DCD donors in the United Kingdom during a 3-month period in 2013. Of those 257, 134 proceeded as an organ donor. Interestingly, of these 134 patient records, 15 had "brain death confirmed or had clinical indications of brain death." Perhaps the most important question, these researchers asked in this study was whether any of the DCD donors could have become DBD donors. This remains a very important question within the global transplant arena as DBD protocols vary from country to country (and even in some areas in a country where DBD is generally accepted as legally dead) (9). Clinically, the assessment of death by neurological criteria (DBD) may not be uniform across geographical areas or even from institution to institution in the same geographical area. This may have consequences in the clinical assessment of possible DBD and declaration of DBD and conversations between clinicians and family members in a more thoughtful and planned way that might result in appropriate organ donations. In addition, the authors also point out the challenges of the ICU clinicians to "reliably identify which patients with devastating brain injuries would progress to brain death to justify recommending a delay in the withdrawal of life support treatment (WLST)" (4). The recommendation to delay WLST may seem to place the ICU physician within a conflict of interest—is it justified to prolong life-sustaining treatment in anticipation of a diagnosis of DBD for the sole reason of increasing the likelihood of organ donation that would be of benefit to others outside of the patient/provider relationship?

"A donation after circulatory death program has the potential to increase the number of donors after brain death" may be a somewhat misleading title to the study by Broderick et al (4). As it turns out in the study conclusions, they state that "The development of a national DCD program has had minimal impact on the number of DBD donors" (4). The most important statement from this study is the argument that in many ICU patients, more time may be required to allow for the "evolution to brain death" that may increase potential organ donation, rather than the withdrawal of life-sustaining treatment without considering the possible DBD clinical outcome.

"The goal of those working within organ donation and transplantation is to develop clinical and/or serologic criteria

*See also p. 352.

Key Words: brain death; donation after circulatory death; donation after neurological death; organ donor; organ transplant

The author has disclosed that she does not have any potential conflicts of interest.

DOI: 10.1097/CCM.0000000000001499

that are sensitive and specific enough to predict whether brain death will develop within an agreed time frame" (4). Eureka! The Eureka effect does not exactly apply here in application as much as it does in aspiration. However, until such a test or criteria is available that can predict a more specific time of death, ICU clinicians will have to rely on their clinical skills, available patient health data, patient/family treatment preferences, social, religious, professional, and legal guidelines as we continue to provide palliation and end-of-life care to those in need of such. Always mindful of the clinical tension "as the changes that would be required to increase rates of brain death would mean conjugating an intimate clinical and cultural focus on the dying patient with the notion of how this person's death might be best managed to be of benefit to others" (10).

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Neurotoxic Properties of Propofol Sedation Following Traumatic Brain Injury*

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Traumatic brain injury (TBI) is one of the leading causes of neurologic disability worldwide. It is estimated that there are 10 million cases severe enough to warrant hospitalization annually and that TBI survivors, many of whom have long-lasting or permanent neurologic sequelae, presently number about 57 million (1). Numerous patients with TBI receive anesthetic drugs for sedation in the ICU in order to alleviate increased intracranial pressure by reducing cerebral metabolic demand. Additionally, sedation may be used following TBI to control hemodynamics and to improve ventilator synchrony in intubated patients. Currently, no strong evidence exists to guide this intervention. Recent findings point to potentially neurotoxic effects of commonly used anesthetics that are either used as sedatives in the ICU or share mechanisms of action with common ICU sedatives, principally via agonist activity at γ-aminobutyric acid (GABA) receptors. Both retrospective clinical studies and preclinical investigations in animal models ranging from rodents to primates demonstrate that anesthetic drugs cause substantial neurotoxic effects when given in early postnatal life (2). Exposure to anesthetics during brain development leads to lasting deficits in learning and memory, and the first mechanism of injury to be described was an increase in neuronal apoptosis seen throughout the brain (3). Subsequent research has revealed a number of additional mechanisms by which transient exposures to anesthetic drugs can cause lasting disruptions in brain circuit formation via effects on neurite growth, axon guidance, and synapse formation (4). Collectively these data may be of tremendous relevance to the question of how to sedate TBI patients of any age, as the process of recovery from brain injury in the adult involves a recapitulation of many features of neuronal development (5). Thus, the use of sedative agents known to have toxic effects in the developing brain may be counterproductive for recovery following TBI.

*See also p. e70.

Key Words: brain-derived neurotrophic factor; neurotoxicity; p75 neurotrophin receptor; propofol; traumatic brain injury

The authors have disclosed that they do not have any potential conflicts of interest.

DOI: 10.1097/CCM.0000000000001322

A Donation After Circulatory Death Program Has the Potential to Increase the Number of Donors After Brain Death*

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Objectives: Donation after circulatory death has been responsible for 75% of the increase in the numbers of deceased organ donors in the United Kingdom. There has been concern that the success of the donation after circulatory death program has been at the expense of donation after brain death. The objective of the study was to ascertain the impact of the donation after circulatory death program on donation after brain death in the United Kingdom.

Design: Retrospective cohort study.

Setting: A national organ procurement organization.

Patients: Patients referred and assessed as donation after circulatory death donors in the United Kingdom between October and December 2013.

Interventions: None.

Measurements and Main Results: A total of 257 patients were assessed for donation after circulatory death. Of these, 193 were eligible donors. Three patients were deemed medically unsuitable following surgical inspection, 56 patients did not proceed due to asystole, and 134 proceeded to donation. Four donors had insufficient data available for analysis. Therefore, 186 cases were analyzed in total. Organ donation would not have been possible in 79 of the 130 actual donors if donation after circulatory death was not available. Thirty-six donation after circulatory death donors (28% of actual donors) were judged to have the potential to progress to brain death if withdrawal of life-sustaining treatment had been delayed by up to a further 36 hours. A further 15 donation after circulatory death donors had brain death confirmed or had clinical indications of brain death with clear mitigating circumstances in all but three cases. We determined that the maximum potential donation after brain death to donation after circulatory death substitution rate observed was 8%; however due to mitigating circumstances, only three patients (2%) could have undergone brain death testing.

Conclusions: The development of a national donation after circulatory death program has had minimal impact on the number of donation after brain death donors. The number of donation after brain death donors could increase with changes in end-of-life care practices to allow the evolution of brain death and increasing the availability of ancillary testing. (*Crit Care Med* 2016; 44:352–359)

Key Words: donation after brain death; donation after circulatory death; end-of-life care; organ donation

***See also p. 454.**

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The study was performed at NHS Blood and Transplant, Bristol, United Kingdom, in collaboration with U.K. Organ Donation Services Teams.

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DOI: 10.1097/CCM.0000000000001384

In the United Kingdom, as elsewhere, the potential solid organ donor pool has been shrinking, in part as a result of better public health measures (1, 2) and improvements

in the management of severe neurologic injuries leading to a reduction in the incidence of brain death (BD) (3–6). Clinicians have turned increasingly to maximizing the donor pool, which includes the use of organs from donors after the circulatory determination of death (donation after circulatory death [DCD]). There are considerable differences in the practice of DCD between different countries (7). In the United Kingdom, United States, Australia, and The Netherlands, DCD donors are predominantly Maastricht category 3 (8) (donation after the planned withdrawal of life-sustaining treatments [WLST] and 5 min after continuous cardiorespiratory arrest). In the United Kingdom, intensivists frequently make decisions regarding the withdrawal of interventions that are judged to be of no overall benefit to an individual. Such decisions are made for approximately 10% of all patients admitted to U.K. ICUs, and 60% of all ICU deaths occur after such a decision has been reached (9, 10). The practice of WLST varies between ICUs but in the majority involves extubating the patient and the use of comfort medications when indicated. In Spain and Italy, DCD donors are more commonly Maastricht category 2 (donation after failed cardiopulmonary resuscitation). DCD donors currently represent around 40% of the U.K. deceased donor population (11).

The fundamental differences between donation after brain death (DBD) and DCD donors and outcomes are highlighted in a recent publication (12). In particular, the median number of organs transplanted from a DCD donor is less than from a DBD donor. In the United Kingdom, the mean number of organs transplanted from a DCD donor is 2.1 and from a DBD donor is 3.6 (13). Furthermore, although the medium-term outcome for kidneys and lungs from DCD donors is similar to those from DBD donors, liver and pancreas outcomes are inferior (14).

Concerns have also been expressed that some donors who are being facilitated as DCD donors may have met the criteria for neurologic testing to confirm death or had the potential to become DBD donors if WLST was delayed to allow the progression of the brain injury (15). There is some evidence that suggests that the increase in DCD donors appears to be associated with a decrease in the number of DBD donors (16) although others have suggested that DCD donors are additional to DBD donors and represent a separate pool of potential organ donors (17, 18). Specifically in the United Kingdom, Summers et al (19) in a retrospective analysis concluded that DCD organ donors have not contributed to a decline in DBD donors.

The report of the U.K. Organ Donation Task Force (20) states that BD testing should be carried out in all patients where BD is a likely diagnosis, even if organ donation is an unlikely outcome. However, there is no legal requirement in the United Kingdom for clinicians to diagnose death using neurologic criteria, even where the preconditions for such testing are met. The preconditions for testing and the actual conduct of the clinical tests are described in detail in the Academy of Royal Medical Colleges U.K. Code of Practice for the Diagnosis and Confirmation of Death (21) Since 2010/2011, the testing rate of patients who are possibly brain dead has increased from 72.1% to 79.6% (11). The remaining 20% are not tested, most commonly because the patient was hemodynamically unstable, the relatives had already declined donation, or the potential donor had a cardiac arrest despite resuscitation (11).

We undertook a retrospective audit of DCD donors in the United Kingdom, over a 3-month period, to explore.

- whether any DCD donors could have become DBD donors,
- whether any DCD donors had potential to progress to BD had WLST been delayed by up to 36 hours,
- to identify the clinical circumstances where delaying WLST by up to 36 hours may result in progression to BD.

MATERIALS AND METHODS

A retrospective audit was undertaken of all U.K. potential DCD donors between October 1, 2013 and December 31, 2013. The study was approved on behalf of the CARE Committee of the Organ Donation and Transplant Directorate of NHS Blood and Transplant. As this was a review of practice, formal approval by Research Ethics Committee was deemed not required. The study team was unaware of any scientifically based criteria that accurately identify which patients have the potential to progress to BD. However, there is evidence that more patients will progress to BD with time: from admission, 45% are brain dead within 48 hours and 85% at 96 hours (15). Therefore, an assessment tool was developed to collate all relevant available clinical information, including the nature of the brain injury, contributory factors, respiratory function, imaging reports, relevant narrative from medical records, and evidence of neurologic deterioration prior to WLST (**Table 1**).

An assessment tool was completed for each DCD donor, by a specialist nurse in organ donation (SN-OD), through a review of information available from medical records, donor records, observation charts, and radiologic records. The assessment tool included essential criteria from the U.K. Code of Practice for the Diagnosis and Confirmation of Death (21) (Summarized in **Table 2**) and summaries of the CT brain reports. In the United Kingdom, the neurologic diagnosis of death is primarily clinical, and there is no requirement for additional ancillary investigations unless clinical testing cannot be performed reliably.

Each completed assessment tool was independently examined by five assessors (one neurosurgeon, two neurointensivists, one SN-OD, and one transplant surgeon). The assessors were selected to provide a measured and unbiased approach. The assessors categorized the DCD donors into one of the five predefined categories using a combination of clinical experience and synthesis of evidence from the assessment tool.

- Category 1. The patients' death was confirmed by using neurologic criteria but underwent withdrawal of ongoing cardiorespiratory support. Cases were assigned to this category if formal neurologic testing to confirm death had been undertaken and death confirmed.

TABLE 1. Data Collected in the Audit Tool for Analysis by the Assessors

Data Collected on the Assessment and Audit Tool
Date of birth
Hospital and unit
Date and time of any trauma
Date and time of hospital admission
Date and time of referral to an SN-OD
Initial GCS
GCS at WLST
Primary diagnosis
Cause of death
Contributory factors
Is patient apneic?
Does patient have a coma of known etiology and is unresponsive?
Have sedative drugs been excluded as a cause of coma?
Sedative drugs not excluded as cause of coma
Any sedative drugs ongoing
Cough reflex present?
Gag reflex present?
Pupil reaction to light?
Corneal reflex present?
Was BSD a likely diagnosis? If so, why?
Were BSD tests performed? If not, why not?
Was BSD confirmed?
Intracranial pressure monitor in situ? If so, last reading?
Was an external ventricular drain in situ? If so, was it on free drainage?
Did patient have a craniectomy?
Any other neurosurgical interventions?
Is there documented evidence of neurologic deterioration in 12 hr preceding assessment?
Was patient treated for diabetes insipidus?
Was a CT scan of the brain carried out? If so, what was the report(s)?
Was WLST suggested following neurosurgical review of the CT scans?
Did the patient experience any hypertensive episodes during admission?
Was patient on a mandatory ventilation mode?
Ventilator set rate?
Fio_2 at assessment?
Respiratory rate at assessment?
Arterial blood gases results at assessment
Heart rate at assessment
Blood pressure at assessment
Central venous pressure at assessment
Sao_2 at assessment
Any hemodynamic support? If so, please detail?
Date and time of decision to WLST
Date and time of WLST
Date and time of asystole
Did patient have respiratory effort following WLST?
Was patient extubated or decannulated?
Organs retrieved
Relevant narrative from the medical, nursing, or SN-OD notes detailing clinical situation and decision making

(*Continued*)

SN-OD = specialist nurse in organ donation; GCS = Glasgow coma score; WLST = withdrawal of life-sustaining treatments; BSD = brain stem death; Fio_2 = fraction of inspired oxygen; Sao_2 = arterial oxygen saturation.

- Category 2. Met the clinical criteria for undertaking neurologic testing to confirm death but underwent WLST. Cases were assigned to this category if clinical information demonstrated that the criteria defined in the U.K. Code of Practice for the Diagnosis and Confirmation of Death using neurologic criteria had been met.
- Category 3. Likely to have met criteria for confirmation of death by using neurologic criteria if WLST had been delayed by a further 36 hours. Cases were assigned to this category by assessors if the clinical information and clinical observations suggested ongoing neurologic deterioration, which was deemed by the assessor as likely to progress to BD within 36 hours.
- Category 4. Unlikely to have met the neurologic criteria for confirmation of death even if the WLST had been delayed a further 36 hours. Cases were assigned to this category by assessors if the clinical information and clinical observations suggested that neurologic deterioration was not ongoing or that there was no indication that BD was likely to occur in the next 36 hours.
- Category 5. Other. Cases were assigned to category 5 only when clinical circumstances prevented classification into categories 1–4.

WLST involved removal from mechanical ventilation in all cases and may have included other measures such as tracheal extubation and the removal of inotropic cardiovascular support.

Futility was determined by the clinical team and the patient's family/surrogate when the anticipated outcomes did not meet

TABLE 2. Requirements for the Confirmation of Death by Using Neurologic Criteria in the United Kingdom

Preconditions
Known etiology of irreversible brain damage
Exclusion of potentially reversible causes of coma
No evidence that the state is due to depressant drugs
Primary hypothermia excluded as the cause of unconsciousness
Potentially reversible circulatory, metabolic, and endocrine disturbances must have been excluded as the cause of the continuation of unconsciousness
Exclusion of potentially reversible causes of apnea
Clinical tests
The pupils are fixed and do not respond to sharp changes in the intensity of incident light
There is no corneal reflex—care should be taken to avoid damage to the cornea
The oculovestibular reflexes are absent
No motor responses within the cranial nerve distribution can be elicited by adequate stimulation of any somatic area
There is no cough reflex response to bronchial stimulation by a suction catheter placed down the trachea to the carina or gag response to stimulation of the posterior pharynx with a spatula
Apnea test
Ancillary tests
Not mandatory in all cases but recommended when confounders cannot be excluded.
Repetition of tests
The tests are conducted twice by two clinicians experienced in testing. One must be a consultant and both must be at least 5-yr postregistration.

the values and preferences of the dying patient and/or the burden of ongoing treatment outweighed any benefits.

The time from ICU admission to a decision to WLST and to death was compared for patients in categories 3 and 4 by using a two-tailed Mann-Whitney *U* test. The absence of brainstem reflexes, evidence of neurologic deterioration in the preceeding 12 hours, and the absence of respiratory effort at WLST were also compared for donors in category 3 with those in category 4 by using chi-square tests.

RESULTS

In the 3 months, there were 257 potential DCD donors whose family had given consent/authorization to donation. Sixty-four patients (25%) did not proceed to assessment of the potential for organ retrieval. This was due to Coroner/Procurator Fiscal refusal (6 patients), family withdrawal of consent (6 patients), organs declined by transplant centers before WLST (34 patients), positive virology (2 patients), cardiac arrest (1 patient), general instability (9 patients), logistic reasons (1 patient), or other reasons (5 patients). These patients were excluded from further analysis.

A total of 193 consented eligible DCD donors underwent WLST following the arrival of the retrieval team at the donor hospital in anticipation of DCD (and underwent full analysis for the purposes of this study). Characteristics of the eligible donors are summarized in **Table 3**. Of these, 56 (29%) did not proceed to donation because of prolonged time (> 3 hr) to asystole. Three (1.5%) were deemed to be medically unsuitable following surgical inspection of the organs.

Of the 193 eligible donors, 134 proceeded to become actual DCD donors, defined as donors from whom at least one organ was retrieved with the intention to transplant. Of these, four cases were excluded from the analysis because there were insufficient data. Categorization of the 134 eligible donors is shown in **Figure 1**.

For the purpose of analysis, we reviewed the case notes and categorized 130 proceeding donors and 56 potential donors who did not proceed due to prolonged time to asystole, a total of 186 cases.

- Category 1. The patients' death was confirmed by using neurologic criteria but underwent withdrawal of ongoing cardiorespiratory support, $n = 2$ of 186 (1%).

Both donors had death confirmed by using neurologic criteria, but during discussions regarding donation of organs, the family members had requested to be with the patient when the heart stopped beating.

- Category 2. Met the clinical criteria for undertaking neurologic testing to confirm death but underwent WLST, $n = 9$ of 186 (5%).

In two cases, the SN-OD had documented that BD appeared to have occurred, but the ICU medical staff disagreed and did not proceed to BD testing. In a third case, the patient was being nursed in the postoperative recovery unit following transfer from another hospital. The consultant responsible for the patient documented that BD was likely to have occurred but that it would not be possible to carry out confirmatory testing in a robust manner. In a further four cases, neurologic testing was initiated, but the patient became hypoxic and/or cardiovascularly unstable; therefore, testing was abandoned and DCD proceeded. In the final two cases, the family were informed of futility and potential for neurologic testing but requested to be with the patient when the heart stopped beating.

- Category 3. Likely to have met criteria for confirmation of death by using neurologic criteria if WLST had been delayed by a further 36 hours, $n = 36$ of 186 (19%).

In 30 of the 36 patients, there was evidence of neurologic deterioration in the 12 hours preceeding referral to an SN-OD. Seventeen of these patients had documented evidence suggestive of an anticipated progression to BD. Of

TABLE 3. Characteristics of Eligible Donation After Circulatory Death Donors in the United Kingdom

Clinical Variable	Eligible DCD Donors Undergoing Withdrawal of Life-Sustaining Treatment, *n* = 193
Male	118 (61%)
Age (yr), median (range)	57 (3–80)
Age (yr) by category, median (range)	
Category 1	50 (37–63)
Category 2	53 (3–77)
Category 3	55 (9–80)
Category 4	62 (7–79)
Category 5	51 (35–78)
Donors with a neurologic diagnosis	113 (86%)
Donation abandoned due to prolonged time to asystole	56 (29%)
Organs deemed medically unsuitable on surgical inspection	3 (1.5%)
Actual DCD organ donor	134 (69%)

DCD = donation after circulatory death.

the 30 patients with evidence of neurologic deterioration in the 12 hours prior to referral, 20 patients were noted to be apneic following WLST, and 4 of whom were noted to have had sedation ongoing at WLST (**Fig. 2**). A further nine patients had weak or minimal respiratory efforts for a short period following WLST.

- Category 4. Unlikely to have met the neurologic criteria for confirmation of death even if the WLST had been delayed a further 36 hours, *n* = 135 of 186 (73%).

Of these, 17 donors had no neurologic injury; therefore, BD was not a possibility, and these cases were excluded from further analysis. Causes of death for this group included respiratory failure, cardiac failure, and multiple organ failure.

Fifty-six patients did not proceed to organ donation because of a prolonged time from the WLST to asystole (usually > 3 hr) and were also excluded from further analysis.

Of the remaining 62 donors, 52 had no documented evidence of neurologic deterioration within the 12 hours preceeding referral to an SN-OD. Fifty-eight patients had respiratory effort at time of assessment and following WLST.

Four donors were apneic following WLST. One had a high cervical spine fracture but with otherwise intact brainstem reflexes, one had been given thiopental prior to WLST, a third had been noted to have very weak and ineffective respirations throughout, and the fourth patient had died following a hanging, which may have resulted in upper airway edema.

- Category 5. Other, *n* = 4 of 186 (2%).

Three patients had high cervical spine fractures. One of these patients had undergone cerebral angiography with equivocal findings, a second had a cervical spine halo brace in situ causing significant artifact on the CT scan, making interpretation unreliable and precluding MRI scanning. No other ancillary testing was available in the hospitals concerned. The third patient had a permanent pacemaker that precluded MRI as an ancillary test—the only option available in the hospital. The final patient had received thiopental in sufficient doses that prevented clinical testing and was morbidly obese that precluded CT scanning. Other ancillary testing options were not available.

In all four patients, cough, gag, pupilar reaction, and respiratory effort were absent. Two had an absent corneal reflex and two had no documented evidence of the corneal reflex being assessed.

Of the 130 DCD donors assessed, there were 15 donors with potential to have become DBD donors (categories 1, 2, and 5). Family wishes to be with the donor when their heart stopped precluded four from becoming DBD donors. Clinical instability and logistic factors prevented confirmation of death by using neurologic criteria in a further eight cases. Only three cases (2%) could potentially have had confirmation of BD by using neurologic criteria and become DBD donors.

Analysis of the Donors in Categories 3 and 4

Analysis of clinical factors in donors in category 3 (donors considered to have the potential to progress to BD) and category 4 (patients not considered to have the potential to progress to BD) was undertaken to identify any clinical differences evident between the two groups.

1. Time from admission to WLST and death

The median interval between admission and a decision to WLST for donors considered to have the potential to progress to BD was 31 hours (interquartile range [IQR], 45 hr), whereas the median interval for those not considered to have the potential to progress to BD was 84 hours (IQR, 81 hr) ($p = 0.001$). The median time interval between admission and death was 47 hours (IQR, 45 hr) for donors considered to have the potential to progress to BD and 97 hours (IQR, 87 hr) for those not considered to have the potential to progress to BD ($p = 0.001$).

2. Brainstem reflexes

The presence or absence of each reflex was compared between categories 3 and 4 by using chi-square tests. The pupillary reflex was absent in 34 donors considered to have the potential to progress to BD versus 31 not considered to have the potential to progress to BD ($p < 0.05$), the corneal reflexes were absent in 28 considered to have the potential to progress to BD versus 19 not considered to have the potential to progress to BD ($p < 0.05$), the cough reflex was absent in 22 donors

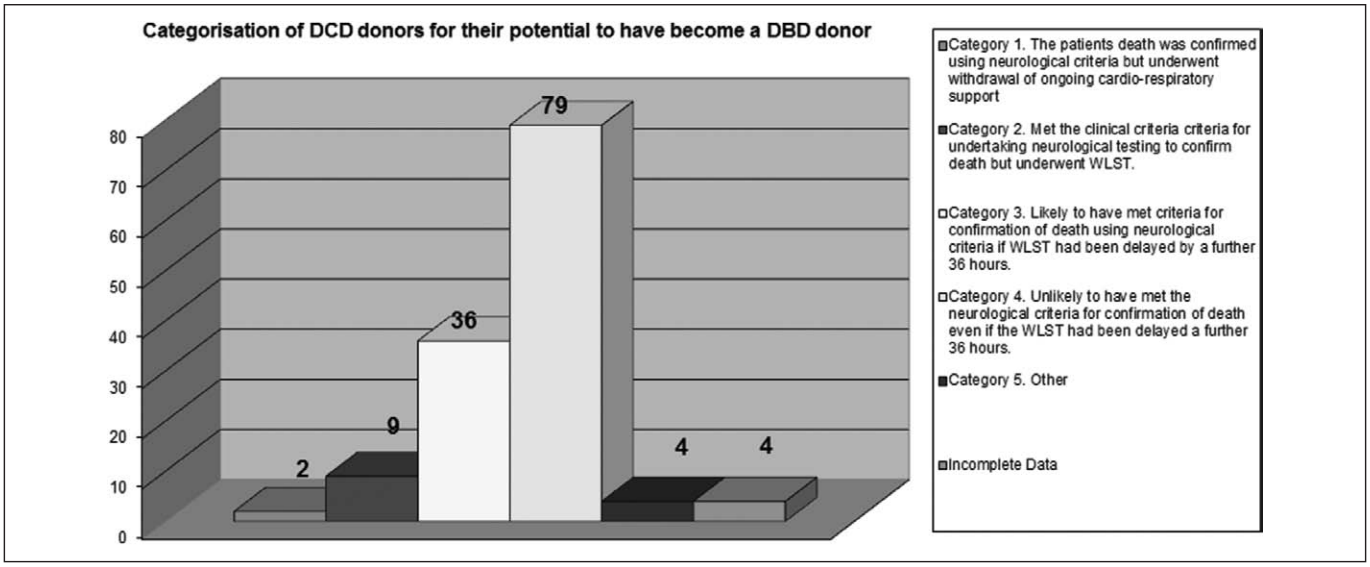

Figure 1. Categorization of the 134 actual donation after circulatory death (DCD) donors between October 1, 2013 and December 31, 2013. DBD = donation after brain death, WLST = withdrawal of life-sustaining treatment.

versus 13 donors ($p < 0.05$), and the gag reflex was absent in 22 donors versus 10 donors ($p < 0.05$).

In the remaining donors in both categories, the reflex was either present or undocumented.

3. Neurologic deterioration in the preceding 12 hours

The presence or absence of neurologic deterioration in the 12 hours preceding referral to an SN-OD was compared between categories 3 and 4 by using chi-square tests. Thirty donors considered to have the potential to progress to BD donors (83%) had a neurologic deterioration versus 10 not considered to have the potential to progress to BD (16%) ($p < 0.05$).

4. Respiratory effort

Absent respiratory effort was noted in 20 of the donors (56%) considered to have the potential to progress to BD at WLST compared with 4 (6%) of those not considered to have the potential to progress to BD ($p < 0.05$).

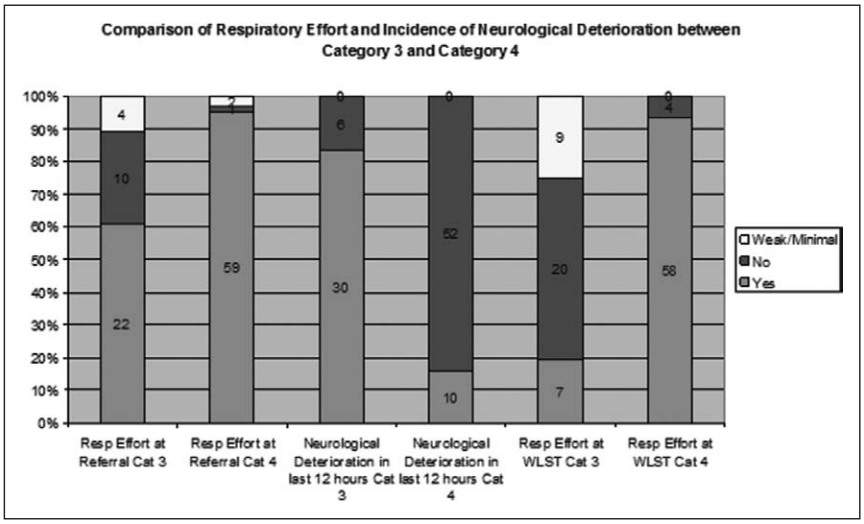

Figure 2. Comparison of respiratory effort, neurologic deterioration in the 12 hr before referral to a specialist nurse in organ donation, and respiratory effort after withdrawal of life-sustaining treatment (WLST).

DISCUSSION

In the 6 years since the publication of the U.K. Organ Donation Taskforce report (20), there has been a 60% increase in the number of deceased donors and a 35% increase in transplants in the United Kingdom. In this time, DCD rates have increased by 170% and have accounted for 75% of the overall increase in deceased organ donor numbers. DCD now accounts for 42% of all deceased organ donors in the United Kingdom (22). Bendorf et al (16) concluded that DCD programs may lead to an overall reduction in the number of transplants performed. This has not been the U.K. experience where the increases in DCD rates have been accompanied by a 28% increase in DBD numbers (13). Similarly, Australia has seen an increase in both DCD and DBD numbers following their organ donation reform program (23). Studies from both the United Kingdom (19) and Australia (18) have concluded that DCD is unlikely to have reduced the DBD donor pool.

We have found that the few times brain-dead patients underwent DCD rather than DBD was almost exclusively for family-centered reasons. Fifteen of the 186 (8%) analyzed eligible DCD donors were either diagnosed brain dead by using neurologic criteria (category 1 donors), were considered to meet the criteria for BD testing (category 2 patients), or were unsuitable for testing due to a lack of ancillary testing that would be required to confirm BD (category 5 patients). Twelve had clear mitigating circumstances why DBD did not proceed. In

the other three cases, there was a difference of opinion between clinicians, ultimately leading to the patient becoming a DCD donor. We concluded that the conversion of DBD donors to DCD donors observed in the study affected just 3 of 186 analyzed eligible donors (2%).

We determined that 135 of the 186 analyzed eligible DCD donors (73%) were considered to have no potential to become brain dead even if WLST had been delayed by a further 36 hours. Seventy-nine of these 135 proceeded to organ donation and accounted for 61% of proceeding DCD donors during the study period. If applied to annual U.K. DCD rates, this would mean that at least 329 of the 540 DCD donors in 2013–2014 would not have donated if a DCD program was not in existence and only patients with potential to become brain dead were considered as donors, with an estimated loss of 855 organs for transplantation.

Assignment into categories 3 and 4 relied heavily on the experience and expertise of the assessors. If categorization was correct, those considered to have the potential to progress to BD had the greatest potential to increase the size of the DBD pool. There were 36 donors in this category (19% of the 186 analyzed eligible DCD donors and 28% of actual 130 analyzed DCD donors). If all donors in this category had become DBD donors, they would have contributed an estimated 200 further transplants in 2013–2014 due to the greater number of organs retrieved on average from DBD donors. It is unknown whether there would be professional, family, and logistic support in the United Kingdom for such a delay in WLST.

The challenge is how to reliably identify which patients with devastating brain injuries would progress to BD to justify recommending a delay in the WLST. The assessors recognized that separating patients likely to progress to BD from those unlikely to progress is more subjective than those in the other categories. This is one of the limitations of the study because there is no validated method of predicting the time for progression from severe brain injury to BD, including the tool we developed and piloted prior to initiation of the study. The subjective nature of the assessments meant that the final categorization of most donors was made on the majority decision rather than unanimity among assessors. Donors considered to have the potential to progress to BD had a significantly shorter time between admission and a decision to WLST (31 vs 84 hr) and a significantly shorter time between admission and death (47 vs 97 hr) than those in category 4. The earlier WLST in those considered to have the potential to progress to BD was interpreted by the assessors as preventing progression to BD. This hypothesis is supported by observational data from Spain, which suggests that 45% of all brain-dead patients would have been diagnosed brain dead within 48 hours of admission compared with approximately 85% at 96 hours (13). Analysis of the U.K. Intensive Care National Audit and Research Centre (ICNARC) (24) data supports this premise. During the period from October to December 2013, the national average time from admission to WLST was 132 hours, whereas the average time from admission to WLST of 31 hours for those considered to have the potential to progress to BD in our study is considerably shorter. Furthermore, the national average time between admission and BD testing was 56 hours. If the WLST in this group had been delayed by 36 hours, the majority would have surpassed the 56-hour average time frame for testing. These data derive from the ICNARC Case Mix Programme Database. The Case Mix Programme is the national comparative audit of patient outcomes from adult critical care coordinated by ICNARC.

End-of-life care practices in ICUs vary considerably across Europe. The Ethicus study (25) found that WLST is undertaken nearly three times more frequently in Northern European countries such as the United Kingdom and The Netherlands compared with Southern European countries such as Spain and Italy and that the incidence of BD was nearly four times more in these Southern European countries compared with the Northern countries. This suggests that the more frequently treatment is withdrawn, the lower the incidence of BD, and this reinforces the argument that more time is required to allow the evolution to BD.

The goal of those working within organ donation and transplantation is to develop clinical and/or serologic criteria that are sensitive and specific enough to predict whether BD will develop within an agreed time frame. This would reassure clinicians that they are not unnecessarily prolonging the dying process and adding distress for the potential donor's family.

This study also highlights some factors that the assessors considered important in deciding if an eligible DCD donor could have progressed to BD in a given time frame. Patients in category 3 had a higher incidence of apnea or poor respiratory effort at the time of WLST, a higher incidence of an absent cough, gag, and pupillary reflexes, and were more likely to have had a significant neurologic deterioration documented in the 12 hours before a referral to an SN-OD was made than those classified as category 4. This suggests that the decision to WLST in category 3 patients was influenced by continued neurologic deterioration, whereas in category 4 the decision to WLST was more likely to have been influenced by a failure to respond to continued treatment.

CONCLUSIONS

We conclude that there is no evidence to suggest widespread conversion of DBD donors to DCD donors in the United Kingdom. However, there is an opportunity to increase the DBD pool, through exploring whether the families of consented, eligible donors who have been identified as having potential to progress to BD in a given time frame would consent to a delay of WLST. Further work is required to define specific and sensitive criteria for delaying WLST and to evaluate if this further alteration in the donation time frame would be acceptable to the patient's families and those working on ICUs.

ACKNOWLEDGMENT

We thank Lucy Dames and Joanna Chalker for assistance with data collection and primary analysis and Lisa Hill for assistance with data collection and collation.

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