

Devastating Brain Injuries: Assessment and Management

Part I: Overview of Brain Death

“To the world you may be one person, but to one person you may be the world.”
-Anonymous

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INTRODUCTION

Perhaps one of the greatest achievements in medicine to date, organ transplantation has transformed the lives of thousands – bringing life to those who would surely have died without it. This achievement is dependent upon a generous gift from another person. From one deceased donor up to 55 lives may be saved or improved.¹ With progressive advances in the trauma system, emergency physicians (EPs) are faced with more severely injured trauma patients, including the potentially brain-dead. The purpose of this three-part series is to present the components of determining brain death, to discuss the pathophysiology unique to brain-dead patients and to outline an algorithm based on that physiology to improve the care of the brain-dead patient. Rather than selectively neglect the brain-dead patient, active management while the patient is still in the emergency department (ED), specialty consultation and critical care can significantly enhance the likelihood of successful organ donation, turning a tragic loss into a rewarding patient encounter.

The majority of transplanted organs come from brain-dead or cadaveric donors. As most of these donors enter the healthcare system through the ED as either trauma patients with brain injuries or medical patients with acute intracranial hemorrhage, EPs are often involved in the diagnosis, referral, and initial stabilization of these patients. When these injuries would not benefit from neurosurgical or neurologic intervention and are deemed to be non-survivable, they are “devastating brain injuries.” The EP’s goal shifts to maintaining hemodynamic stability to diagnose brain death, should it occur. Furthermore, we must prepare the family for devastating news and allow them to begin the grieving process. EPs and trauma surgeons are often involved in discussions of end-of-life care and intensive care management of critical illness and injury. Therefore, both groups have the ability to impact organ donation, transplant frequency and success.

Table 1. Glasgow Coma Scale

Motor		
6		Purposeful; follows commands
5		Localizes to pain
4		Withdraws to pain
3		Decorticate posture
2		Decerebrate posture
1		No movement
Verbal		
5		Oriented
4		Confused
3		Inappropriate
2		Incomprehensible
1		Nonverbal
Eye		
4		Open spontaneously
3		Open to voice
2		Open to pain
1		No eye opening
Total Score:		3-15

Table 2. Brainstem Reflexes

Pupillary response to light
Corneal reflexes
Caloric responses
Gag reflex
Coughing reflex

Table 3. Apnea Test Sequence (Derived from reference 9 and UCI Declaration of Brain Death Policy and Form - see Figure 2)

1. Preoxygenate the patient with 100% FiO₂
2. Ensure the patient is not hypocarbic via ABG
3. Disconnect the ventilator, but supply oropharyngeal oxygen
4. Monitor the patient for any signs of respiration
5. Obtain ABGs at selected intervals (q3-4 min)
6. Stop the test and return to mechanical ventilation if
 - hemodynamic instability occurs, or
 - the patient exhibits attempts to breathe, or
 - the pCO₂ is >60 mmHg or rises > 20 mmHg above baseline in the setting of an arterial pH < 7.3

*FiO₂ fraction of inspired oxygen; ABG, arterial blood gas; pCO₂, partial pressure of arterial carbon dioxide

Organ Donation and Transplantation

Dr. Joseph Murray performed the world's first transplant at Brigham and Women's Hospital in 1954, and since then over 400,000 transplants have been performed.² In 2007 there were 21,403 transplants performed in the United States (U.S.) alone.³ In medically suitable patients, transplantation for end-stage organ failure is the standard of care.⁴ The most commonly needed and transplanted organs, in descending order, are the kidney, liver, heart, lung, and pancreas. Kidney transplants made up 60% of all transplants in 2007 in the U.S. and have been shown to improve quality of life and to be cost-effective compared to hemodialysis.⁵

To comprehend the potential impact of organ donation, several statistics are relevant. The five-year survival rates for patients on the transplant waiting list compared to those that are transplanted are 80.3% vs. 91% for pancreas, 66.5% vs. 92% for kidney, and 37.7% vs. 48% for lung. Two-year survival rates for heart transplantation wait-listed patients range from 44-70%, depending on the severity of heart failure, while the five-year survival after heart transplantation is 73%. Similarly, the one-year survival rate for patients awaiting liver transplantation based on severity ranges from 0-60% and the five-year survival after liver transplantation is 73%. It has been estimated that an average of 30 life-years are saved per organ and tissue donor, based on 2002 statistics, and 55 life-years would be saved if all organs were maximally utilized.⁶ Despite this potential, there are currently 98,161 people on the United Network for Organ Sharing (UNOS) waiting list³, 77,758 patients went without transplant in 2007, and approximately 7,000 died waiting.⁷

There are several strategies to address the mismatch between available and needed organs. Education programs increase awareness of transplant needs and thereby increase the number of people who choose to donate, while prevention

Table 4. Additional Confirmatory Testing for Determination of Brain Death

Cerebral angiography

The contrast medium should be injected under high pressure in both anterior and posterior circulation.

No intracerebral filling should be detected at the level of entry of the carotid or vertebral artery to the skull.

The external carotid circulation should be patent.

The filling of the superior longitudinal sinus may be delayed.

Electroencephalography

A minimum of eight scalp electrodes should be used.

Interelectrode impedances should be between 100 and 10,000 Ω

The integrity of the entire recording system should be tested.

The distance between electrodes should be at least 10 cm.

The sensitivity should be increase to at least 2 μV for 30 minutes with inclusion of appropriate calibrations.

The high-frequency filter setting should not be set below 30Hz, and the low-frequency setting should not be above 1 Hz.

Electroencephalography should demonstrate a lack of reactivity to intense somatosensory or audiovisual stimuli.

Transcranial Doppler ultrasonography

There should be bilateral insonation. The probe should be placed at the temporal bone above the zygomatic arch or the vertebrobasilar arteries through the suboccipital transcranial window.

The abnormalities should include a lack of diastolic or reverberating flow and documentation of small systolic peaks in early systole. A finding of a complete absence of flow may not be reliable owing to inadequate transtemporal windows for insonation.

Cerebral scintigraphy (technetium Tc 99m hexametzime)

The isotope should be injected within 30 minutes after its reconstitution.

A static image of 500,000 counts should be obtained at several time points: immediately, between 30 and 60 minutes later, and at 2 hours.

A correct intravenous injection may be confirmed with additional images of the liver demonstrating uptake (optional).

efforts lessen the burden of chronic diseases that require a transplant. Additionally, UNOS has an extended criteria donor program, which matches high-risk patients with advanced age or chronic diseases such as Hepatitis with high-risk donors. Expanding the donor pool from brain-dead donors to living donors and donors after cardiac death also helps to close

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CLINICAL ALGORITHM – MANAGEMENT OF ADULT PATIENTS WITH DEVASTATING BRAIN INJURIES

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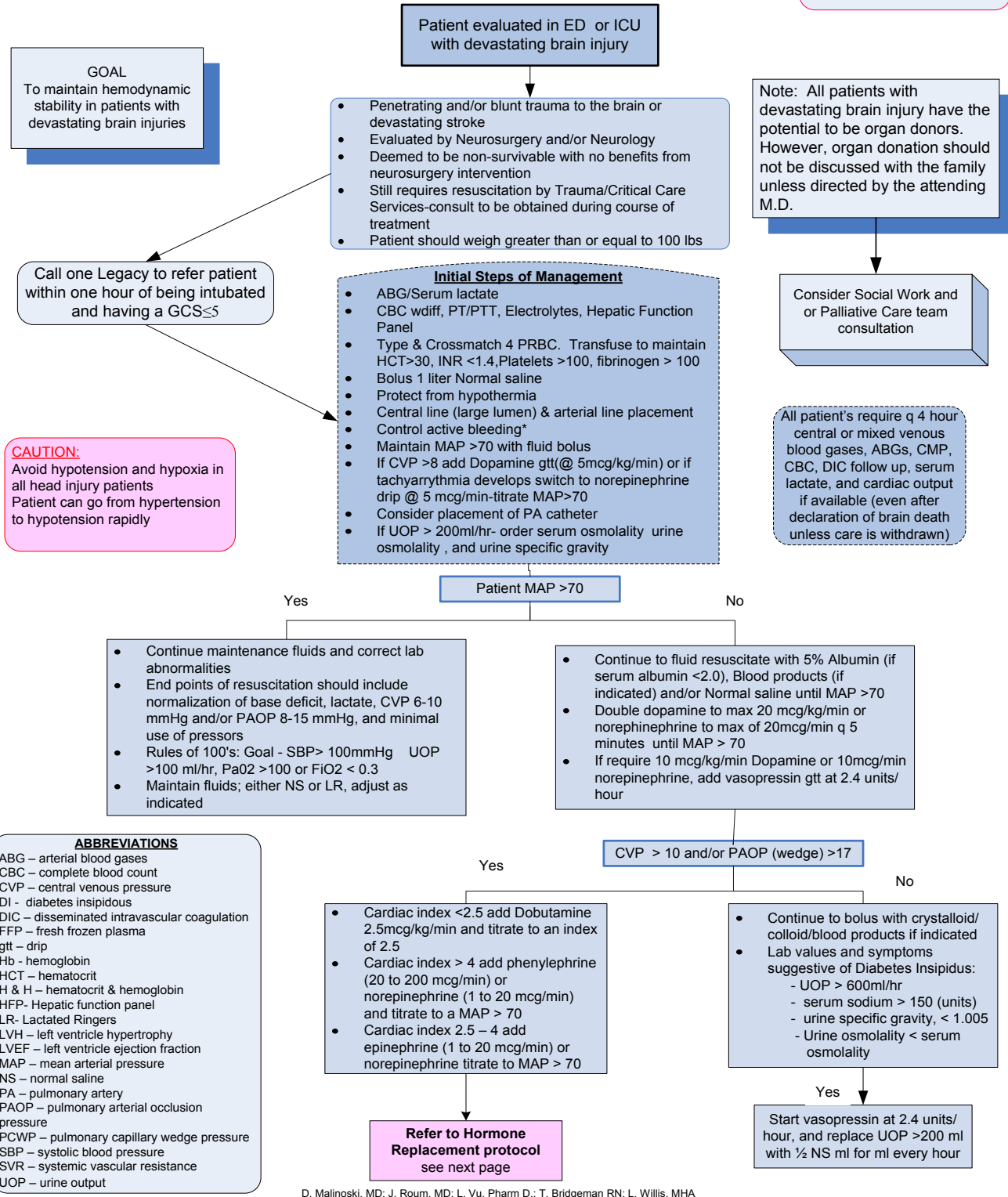


Figure 1. University of California Irvine Medical Center Devastating Brain Injury Pathway (Included with permission from and only approved for use at UCIMC)

the gap. Finally, this series of articles focuses on improving pre-mortem care of brain-dead donors, which decreases the number who succumb to cardiovascular collapse, and increases the number and function of viable organs procured per donor.¹⁰

In the first part of this series, we examine the concept and definition of brain death and provide an overview of the organ donation process. We will outline the clinician's role in determining brain death and introduce our Devastating Brain Injury Algorithm, Figure 1, which is the basis of this series.

BRAIN DEATH

The concept of brain death has caused great controversy in medicine and politics. It is debated by ethicists, law professors, government agencies and healthcare workers.⁸⁻¹¹ First introduced by Mollaret and Goulon in 1959, brain death was originally described as a persistent vegetative state or permanent coma.¹² After 1959, the definition evolved until 1968 when a Harvard Medical School ad hoc committee created the current definition, which was later affirmed by the Uniform Determination of Death Act in 1981.^{12,13}

In general, brain death is the irreversible loss of all brain function. Most agree that complex mental abilities alone do not singularly constitute being alive, lest those in a vegetative state or with severe cerebral malformations be inappropriately declared devoid of life.¹⁴ Ultimately, the brainstem controls brain function and is responsible for regulating breathing, heart rate, and reflexes such as gagging or coughing when the airway is obstructed, withdrawal from pain, and pupillary function. Without a functioning brainstem, life cannot exist. Therefore, diagnosing brain death requires the absence of brainstem function.

To establish a diagnosis of brain death, the clinician must first identify the underlying causes and determine that they are irreversible.¹² Trauma, stroke, cerebral hypoxia, intracranial hemorrhage, tumors, meningitis, and encephalitis are all well-known causes.¹⁵ All confounding factors must be eliminated, such as hypothermia (< 35°C), hypoxia, intoxication by legal or illegal drugs, shock/hypotension, and severe electrolyte disturbances.¹² Figure 2 shows the brain death declaration form and instruction sheet used at our institution.

The clinical brain death assessment is usually made in the intensive care unit (ICU), but if delayed in the ED, patients may warrant a brain death exam before admission. This evaluation involves three steps: verifying unconsciousness, documenting absent brainstem reflexes, and performing the apnea test. To verify unconsciousness, a Glasgow score of 3 is required (Table 1). The five brainstem reflexes that should be assessed in adults are shown in Figure 3 and Table 2.¹² If all brainstem reflexes are absent, an apnea test is performed. The patient should have a pCO₂ within the normal range and be pre-oxygenated with 100% FiO₂. The apnea test ensures the patient has lost the drive to breathe

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BRAIN DEATH DECLARATION FORM

	RESULTS	
Patient Label	Check Box	Comments
Initial Evaluation		
Mechanism consistent with brain death	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Other causes of death excluded, for example:	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Toxins / drugs (no contributory abnormalities)		
Metabolic parameters (no contributory abnormalities)		
Vital Signs		
Temperature (> 35°C) (record: _____)	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Blood pressure normal for age (record: _____)	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Oxygen saturation (> 90%) (record: _____)	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Neurological Examination		
Response to verbal stimuli absent	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Pupils fixed and dilated	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Corneal reflex absent	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Oculocephalic reflex absent (pt not in C-spine precautions)	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Oculovestibular reflex absent (pt in C-spine precautions)	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Motor response to noxious stimulation absent	<input type="checkbox"/> Yes <input type="checkbox"/> No	
For infants Only		
Sucking/rooting reflexes absent (for infants)	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Apnea Test (no respiratory effort in the setting of):		
pH < 7.30 AND EITHER	<input type="checkbox"/> Yes <input type="checkbox"/> No	
pCO ₂ > 60 mm Hg OR ≥ 20 mm Hg over baseline	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Other Confirmatory Tests (as needed)		
4-vessel cerebral angiography	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Radionuclide cerebral blood flow study	<input type="checkbox"/> Yes <input type="checkbox"/> No	
EEG	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Doppler/Ultrasound	<input type="checkbox"/> Yes <input type="checkbox"/> No	
*AFTER ALL CLINICAL CRITERIA ARE MET, EITHER AN APNEA OR OTHER CONFIRMATORY TEST IS REQUIRED TO COMPLETE THE FIRST EXAM. THE SECOND EXAM CAN REFER TO THE APNEA OR OTHER CONFIRMATORY TEST OF THE FIRST EXAM.		
I certify that the above tests have been performed and that according to hospital policy this patient is brain dead.		
California Licensed Physician's Signature _____	License Number _____	Date _____ Time _____
Indicate if examination is first or second examination: _____		
If second exam, indicate: Identity of the first examiner: _____		
Date and time of the first exam: _____		
Notes: The second page of this form is for information only and does not need to be placed in the medical record.		
All documentation must indicate the specific date and time of entry and a signature complete with identifying credential, title or classification.		
88090 (Rev. 4/21/08)		

Figure 2. University of California Irvine Medical Center Brain Death Declaration Form and Instruction Sheet (Included with permission from and only approved for use at UCIMC)

and confirms the diagnosis of brain death.

An overview of the procedure and an example of our institution's brain death declaration protocol can be found in Table 3 and Figure 2, respectively. Criteria for a positive apnea test include: no attempt to breathe while disconnected from the ventilator (as oxygen is still delivered to the airway), a pCO₂ greater than 60mmHg or a rise greater than 20mmHg above base-line, and an arterial pH less than 7.3. It usually takes 5-10 minutes of apnea for the pCO₂ to meet criteria, and we recommend drawing blood gasses every three minutes until either brain death is confirmed or the patient becomes hemodynamically unstable, at which point the patient should be reconnected to the ventilator. Some institutions recommend that the clinical exam, including the apnea test, be performed twice, six hours apart for adults and as much as 48 hours apart for neonates, but second assessment remains controversial.^{9,12}

If the patient is hemodynamically unstable and would not tolerate even a few minutes off the ventilator for fear

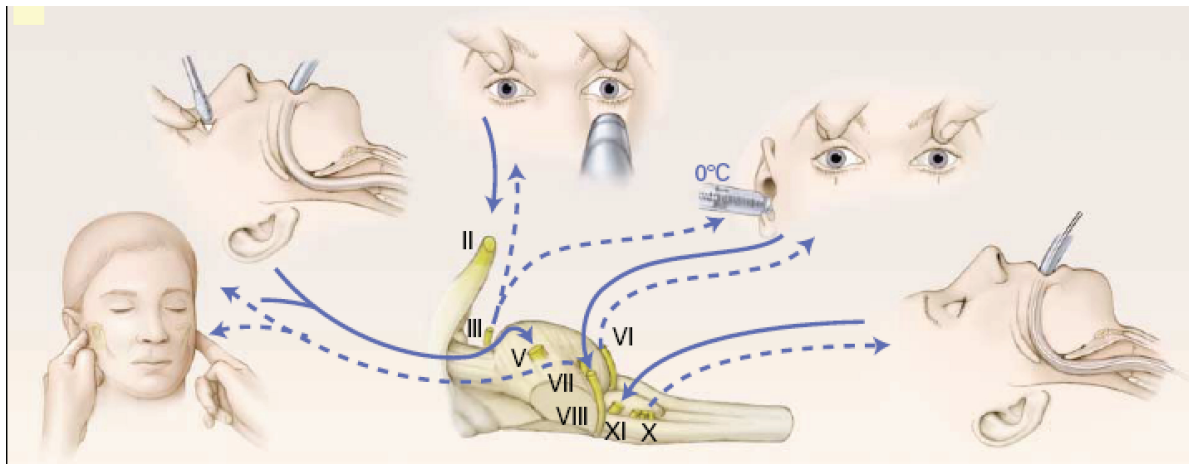


Figure 3. The Steps in a Clinical Examination to Assess Brainstem Reflexes

The tested cranial nerves are indicated by Roman numerals; the solid arrows represent afferent limbs, and the broken arrows efferent limbs. Depicted are the absence of grimacing or eye opening with deep pressure on both condyles at the level of the temporomandibular joint (afferent nerve V and efferent nerve VII), the absent corneal reflex elicited by touching the edge of the cornea (V and VII), the absent light reflex (II and III), the absent oculovestibular response toward the side of the cold stimulus provided by ice water (pen marks at the level of the pupils can be used as reference) (VIII and III and VI), and the absent cough reflex elicited through the introduction of a suction catheter deep in the trachea (IX and X). (Adapted from Wijdicks⁹ and reproduced with permission from Mayo Foundation for Medical Education and Research.)

of causing cardiopulmonary arrest, other confirmatory tests may be used (Table 4). The most common in the U.S. is cerebral angiography. If the carotid arteries cut off at the base of the skull and there is no blood flow within the calvarium, the patient is brain dead. Recently, clinicians have used magnetic resonance or computed tomography angiograms in lieu of more invasive traditional angiography.¹⁶ Electroencephalography (EEG) is well-validated and frequently used to confirm brain death with absent electrical activity. The disadvantage of EEG is that devices in the ICU may cause artifacts, leading to spurious results.¹² Other tests include transcranial Doppler ultrasound to assess cerebral blood flow and nuclear imaging to assess uptake of tracer in the brain. The latter is preferred for secondary confirmation in our institution. None of these confirmatory tests replaces the clinical exam.

Since children are more resilient than adults, a longer time between assessments has been advocated.¹² Additionally, many institutions require other confirmatory tests, in addition to the apnea test, in children less than one year of age. Deciding who is qualified to determine brain death is another variable. Some centers advocate that at least two clinicians concur on the diagnosis of brain death and that at least one of those clinicians be a neurologist or neurosurgeon. Beyond these minor differences, the declaration of brain death is otherwise similar worldwide.

Once declared brain dead, the patient may become an organ donor with family consent or advanced directive. This may be verified by living wills or, in some states, by registration when obtaining a driver's license.³ Brain death can be a challenging concept for a patient's family, and

it is important to equate brain death with the layperson's understanding of bodily death, which usually means that the heart has stopped. The essential connection between brain function and conscious thought may not be obvious to laypersons, and should be stated explicitly.

It is imperative to separate end-of-life discussions surrounding brain death and the withdrawal of medical support from conversations about organ donation, to avoid any perceived conflict of interest. It is recommended that healthcare providers NOT approach family about organ donation without first consulting with their local organ procurement organization (OPO). In general, representatives from the OPO who are formally trained to talk with families about organ donation make the first, formal approach after end-of-life discussions have taken place. Healthcare providers with a close relationship to the family may be involved in the process as well.

Donor Management

The goal prior to and after the determination of brain death is to maintain perfusion of vital organs. This is, at times, as much the responsibility of the EP as the intensivist. After a family consents to donate organs, the OPO assumes care of the donor, both medically and financially, but physician involvement is still important to perform procedures and provide expert critical care advice. The brain is so central to bodily homeostasis, that once dead, it wreaks havoc on all other organ systems. Preserving organs is quite challenging in the face of brain death, and it is not uncommon to lose donors to the spiral of hormonal and cardiovascular collapse.

Recently, studies have proven that aggressive donor

management (ADM) can improve the quantity and quality of donated organs from brain dead donors.^{4,17-19} After a dedicated team of physicians assumed responsibility for the management of all potential organ donors at the Los Angeles County / University of Southern California Medical Center, there was an 82% increase in the number of organ donors and a 71% increase in the number of organs recovered.⁴ Furthermore, organizing the care of the brain-dead donor into an evidence-based clinical protocol has been shown to both decrease donors lost to cardiovascular collapse, as well as increase the number of organs procured per brain-dead donor.¹⁷

The intensive care of the brain-dead donor does increase overall cost of care, but there is no cost to the donor's estate or family.²⁰ The cost-effectiveness of transplantation has been well established and has been most extensively reviewed for kidney transplantation.^{3,20-24} Furthermore, it is imperative to remember that the care of the donor potentially benefits eight patients with end-stage organ failure, and many more who will benefit from tissue donation.^{6,25} Traditionally, 75% of U.S. transplantations have been paid by Medicare.²² The transplanted patient or the patient's insurance company pay for the remaining 16% and 9%, respectively.²² Costs incurred while caring for the brain-dead donor are ultimately distributed amongst the patients receiving the donated organs and are usually covered through insurance or Medicare/Medicaid.²⁶

CONCLUSION

The active participation of all healthcare providers involved in the care of patients with severe neurologic insults preserves the option of organ donation for patients and their families. This care often begins in the ED. Recently, our institution implemented a Devastating Brain Injury Pathway – an evidence-based protocol designed to improve care of this unique population. The primary purposes of the pathway are to maintain hemodynamic stability by providing comprehensive critical care in order for brain death to be diagnosed, should it occur; to give families time to come to the hospital and grieve; and to preserve the opportunity of donation for patients and their families. It is imperative to explicitly state that the primary purpose is not to improve the number of organs that can be transplanted, as this would represent a potential conflict of interest for the physician caring for the injured patient. However, the pathway does represent sound neurologic critical care that will improve perfusion to the brain and has the potential to turn a devastating brain injury into a salvageable one. If a patient does regress to brain death, organ perfusion will be maintained should the patient's family decide to donate. In the next two reviews we will discuss the pathophysiology of brain death that causes so many donors to be lost to cardiovascular collapse (part 2) and the resuscitation and management of these donors to preserve the maximum amount and function of organs per donor (part 3).

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REFERENCES

1. United Network for Organ Sharing. Talking about transplantation: what every patient needs to know. 2004. Available at: <http://www.unos.org>.
2. Transplant pioneers recall medical milestone. Morning Edition, NPR. December 20, 2004. Available at: <http://www.npr.org>.
3. United Network for Organ Sharing. Dec 21, 2007. Available at: <http://www.unos.org>.
4. Salim A, Velmahos GC, Brown C, et al. Aggressive organ donor management significantly increases the number of organs available for transplantation. *J Trauma*. 2005; 58:991-994.
5. Smith CR, Woodward RS, Cohen DS, et al. Cadaveric versus living donor kidney transplantation: a medicare payment analysis. *Transplant*. 2000; 69:311-314.
6. Schnitzler MA, Whiting JF, Brennan DC, et al. The life-years saved by a deceased organ donor. *Am J of Transplant*. 2005; 5:2289-2296.
7. Novitzky D, Cooper DKC, Rosendale JA, et al. Hormonal therapy of the brain-dead donor: experimental and clinical studies. *Transplant*. 2006; 82:1396-1401.
8. Hanto DW. Ethical challenges posed by the solicitation of deceased and living organ donors. *NEJM*. 2007; 356:1062-1066.
9. Shemie SD, Pollack MM, Morioka M, et al. Forum. *Lancet Neurol*. 2007; 6:87-92.
10. Sheehy E, Conrad SL, Brigham LE, et al. Estimating the number of potential organ donors in the United States. *NEJM*. 2003; 349:667-674.
11. Capron AM. Brain death – well settled yet still unresolved. *NEJM*. 2001; 344:1244-1246.
12. Wijdicks EFM. The diagnosis of brain death. *NEJM*. 2001; 344:1215-1221.
13. Todd PM, Jerome RN, Jarquin-Valdivia AA. Organ preservation in a brain dead patient: information support for neurocritical care protocol development. *J Med Libr Assoc*. 2007; 95:238-245.
14. Bagheri A. Individual choice in the definition of death. *J Med Ethics*. 2007; 33:146-149.
15. Karcioğlu O, Ayrik C, Erbil B. The brain-dead patient or a flower in the vase: the emergency department approach to the preservation of the organ donor. *Eur J Emerg Med*. 2003; 10:52-57.

16. Young GB, Shemie SD, Doig CJ, et al. Brief review: the role of ancillary tests in the neurological determination of death. *Can J Anesth*. 2006; 53:533-539.
17. Salim A, Martin M, Brown C, et al. The effect of aggressive donor management: implications for the national organ donor shortage. *J Trauma*. 2006; 61:429-432.
18. Rosendale JD, Chabalewski FL, McBride MA, et al. Increased transplanted organs from the use of a standardized donor management protocol. *Am J Transplant*. 2002; 2:761-768.
19. Roth BJ, Sher L, Murray JA, Belzberg H, Mateo R, Heeran A, Romero J, Mone T, Chan L, Selby R. Cadaveric organ donor recruitment at Los Angeles County Hospital: improvement after formation of a structured clinical, educational and administrative service. *Clin Transplant*. 2003; 17(suppl9):52-57.
20. Donate Life America. December 26, 2007. Available at: <http://www.donatelife.net>.
21. Suthanthiran M and Strom TB. Renal transplantation. *NEJM*. 1994; 331:365-376.
22. Evans RW and Kitzmann DJ. An economic analysis of kidney transplantation. *Surg Clin N Amer*. 1998; 78:149-174.
23. Kim SJ, Gordon EJ and Powe NR. The economics and ethics of kidney transplantation: perspectives in 2006. *Curr Opin Nephrol Hypertens*. 2006; 15:593-598.
24. Oostenbrink JB, Kok ET and Verheul RM. A comparative study of resource use and costs of renal, liver and heart transplantation. *Transpl Internat*. 2005; 18:437-443.
25. Meier-Kriesche H, Schold JD, Gaston RS, et al. Kidneys from deceased donors: maximizing the value of a scarce resource. *Am J Transpl*. 2005; 5:1725-1730.
26. United States Department of Health and Human Services January 8, 2008. Available at: <http://answers.hrsa.gov> via www.organdonor.gov.