Organ preservation in a brain dead patient: information support for neurocritical care protocol development

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THE CASE: BACKGROUND

In response to a traumatic brain injury or another tremendous physiologic “insult” to the brain (e.g., hemorrhagic or ischemic stroke), some patients suffer global and irreversible loss of brain stem function, leading to a diagnosis of brain death. Some of these patients may be candidates for organ and tissue donation, a decision mediated by the patient’s previously expressed wishes, sometimes in the form of an advance directive or organ donor card, and the preferences of the patient’s family [1].

Organ donation is truly a family-driven process and can be affected by various social, educational, and spiritual considerations. An organ procurement organization (OPO) representative or specially trained hospital staff member is typically responsible for communicating with family members about the process of organ donor management and the ways tissue and organ donation will benefit other patients in need. Because significant emotional issues may be involved with the loss of a loved one, educating the family and sincere sensitivity regarding their needs and wishes are crucial to the organ donation process.

Organ donation also includes a complex set of medical practices. Key steps in beginning the process involve diagnosing and managing the brain dead patient, referred to in the literature as the brain dead cadaver and clinically defined as a patient who is comatose and shows no evidence of brain stem reflexes (e.g., spontaneous breathing, further defined in Table 1). These are important issues, given the ever-increasing demand for viable organs and list of individuals waiting for transplants. According to the US Organ Procurement and Tissue Transplantation Network in January 2007, nearly 100,000 people were waiting for organ transplants, with only approximately 26,000 patients receiving transplants between November 2006 and January 2007 [2].

A major issue in a hospital’s neurocritical care unit (NCU) setting is management of the brain dead cadaver, with a focus on optimizing the preservation of donor organs and the transfer of those organs to transplant candidates in other care facilities. Managing the organ donor following determination of brain death is multifaceted and involves a comprehensive system for medical care of the donor, which may include administering appropriate medications to maintain basic body and organ functions and monitoring physiologic values like oxygen, hormone, and electrolyte levels in the blood. Proper management of the organ donor is extremely important to ensure that organs are preserved and protected prior to harvesting and to optimize the number and quality of organs and tissues available for transplantation.

Organ preservation prior to withdrawal of extraordinary means of support (e.g., pharmacologic support of hemodynamics, ventilator support of respiration) involves both monitoring and maintaining physiologic values within set parameters to avoid damage and maintain organ function. These parameters include blood pressure, respiratory rate, and fluid and electrolyte status. Function and levels can be maintained through administration of medications such as corticosteroids and thyroid hormones, as well as through adjustments to ventilator settings and fluid administration to maintain respiratory rate and electrolyte balance.

Synchronous management of the brain dead cadaver, the patient’s family, and the members of the clinical team is crucial to ensure functioning of the implanted organ once it is transplanted. Transferring the organ from donor to recipient should be executed as quickly as possible. The wishes of family members and the actions of the care team and of the OPO representatives are important elements in managing the treatment course and process outcomes.

THE LIBRARIAN’S ROLE IN ESTABLISHING BEST PRACTICES

Given the complexity and time-sensitive nature of this entire process, providing the members of the clinical team with appropriate education and guidance regarding the use of appropriate procedures is vital to the successful procurement process. You serve as the liaison to your hospital’s NCU committee, which is charged with identifying and implementing guidelines to assist care providers in using appropriate management strategies for patient care in the unit. This multidisciplinary team also includes physician intensivists, critical care nurses, pharmacists, respiratory therapists, ethicists, and hospital epidemiologists. Given the complexity of the organ donation process, the NCU committee turns its attention to verifying and implementing best practices for organ donor management.

The main concerns during the committee’s initial discussion of organ procurement practices center around standardizing different aspects of donor care, including appropriate interventions to maintain organs prior to removal for transplant and to ensure effective and timely communication with family members. The team’s goal is to achieve appropriate management of the body from the point at which brain death is perceived to be imminent to the time when organs are removed for transplantation. They hope that by optimizing the unit’s practices, they will also ultimately increase the number of viable organs available for transplant. Discussion among group members
Table 1  
Concept definitions with references to introductory-level information

<table>
<thead>
<tr>
<th>Medical concept</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Brain death</td>
<td>Defined as the irreversible loss of brain function. Brain function is controlled by the brainstem, which serves as the human body’s “control center” for breathing and other involuntary processes. Lack of brainstem reflexes, such as the ability to breathe independently, pupil reactions to light, eye movement, or arms and legs pulling away when pinched or poked (referred to clinically as “withdrawal to pain” or “withdrawal to noxious stimuli”) are indications of brain death. Certain conditions need to be ruled out before brain death can be diagnosed, including effects of phenobarbital drug and alcohol overdose. Diagnosis of brain death is a controversial issue and the focus of continuing debate, given the constant development of medical research in neuroregeneration, recovery of brain tissue after stroke or injury, and variability in diagnostic methods, such as the apnea test and confirmatory lab results. A brain dead cadaver is a patient who has suffered brain death after stroke; an episode such as cardiac arrest, near-drowning, or other events causing a lack of oxygen supply to the brain; or traumatic brain injury. The body no longer has any brainstem reflexes, as defined above, though heart beat and breathing continue through support by a mechanical ventilator and medications administered by intensive care unit staff caring for the patient [17].</td>
</tr>
<tr>
<td>Organ procurement organization (OPO)</td>
<td>In the United States, OPOs coordinate organ procurement in designated service areas, which may cover all or part of a state. OPOs evaluate potential donors, discuss donation with family members, arrange for surgical removal of donated organs, and preserve organs and arrange for their distribution according to national organ sharing policies. Most hospitals and medical centers call on specially trained OPO representatives or an organ recovery coordinator to act as direct liaisons with family members about tissue and organ procurement. These organizations aid health care facilities in proper management of family needs [18].</td>
</tr>
<tr>
<td>Organ procurement</td>
<td>This is a complex process involving a multifaceted approach to preserving the donor organs through medical support with medications and monitoring of breathing and blood values that serve as indicators of how well the body is functioning. The process also involves delivering donor organs to the appropriate hospital or organization for transplantation into recipients, which is usually overseen by the local OPO [18–20].</td>
</tr>
<tr>
<td>Uniform Determination of Death Act</td>
<td>According the Uniform Determination of Death Act of 1981, in the United States, death is declared by meeting criteria for the irreversible cessation of either cardiopulmonary function or the cessation of function of the entire brain. When either criterion is met, the individual is defined as a cadaver [20].</td>
</tr>
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</table>

Figure 1  
Clinician commentary

Organ donation and transplantation is one of the most powerful and dramatic practices in modern medicine. It is the pinnacle of centuries of dreams, massive amounts of accrued knowledge, and impressive technical developments. One organ donor has the potential of saving more than five lives and impacting the quality of life of many others via tissue donation. N oting the number of successful transplants or improve quality of the organs removed from potential donors. Noting the daunting potential volume and complexity of literature that is needed to guide them in developing a care protocol for brain dead cadaver care, they ask you, as the group’s librarian, to aid them in identifying, summarizing, and appraising guidelines and articles addressing these issues.

THE QUESTION

Please identify literature that the NCU committee can use to develop guidelines for implementing evidence-based strategies for preserving organs in a brain dead adult cadaver prior to harvesting organs for donation. Clinical commentary in Figure 1 provides further information regarding the significance of this topic in neurocritical care practices.

UNDERSTANDING THE CONCEPTS

Your first step in exploring the literature focuses on understanding the medical concepts encompassed by the committee’s request. This question has two main concepts: the definition of brain death, including diagnosis, and the organ preservation process and the way it is carried out by hospital staff and regional organ procurement organization (OPO) representatives (Table 1).

EXPLORING THE LITERATURE

Once you better understand these main concepts, the National Guidelines Clearinghouse (NGC) and PubMed are two good places to explore for guidelines to help the committee answer this question [3, 4]. You search NGC using keywords identified during your background reading, such as brain death, organ donation, organ procurement, and organ preservation. However, you find that NGC currently does not con-
tain any relevant guidelines discussing organ preservation in brain dead patients.

Given the committee’s focus on identifying guidelines to support their efforts, you extend your literature search to PubMed with an initial focus on identifying these types of articles using relevant publication types and Medical Subject Heading (MeSH) terms. In addition to terms used to represent guidelines, you also find a term in the MeSH Publication Types hierarchy, “Consensus Development Conference,” defined in its MeSH scope note as a “work that consists of summary statements representing the majority and current agreement of physicians, scientists, and other professionals meeting to reach a consensus on a selected subject” [5]. This article type would also be useful in answering the question. For this first foray into PubMed to find guideline-level information, your search strategy may look something like this:


This initial approach will determine if there are established guidelines specifically focusing on the process of organ preservation prior to harvesting. In addition to addressing the request of the committee, such guidelines will also give you a good starting point from which to begin exploring the relevant evidence, providing an overview of the state of the literature as it is reflected in these secondary sources. A quick review of your PubMed search retrieval reveals primarily guidelines that focus on assessing brain death [6] and Canadian guidelines discussing optimal strategies for organ preservation [7].

Next, you move to a broader search to identify relevant primary literature (i.e., clinical studies exploring facets of this topic). Your expanded search may include other relevant MeSH terms and text-words regarding organ transplantation concepts you retrieved from your background reading and observations you have made while looking through citations in your previous search retrieval. For example, you consider such terms as support, quality, donor management, and preservation. This technique takes into account the variation in how articles are indexed in MEDLINE for this topic over time as the fields of transplantation research and technology have evolved.

You may also want to include a third concept involving organ preservation to refine your results to those that are most relevant to the team’s question. During your examination of the literature, you quickly begin to realize that the concept of “organ preservation” varies quite a bit in how it is represented in different articles. You find specific synonyms and terms that would be especially helpful including words like protection, quality, donor management, and preservation. Your final, more complex search strategy may look something like this:


To ensure comprehensive representation of expert opinion and research relevant to the question, you also find it useful to expand your search to several other resources, including various government and organization Websites (Table 2).

### SELECTING THE ARTICLES

You now turn to the challenging task of sifting through the plethora of information on this topic identified during your searching efforts. You focus on selecting articles that discuss complete protocols and guidelines. Consensus documents are useful for their pro-
vision of useful synthesis of related research, while protocols from individual institutions may provide additional process-oriented information for the committee to consider. Recommendations developed by the Canadian forum on Medical Management to Optimize Donor Organ Potential [7], for example, include a synthesis of the literature describing all medical aspects of organ preservation, including exact parameters for heart rate, respiratory rate, chemical blood levels, and other measurements. These guidelines, however, do not include detailed discussion of family management and staff training, so you also turn to other articles to describe these aspects of the process.

You find several papers that include protocols with specific reference to family and staff issues related to organ management. For example, a retrospective study by Roth et al. assesses the impact of a donor management protocol on patient referrals, number of suitable donors, actual donors, and organs donated at the Los Angeles County trauma service [8]. This system includes an in-house coordinator, a dedicated resuscitation service, and a formal resuscitation pathway, as well as training for staff members to ensure appropriate use of the protocol. This article may be particularly relevant due to its consideration of both social and medical aspects of the organ management protocol.

You also note that several articles address controversial issues in organ preservation [9, 10]. Although you may not summarize such items in detail, the team will likely appreciate brief mention of this kind of supplemental information to aid them in more fully understanding the issues surrounding the question. For example, the prospective study by Rosendale et al. describes the use of hormonal resuscitation to improve the organ preservation in brain dead patients [9]. This article focuses on one specific aspect of organ donor management that seems to be the topic of some debate in the literature and thus may help the committee understand areas of debate in the literature and directions for future research. You also include citations and brief explanations discussing the management of social and family concerns involved in organ donation [11]. In addition, you select articles that focus on staff training in the use of appropriate resuscitation protocol methods (i.e., managing respiratory and physiologic parameters to preserve organ function and prevent damage), in providing timely communication with the OPO, and in recognizing specific medical needs that should be appropriately addressed in the organ donor [10].

As you sift through the literature, you consider several citations that may not be useful to include in your summary. For instance, a review article by Hicks et al. describes some of the issues surrounding organ preservation and management of the organ donor following brain death [12]. This article may be very useful as background reading and may lead you to studies and other papers cited in the text but does not provide primary evidence that answers your question directly. You also choose not to include an article describing improvements in the number of organs harvested from minority patients due to the inclusion of an in-house OPO staff member [11], because it focuses on a specific patient subset rather than an overarching protocol.

**SUMMARIZING THE ARTICLES**

Now that you have selected the guidelines and primary data that seem most relevant to the team’s question, you begin to think about how to summarize the key elements of these items for the committee’s quick reference. Because the research articles are fairly comparable in structure and general content, useful column headings for a table summarizing the articles you selected include:

- **First author or year**: allowing the reader to view a quick surrogate for the citation information
- **Study design and objective**: describing the research methodology used in the study (e.g., prospective or retrospective; clinical trial, cohort, etc.) and brief details of the study’s purpose
- **Patient information**: providing key information about the number of patients in the study, age, sex, and other demographic information that may be relevant to the question
- **Protocol**: explicitly defining details including medical maintenance of the organ donor, management of the family, and staff education issues
- **Relevant results**: detailing specific outcomes, including the number of viable organs harvested or successfully transplanted; for some of the items you selected, not all of the study results described in the article are relevant; for example, the cause of brain death (e.g., stroke, brain injury, etc.) is likely not critical to report given that this does not affect the protocol or pathway used to manage organ donors
- **Limitations**: allowing you to highlight that these results may not have the strength of a randomized controlled trial, as the majority of the literature comprises retrospective or ecologic studies comparing hospital populations before and after implementation of a management protocol, to help the team understand how the protocols may be implemented in practice; these studies may, however, provide information about the population effects of implementing such a protocol or provide hypotheses for other researchers to conduct a prospective study

Table 3 provides an example of how you might use this structure to summarize several of the studies you selected for this question. Because you are also including guidelines and other consensus documents in your summary that do not lend themselves to the same tabular format, you might prefer to summarize these in a more narrative format, describing their significance and any relevant details that help to answer the question (a simple, brief summary example provided in Figure 2).

**OVERALL STATE OF THE LITERATURE**

Determining the content and length of the overall summation of the data related to your question (Figure 3) can be challenging, and you may need to be sensitive to the needs of your requestors. The team has re-
Table 3
Summarizing the individual articles

<table>
<thead>
<tr>
<th>Author (yr)</th>
<th>Study design/objective</th>
<th>Patient characteristics</th>
<th>Protocol</th>
<th>Relevant results</th>
<th>Comments/limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rosendale et al. (2002) [14]</td>
<td>Ecologic study; assess the effect of a critical pathway algorithm on efficiency and effectiveness of organ procurement process</td>
<td>7/11 OPO regions represented in the study; 130 donors accrued during study period (CP); 140 donors selected from a period before pathway implementation (P-CP)</td>
<td>Critical care staff in each center were trained in the use of the pathway; critical pathway for organ donors: 5-phase protocol, involving care of the organ donor through hospital admission, diagnosis of brain death, donor assessment, donor management, and recipient recovery (details in Appendix 1 of the article)</td>
<td>CP group had 10.3% greater number of organs recovered/100 donors compared to P-CP (420.8 vs. 381.4); CP group had 3.3% greater number of organs transplanted compared to P-CP donors; no significant increase in 1-year graft survival rates between groups for any organ</td>
<td>Limitations: Results may be limited by comparison of retrospective data with prospective data; groups may not be comparable</td>
</tr>
<tr>
<td>Roth et al. (2003) [8]</td>
<td>Single-center, retrospective review of death records; assess impact of a donor management protocol involving an in-house coordinator, dedicated resuscitation service, and resuscitation protocol on patient referrals, number of suitable donors, actual donors, and organs donated at one institution</td>
<td>Reviewed medical records of all patients treated by the institution who expired with a diagnosis of severe neurological injury or brain death from 1996 through 2001</td>
<td>Phase I: period prior to protocol implementation (1996–1998); phase II: Protocol included full-time in-house nurse coordinator from local OPO; trauma/critical care teams were trained to identify and stabilize potential donors, a resuscitation protocol was developed (Figure 1 of the article), and biweekly morbidity/mortality conferences were held to review donor failures</td>
<td>46% increase in donor referrals in phase II compared to phase I (124/year vs. 86/year, P = 0.0495); increase in mean number of actual donors from phase I to phase II (15/year vs. 26/year, P = 0.0495); increase in number of organs donated between phase I and phase II (52/year vs. 89/year, P = 0.0495)</td>
<td>Authors note that the inclusion of dedicated in-house coordinators in a standardized protocol can improve number of donors and organs harvested</td>
</tr>
<tr>
<td>Salim et al. (2005) [16]</td>
<td>Retrospective study: evaluate the impact of aggressive donor management (ADM) protocol on number of organ referrals and procurement rate</td>
<td>Reviewed records of 878 patients referred for organ donation over 8 years (1995–2002) in regional OPO; 469 were confirmed as potential donors; 161 became actual donors</td>
<td>Potential organ donors referred to the surgical intensive care unit (SICU) where a dedicated team managed care; protocol of ADM: (1) pulmonary artery catheterization; (2) aggressive fluid resuscitation; (3) vasopressors infused till mean arterial pressure less than 70 mm Hg; (4) hormone therapy (IV bolus of 1 ampule 50% dextrose, 2g Solumedrol, 20 units insulin, 20 mcg of T4, followed by continuous T4 infusion of 10 mcg/hr; (5) identification of brain death–related complications and prompt intervention to address them</td>
<td>Pre-ADM (1995–1998): 214 confirmed potential donors, 57 actual donors (27%); post-ADM (1999–2002): 255 confirmed potential donors, 104 actual donors (41%); increase in both potential and actual donors post-ADM were statistically significant (P = 0.001 and P &lt; 0.001, respectively); 71% increase in total number of organs recovered compared to pre-ADM (P &lt; 0.001); 370 organs recovered post-ADM, 217 recovered pre-ADM; 9% decrease in family decline of organ donation to 42% post-ADM (n = 106) compared to 51% pre-ADM (n = 108, P &lt; 0.05)</td>
<td>Limitations: Retrospective nature of the data may limit application of study results</td>
</tr>
<tr>
<td>Salim (2006) [16]</td>
<td>Retrospective study: compare centers who have adopted early ADM protocols versus those who did not in terms of decrease in loss of organs from donor cardiovascular collapse (CVC)</td>
<td>Searched database of southern California OPO between 1995–2003, included level 1 trauma centers and teaching hospitals in region; 1 trauma center (Los Angeles County, LAC) adopted early resuscitation protocol (ADM), all other 8 centers were combined into 1 group for comparison purposes (Center A)</td>
<td>Number of referrals for organ donation, potential donors, actual donors, family decline, donors lost from CVC, and organs recovered was documented for each medical center; data from period before ADM adoption at LAC (LAC-preADM) was compared to period after protocol implementation (LAC-postADM); pooled data from the other centers were also compared (Center A)</td>
<td>Incidence of CVC was significantly higher in LAC-preADM (19.63%, OR 15.04; 95% CI: 5.84–38.73) and Center A (8.67%, OR 5.85; 95% CI: 2.37–14.42) compared to LAC-postADM; the number of organs harvested per potential donor was higher in LAC-postADM (2.41) versus LAC-preADM (2.07, P = 0.003) and Center A (2.09, P &lt; 0.01); authors note an increased conversion rate (number of actual donors/number of potential donors) LAC-postADM compared with LAC-preADM (41.2% versus 26.6%); the conversion rate for Center A was comparable to LAC-postADM (41.4%)</td>
<td>Limitations: because all other centers were combined, unclear if parameters of individual institutions compared with LAC may have shown a significant difference; authors note that low conversion rate indicates need for further development of methods for better communication with families; retrospective nature of the data may limit results</td>
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</table>
quested that you share your summary by email before the next committee meeting to allow team members to prepare for discussing the literature at the session. Thus, this overall summary will likely be very important to the group in understanding the key points of the literature you have selected.

You may begin your summary with a brief characterization of the literature as a whole by describing the complexity of donor care, noting the multifaceted medical management protocol involving body processes that need to be monitored (e.g., electrolytes, blood pressure, respiratory parameters) and concerns surrounding communication between donor family members and hospital staff.

You also note several related controversies in social and medical management of the donor and family members. For instance, several papers mention the difficulty in communicating properly with the family [10, 13] and comment that hospital staff may always not be the most appropriate group to discuss organ donation with relatives because special training is needed in terms of approaching the family and in using correct terminology when discussing organ donation. The literature also discusses that this duty can be carried out by an OPO representative or a designated in-house team, with a beneficial impact on number of organ transplants [10].

You may briefly summarize the level of evidence available to answer this question, characterizing the nature of the literature for this question as retrospective or ecologic in design and noting the limitations of such approaches.

For this case, information related to organ preservation and related processes varies significantly. The overall summary provides a good opportunity to indicate that you limited your selection to articles discussing care pathways and comprehensive protocols, as requested by the committee. Several articles assess different management strategies [8, 14, 15], comparing pathway algorithms for improving the efficiency of the organ procurement process [8, 14] or evaluating the impact of an aggressive organ donor management protocol on the number of successful organ referrals [15, 16].

You may want to include pertinent details from individual articles used to answer the question in the overall summary. This section can include specific results or outcome data related to the question. For this example, the increase in number of available organs for donations was an important outcome in all the assessed studies, given that this was a direct measurement of the success of a management protocol for organ preservation.

The overall summary can be concluded by mentioning other related issues you have come across in the literature. Several issues are emphasized in the literature regarding organ preservation, including the impact of maintaining an in-hospital OPO representative and impact of using hormone therapy in brain dead patients to preserve the organs.

CONCLUDING REMARKS

Your expert synthesis of the literature related to organ preservation prior to harvesting for donation provides the committee the basis to begin developing a comprehensive, evidence-based care pathway for the NCU (draft protocol in Figure 4). By summarizing and sharing the most relevant literature for this question, you


This consensus document provides an overview of the evidence describing appropriate strategies for medical management of a brain dead organ donor. It focuses on hemodynamic support, blood and electrolyte balance, respiratory support, and drug administration to provide specific parameters for health care providers.

**Note:** Appendix 3 of the article provides a full list of standing orders recommended for management of the organ donor prior to organ harvest.
directly contribute to the improvement of care processes for brain dead cadavers, their families, and the recipient patients. Your involvement may also affect the number of viable organs available for transplantation by contributing examples of validated methods and systems used in other institutions that can be incorporated into policies and procedures in your institution. The development of a post–brain death organ preservation protocol provides a visible example of the value of your participation and the contributions that librarians can make to teams across the spectrum of clinical care.

REFERENCES


AUTHORS’ AFFILIATIONS

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