Chapter 5

The Process of Organ Donation from Non-Living Donors: A Case-Based Journey from Potential Donor Identification to Organ Procurement

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Additional information is available at the end of the chapter

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Abstract

Each year, thousands of people worldwide succumb to end-organ failure while awaiting life-saving transplantation procedures. The shortage of organs continues with no signs of easing in the foreseeable future. The availability of organs from living donors continues to be constrained. At the same time, the cumulative knowledge of organ preservation is advancing steadily resulting in an enhanced ability to utilize a growing number of previously unsuitable tissue and organ gifts. Our ability to procure and preserve more organs is accompanied by the increasing use of so-called "expanded criteria" donors, or those whose organs may not have been suitable without modern advances in organ preservation science. Within the overall context of organ donation from non-living donors, the importance of physiologic and end-organ optimization cannot be understated. This chapter discusses our current state of understanding of optimized organ procurement approaches derived from practical experiences and "lessons learned" at a high-performing, community-based tertiary referral hospital.

Keywords: clinical optimization, ethical considerations, organ donation, organ procurement, organ procurement organization, transplantation

1. Introduction

The process of organ procurement from non-living donors (OPNLD) is multi-factorial and complex [1]. In the United States, significant progress has been made toward wider availability

of organs for transplantation [2, 3]. This includes increased use of organs from donors after cardiac death (DCD) as well as the inclusion of "expanded criteria" donors (ECD) and the introduction of information technology-based tools for better organ allocation [3]. Despite tremendous progress, major challenges remain including the growing number of patients entering transplant waiting lists [4].

It has long been known that more organs may be available than are being currently captured within the existing organ procurement organization (OPO) network [5]. In addition, some organs are lost through suboptimal organ donor resuscitation and/or lack of timely OPO notification [6, 7]. In this chapter, the authors will discuss the modern process of OPNLD, beginning with potential donor identification, then proceeding with physiological optimization, and finally ending with the procurement procedure. To illustrate key points more effectively, a realistic hypothetical case-based scenario will be presented.

2. Case vignette

A 65-year-old male presents via aeromedical flight after a head-on, two-car collision in which he was the restrained passenger. The crash occurred at 7:45 pm–approximately 45 min prior to his arrival at the regional Trauma Center. The patient's wife, the driver, was pronounced dead at the scene. According to the Emergency Medical Services (EMS) report, the patient had Glasgow Coma Scale (GCS) of 9 shortly after the incident and was complaining of left-sided chest pain. It took 30 min to extract the patient from the car.

The patient arrived at the regional Trauma Center at 8:32 pm. On initial assessment, blood pressure was 90/65 mmHg, pulse was 120 beats/min, respiratory rate was 28 breaths/min and the patient had a GCS of 4. Intravenous fluid administration was started and the patient was immediately tracheally intubated. The FAST ultrasound exam was negative. Chest radiograph showed multiple rib fractures and a pneumothorax on the left, for which a chest tube was placed. The secondary trauma survey showed an obvious deformity of the left parietal skull, a left chest wall injury, and a visibly displaced left-sided hip fracture.

Hypertonic saline infusion was begun for treatment of a presumed severe traumatic brain injury (TBI). Detailed timeline of subsequent events now follows:

- 9:00 pm: Once the patient was hemodynamically stabilized, he was taken for computed tomography (CT) of the head, cervical spine, chest, abdomen and pelvis. Immediate review of imaging confirmed left hip fracture-dislocation, multiple left-sided rib fractures and a pneumothorax on the left. Of special concern was the presence of large left epidural and subdural hematomas with evidence of diffuse axonal injury, as well as extensive subarachnoid hemorrhage. The patient was found to have 1.5 cm midline shift with uncal herniation.
- 9:15 pm: Emergent neurosurgery consultation was placed, with immediate arrival of the on-call neurosurgeon. The patient experienced a brief period of hemodynamic instability featuring both bradycardia and tachycardia, followed by the appearance of severe hypertension (systolic blood pressures >200 mmHg), and finally the appearance of bilaterally dilated, unresponsive pupillary exam. The injury was deemed non-survivable.

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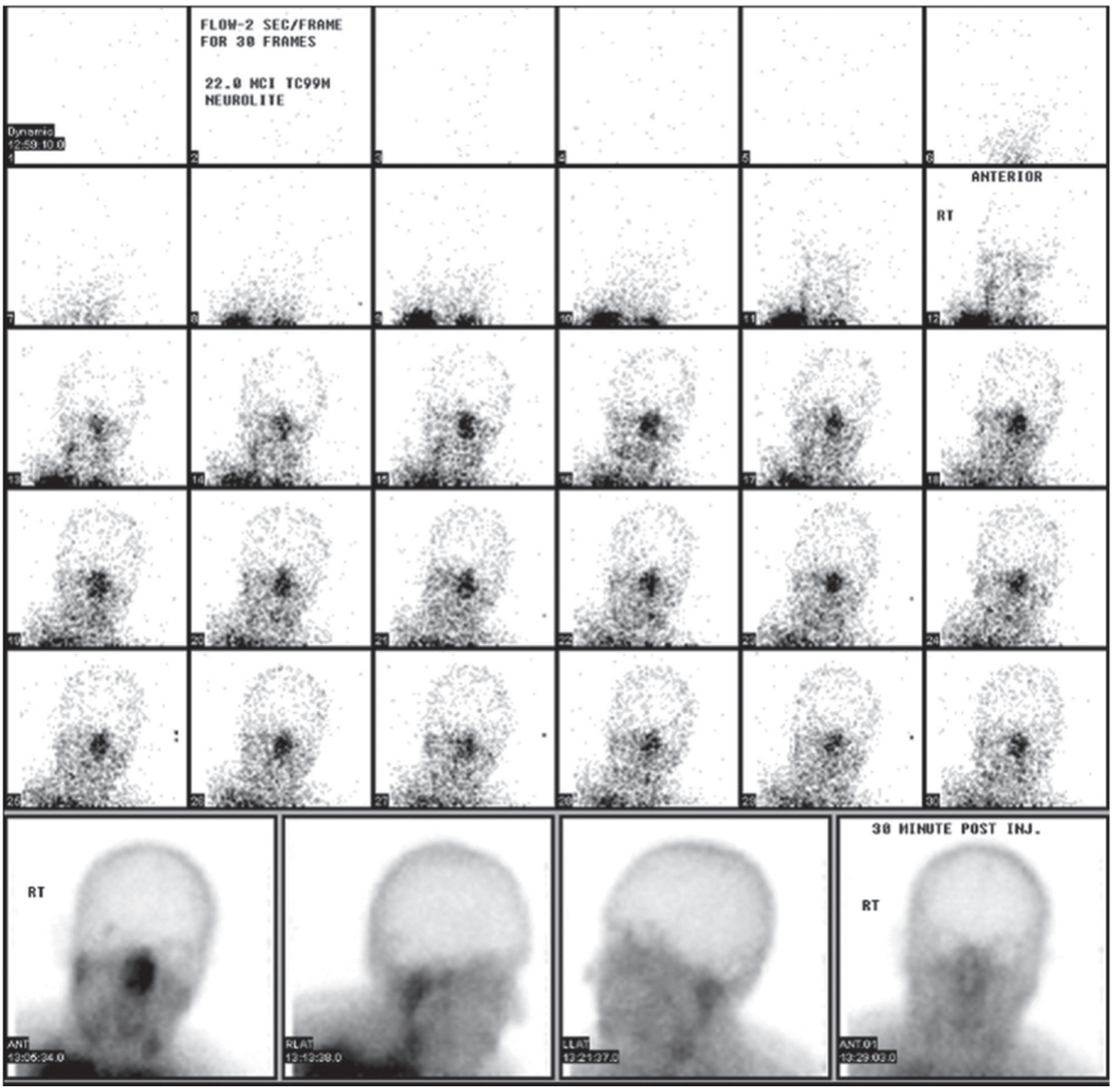

Figure 1. An example of a Tc-99 m radionuclide cerebral blood flow study showing typical appearance of "no flow" within the cranial vault (e.g., the white appearance). At the same time, the facial region is richly perfused with blood (e.g., the "hot-nose" sign), providing a stark comparison to the lack of intracranial flow. **Credit**: Jason Robert Young, M.D. Image used under Creative Commons Attribution-Share Alike 4.0 International license.

- 9:25 pm: The patient's neurological exam was consistent with brain death, as confirmed by two independent physicians credentialed in this clinical area of expertise. Confirmatory testing in the form of cerebral perfusion study was ordered and the patient was taken to the intensive care unit (ICU) in the interim for ongoing medical management. In accordance with applicable State Laws, The Local Organ Procurement Organization (OPO) was contacted for possible organ donation.
- 10:30 pm: The patient's family arrived at the hospital and discussed prognosis and goals of care with the clinical team. At that time, his family members indicated understanding of the diagnosis, and the gravity and irreversibility of his condition. They informed staff that the patient was an organ donor and that they would like to honor his wishes in the event of brain death. Medical management and stabilization continued in anticipation of the cerebral perfusion study.

- 8:30 am: After stabilizing the patient sufficiently for transfer to the radiology department for confirmatory brain flow study, determination was made to proceed with such testing (**Figure 1**). Following the confirmatory study to determine brain death, the patient continued to receive maximum medical management to ensure adequate organ perfusion and maintain tissue oxygenation. Representatives of the local OPO were introduced to the family and the formal process of organ donation was initiated.

- 9:00 am: All required procedures for determining blood type and tissue match were progressing as planned. Organ placement discussions between the local OPO and potential receiving institutions were ongoing. The patient underwent trans-esophageal echocardiography and bronchoscopy to determine his suitability as a heart and lung donor, respectively. Throughout this process, medical optimization of end-organ perfusion continued, including the use of advanced cardiac monitoring, as well as intermittent use of vasopressors and inotropes.

- 11:00 am: After determining that the patient will be able to donate his kidneys, pancreas, and liver. However, due to severe chest trauma his lungs and heart were not suitable for transplantation. At this time, final placement decisions were made.

- 12:00 pm: The patient's family members were allowed to see him prior to the organ procurement operation. The process was to occur within the next several hours, and was predicated on finding a suitable recipient for one of the kidneys. Medical optimization therapy continued.

- 15:30 pm: The patient was taken to the Operating Room for the procurement of bilateral kidneys, pancreas and liver. Three different institutions received kidney, liver and combined kidney-pancreas for transplantation, respectively. Recipients of the above organs underwent uneventful immediate post-transplantation recovery and were able to resume normal lives.

3. Historical background

Organ transplantation and procurement has a rich history, with early accounts of tissue removal and re-implantation involving skin, bone and teeth [8]. During the past several decades, significant progress was made in the area of human transplantation. The evolution of both surgical techniques and immunosuppression resulted in organ transplantation becoming commonplace [9, 10]. Notable medical pioneers of modern transplantation include Dr Christiaan Barnard, Dr Alexis Carrel, Dr Joseph Murray, Dr Thomas Starzl and many others who helped advance the basic scientific and medical understanding required to achieve today's state of knowledge and clinical reliability [11, 12].

From a clinical perspective, the first successful transplants of the modern era involved skin and corneal tissues, and took place in the early 1900s [8]. These experiences, especially involving skin grafting, were plagued by failures well before the concept of tissue compatibility and rejection was fully elucidated [11]. Solid organ transplantation beginning with the kidney was even more challenging. Russian surgeon, Dr Yuri Voronov is credited with the first recorded

report of a kidney transplant from a recently deceased donor in the mid-1930s [8, 13, 14]. Although unsuccessful, this procedure foreshadowed the various technical and ethical challenges modern transplantation would face well into the future.

The subsequent years and decades were characterized by a mixture of "trial and error" until the first successful living donor kidney transplant was performed in the mid-1950s by Nobel prize winner, Dr Joseph Murray [8, 11, 13]. The procedure was performed between identical twin brothers, both of whom survived for some time after [15]. Although the understanding of the organ rejection process was still very poor, Murray's successful transplantation strongly implied the need of genetic congruity between donor and recipient. Shortly thereafter, Main and Prehn discovered that chimerism could be induced by using radiation to weaken the immune system of mice, leading to improved acceptance of donor tissue [16, 17]. Several years later, Dr Murray attempted this method in his next successful kidney transplantation, but this was unfortunately preceded by significant mortality among patients who underwent total body irradiation prior to receiving new organs [11, 18]. Of note, this successful non-twin-twin transplant recipient was the first well-documented case to recover from rejection [11, 19]. Subsequent failures associated with total body irradiation, including significant morbidity and mortality, led to increased interest in other potential methods of immunosuppression [13].

As a result of intensive research efforts, immunosuppressive medications were soon introduced to help address the problem of graft rejection [20, 21]. Initially the use of monotherapy was attempted with limited effectiveness. It was Dr Thomas Starzl (whose success rates exceeded most in the field at the time) who proposed a cocktail of immunosuppressive agents capable of reversing rejection [11]. This was yet another critical discovery that over time facilitated the expansion of efforts into transplantation of other solid organs, including the first liver transplant in 1963 by Dr Starzl, the pancreas in 1966 by Dr Lillehei and the heart in 1967 by Dr Barnard [8, 22–24]. Although long-term survival of early transplants and their recipients varied, the 1960s ushered in a new era with transplant centers appearing across the world [8, 11, 24]. Organ preservation science developed out of the necessity to ensure organ viability during transport from donor to recipient [25].

Beginning in the early 1900s, Charles Guthrie proposed that cooling of organs may offer a way to preserve them during transport [11]. It was not until the mid-1960s that the use of cooling agents became standard practice with the introduction of the now widely accepted University of Wisconsin solution [11, 26, 27]. With progress being made in multiple aspects of transplantation, new hope arose for patients suffering from various forms of end-stage organ failure. As organ preservation and technical aspects of transplantation advanced, attention shifted to ensuring adequate organ availability [7]. Along with this challenge came the ethical and legal considerations surrounding death and organ donation, which will be addressed in greater detail later on in this chapter.

4. Ethical considerations

It is the responsibility of physicians to "above all, do no harm" [28]. This concept should permeate each clinical decision made. In theory, this ethical principle is paramount to an equitable

and just system of medicine, but oftentimes physicians find themselves in situations where they must weigh the risks and benefits of treatment, and answers are far from apparent [29–32]. The field of transplantation is among the most complex medical settings to navigate from the ethics standpoint. This is even more evident with the emergence of extremity and face transplants [33–35].

As Dr Murray embarked on the first living donor transplant, he faced an ethical dilemma. The concept of retrieving an organ from a perfectly healthy individual for implantation in another patient was, and still is, a gray area considering that by removing an organ from a perfectly healthy donor, you are exposing them to a number of risks. [36]. At the same time, certain organs (e.g., heart and pancreas) can only be procured from deceased donors, which raises a completely different set of ethical issues. These include questions of donor and recipient eligibility, fairness, procurement procedures, the legal definition of death, donor designation versus family permission and compensation [7, 36]. There is also a major concern regarding the potential of inequitable allocation of organs [36, 37]. This dilemma gained international attention with the first successful cardiac transplant in 1967 by Dr Barnard [38]. The concept of taking a still beating heart from someone considered "dead" created a significant conceptual and ethical problem in the eyes of many, with calls for a more concrete definition or list of objective criteria including non-responsiveness and other neurological signs that defined irreversible coma [8, 36]. It would be another 10 years before the Presidential Commission of the Study of the Ethics in Medicine proposed the current legal definition of death which included "irreversible cessation of circulatory and respiratory function" or "irreversible cessation of brain function including brainstem function" [36, 39]. The concepts of brain death and circulatory death will be discussed in greater detail later in this chapter.

Over 33,000 organ transplants were performed in the US in 2016, representing a 20% increase in donations over the past 5 years [40]. Yet about 115,000 individuals are currently on the waitlist for organ donation and 7000 waitlist candidates died in 2016, while awaiting a life-saving transplantation [40]. Although significant strides were made with regard to increasing donations, there continues to be an organ shortage, which has led to some ethically questionable practices [35, 41]. The National Organ Transplant Act of 1984 brought together top content experts and outlined key issues related to the different aspects of the organ procurement process [42–44]. This group established key ethical principles, including the requirement that there would be no payment in exchange for organs and that organs must be voluntarily given [36, 43, 44]. This act also established our current U.S. system of organ allocation [45]. As one can see, there are numerous ethical concerns to take into account from a purely systematic viewpoint. This does not even account for the sensitivity of broaching the topic of organ donation to a grieving family coming to grips with the loss of a loved one. Even with efforts to encourage individuals to make these end-of-life decisions early on through donor registries, it is still common practice in many states to consult the family prior to proceeding with the organ procurement process [7]. Because the primary focus of this chapter is to describe the organ donation process in non-living donors, we will not be discussing numerous other ethical issues that arise when taking into account living donors. The subsequent sections of this chapter will outline OPO's and their critical role in the donation process. We will then proceed to describe the organ donation process in the context of both the above ethical and historical considerations, as well as the vignette presented earlier in the text.

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5. Organ procurement organizations

The organ procurement process begins with the identification of a potential organ donor, then proceeds through the stages of notification of next of kin, the decision to donate, the process of physiologic donor optimization, the process of organ procurement and finally the transplantation of donated organs. Throughout this entire sequence of events, the OPO plays a central and an integral role [7]. The evolution of OPOs stems from the increased demand for organ donation, the need to organize and prioritize the process, and the necessity to ensure that organ allocation is performed in a fair and impartial fashion while at the same time efficiently and effectively providing organs to those in need [8, 46].

Prior to the inception of the modern network of OPOs, the organ procurement and allocation process was the responsibility of individual transplant centers [8]. They also shouldered the costs of the procurement and transportation process. As one can imagine this created a fragmented system in which each center would instinctively focus on providing resources to those in need of organs within their own hospital or locality [47, 48]. The evolution of OPO's provided a structured, equitable solution to streamline the process from organ donation to transplantation [7]. The current scope of functions of OPOs is vast and diverse, including interfacing with patient families; providing support to grieving relatives while helping them make critical decisions concerning organ donation; working in conjunction with hospitals and health care practitioners to physiologically optimize donors prior to organ procurement; coordinating with the United Network for Organ Sharing (UNOS) to find proper donor matches; and facilitating professional and public education as well as related research [7, 49].

6. The process of organ procurement

From the time of identification of potential donor to successful procurement and transplant, the process of organ procurement is a complex and intricate undertaking that we will discuss in greater detail in this section. For the purposes of our discussion, we will direct our attention to donation after death since the subject of live donors is outlined in other chapters. A simplified schematic of the overall process is shown in **Figure 2**.

The initial step in donation is centered on the potential organ donor. Although each clinical situation is uniquely different, the first step in the process is the recognition of the irreversible process of brain death, or the circumstances leading to non-heart beating donation [7, 50]. When examining the topic of donation after cardiac or circulatory death, we must go back to the corresponding legal and ethical definitions [23, 51, 52]. How and when does one determine brain death and circulatory death? In the current chapter's vignette, the circumstances of brain death were unequivocal as the patient had suffered a non-survivable injury. We realize that in clinical practice it may not be this straightforward, and repeated exams or confirmatory testing may provide the family with a greater degree of certainty regarding the finality of this devastating diagnosis. More specifically, confirmatory brain death determination with the brain scan showing "no blood flow" to the brain was helpful in the current scenario.

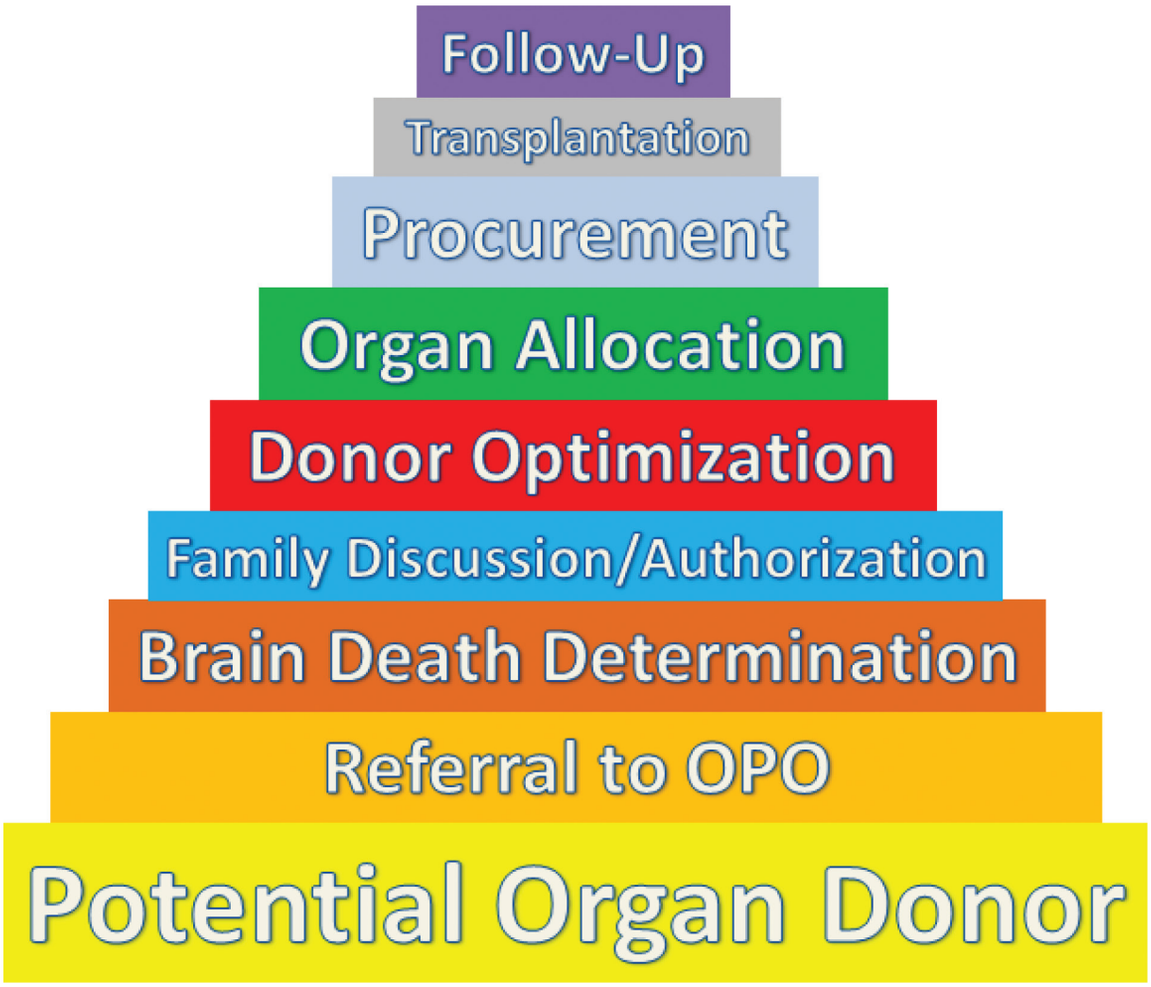

Figure 2. Simplified schematic of the organ donation process. Following the identification of potential organ donor, a cascade of events takes place that ultimately ends with successful organ transplantation. Further details regarding this complex process can be obtained from Wojda et al. [7].

Another critically important consideration is the emotional state of a family coming to grips with the untimely and unexpected loss of a loved one. The grief combined with the immense responsibility of determining what a loved one "may have wanted" can place a significant burden on his or her relatives. This can be especially difficult for families of patients with no advance directive, living will, power of attorney, or prior conversation concerning their organ donation wishes. When dealing with issues related to organ donation, health care providers must be extremely sensitive to family needs and ensure that their local OPO is involved early on in the process in order to prevent any potential conflict of interest [7]. The separation of responsibilities during these proceedings is critical in alleviating any concerns regarding the simultaneous provision of care for the patient along with facilitation of the organ donation process by the same individual and/or team [53, 54].

From the time a potential donor arrives to the hospital and is determined to have non-survivable injury, it is important that they are managed under the assumption that they may donate organs, and that care is both optimal and timely [6, 55, 56]. This includes early notification of the local OPO regarding the presence of a potential donor [7]. A great deal of attention must be paid to prevent hypoxia and systemic hypo-perfusion, both of which could compromise the

viability of the donor's organs [56, 57]. As was the case in our hypothetical vignette, the patient should be stable before undergoing any confirmatory testing. In the current example, such stabilization required approximately 10–12 h of continuous effort by the critical care team. Once the decision is made to donate by the family in the case of brain death or circulatory death, the OPO helps coordinate the remainder of the care process, including the distribution of the organs and the provision of highly trained staff to prepare for the actual organ procurement and preservation, as well as highly efficient transport of preserved organs to each recipient's institution [7]. At this time, we will discuss key components of the process of organ donation, including the determination of death and physiologic optimization of the donor.

7. Determination of death

As discussed earlier in the chapter, declaration of death—whether that be circulatory death or brain death—has been a controversial topic over the years. In 2014, an international forum was held in Montreal, Canada with the objective to provide a functional definition of death that encompassed the concepts of brain and circulatory death. They reported that "Death is the permanent loss of capacity for consciousness and all brainstem functions. This may result from permanent cessation of circulation or catastrophic brain injury. In the context of death determination, 'permanent' refers to loss of function that cannot resume spontaneously and will not be restored through intervention" [58]. It is important for health care practitioners of all levels working with potential donor patients to have a good understanding of the definition of death in order to be able to explain to grieving families the reality of the situation and its finality [59]. It is well established that adequate explanation of brain death is one of the critical components of the donation process [60]. The optimal timing of the consent process is also of great importance [61]. Checklists are helpful in maintaining the thoroughness of brain death determination, but do not replace the expertise, knowledge and compassion of physicians in end-of-life discussions with families of the potential donor.

8. Brain death determination

When a patient presents to the hospital with concern for altered consciousness, it is imperative to rule out all reversible causes of coma, first excluding the presence of any substances of abuse, medication side effects, electrolyte, metabolic or acid-base derangements [62]. Once these are ruled out, imaging can often shed some light on potential causes of neurological compromise. In the current case vignette, the CT was utilized in order to give the treating physician an indication of the magnitude of injury and likelihood of recovery. With that being said, official declaration of BD is actually a clinical one [63]. From definitional standpoint, BD is considered to be present when there is irreversible damage to the brain and brainstem [36]. In order to assess brain function, several key components are required, with the most important one being a thorough neurological examination including assessment of brainstem reflexes [62]. Various ancillary tests can also be performed to assess cerebral blood flow and brain electrical activity in cases with equivocal exam findings. The final declaration of BD (including the official time of death) rests with the treating physician.

Determination of brain death (BD) can be a complex issue in the evaluation of catastrophic neurological injury. Clinical diagnosis of BD is relatively uncommon in the acute care setting. Usually acute injury does not progress to the degree of absent brainstem reflexes and apnea. "The small percentage of…cases may be related to many factors including early aggressive care like decompressive craniectomies, change in referral patterns, and early withdrawal of care or decision to proceed with a donation after cardiac death protocol" [64]. There are predefined criteria for the clinical determination of BD which may vary slightly from country to country. The neurological assessment of suspected BD typically requires at least 25 tests and verifications. "The overriding principle is simple: establish cause, exclude confounders, determine futility of interventions, examine brainstem reflexes and test for apnea" [64].

Due to frequent inconsistencies related to the determination of BD, the Quality Standards Subcommittee of the American Academy of Neurology (AAN) met in the 1990s to establish clear definitions of clinical terms and associated testing. The group also determined the validity of ancillary testing versus the clinical exam and its applicability to the organ donation process. Clinical criteria for BD require a formal assessment and are only undertaken once all other potentially reversible cause are excluded. The initial evaluation needs to ensure there are "no lingering effects of prior sedation, or prior use of illegal drugs or alcohol. A reasonable guideline is to calculate 5–7 times the drug's elimination half-life in hours and allow that time to pass before clinical exam is performed" [64]. A core temperature of 36°C is also recommended which can be aided by use of warming blankets if necessary. As in the current chapter's vignette, neuroimaging such as a CT scan of the head should be performed to help determine cause of mental status deterioration. Clinical examination must include a thorough neurological examination including assessment of patient's level consciousness, as well as evaluation for verbal and motor deficits. The above exam must also include the interrogation of brainstem reflexes including pupillary, corneal, pharyngeal, and tracheal responses, as well as oculocephalic reflexes with doll's eye and cold caloric assessments. Apnea testing requires documentation of absence of a respiratory drive after a CO_2 challenge. This methodology also has strict criteria that must be followed to ensure accurate determination of absent respiratory drive [65, 66].

Although ancillary testing, such as electroencephalography (EEG), cerebral angiography, nuclear flow scan, transcranial Doppler, CT angiography and magnetic resonance (MR) angiography, can be utilized in the process of determining BD—due to variability in the interpretation of these studies—it is not a substitute for the clinical examination [67–70]. In aggregate, the above tests can provide additional data on electrical brain function and cerebral blood flow and "…can be used when uncertainty exist about the reliability of parts of the neurological examination or when the apnea test cannot be performed" [71, 72]. Expertise in determining brain death can be inadequate due to multitude of factors, including lack of clinical experience. This is likely one of the reasons why 6 US states require confirmation by a second examiner and some specifically require at least one of these examiners to be either a neurologist, neurosurgeon or intensivist [73].

As one can see, the determination of brain death can be quite complex in and of itself and can be even further complicated when the question of organ donation is raised. This is why we stress the importance of early involvement of a local OPO [73]. After the declaration of BD, assuming the presence of consent for organ and tissue donation, the care of the donor shifts to optimizing organ perfusion and viability [7]. The preservation of organs after determination

of BD also requires excellent coordination between the OPO and the medical management team [7, 64]. The key concerns for the medical team are to ensure hemodynamic stability and avoid the development of hyper/hypo-glycemia, acid-base or electrolyte derangements and pulmonary edema [7]. Many diagnostic tests and interventions occur during this phase specifically to ensure viability of key body systems and organs. Accumulated clinical evidence suggests "that a delay in declaration of brain death not only prolongs the time to organ recovery but also may increase the risks to transplantable organs, resulting in more complicated post-operative phases for the recipient" [64]. Finally, there is also evidence suggesting that second BD examination may negatively affect organ donor physiology due to inherent time delays [74], thus lending indirect support for ancillary/confirmatory BD testing.

From historical perspective, transplantation of organs was premised on the so-called "dead donor rule", where donors must be declared dead according to established medical and legal criteria prior to donation [75]. According to Chaten [76], "the dead donor rule (DDR) maintains that it is illicit to procure vital organs from donors until after they have been declared dead". This rule also required adherence to strict BD criteria, directly referencing that the "dead donor rule mandates simultaneous life and death within the same body for organ donation, a biological status that is inherently contradictory" [76]. The best way to decrease variability in BD determination is for all hospitals to implement the established set of AAN brain death guidelines [71, 77]. This would lead to less confusion and fewer inconsistencies among institutions. Due to the many complexities of end-of-life discussions, it is imperative that BD determination protocols become increasingly uniform in both content and application. Wahlster et al. [78] looked at practices and perceptions regarding BD declaration in 91 countries, noting that "countries with an organized transplant network were more likely to have a brain death provision compared with countries without" [78]. Barriers to consensus on universal BD standardization include social, religious and economic factors specific to each country and/or culture. Wahlster et al. [78] further note that "future efforts for uniform policies will need to include physicians with neurologic and critical care expertise, representatives of national and international major medical organizations such as the World Health Organization or World Federation of Neurology, and scientific and medical advisors of government agencies" [76].

9. Circulatory death determination

The shortage of organ donors has prompted resurgence in the utilization of donation after circulatory or cardiac death (DCD) [23, 51, 79]. While the concept of BD has been extensively discussed and there is a reasonable consensus as far as applicable criteria and assessments are concerned, definitive guidelines with respect to DCD continue to pose a challenge. In 1993, the Pittsburg non-beating heart organ donation protocol was proposed in order to provide criterion for organ procurement in the case of circulatory death. This protocol has come under criticism due to its questionable ethical application [80]. Although a definitive consensus is yet to be made from a legal and ethical standpoint, various OPOs are performing organ procurements with their own sets of standards and protocols [80]. Of interest, DCD historically constituted the largest proportion of organ donations prior to the advent of donation after BD. Subsequently, its utilization decreased substantially due to superior graft survival outcomes following donation after BD [81, 82].

10. Physiological optimization of the organ donor

Throughout the process of organ procurement, it is critical to achieve physiologic normalization and maintain systemic homeostasis in order to optimize the number of organs procured from each donor [6, 7, 83]. With this in mind, it is essential that potential donors be attentively managed in order to prevent systemic hypoxia and hypoperfusion to vital organs [7]. As in the current chapter's vignette, the ICU is the ideal location for the resuscitation of organ donors and the associated complex physiological and management needs [56, 84]. Cessation of brain function sets off a myriad of multi-system manifestations (e.g. cardiac arrhythmia, hypotension, profound acid-base and electrolyte imbalances) many of which can result in subsequent end-organ insufficiency and/or failure [56]. Consequently, ICU teams must be cognizant of these considerations and proactively work to counteract deleterious effects of BD through a number of intensive interventions. Adherence to strict protocols for management of the organ donor is of utmost importance to ensure optimal conversion rates and graft survival among recipients [7, 84]. Because such protocols may differ from center to center, it is essential for ICU teams to work with local OPOs to ensure standardization in the approach taken to optimize the organ donor prior to the procurement procedure [7, 84]. This alliance can help standardize the care received by each patient, regardless of the institution, and also provide important feedback on what is working and what may not be working. This then helps facilitate performance improvement from an OPO system standpoint [7].

As previously mentioned, there are multiple adverse physiologic events that may occur when the brain ceases to function (**Figure 3**). These include reflexive hypertension and subsequent hypotension; systemic "endocrine failure" leading to significant hormonal derangements including diabetes insipidus; and finally secondary phenomena such as acute lung injury and neurogenic pulmonary edema [85–88]. When managing patients, who succumbed to BD following TBI and multi-system trauma, special care must be dedicated to preventing any secondary insults

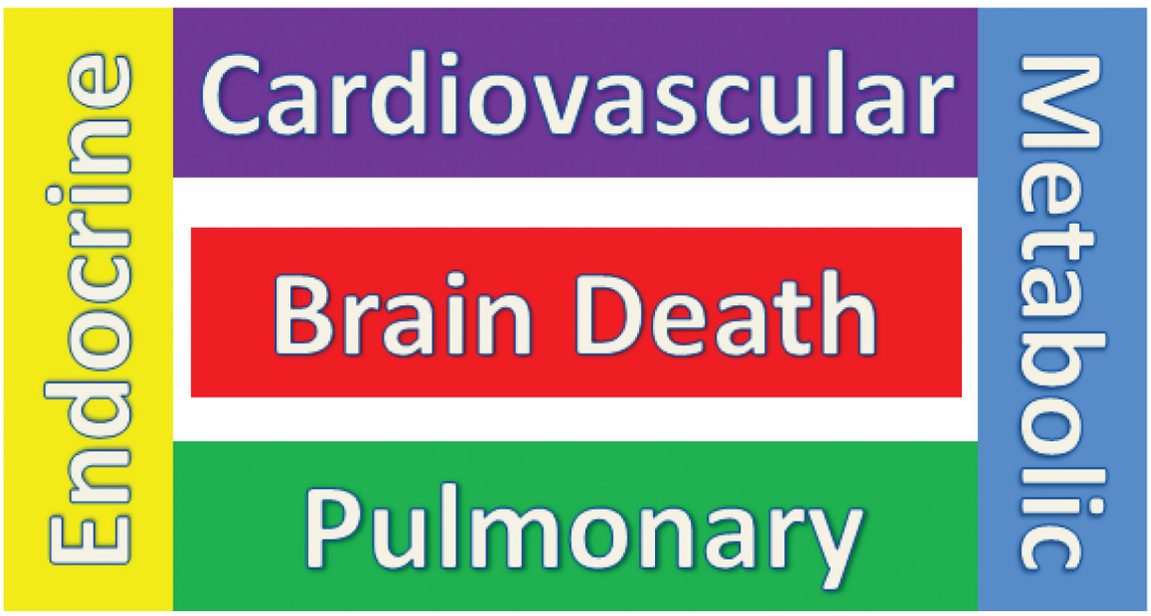

Figure 3. A diagram showing the most important and most commonly reported systemic manifestations following brain death. In the management of an organ donor consideration must be made to all of the above changes, including proactive approaches to normalize any deleterious physiologic disturbances.

from any injury that may pose a potential threat to end-organ viability [87, 89–91]. In order to properly monitor the various changes that may be rapidly occurring within the donor, frequent laboratory assessments and advanced cardiopulmonary monitoring are recommended [7, 57, 62, 92]. Correcting electrolyte and metabolic abnormalities can increase viability of donated organs according to an observational study conducted by UNOS [92]. Another important UNOS report stated that by setting certain parameters or goals for managing donors during the period leading up to organ procurement, care teams were able to augment the number of viable organs from each donor [83]. Among endpoints that increased likelihood of organ viability were maintenance of central venous pressure as well as PaO_2:FiO_2 ratio, optimization of cardiac ejection fraction and normalization of serum sodium and creatinine [83]. Thyroid hormone levels are another important element to closely monitor and correct during organ optimization. Exogenous thyroid hormone is routinely administered along with methylprednisolone and insulin to maximize organ donor viability [62, 83, 92]. Among more progressive developments, the use of extracorporeal membrane oxygenation has been proposed as a method for expanding the donor pool after cardiac death [93]. However, this approach may be prohibitive from a financial standpoint.

11. Conclusion

In summary, the field of transplantation has made significant strides throughout the years. Following its humble beginnings as an experimental science, it evolved into the primary therapeutic option for patients suffering from end-stage-organ failure. Modern transplantation offers hope to those who even a few decades ago would have none. Going hand-in-hand with that hope are the ethical and legal ramifications related to the donor and their families. With the demand for organs far exceeding the current availability, a better framework is needed for both maximizing the procurement of organs from eligible donors and better allocation of these gifts-of-life across patients on transplant waiting lists. Closer examination of all available organ donation avenues is warranted, including the assessment of opportunities offered by the use of expanded criteria donors and greater utilization of donation after cardiac death.

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