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Intensive Care Management of Post-Transplant Patients

A Guide for Critical Care Specialists

(General)

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Volume 1

JAYPEE

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CHAPTER 4

Optimization of Physiological Parameters in Brain-dead Patients Before Organ Donation

Suvadeep Sen, Gunadhar Padhi

INTRODUCTION

Organ donation is a critical component of modern medical practice, providing an alternative life-saving treatment, especially for individuals suffering from end-stage organ failure. The availability of healthy, well-functioning donor organs is essential and often remains challenging for successful transplantation procedures and improving patient outcomes. Despite its significance, there remains a substantial gap between the demand for donor organs and their availability, highlighting the importance of increasing awareness and registration rates. In 2022, approximately 157,494 organ transplants were conducted worldwide, with kidney transplants being common followed by liver and heart; yet the need for organs far exceeded supply.[1] Data from the United States shows, on average, 21 patients die each day waiting for organ donation while staying on the list.[2] If we look into the Indian data from the National Organ and Tissue Transplant Organization (NOTTO), the total number of deceased donor transplantation was a mere 2,694 in the year 2022 from 941 willing brain-stem death (BSD) donors.[3]

Several organs may be harvested from a single organ donor including kidneys, hearts, livers, lungs, pancreas, and intestines. Even tissues like skin, bone, and corneas help people with burns, fractures, and other medical conditions. It is estimated as many as eight and sometimes even nine lives may be saved from one suitable BSD organ donor and the lives of up to 75 people may be improved through tissue donation.[4,5] Therefore, this raises a significant requirement of mass awareness regarding organ donation. However, the lifespan of transplanted organs varies depending on factors such as the organ type, the donor's medical history, preharvesting condition of donor organ, and the recipient's overall health. With the advancements in the medical field, organ donation has become a safe and well-regulated process. The process primarily starts with the identification of potential donors in the intensive care unit (ICU), where they are screened meticulously to ensure that their organs are healthy and suitable for transplantation. Apart from the benefit it brings by saving a recipient's life, organ donation also has a profound positive impact on families that can further forward the merits of organ donation to society.[6] Effective donor management requires a multidisciplinary approach involving critical care physicians, transplant surgeons, and other healthcare professionals. Adherence to standardized protocols and ethical guidelines is essential to preserve donor dignity and ensure successful organ transplantation. Despite the advancements in donor care, there are still areas needing improvement, such as hemodynamic management, respiratory support, endocrine regulation, and thermoregulation. This chapter aims to introduce the importance of the optimization of donor care, meanwhile highlighting the potential challenges that are faced during the intensive care of potential brain-dead organ donors.

DEFINITION, CRITERIA, AND CONFIRMATION OF BRAIN DEATH

Currently, there are two major organ donation pathways followed by transplantation units across the world: Donation after brain death (DBD) that confirms the death of the donor via neurological criteria and another is Donation after circulatory death (DCD) that follows cardiorespiratory criteria to confirm donor death. This current definition of brain death (BD) is based on the American Association of Neurology (AAN) guidelines, which were last updated in 2023, and is in synchrony with the Uniform Determination of Death Act (UDDA), which states that BD or death by neurological criteria (DNC)[7] is a state of irreversible cessation of "all functions of entire brain" including the brain stem. This is manifested by three cardinal features: (1) Coma (no response to noxious stimulation), (2) absent brainstem reflexes (absence of pupillary reflexes, corneal reflexes, and gag reflexes), and (3) absent breathing even in the presence of adequate stimulus (positive apnea testing). The important

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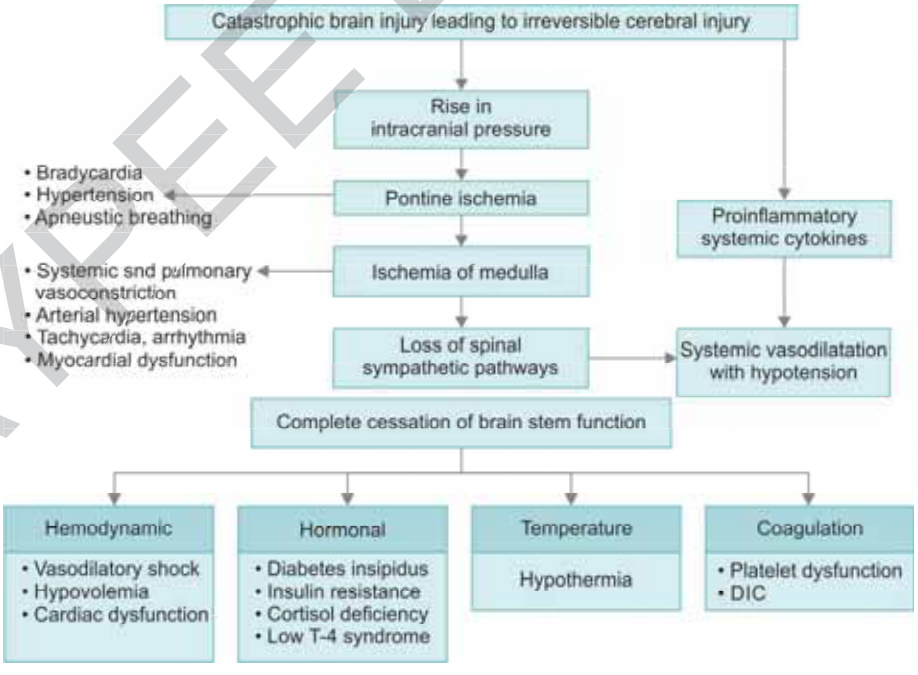
prerequisites are (1) patients must have sustained some form of catastrophic brain injury that is known to cause to BD/DNC state; (2) they should not have any confounders like hypothermia, dyselectrolytemia, sedative and muscle relaxant effect, systemic acidosis or alkalosis that can affect the result of apnea test; (3) clinicians are aware of the mimickers of brain-death state such as Guillain–Barré syndrome, snake bite, botulism, high cervical cord injuries, leptomeningeal carcinomatosis, etc.; (4) clinicians should be aware of spinally-mediated reflex causing motor response that may result in false negative brain-death testing; (5) clinicians involved in the entire process of the testing should not be the part of organ procurement and transplant team and absolute confidentiality is maintained of donor identity; and (6) two separate testings need to be conducted with an interval period of at least 6 hours by two different designated physicians to declare BD for any patient. Certain ancillary tests, such as electroencephalography (EEG) or transcranial Doppler ultrasound, may be used to further confirm the diagnosis of brain death, especially in cases where the clinical examination or apnea testing is inconclusive.

The diagnosis and confirmation of brain death have essential legal and ethical implications. In many countries, including India, the documentation of the diagnosis of BD is mandatory and requires fulfilling all the mandatory criteria and a confirmatory report from the apnea testing. Although the legal framework for organ donation and transplantation varies globally, proper consent for the removal of organs from a deceased donor is a universal mandatory requirement.[8]

ROLE OF INTENSIVE CARE IN ORGAN DONATION

Intensive care units play an essential role in the management of potential organ donors and the success of transplantation. Pathophysiology of the brain-dead condition is complex and necessitates focused understanding **(Flowchart 1)**. Intensivists are fundamentally responsible for the maintaining the physiological stability of the donor, optimizing organ function, and ensuring the successful procurement and transplantation of viable organs. The role of intensivists in the organ donation process is outlined in **Flowchart 2**. Identification of potential candidates with 'BD alert signs' is the fundamental step. Undue delay in recognition of the condition leads to more profound organ injury before harvesting and sometimes, loss of precious time due to which an organ becomes nontransplantable.

Flowchart 1: Illustrated pathophysiology of brain-death state.



(DIC: disseminated intravascular coagulation)

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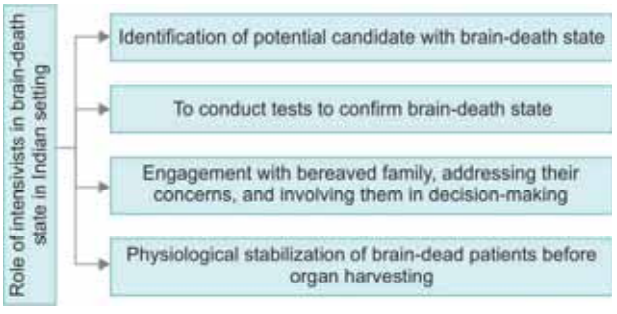
Flowchart 2: Role of an intensivist in case of brain-death condition.



Intensivists should know the standard contraindications to organ donations, where such conversation with the bereaved family is futile. In all cases, it is essential to engage with the family early preferably from the time of admission and before reaching the state of irreversibility. It is important to be part of the entire journey of the family's emotional turmoil and build a relationship of trust and confidence. Starting the talk in the midway after performing an apnea test is usually futile and often rouses suspicion and mistrust. Discussion about organ donation should be part of all end-of-life (EOL) decisions.[9] Absolute dignity and confidentiality need to be maintained to ensure donor identity, and adherence to the rules set by NOTTO is mandatory. Society of Critical Care Medicine (SCCM) guideline recommends that intensivists should notify organ procurement organizations (OPOs) and OPO coordinators as soon as a patient with nonrecoverable neurologic injury meets specified clinical triggers (like loss of brain-stem reflexes, when formal brain-death testing is contemplated), before engaging with family for discussion of organ donation.[9] Soon after the identification of the donor, intensivists aim to optimize the physiological condition with specific donor management goals (DMGs) to ensure the best possible organ function and condition at the time of organ harvesting. Intensivists must act as a bridge among various stakeholders in the process, starting from family members of the patient, donor counselors, government bodies participating in the allocation process, legal authorities, and medical professionals of the recipient institution, for smooth coordination of the entire process of organ donation.

ORGAN SUPPORT IN CASE OF BRAIN-DEATH STATE

The protocol for intensive care management of BSD patients to maximize organ procurement is based on the guidelines laid by the Indian Society of Critical Care Medicine (ISCCM),[10] the latest updated version of which was published in August 2024, and a consensus statement from the SCCM, American College of Chest Physicians (ACP), and Association of Organ Procurement Organizations.[9] It is important to note that achieving specific donor management goals requires high-quality intensive care with commitment and knowledge and a specific time frame to manage the physiological disharmony in BSD patients. The optimal maintenance duration is not known. It is found that a period of at least 18 hours needs to be provided to the intensivist for organ optimization and achieving control over autonomic storm injury.[11] Sometimes, longer time is needed for organ optimization. Cardiac function recovery takes almost 48 hours after the onset of autonomic storm.[10] However, a multicentric Brazilian study on retrospective analysis of brain-dead potential donors (BDPD) revealed that a duration of greater than 30 hours after the first clinical test of BD diagnosis was associated with a higher incidence of cardiac arrests among potential deceased donors.[12]

Hemodynamic Monitoring and Support

As brain-dead donors are prone to severe cardiovascular complications, continuous hemodynamic monitoring, including invasive arterial blood pressure, central venous pressure, and cardiac output measurements, is essential for the management of brain-dead donors. Loss of vagal tone in BSD patients and unopposed sympathetic nervous system influence leads to high circulatory catecholamines, which increase systemic arterial blood pressure, increase cardiac afterload, and leads to increased global oxygen consumption, pulmonary capillary pressure, and cardiac myocyte injury and arrhythmia. This phase is soon overwhelmed by generalized loss of vasomotor tone leading to systemic vasodilatation and consequent hypotension. Hypotension is also contributed by the hypovolemic status in these patients from osmotic or loop diuretics, and free water loss due to central diabetes insipidus (cDI). Systemic vasodilatation is aggravated by inflammatory mediators released in severe brain injury conditions.

The ultimate goal of cardiovascular management in brain-dead donors is to optimize cardiac output and ensure adequate perfusion to all organs, thereby maximizing the potential for successful organ transplantation. Goal-directed fluid therapy and the use of isotonic balanced crystalloid solutions are employed to optimize fluid management in hemodynamically unstable patients.

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Systemic hyperchloremia should be avoided in case of renal transplant.[4] Colloids like hydroxyethyl starch are generally avoided and are associated with delayed graft failure after kidney transplant.[13] A conservative fluid strategy is beneficial before harvesting lungs whereas a liberal fluid administration is usually practiced for better liver and kidney graft function in the absence of lung donation. However, a recently published cohort trial has not been found to have any adverse effect on kidney graft survival when a lung-specific restrictive fluid strategy was adopted in donor management.[14] The use of vasoactive agents, such as vasopressors and inotropes, is highly recommended. Noradrenaline is the first vasopressor of choice traditionally in vasodilatory shock. In patients with diabetes insipidus with hemodynamic instability, vasopressin should be used. The use of vasopressin instead of catecholamines as the preferred first choice is beneficial in case of cardiac donation.[15] Noradrenaline and adrenaline can theoretically cause downregulation of β receptor in donor's heart and may affect the recovery of contractility post-transplant. Dopamine may also be used as inotropic support, especially when there is a component of predominant cardiac pump dysfunction. Dopamine has an additional immunomodulatory effect and protects against ischemia–reperfusion injury. While earlier randomized controlled trials (RCTs) highlighted better renal allograft function with low-dose dopamine infusion (4 μg/kg/min) in donor,[16] subsequent RCTs with intention-to-treat (ITT) analysis have failed to prove this effect with a proper exposure–response relationship.[17] Cardiac arrhythmias and myocardial dysfunction are commonly reported challenges in brain-dead donors. Bradyarrhythmia is usually not responsive to atropine and needs to be treated with isoprenaline, adrenaline, or sometimes, temporary pacing. Cardiac arrest is a dreaded complication in brain-dead conditions that leads to low-quality organs or sometimes loss of opportunity for organ donation. The incidence of cardiac arrest varied in different literature and ranged from 3.1% to as high as 20%.[18] Loss of organs due to cardiac arrest in BSD candidates reflects overall ICU care, and protocol-based management is said to reduce the incidence of cardiac arrest. Availability and accessibility of appropriate pharmacological and electrical interventions must be ensured to manage these complications and preserve cardiac function.

Standard monitoring devices should be employed in this group of patients. The upstream and downstream markers (mixed venous oxygen saturation, arterial lactate, and base deficit) of perfusion status should be monitored periodically. Fluid responsiveness should be periodically checked either with noninvasive bedside echocardiography with left ventricular outflow tract (LVOT) velocity-time integral (VTI) parameters or invasive hemodynamic parameters such as pulse pressure variation (PPV) or stroke volume variation (SVV) that work reliably in the absence of spontaneous breathing. In patients with left ventricular (LV) dysfunction, invasive cardiac output (CO) monitors may be used to assess stroke volume and fluid responsiveness. LV systolic and diastolic function assessment should be a part of routine fluid administration protocol in ICU. Lung ultrasound, left atrial (LA) pressure estimation, and inferior vena cava (IVC) distensibility provide clues to overresuscitation and should act as endpoint of fluid administration. It is important to understand echocardiographic assessment of LV function, or ventricular wall motion may be unreliable in the presence of catecholamine storm and should be performed either early before the impending BD situation or delayed when donor is on minimal or no support of catecholamines. The consensus guideline from the International Society for Heart and Lung Transplantation (ISHLT) for heart and lung procurement suggests maintaining a mean arterial pressure (MAP) of at least 60 mm Hg, central venous pressure in a range of 6–10 mm Hg, urine output of at least 1 mL/kg/h, and left ventricular ejection fraction (LVEF) should be at least 45%.[15] Coronary angiography for donors should be performed in patients who have regional wall motion abnormalities on echocardiography or with risk factors for coronary artery disease (CAD)—such as those with hypertension, hyperlipidemia, significant smoking history, age >40 years, and drug abusers. The criteria may sometimes vary as per institutional protocol.

RESPIRATORY DYSFUNCTION AND CHALLENGES

The irreversible brain damage releases numerous inflammatory mediators that increase the vulnerability of lungs with ischemia–reperfusion injury and alveolar damage leading to increased capillary leakage and a clinical picture similar to acute respiratory distress syndrome (ARDS). Pulmonary management of potential donors should consider this and ensure lung-protective ventilation with optimal positive end-expiratory pressure (PEEP) and tidal volume management. Driving pressure should be under 15 cmH_2O. The aim should be to prevent ventilator-induced lung injury and any form of ventilator-associated

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events (VAE) and infection-related ventilator-associated complications (IVAC). During ventilation, normocarbia and normal oxygen level [partial pressure of oxygen (PaO_2) 70 mm Hg] should be maintained. Conducting an apnea test with complete disconnection of the ventilator leads to further recruitment of lung, hampering gas exchange. A multicenter RCT conducted in 12 ICUs showed that apnea testing with continuous PEEP is better than complete disconnection of the ventilator and increases the number of eligible and harvested lungs.[19] On the contrary, a high PEEP strategy sometimes retards venous return and causes hepatic congestion, and is usually avoided from the perspective of liver harvesting.[4]

Existing guidelines on ICU management of potential BSD donors recommend low stretch protocol for ventilating lungs in brain-dead patients with tidal volume 6 mL/kg predicted body weight, plateau pressure <30 cmH_2O, and recruitment maneuvers.[9] PaO_2/fraction of inspired oxygen (FiO_2) ratio is monitored routinely to assess native lung function. A PaO_2/FiO_2 ratio >300 with a clear lung field indicates lungs are suitable for transplantation.

In addition to this, regular bronchial toileting, chest physiotherapy, and change in position are required for clearance of secretions and to prevent superadded infection in the lungs.

Bronchoscopy is performed routinely before lung transplant for evaluation of the tracheobronchial tree, and bronchoalveolar lavage samples are sent for Gram stain and other microbiological assessment before harvesting.

The general tendency is to keep lungs as dry as possible before procurement of lungs from a BSD donor.[15]

Use of Adjunctive Respiratory Therapies

In case of severe respiratory dysfunctions, adjunctive respiratory therapies, such as prone positioning, extracorporeal membrane oxygenation (ECMO), and the use of surfactant, may be considered to support organ function and prevent any damage to the organs.[20] Multiple case reports have been published in the last decade, where venovenous (VV) and venoarterial (VA)-ECMO were initiated to provide respiratory or cardiovascular support to a potential BSD organ donor, which led to successful organ retrieval. Performance of apnea tests in patients supported with VA-ECMO is challenging. This issue has been addressed systemically in the latest ISCCM position statement.[10]

Endocrine and Metabolic Dysregulation

Brain-death situation is associated with ischemic injury to the hypothalamic–pituitary axis. This leads to deficiency of antidiuretic hormone (ADH) causing cDI and consequent hypernatremia in almost 80% of patients.[21] Thyroid and cortisol deficiency also sets in a variable number of patients which further jeopardizes the hemodynamic control and temperature regulation in the body. Several preclinical and clinical studies have shown that hormone replacement therapy (HRT) in potential BD donors can enhance hemodynamic stability, improve organ function, and increase the chances of successful organ retrieval. The recently published ISCCM position statement supports hormonal replacement with thyroxine (T4) and methylprednisolone for hemodynamically unstable patients who are adequately fluid resuscitated and are on vasopressor support.[10]

Doses of all medications included in HRT have been tabulated in **Table 1**.

Thyroid hormone supplementation is a routine practice in cadaver management. This recommendation is supported by a large retrospective analysis performed on the data of 63,593 brain-dead potential organ donors published in 2014.[22] This observational study showed that thyroid hormone supplementation in the specific patient group helps attain a significantly greater number of organ (heart, lungs, kidney, intestine, and pancreas) procurement and improves post-transplant graft survival. However, the subsequent RCT in a smaller patient population has not shown a proven benefit in terms of organ procurement following administration of intravenous levothyroxine in cadaver donors.[23] It is important to know in this context that the thyroid dysfunction in the BD state is more a result of sick-euthyroid state than the state of central hypopituitarism. Because the anterior pituitary retains its blood supply from the internal carotid, and residual pituitary function remains normal in most BD patients, this group of patients develop a low triiodothyronine (T3) state due to peripheral conversion of T4 into reverse T3. Hence, routine supplementation of thyroid hormone may not have practical benefits but may be considered in selected DBD patients who have severe myocardial depression.[24] The SCCM guideline.[9] suggests thyroid hormone supplementation in hemodynamically unstable donors.

Replacement of corticosteroids is also a routine consideration in ICU for DBD patients. This has two major

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TABLE 1: Dosage of drugs in HRT in BSD condition.

Thyroxin	• *T4:* 20 µg IV bolus followed by infusions of 10 µg/h (preferred) • *T3:* 4 µg bolus followed by an infusion of 3 µg/h • Thyroxine (T4) 300–400 µg through the nasogastric route (ISCCM 2024)
Steroid	• Methylprednisolone 15 mg/kg or 1,000 mg IV immediately after diagnosis of BD and every 24 hours thereafter (ISCCM 2024) • Methylprednisolone 250 mg IV followed by 100 mg/h till the organ retrieval (SCCM 2015) • *Hydrocortisone:* 300 mg IV/D or 50 mg IV bolus followed by infusion 10 mg/h[27]
AVP	• *Hemodynamically stable patients:* Desmopressin initial dose of 1–4 µg IV followed by 1–2 µg IV every 6 hours • *Hemodynamically unstable:* – Vasopressin 1 U bolus followed by infusion of 0.5–4.0 U/h (ISCCM 2024) – Vasopressin infusion 0.03–0.04 IU/min; higher doses up to 0.067 IU/min can be tried with caution (SCCM 2015)
Insulin	Insulin infusion to maintain blood glucose between 80 and 150 mg

(AVP: arginine vasopressin; BD: brain death; BSD: brain-stem death; HRT: hormone replacement therapy; IV: intravenous; ISCCM: Indian Society of Critical Care Medicine; SCCM: Society of Critical Care Medicine)

theoretical benefits; firstly, it reduces the inflammatory cascade in the setting of acute brain injury, which negatively affects hemodynamic status in prospective BD donors and also the graft function of recipient post-transplant, and second, counteracts the relative cortisol deficiency in the presence of deranged hypothalamic–pituitary axis in brain death state. However, as stated previously, central adrenal deficiency is not universally common in DBD patients, and they are not associated with low cortisol levels in a majority of cases. In a prospective multicenter CORTICOME study,[24] on 259 DBD patients, low-dose corticosteroid was found to be associated with better hemodynamic control, but no observed benefit on post-transplant graft function was observed. The SCCM guideline suggests using high-dose intravenous (IV) methylprednisolone 1,000 mg (or 15 mg/kg or 250 mg IV bolus followed by infusion at 100 mg/h), at the diagnosis of BD state. The choice of corticosteroid and its dosing guideline is mainly to counteract the inflammatory mediator-related organ dysfunction and systemic vasodilatation in the BD state and to improve the outcome of harvested

BOX 1: Causes of polyuria encountered in a patient with brain-stem death.

- Central diabetes insipidus
- Osmotic diuresis from hyperglycemia and inadequate sugar control
- Osmotic diuretics such as mannitol administration
- Administration of loop diuretics
- Physiological diuresis
- Hypothermia-induced diuresis
- Combination of any of the above

organ in potential recipient. There are a few RCTs where downregulation of inflammatory signaling pathways with high-dose corticosteroids helps achieve better hemodynamic control[25] and was found to be associated with improved graft function postkidney transplant.[26] Earlier studies also reported a beneficial effect of steroid administration in donors on post-transplant graft function in liver, lung, and heart transplantation. However, most of the studies published recently on this aspect did not reveal any benefit in terms of recipient outcome and graft function. The major disadvantages of high-dose steroids are insulin resistance with hyperglycemia and increased probability of infection both of which negatively impact post-transplant graft function. In the absence of large RCTs in this section, the current use of steroids should be reserved for hemodynamically unstable patients only and should be administered after taking samples for tissue typing.[27]

Central diabetes mellitus (cDI) occurs in 46–86% of BD patients[20] and results in polyuria and hypernatremia. Excessive volume loss may aggravate hypovolemia potentiating hemodynamic instability, whereas hypernatremia (serum sodium ≥155 mmol/L) has been associated with poor graft function postharvesting in case of liver transplantation. Early diagnosis is important, and it is important to distinguish the different causes of polyuria in BD state **(Box 1)**. The standard criteria for diagnosis of cDI (urine output >3–4 L/day, serum sodium concentration >145 mmol/L, serum osmolality >305 mOsm/kg of H_2O, urine osmolality <200 mOsm/kg of H_2O or specific gravity <1.005) should be used. Prevention of control of rise in sodium reflects overall ICU care and vigilance in the management of such types of patients. The treatment is IV desmopressin (1-deamino-8-d-arginine vasopressin), which is a selective V2 receptor agonist. This should be continued till urine volume and plasma sodium level come under control. Administration of hypotonic solution like 5% dextrose is sometimes warranted, but this

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increases the risk of hyperglycemia and systemic third spacing as the tonicity of such solution is zero. If the patient is hemodynamically unstable, vasopressin infusion is preferred as it works on both V1 (vasopressor effect) and V2 (antidiuretic effect) receptors. Both desmopressin and vasopressin may be administered in hemodynamically unstable patients with severe hypernatremia. Patients with diabetes insipidus and polyuria may lose electrolytes through urine, which can result in hypokalemia, hypophosphatemia, and hypomagnesemia, so regular monitoring and supplementation are essential.

Glycemic control is important in the case of potential organ transplantation. Insulin resistance is common in this group of patients. High blood sugar in BD patients leads to osmotic diuresis with resulting hypovolemia and electrolyte loss and increases risk of infection. Retrospective analysis has been found to negatively impact allograft function in kidney and pancreas transplantation[27] in the presence of hyperglycemia. The United Network for Organ Sharing (UNOS) and SCCM recommend keeping target blood sugar in BD donors <180 mg/dL[9] and the ISSCM position statement[10] recommends blood sugar level to be maintained between 80 and 150 mg/dL.

TEMPERATURE MANAGEMENT

Hypothermia is common in patients with a BD state and happens in almost all such patients.[10] This happens due to loss of hypothalamic control, increased loss of body heat in vasoplegic state, decline in metabolic rate, and absence of muscle activity. Hypothermia may induce cardiac arrhythmia, immune dysregulation, disruption of coagulation cascade, and disseminated intravascular coagulation DIC and potentiate organ dysfunction. Maintaining core body temperature at ≥36°C is an important absolute prerequisite before initiation of apnea test.[7] A decade ago, an RCT was published showing the effect of permissive hypothermia after the declaration of brain-dead state improved early graft function in kidney transplant recipients.[28] However, this is not a widely practiced approach and maintaining normothermia is the standard of care as per existing guidelines. The use of thermal blankets to prevent heat loss, forced-air warming devices, and systemic administration of warm IV solutions are commonly used measures. In addition to that, there must be proper infrastructure that carefully monitors and adjusts the environmental factors, such as ambient temperature, humidity, and air circulation. The ISSCM position statement recommends maintaining a core body temperature above 35°C.

Other Ancillary Intensive Care Unit Management

The general FAST-HUG-BID approach should be applied for routine care in all BSD patients. All patients should be given care in propped-up position 30–45°. Routine nursing care, with regular changes of position to prevent pressure ulcers, eye care to prevent corneal ulcers, skin care, change of dressing at regular intervals, stress ulcer prophylaxis, and mechanical or pharmacological prophylaxis to prevent deep vein thrombosis should be at per any standard ICU care.

Nutrition

Standard nutritional recommendations should apply in BSD patients, and it is recommended to continue enteral nutrition till organ harvesting.

Infection Control

The prevalence of donor-derived disease transmission to transplant recipients is historically shown to be <1%,[29] but it adversely affects post-transplant graft and patient outcomes. All BSD patients are routinely screened for infection before elective organ harvesting. It is important to have a thorough history of their medical and social history including history of travel, sexual exposure, IV drug abuse, past infection, and blood transfusion. Care of invasive lines and tubes is extremely important to prevent device-related nosocomial infection. The risk of hospital-acquired infection increases with length of ICU stay, antibiotics exposure, and number of device days. Bacteremia is not a contraindication of organ harvesting as long as the donor has received sensitive antibiotics for at least 48 hours. All potential donors should be sought for clinical and radiological +/– microbiological evidence of active tuberculosis. Routine screening for hepatitis B, C, and human immunodeficiency virus (HIV) with nucleic acid test (NAT) testing is recommended. With a history of travel, screening for severe acute respiratory syndrome–coronavirus 2019 (SARS–COVID-19) virus infection, ZIKA virus, and yellow fever virus is recommended if there is a history of travel from a particular endemic region. Cytomegalovirus (CMV) and Epstein–Barr Virus (EBV) serological status determination is important for both donor and recipient.

A bundle care approach is important to prevent hospital-acquired infections. Standard hand hygiene protocol needs to be maintained. Sterile precautions need to be maintained while handling urinary and intravascular

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catheters. Although routine antibiotics are not recommended, strong clinical suspicion of identification of sepsis and its source is needed in all patients in ICU staying for >48 hours.

TRANSFUSION PROTOCOL

Standard ICU guideline is followed in terms of transfusion triggers and protocols. In the absence of standardized RCTs, it is suggested to adhere to the transfusion threshold of 7 g/dL as per the practice in other critical patients in the ICU.[9] However, the current ISCCM guideline[10] still suggests packed red blood cell (PRBC) transfusion if the hematocrit level is <30%. A recently published retrospective analysis of 20,294 lung transplant recipients has shown that multiple PRBC transfusions in donors may adversely affect graft function and 90-day mortality in the postoperative period.[30]

While good clinical evidence is lacking, existing literature[27] suggests maintaining normal coagulation status in brain-dead patients with International Normalized Ratio (INR) <1.5 and platelet count >50,000/mm^3. Organ retrieval should be expedited in case of worsening coagulopathy.[10]

It is reasonable to continue low-molecular-weight heparin (LMWH) as deep vein thrombosis (DVT) prophylaxis in all patients with BSD in the absence of specific contraindications.

The specific consideration concerning particular organ donation has been mentioned in **Table 2**.

TABLE 2: Organ-specific management in BSD patients.

Lung donation	• Restrictive fluid strategy • PEEP optimization with a "open lung" strategy and low-stretch ventilation protocols • Recruitment maneuvers after any disconnection from the ventilator • Preassessment with bronchoscopy as routine evaluation • Use of CPAP during apnea testing to prevent derecruitment • Closed circuit for airway suctioning • Avoid barotrauma and volutrauma • Regular monitoring of PaO_2/FiO_2 ratio
Cardiac donation	• Use of vasopressin instead of norepinephrine and epinephrine to prevent downregulation of β receptors in donor management • HRT for potential cardiac donor with evidence of left ventricular dysfunction (SCCM 2015) • Serial echocardiography for cardiac assessment, to check for reversibility and preferably, after weaning off of catecholamine support in donor • Transesophageal echocardiography (TEE) provides better image than transthoracic echocardiography • Coronary angiography in specific population
Liver donation	• Keep serum sodium <150 mEq/L • A little liberal fluid strategy for better graft function but avoid volume overload • Hemodynamic management to maintain MAP 60–70 mm Hg in potential donor to avoid ischemic injury • Avoid hypotension and ischemic insult to donor liver • Avoid high PEEP to prevent hepatic venous congestion
Kidney donation	• Euvolemia and restrictive strategy are usually not advocated in isolated kidney donation • Avoid nephrotoxic medication and Hydroxyethyl starch in donor • Optimize cardiac contractility to maintain renal perfusion • Avoid hyperchloremia • Use of low-dose dopamine (4 µg/kg/min)
Pancreas donation	• Avoid overzealous fluid administration to prevent pancreatic edema • Use of HRT in donors (SCCM 2015)
Small-bowel donation	• Donor with excessive vasopressor requirement or having prolonged cardiac arrest is usually avoided • Small-bowel decontamination regimen • Broad-spectrum IV antibiotics for donors as per institutional protocol • Continuation of enteral feeding to maintain gut mucosal integrity

(BSD: brain-stem death; CPAP: continuous positive airway pressure; FiO_2: fraction of inspired oxygen; HRT: hormone replacement therapy; MAP: mean arterial pressure; PaO_2: partial pressure of oxygen; PEEP: positive end-expiratory pressure)

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STANDARDIZED PROTOCOLS AND CHECKLISTS

It has been reported that a large number of potential brain-dead donors and at least 20% of the organs are lost due to the clinical negligence of the management.[31] The implementation of standardized protocols and checklists can help ensure early identification and evaluation of potential brain-death donors (PBDD), comprehensive goal-directed organ support to optimize their function in the setting of physiological disharmony, improved communication with the entire team to smoothen the process of donation, analysis of data to identify the knowledge gaps, and subsequent process building to improve overall outcomes of organ transplantation. Adherence to a bedside checklist in donor management has been found to decrease the reduction of odds of cardiac arrest episodes and increase the supply of organs suitable for transplant.[32]

ETHICAL CONSIDERATIONS AND FAMILY COMMUNICATION

One of the essential and mandatory aspects of the whole organ donation landscape is compliance with the ethical guidelines. This compliance is what differentiates it from the crime of organ trafficking. Ethical considerations, which include informed consent, the preservation of donor dignity, and effective communication with the family of the donor, are crucial aspects of the intensive care management of brain-dead donors.

DOCUMENTATION AND LEGAL REQUIREMENTS

In addition to the consent formalities, meticulous documentation of the clinical course of donor, management, and the fulfillment of legal requirements are essential for the successful procurement, record maintenance, and are one of the prerequisites during transplantation of donor organs.

CONCLUSION

The care for potential organ donors in the ICU necessitates a holistic and compassionate approach that prioritizes the well-being of the patient, and their family, and the coordination among the several healthcare and administration teams. This is a complex process that necessitates intensive training with experience, dedication, and a thorough plan and team management. Various complications are associated with BD, as a condition may lead to a cascade of neurological and systemic pathophysiological changes. Effective management of brain-dead donors leads to increased organ availability, better graft function, and enhanced long-term survival for transplant recipients. Suboptimal and unstandardized management of BD patients often results in lower organ quality and increases the risk of losing donors often due to cardiac arrest. Following proper checklist-based intensive care protocols, a multidisciplinary team approach, and adherence to ethical and legal requirements are essential for optimizing donor management and improving recipient outcomes.

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