Autoresuscitation after asystole in patients being considered for organ donation*

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Objectives: **A fundamental issue in organ donation after circulatory death is the determination of death. There are limited data regarding the incidence and timing of autoresuscitation after asystole. Prevailing guidelines suggest a 2- to 5-min observation after mechanical asystole before the declaration of death. This study tested the hypothesis that a 2-min observation period after asystole is sufficient for the declaration of death in patients being considered for organ donation after circulatory death.**

Design: **Single-center observational study using prospectively collected data.**

Setting: **University hospital, Level I trauma center.**

Patients: **Those patients identified by the organ donation registry that underwent organ donation after circulatory death from 2000 to 2008, during which time the institutional protocol required a 5-min observation period.**

Interventions: **None.**

Measurements and Main Results: **Documentation of medical history, serial Glasgow Coma Scale scores, time of extubation, and time to asystole, hypotension, pulseless electrical activity, and declaration of death were ascertained. Seventy-three patients were identified. The most common mechanism of injury was traumatic brain injury, and eight patients were aged <18 yrs. Patients had a mean Glasgow Coma Scale score of 5 on admission and were taken to organ donation after circulatory death an average of 6.6 days after admission. The average time from extubation to death was 22 mins. No patients exhibited autoresuscitation during the 5-min waiting observation period, including the first 2 mins after asystole.**

Conclusions: **The absence of autoresuscitation in our series suggests that a 2-min observation period is sufficient for the determination of death after cardiac arrest, including patients younger than 18 yrs. These data may inform practice guidelines. (Crit Care Med 2012; 40:158–161)**

KEY WORDS: donation after circulatory death; organ donation; traumatic brain injury

The determination of the exact moment of death has come under scrutiny in the era of modern medicine, especially in the setting of invasive organ support. Because of the natural link between the declaration of death and organ donation, procedures surrounding organ retrieval demand precise protocols. The Uniform Anatomical Gift Act established the "Dead Donor Rule" declaring that donors must be declared dead before organ removal rather than dying as a result of organ removal (1). In the case of brain death, the donor, after the declaration of death, remains on a ventilator with circulation to the organs maintained. However, in the case of donation after circulatory death (DCD), cessation of circulation is needed for the determination of death. Incision for organ procurement follows the certification of death. The precise minimal duration of cessation of circulation in this context is a matter of debate and practice variability (2–4).

Beginning with the 1995 International Maastricht Workshop, which recommended an observation period of 10 mins (5), more recent guidelines have recommended shorter time periods ranging from 2 to 5 mins (6, 7). Recently, cardiac transplantation was performed from newborns at 75 secs, leading to considerable controversy and highlighting the lack of consensus regarding autoresuscitation (AR) (8).

AR is said to occur when a heart that has stopped beating spontaneously "restarts" and generates forward circulation. Although intrinsic cardiac conduction system electrical activity is necessary for AR, it is not alone sufficient because pulseless electrical activity is not equivalent to AR (9). Evidence of anterograde circulation such as pulse, blood pressure, or neurologic function is necessary because death determination is based on the permanent absence of circulation, not cardiac activity. Death cannot be declared in any time window during which AR can be observed because such an observation would demonstrate that the termination of circulation was not permanent.

A recent meta-analysis of AR identified 32 cases, all of which were reported after failed cardiopulmonary resuscitation and none of which were reported during withdrawal of life-sustaining therapy in the absence of cardiopulmonary resuscitation (10). One small other series of 15 DCD patients, the youngest of whom was 23 yrs of age, reported no AR after 1 min of absent circulation (11). According to several Institute of Medicine reports, evidence about the incidence and timing of AR is urgently needed. To our knowledge, we report the largest series to date that tests the hypothesis that a 2-min obser-

*See also p. 329.

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vation period after asystole is sufficient for the declaration of death in DCD patients.

PATIENTS AND METHODS

From 2000 to 2008, the University of Maryland Medical Center and R Adams Cowley Shock Trauma Center required a 5-min observation period for patients eligible for DCD. The University of Maryland institutional review board approved the identification and review of records of DCD patients during this time period. The local organ procurement organization identified patients who participated in DCD.

According to our institutional protocol, the process of organ procurement, including consent for organ donation, is initiated only after the decision is made to discontinue life-sustaining therapies. After consent for evaluation and procurement is obtained, the local organ procurement organization, including their medical directors and the critical care physician, evaluate the patient for suitability for organ donation.

During the study period, all patients had continuous arterial line monitoring for at least 5 mins and documentation included times of extubation, death, pulse, hypotension, and asystole. Patient records were reviewed and demographic information and medical history, including mechanism of initial injury, were recorded. For the purposes of this study (11), continuous criteria for death, after the presence of asystole, included the absence of pulse pressure by arterial catheter, absence of heart sounds, apnea, and unresponsiveness. During the study period, 5 mins of continuous asystole were required for the declaration of death. This clinical determination was made by the physician by visualizing the arterial tracing and cardiac auscultation. Hypotension was defined as systolic blood pressure <50 mm Hg as has been done previously (11). Procedures for withdrawal of mechanical ventilation, consistent with institutional practice, include the use of analgesic medication to relieve pain.

Before extubation, patients were administered a heparin bolus for the possibility of organ donation. Postextubation, pressor support was discontinued and vital signs closely monitored. The treating team included an attending physician or their physician designee, nurse, respiratory therapist, and, if requested by the family, a representative from the local organ procurement organization.

RESULTS

From 2000 to 2008, we identified 73 patients who underwent DCD at the University of Maryland Medical Center. Demographic information and etiology of injury are shown in Table 1. The mean age was 33 yrs, and eight patients were <18 yrs. The majority of patients had severe brain injury, as evidenced by a mean Glasgow Coma Scale score of 5.1, and as expected, the Glasgow Coma Scale deteriorated before DCD. Most patients presented with a primary brain injury, and the most common diagnosis was traumatic brain injury; however, no patient from this cohort had received a diagnosis of brain death.

Table 1. Characteristics of 73 donation after circulatory death patients

Characteristic	Mean or Percent	Range
Age, yrs	36	16–63
Female gender	27.4	—
History of coronary artery disease	9.6	—
Admission Glasgow Coma Scale score	5.1	3–14
Glasgow Coma Scale score before extubation	3.5	3–6
Days from injury to donation after circulatory death	6.8	1–67
Etiology of injury		
Traumatic brain injury	64.4	
Intracerebral hemorrhage	8.2	
Subarachnoid hemorrhage	4.1	
Ischemic stroke	6.8	
Trauma	5.5	
Cardiac arrest	11.0	

Table 2. Latency in minutes from between events certified

Event	Mean	SD	Range
Extubation to death	22.0	10.8	6–53
Extubation to systolic blood pressure <50 mm Hg	12.3	9.1	1–55
Systolic blood pressure <50 mm Hg to death	10.2	9.9	2–29
Extubation to Pulselessness	16.5	10.9	1–57
Pulselessness to death	5.8	0	5–15

All patients had an arterial catheter, and the latencies from extubation, hypotension, and pulselessness to death were reviewed (Table 2). The mean time from extubation to death was 22 mins. There were no episodes of AR after 2 mins of observation.

DCD information is catalogued by injury subtype in Table 3. Traumatic brain injury was the most common subtype; however, epochs of inpatient stay and DCD event times were similar. In addition, eight patients <18 yrs of age underwent DCD with similar characteristics and no episodes of AR.

DISCUSSION

The national shortage of organs available for transplantation demonstrates a clear and urgent need to increase the supply in accordance with accepted ethical and societal principles. Nonheart-beating organ donors in the setting of donation after circulatory death continue to be a population of special interest for increasing organ supply. An obvious limitation to the expansion of DCD programs is the debate surrounding appropriate waiting times between cardiac arrest and the determination of death. The Institute of Medicine, President's Council on Bioethics, and a recent Health and Human Services Panel (12, 13) have all called for further research on the natural history of AR. In this article, we report, to our knowledge, the largest series (73 patients) with continuous monitoring by arterial line and assessment of the return of spontaneous circulation in the context of DCD. In our experience, there were no cases of AR after 1 min.

A recent comprehensive review of published AR accounts revealed no reports of AR in the absence of cardiopulmonary resuscitation (10). All 32 reported cases of AR were observed after failed cardiopulmonary resuscitation. The range of AR times ranged from a few seconds to 33 mins; however, the method of monitoring was highly variable across parent reports. Previously, a study by Wijdicks and colleagues (14) monitored electrocardiographic activity after asystole in 12 neurologically devastated patients on withdrawal of mechanical ventilation. Electrocardiographic complexes were noted; however, return of spontane-

Table 3. Patient and donation after circulatory death event characteristics by injury subtype

Diagnosis	No.	Age, yrs	Female Gender, %	Coronary Artery Disease, %	Injury to Donation After Circulatory Death, days	Admission Glasgow Coma Scale Score/Glasgow Coma Scale Score Before Donation After Circulatory Death	Extubation to Death, mins	Extubation to Peak Endocardial Acceleration, mins	Extubation to Asystole, mins	Extubation to Systolic Blood Pressure <50 mm Hg
Traumatic brain injury	49	33 (14–62)	29	8.2	4.9 (1–17)	4.4/3.5	21.7 (6–62)	15.7 (1–57)	16.6 (1–57)	12.2 (1–55)
Trauma	3	52 (41–63)	0	0	11.3 (8–22)	7.3/4.0	26 (18–41)	21 (13–36)	21 (13–36)	14 (7–25)
Intracerebral hemorrhage	6	44 (19–55)	33	16.7	11.3 (1–58)	3.7/3.5	20 (14–39)	13.8 (8–34)	13.8 (8–34)	9.8 (4–16)
Subarachnoid hemorrhage	3	43 (30–56)	0	0	8.3 (2–15)	9/3	21 (15–27)	16 (10–22)	16 (10–22)	7.3 (1–11)
Ischemic stroke	4	39 (19–57)	25	25	4.8 (1–7)	8.5/4.5	16.8 (10–26)	14 (9–21)	14 (9–21)	10.3 (5–21)
Cardiac arrest	8	38 (16–59)	50	33	13.5 (3–67)	6.5/3.4	26.9 (7–53)	24.9 (12–48)	24.9 (12–48)	17.2 (2–35)
Patients <18 yrs	8	16 (14–17)	38	0	6.75 (1–14)	3.6/3.2	19.9 (7–36)	15.1 (8–31)	15.1 (8–31)	12.4 (5–30)

ous circulation was not measured in most patients. In two patients with arterial line monitoring, there was no evidence of circulation in the presence of any electrocardiographic activity.

Based, in part, on animal evidence of neurologic recovery after approximately 10 mins of cardiac arrest (15), the Dutch have proposed that because all death is "brain death," the duration of time required to declare death is that interval necessary to produce brain death (16). In the United States, expert groups recommend waiting periods varying from 2 to 5 min. These time periods are, in part, justified on the presumed equivalence of irreversibility and permanence of loss of circulation in the absence of cardiopulmonary resuscitation or AR. Patients who become nonheart-beating organ donors have refused life-prolonging therapies and all forms of resuscitation. Therefore, the ability to restore circulation in the setting of withdrawal of mechanical ventilation can be achieved only by spontaneous AR. If AR can be excluded, the permanent loss of circulation equals its irreversible loss (17). The use of extracorporeal membrane oxygenation as a bridge to transplantation is controversial because it is a form of resuscitation that confounds the previous death determination (18).

Before the Hornby et al study, there had been few reports of the natural history and incidence of AR in the setting of DCD. A study by Devita and colleagues (11) reported 15 patients who were reviewed for any AR in the setting of DCD. However, only 12 patients had records for adequate evaluation, and in all of these patients, there was no record of continuous monitoring after 2 mins, only the absence of circulation until the 2-min time point. Because our institutional protocol required continuous assessment of return of spontaneous circulation and the presence of continuous monitoring in the setting of a 5-min wait time during the study period, we were able to assess for evidence of AR from 2–5 mins. The lack of AR in our series was seen across a number of injury subtypes. The latency to hypotension, peak endocardial acceleration, and asystole was longer in victims of trauma and cardiac arrest; however, the 2-min observation was sufficient in all cases. Because the mechanism of death may be different from in brain-injured patients, future studies should confirm our observations in nonneurologic patients. Our data are a retrospective analysis of prospectively recorded data, so we rely on the fidelity of prior observations. These observations are exclusively from potential candidates for DCD instead of a wider range of patients who receive withdrawal of mechanical ventilation; however, the latter group does not routinely undergo invasive physiological monitoring, essential for this study.

Our series is also the first, to our knowledge, to report the lack of AR in DCD patients <18 yrs of age, the youngest of which was 14 yrs. Withdrawal of mechanical ventilation and other supportive measures in adolescents and children is challenging. There is even more limited data on the irreversibility and incidence of AR children. It is unclear if the physiological and temporal relationship between cessation of circulation and cerebral activity is the same in adult and pediatric patients. In our series, all pediatric patient had traumatic brain injury, except one with cardiac arrest.

This report provides further evidence that a 2-min waiting period is sufficient for organ donation after circulatory death. Fewer organs are procured after DCD than after brain death (19), and this may be, in part, the result of increased warm ischemia times (20). A reduction in warm ischemia time may lead to procurement of more organs. In addition to the medical benefits of organ and tissue survival, more widespread adoption of a uniform waiting period of 2 mins would increase consistency of DCD protocols among centers. Increased consistency of procedures, along with complete transparency, serves directly to increase public trust in DCD as an ethical means of organ retrieval (21). Consistency in DCD and transparency are increasingly important as the practice of controlled DCD continues to expand. From 1997 to 2007, the number of organ procurement organizations that reported five or more controlled DCDs in their region increased from six to 41 (13).

CONCLUSION

There continues to be an urgent need to increase DCD to reduce the shortage of available organs for transplantation. Increasing consistency and transparency are essential for DCD protocols to have continued widespread acceptance and implementation. We describe a longitudinal experience with DCD in which donor death occurred reliably and rapidly after extubation, and no patient exhibited any evidence of AR after 1 min. These data are consistent with prior reports and may inform practice guidelines. A 2-min waiting period appears to be sufficient in adult and adolescent patients to exclude AR. Further prospective observation in adults and children is urgently needed as are studies directed at improving organ viability after this time period.

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