GUIDELINES

Management of Potential Organ Donor: Indian Society of Critical Care Medicine—Position Statement

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Abstract

This position statement is documented based on the input from all contributing coauthors from the Indian Society of Critical Care Medicine (ISCCM), following a comprehensive literature review and summary of current scientific evidence. Its objective is to provide the standard perspective for the management of potential organ/tissue donors after brain death (BD) in adults only, regardless of the availability of technology. This document should only be used for guidance only and is not a substitute for proper clinical decision making in particular circumstances of any case. Endorsement by the ISCCM does not imply that the statements given in the document are applicable in all or in a particular case; however, they may provide guidance for the users thus facilitating maximum organ availability from brain-dead patients. Thus, the care of potential brain-dead organ donors is "caring for multiple recipients."

Keywords: Apnea test, Ancillary tests, Brainstem death, Extended organ donation criteria, Hurdles for organ donation in India, Infusion and pumping, Pharmacological treatment approach in management of organ donation, Ventilation.

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Introduction

As per the Indian Society of Organ Transplant (ISOT), out of 3.17 lakh people waiting for organs (such as the liver, kidney, heart, lung, and pancreas) only 3.25% received them in the year 2020.[1] According to the figures on the Global Observatory of Donation and Transplant (GODT) website from India, the total number of organs donated from deceased donors in 2022 was 941 [0.67 per million population (pmp)], which is lower than southeast Asian regional average of 0.76 pmp and much lower than the global average of 8.67 pmp.[2] Actions taken by the Government, under the National Organ and Tissue Transplant Program (NOTP), the formation of the National Organ and Tissue Transplant Organization (NOTTO), and non-governmental organizations (NGOs) have led to an increase in the number of total organ transplants from 4,990 in 2013 to 16,041 in 2022. Despite these rising numbers of transplants per year, proportions from deceased donor organs, 17% (837 of 4,990) in 2013 and 16.7% (2,694 of 16,041) in 2022 have remained static.[3]

Demand for transplants is increasing due to many reasons. This includes (A) rising population and longevity, (B) burden of disease requiring transplants, (C) removal of upper age limit to register as the recipient on the waiting list, (D) increased number of transplant centers, and (E) ease of registration in statewide recipient waiting list (no fixed age limit, no domicile certificate is required, and no fee for registration is required). National Organ and Tissue Transplant Organization and ISOT have started national recipient waiting lists and transplant registries, respectively.[3,4] As per one approximate estimate, the gap between actual transplants and demand in 2022 was huge, that is, total transplants 16,041 vs demand 3,17,000; kidney 11,705 vs 1,75,000, liver 3,911 vs 80,000, and heart 243 vs 10,000.[5]

On the background of increasing organ demand, compared to the number of organs available for transplantation, the

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responsibility to care for each potential donor increases.[6] Optimal management of potential organ donors is done with the intention that maximum organs can be procured from the donor and graft functions improve after transplantation. Thus, a multidisciplinary team approach is necessary for successful organ donation.[7] It is necessary to understand the physiology of brain death (BD) so that necessary measures can be initiated at steps where organ damage can occur. Often, elderly and borderline/marginal donors are also potential donor candidates and such cases need to be managed carefully, to improve the conversion rate, quality of organs, and graft survival after donation.[6]

The healthcare system needs to look into the feasibilities of expanding the donor pool by the use of modern methodologies such as Domino liver transplantation, split grafting, extracorporeal cardiopulmonary resuscitation (E-CPR), or organ preserving cardiopulmonary resuscitation (OP-CPR) hypothermic oxygenated perfusion (HOPE) and normothermic regional perfusion (nRP) and increase donation after circulatory death (DCD).[8–10] However, in the zeal to increase the number of organs, we must not overlook "the dead donor rule" as quoted by Robert in the New England Journal of Medicine (NEJM) in 2013, which states "patients may become donors only after death, and the recovery of organs must not cause a donor's death."[11,12] Furthermore, the safety of recipients must be at the center stage by avoidance of transfer of infection or cancer from transplanted organs.

Role of Intensivist

Recommendation 1

- The ISCCM recommends that trained critical care personnel be involved in the management of potential organ donors.
- The ISCCM recommends for early identification, assessment and maintenance of potential organ donors.
- The ISCCM recommends that an intensivist play vital role in evaluating the deceased donor.

Justification

An intensivist is a specialist who has specific training, certification, and experience in managing critically ill patients in an intensive care unit (ICU) or has extensive experience in intensive care in India after a Bachelor of Medicine and Bachelor of Surgery (MBBS), quantified as at least 3 years' experience in ICU (at least 50% time spent in the ICU). Most of the potential donors are critical and thus are admitted to critical care units. A time comes when the healthcare team realizes that the medical care to patient is futile in terms of saving the life of the patient. This timing is very crucial. It should be picked up, and hemodynamic instability should be prevented, thereby preserving organ perfusion and maintaining the quality of organs, in case the relatives or surrogate decision makers opt for organ donation. Thus, the healthcare team can save the lives of patients on the waiting list for organ transplantation, by early recognition of a potential donor. The critical care team can thus not only preserve the opportunity for organ donation for the family but also improve the quality of organs if the next of kin opts for organ donation. Thus, the intensivist helps in providing the "gift of life" to many recipients on the waiting list. Intensivists play a vital role in the following ways:

- Early recognition of potential donor: Critically ill patients with low Glasgow Coma Scale (GCS <4) due to head trauma, stroke (ischemic and bleeding), or loss of blood flow to the brain after cardiac arrest are usually admitted to critical units. Hence, early recognition of BD alert signs (loss of one or more cranial nerve reflexes; GCS <4 that is not explained by sedation) is important so that we do not lose any potential donor—the main responsibility of the intensivist.
- Preserving and optimizing organ function: The physiological changes that follow BD are not uniform. The severity and occurrence of dysfunctions after BD are related to the etiology and time course of brainstem death. Thus, the intensivist along with the organ procuring team provides medical care to potential organ donors and thus helps in improving rates of graft survival, that is, the quality of organ donation when done[7,13,14] (Table 1).
- Evaluation of deceased donor (please refer points under recommendation 13): Although we want potential donors to be multiorgan donors, our main aim while evaluating deceased donors is to minimize the risks of transmission of infection and malignancy. The suggested list of investigation are included under recommendation 13.

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Table 1: Role of intensivist in the care of the potential brain-dead patient

1.	Early pickup of brainstem death alert signs/recognize potential organ donor.
2.	Maintaining hemodynamic stability to improve the organ quality.
3.	Diagnosing and certification of neurological death.
4.	Preparing the family for devastating news.
5.	Counselling family for end-of-life (EOL).
6.	Implementing policies and protocols for the option of organ donation.
7.	Communication with the transplant coordinator, organ procurement team, and family members.
8.	Handover protocol to the organ procurement team.

Potential Organ Donor and Brain Death

A potential organ donor is defined by the presence of either BD or a catastrophic injury to the brain which could progress beyond reversibility and may fulfill BD criteria.[15]

Diagnosing Brain Stem Death in Patients

Recommendation 2

The ISCCM recommends that for the declaration of brain stem death, there should be a potential irreversible cause of catastrophic brain injury (supported radiologically), confounding factors be ruled out and precondition criteria strictly checked.

Justification

According to the Transplantation of Human Organ Act (THOA; Central Act 42 of 1994), the definition of death is defined as follows:[16]

"Deceased person" means a person in whom permanent disappearance of all evidence of life has occurred:

- By the reason of supported by brainstem death or by cardiopulmonary arrest.
- In a cardiopulmonary sense at any time after live birth has taken place.

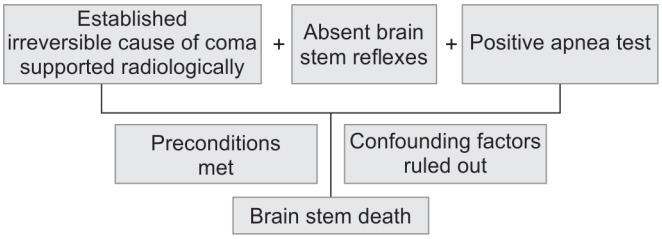


Fig. 1: Prerequisites for brainstem death diagnosis

"Brainstem death" means the stage at which all functions of the brainstem have permanently and irreversibly ceased. However, the cause of irreversible coma has to be established, preconditions should be met, and confounding factors are to be ruled out (Fig. 1).[15,17,18] Preconditions include core temperature ≥34°C (Canadian guidelines recommend 32.2°C while American guidelines recommend above 36.0°C) metabolic parameters within acceptable range (sodium, potassium, blood sugars, and acid–base status); no endocrine disturbance; and drug intoxication ruled out.[18]

Brain death is commonly caused by the following:[19,20]

- Spontaneous intracranial hemorrhage.
- Head injury due to motor vehicle accidents, recreational and industrial accidents, gunshot assault, etc.
- Cerebral anoxia/ischemic injury (cardiac arrest due to asthma, asphyxiation, drug overdose, hanging, drowning, meningitis, carbon monoxide poisoning, or primary cardiac arrest).
- Primary cerebral tumor.

India follows the UK concept of brainstem death, and the THOA was passed by the Indian Parliament in 1994 which legalized brainstem death.[21] In 1995, THO rules were laid down which describe the BD certification procedure.

Recommendation 3

The ISCCM describes the National Organ and Tissue Transplant Organization (NOTTO), State Organ and Tissue Transplant Organization (SOTTO), and Regional Organ and Tissue Transplant Organization (ROTTO).

Justification

Prior to the 1950s, death was conceptualized as cessation of cardiorespiratory function. This was followed naturally by cessation of brain function. In the subsequent years later, the development of advanced life support measures including cardiopulmonary resuscitation (CPR) and positive pressure ventilation (PPV) brought this interdependence and the traditional definition of death into question.

In 1959, the concept of BD was first theorized as "le coma dépassé," by Mollaret and Goulon, who described an apneic, comatose patient without brainstem reflexes or electroencephalographic (EEG) activity.[22]

In 1968, a group from Harvard Medical School proposed the first clinical definition as the Harvard Brain Death Criteria, which consisted of clinical and EEG criteria.[23]

In 1976, the Conference of Medical Royal Colleges published a statement on the diagnosis of BD, and clinical diagnostic testing for BD became more refined.

In 1980, the Uniform Determination of Death Act established a legal basis for a neurologic determination of death in the US, and adult guidelines were put forth in 1995 (revised in 2010) American Academy of Neurology (AAN) guidelines on the determination

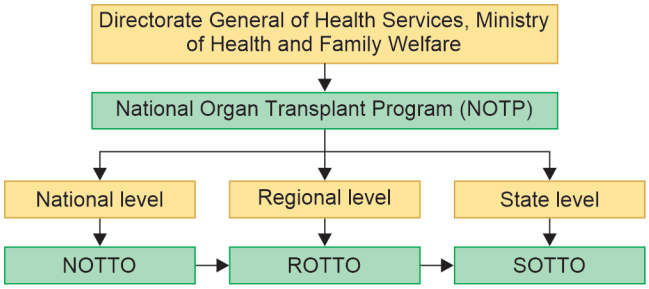


Fig. 2: Structure of National Organ Transplantation Program

NOTTO, National organ and tissue transplant organization; ROTTO, Regional organ and tissue transplant organization; SOTTO, State organ and tissue transplant organization

of BD were framed. In 1987, the American Academy of Pediatrics task force on BD in children published guidelines for the pediatric population, which was updated in 2011.[24–26]

India abides by the UK standards. The legal foundation for organ donation has been put in place in India. The transplantation of human organ act (THOA) legislation has made deceased donation a legal activity (THOA – 1994).[16,21] The THOA – 1994 was amended in 2011. The amended act is now named as Transplantation of Human Organs and Tissues Act (THOTA – 1994). The THOTA – 1994 provides for the regulation of removal, storage, and transplantation of human organs and tissues for therapeutic purposes and for the prevention of commercial dealings in human organs and tissues.

The National Organ Transplant Program (NOTP, 2010–2012) in November 2010 approved the establishment of NOTTO. The NOTP was implemented to establish a network of organ and tissue transplant organizations at national, regional, and state levels; and to link them with transplant and retrieval hospitals and tissue banks. National Organ and Tissue Transplant Organization is a national-level organization—a set up under the Directorate General of Health Services, Ministry of Health and Family Welfare which functions as an apex center for all Indian activities of coordination and networking for procurement and distribution of organs and tissues and is the Registry of Organs and Tissues Donation and Transplantation in the country (Fig. 2).

The National Organ and Tissue Transplant Organization has five regional networks (ROTTO). The SOTTO will be developed in every state and union territory. This was based on the THOTA – 2014 rules. As part of the national networking effort, every hospital in the nation involved in organ retrieval, transplantation, or both, must connect with NOTTO *via* ROTTO or SOTTO.

The THOTA – 2014 rules have many provisions to remove the impediments to organ donation while curbing misuse/misinterpretation of the rules. The National Registry of organ and tissue donors and recipients provides an efficient system for the procurement and distribution of organs and tissues from deceased donors.

The state of Maharashtra, India has passed a resolution making it mandatory to declare and certify "brain death." The government resolution underlines the responsibilities of authorized transplant centers registered under the THOA – 1994. As a large number of BDs occur in nontransplant hospitals, all hospitals in the state that have an operation theater and ICU should be registered as Nontransplant Organ Retrieval Centers (NTORCs) with the appropriate authority (Director of Health Services). These hospitals are permitted to certify brain death as per procedure and then conduct organ retrieval for therapeutic purposes but are not permitted to perform actual

transplantation. Thus, it is mandatory now for all NTORCs and authorized transplant centers in the State to certify and notify the BD cases to the Zonal Transplantation Coordination Committee. This is a strong step to streamline the procedure for cadaveric organ retrieval and transplantation.

The readers are advised to refer to the amendments and adoptions made to the act by their respective states regarding the structure of the deceased donor organ donation process.

Recommendation 4

The ISCCM recommends a thorough evaluation of potential/deceased organ donors which includes ensuring the potential cause of devastating brain injury, detailed medical history of the patient, clinical/neurological examination, and apnea test (AT).

History and clinical examination are important for the determination of brainstem death.[19,20,27]

- History taking and physical examination findings that help us to establish the etiology of brain dysfunction should be done. The determination of BD requires the identification of the proximate cause and irreversibility of coma. The evaluation of a potentially irreversible coma should be established with appropriate clinical or neuroimaging evidence.
- Exclusion of confounding factors that interfere in the clinical diagnosis of BD (Table 2).[19,20,27]
  - Shock/hypotension: Aim to have systolic blood pressure (SBP) ≥90–100 mm Hg with vasopressors, if required.
  - Hypothermia: Temperature below 32°C (core temperature); aim for core temperature between 32 and 36°C (32°C for BD declaration and 36°C for carrying out AT).
  - Drugs that are known to alter neurologic, neuromuscular function, and EEG testing: Administration of medications such as anesthetic agents, neuroparalytic drugs, methaqualone, barbiturates, benzodiazepines, high-dose bretylium, amitriptyline, and trichloroethylene should be ruled out. Consumption of alcohol should be excluded. Medication and ICU observation charts may be reviewed for drugs given. If any medication administration is documented or is doubtful it is advisable to wait for at least 5 half-lives with normal renal and liver function to exclude a drug effect. Peripheral nerve stimulator for train-of-four response (TOF) should be used to rule out muscle relaxant effect. This is particularly important when patients are referred from the periphery care center to the tertiary care center.
  - Brainstem encephalitis: Review history and imaging.
  - Guillain–Barre syndrome: Review history and imaging.
  - Encephalopathy associated with hepatic failure, uremia, and hyperosmolar coma: Review history and imaging.
  - Severe hypophosphatemia: Check phosphate levels if in doubt.
  - Neurotoxic snake envenomation: Review history.

Table 2: Confounding factors that interfere in clinical diagnosis of BD

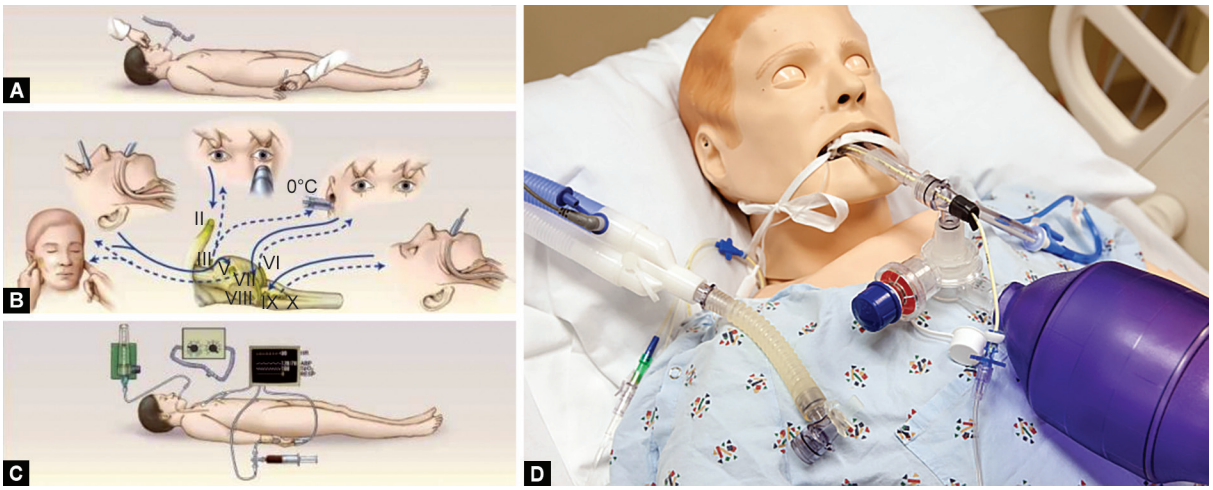
Shock/hypotension.
Hypothermia temperature below 32°C (core temperature).
Neurotoxic snake envenomation.
Brainstem encephalitis.
Guillain–Barré syndrome.
Encephalopathy.
Severe hypophosphatemia.
Drugs are known to alter neurologic, neuromuscular function, and EEG testing, such as anesthetic agents, neuroparalytic drugs, sedatives, GABA antagonists, and ethanol.

GABA, Gamma-aminobutyric acid

The performance of a complete neurological examination needs to be as follows:[28,29]

- Examination of the patient for the response to noxious stimuli, administered through a cranial nerve pathway should be carried out. Suggested sites for noxious stimuli are the supraorbital grove bilaterally and, trapezius squeeze bilaterally, the condyles at the level of the temporomandibular joints, and the sternal notch (Fig. 3A). A history of severe neuromuscular disease or facial trauma necessitates an ancillary test, as these conditions potentially mask motor responses. It is necessary to differentiate spinal- from brain-mediated movement responses. If one is in doubt, ancillary tests are required.

  In brainstem death patients, there is no response to pain.
- Absent pupillary reflex to direct and consensual light (cranial nerves II and III); pupils need not be equal or dilated. Conditions interfering with the pupillary reflex are orbital trauma, head



Figs 3A to D: Neurological examination and AT with PEEP valve

AT, apnea Test; PEEP valve, positive end expiratory pressure valve

injury, cataracts, and medications such as high-dose dopamine, glutethimide, scopolamine, atropine, bretylium, or monoamine oxidase inhibitors (Fig. 3B).

- Absent corneal reflex and oculocephalic reflex (cranial nerves V and VII) (Fig. 3C).

  Test: The corneal reflex may be altered as a result of facial weakness. A corneal reflex is performed, elicited by touching a cotton swab on a stick to the outer edge of the iris. This reflex needs to be carried carefully taking care not to damage the cornea.

  In a braindead patient, the corneal reflex is absent, and no eyelid movement is seen.
- Absent oculocephalic reflex: Head is moved horizontally on both sides and look at bilateral eye movements. Sometimes, it can also be performed by moving the head vertically.

  In patients with brainstem death, no movement of the eyes occurs relative to the head, and it is documented as an absent reflex.

  Contraindications for this test: A spinal cord injury or cervical spine instability.
- No cough, and gag reflexes (cranial nerves IX and X): Using a suction catheter or tongue depressor, stimulate the posterior pharyngeal wall bilaterally. To test a cough reflex, stimulate the trachea near the carina with the use of a deep endotracheal suction catheter (close suction catheter suction can be used) (Fig. 3B).

  In brainstem death patients, the cough reflex is absent for the stimulus.
- Absent oculovestibular reflex cold caloric test/cranial nerves VIII, III, and VI) (Fig. 3B).

  Test: The external auditory canal should be clear of cerumen, and tympanic membranes should be intact. Elevate the patient's head by 30°. Irrigate 20–50 mL of ice water into the external auditory canal and over the tympanic membrane using a soft irrigation cannula. One should look for eyeball movement for which upper eyelids need to be retracted. Allow 1-minute response time after injection/irrigation of fluid and at least 5 minutes between testing on each side.

  In brainstem death patient, no eyeball movements will be seen. Labyrinthine injury or disease, anticholinergics, anticonvulsants, tricyclic antidepressants, and some sedatives may alter the response.

Recommendation 5

- The ISCCM recommends AT is mandatory in confirming the diagnosis of brainstem death and AT should be performed only after prerequisites are met and a thorough clinical examination of brainstem reflexes is done.
- Steps for AT should be strictly followed to avoid failure and complications.
- Apnea test can be performed with an oxygen insufflation catheter, positive end-expiratory pressure (PEEP) valve, T-piece, Bains circuit, and continuous positive airway pressure (CPAP) on the ventilator.

Absent respiratory efforts in the presence of hypercarbia is the principle of AT (Table 3).[18,20,27–30]

The following prerequisites must be met before carrying out the AT:

- Core temperature ≥ 36.5°C or 97.7°F.
- Euvolemia or positive fluid balance in the previous 6 hours.
- Normal PCO_2 or arterial PCO_2 ≥ 40 mm Hg.
- Normal PO_2.
- Pulse oximeter, electrocardiogram (ECG) monitor, and blood pressure (BP) should be monitored continuously.

Following are the steps to be followed for AT (Figs 3C and 4):

Step 1: Preoxygenate the patient with 100% O_2 for 10–15 minutes (to ensure denitrogenation of lungs) and do an arterial blood gas analysis on these ventilator settings. A curtain should be used while carrying out the test (safety of patients on adjacent beds).

Step 2: Check for pulse oximeter, ECG monitor, and BP monitors.

Step 3: Patient's chest and abdomen should be exposed.

Step 4: Disconnect the ventilator.

Step 5: Deliver 4–6 L/minute of O_2 through an endotracheal tube (ETT) into the trachea using a soft catheter.

Step 6: Look closely for any respiratory movements (abdominal or chest excursions that produce adequate tidal volumes).

Table 3: Apnea test – queries about AT

1.	Prerequisites for AT.
2.	Steps for performing AT (standard, PEEP valve, CPAP, and Bains circuit).
3.	Interpretation.
4.	Complications.
5.	Observation period before performing AT.
6.	Is consent necessary for AT?
7.	Troubleshooting in AT.

Fig. 4: A PEEP valve

Step 7: After 8–10 minutes send the ABG (for every minute of apnea, $PaCO_2$ rises by approximately 3 mm Hg).

- If respiratory movements are observed, the AT result is negative (i.e., it does not support the clinical diagnosis of BD).
- Connect the ventilator if during testing:
  - The SBP becomes below 90 mm Hg (or below age-appropriate thresholds in children below 18 years of age).
  - Or the pulse oximetry indicates significant oxygen desaturation.
  - Or cardiac arrhythmias develop.

Interpretation

- If respiratory movements are absent and arterial PCO_2 is ≥60 mm Hg (or increase in $PaCO_2$ by 20 mm Hg above the baseline $PaCo_2$), the AT result is positive (i.e., it supports the diagnosis of BD).[13,15]
- If PCO_2 is below 60 mm Hg and PCO_2 increase is below 20 mm Hg over baseline, the result is indeterminate and a confirmatory test can be considered or AT can be repeated.

Following are the complications of AT:[30]

The various complications seen while performing AT are hypotension (7–9%), hypoxemia (4–6.3%), cardiac arrhythmias (from less than 1 to 1%), cardiac arrest (0–0.7%) pneumothorax, pneumomediastinum, and pneumoperitoneum (rare).

Queries about AT are listed in the following:

- **When should the AT be performed?**
  Determination of BD should be thorough and meticulous. A formal evaluation of the brainstem reflexes is undertaken before AT. After the first clinical examination, the patient should be observed for a defined period of time for clinical manifestations that are consistent with the diagnosis of BD. Most experts agree that a 6-hour observation period is sufficient and reasonable in adults and children over the age of 2 years.
- **Is consent necessary for AT?**
  Consent is not necessary for carrying out AT (though the assent of the family—informing them about the test being done—would be appreciated).
- **How many times AT should be done?**
  Apnea test should be done twice, 6 hours apart by the registered medical practitioner (RMP).

The following lists the troubleshooting during the performance of AT (Fig. 5):

- Patient's SBP ≤ 100 mm Hg: Vasopressors, inotropes, and fluid boluses need to be administered to keep the BP above the target. The AT is aborted if SBP is ≤90 mm Hg and the test needs to be repeated after stabilization.
- Oxygen saturation not maintained during apnea testing: The apnea testing is terminated if the saturation is ≤85% for more than 30 seconds. The test can be attempted with a T-piece and continuous positive airway pressure of 10 cm H_2O or more and oxygen flow of 12.0 L/minute. Reducing the PEEP to 5 cm H_2O prior to disconnection from the ventilator for apnea testing can predict the tolerance to apnea. With the help of a PEEP valve, one can give PEEP up to 25 cm H_2O (Fig. 4).

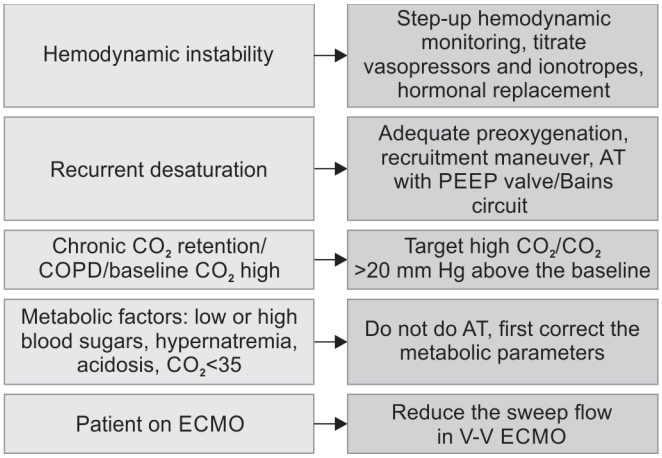


Fig. 5: Troubleshooting in AT

AT, apnea test; CO_2, carbon dioxide; COPD, chronic obstructive pulmonary disease; ECMO, extra corporeal membrane oxygenation; PEEP, positive end expiratory pressure; V-V ECMO, veno-venous ECMO

- Patient repeatedly desaturates or becomes hypotensive during apnea testing: One should consider ancillary tests for confirming BD. Ancillary tests for confirming BD such as EEG, cerebral angiography, transcranial Doppler (TCD), and scintigraphy may be considered if available. These do not replace clinical assessment and, notably, THOA in India does not mandate the use of ancillary tests (Section 1.7).[13,15]
- Baseline $PaCO_2$ ≥40 mm Hg or ≤35 mm Hg: Reducing the frequency of ventilation to allow a $PaCO_2$ in the recommended range should be considered prior to testing of apnea. Hypoventilation can be done while taking care that pH does not become acidotic. A rise of ≥20 mm Hg above baseline can be considered a positive AT in patients with elevated baseline $PaCO_2$. For $PaCO_2$ ≥40, try to increase minute ventilation (minute ventilation = tidal volume × respiratory rate), check on end-tidal CO_2 or on arterial blood gas, and then proceed to AT.
- The AT can be modified if attempts to carry out AT in a conventional manner fail; the oxygen requirement of the donor is high [PaO_2/FiO_2 ratio (PF) <150], the potential donor desaturates after disconnecting from the ventilator and has high requirements of vasoconstrictor or inotropic medications. Continuous positive airway pressure during AT can be generated in the following three ways: Directly by the ventilator; through the use of a CPAP/PEEP valve at the outflow end; and through the use of a traditional T-piece system with connection to a reservoir bag connected at one end with the distal outflow tubing immersed in water at a depth that can be adjusted depending on the target PEEP or Bains circuit.

The first approach requires the use of a ventilator that allows the disabling of rescue breaths for apnea. The 2010 American academy of neurology (AAN) guidelines and the Austrian guidelines support AT with a T-piece and CPAP (second approach) if conventional AT results in poor oxygenation. The Polish recommend the use of CPAP on a ventilator (CPAP-AT) for all brainstem death tests. The advantage of these methods is they can prevent the derecruitment of lungs, reduce the risk of

hypoxemia, and increase hemodynamic stability by preventing BP fluctuation compared to the traditional O_2 insufflation method.
- Apnea test for a patient on extracorporeal membrane oxygenator (ECMO):[31] The gas exchange for patients on ECMO occurs through the membrane oxygenator. Carbon dioxide elimination is dependent on the sweep gas flow rate. After preoxygenating by increasing the ECMO circuit FiO_2 to 100%, the patient is taken on CPAP with FiO_2 100% administered through a flow-inflating anesthesia bag connected to the ETT. The blood flow rate is left unchanged while the sweep gas flow rate is decreased.

Steps for AT for a patient on venovenous (V-V ECMO) include the following:

- Preoxygenation with 100% FiO_2 on the ventilator and 100% O_2 on the ECMO flow for at least 10 minutes.
- Reduction in the sweep gas flow to 0–1 L/minute.
- Either continue to keep the patient on the ventilator or disconnect and take on a T-piece or insert an insufflation cannula inside the ETT with oxygen flow at 6–9 L/minute or use CPAP.
- Do blood gas analysis before reducing the gas flow rate.
- Observe SpO_2 and respiratory movements.

Recommendation 6

ISCCM recommends that intensivists should be aware of compatible and incompatible observations seen in brainstem death patients.

Justification

The following lists the observations that are compatible and incompatible with brainstem death:[28,31]

Compatible

- Spinal reflexes.
- Sweating, blushing, and tachycardia.
- Normotension without pharmacologic support.
- Absence of diabetes insipidus (DI).

Incompatible

- Decerebrate or decorticate posturing.
- Extensor or flexor motor responses to painful stimuli.
- Seizures.

Reason for spinal reflexes according to one hypothesis: the reflex movements represent hypoxia- and hypercapnia-induced activity of cervical cord neurons. Alternatively, they might be due to the disinhibition of movement generators of the spinal cord. Another hypothesis is that mechanical compression/decompression of the spinal root or cervical spinal cord by neck flexion/extension can generate movement.

Recommendation 7

- The ISCCM recommends that ancillary tests are not mandatory for diagnosing brainstem death.
- The ISCCM recommends conducting ancillary tests only if a panel of doctors who are in doubt or disagreement with the diagnosis, establish a clear, irreversible cause of brain injury or if there is any contraindication to carry out clinical examination.

When the full clinical examination, including both assessments of brainstem reflexes and the AT, is conclusively performed, no additional testing is required to determine BD. Confirmatory tests such as EEG, cerebral angiography, TCD, and radionuclide scan are not mandatory.

As per the TOHA, the ancillary tests are not mentioned at all; hence, its legal acceptability is challenging. Harvard Brain Death Criteria were initially proposed, and EEG was recommended for every evaluation.[2] Listed in the following are indications for ancillary tests:

- Patients with cranial or cervical injuries, and cardiovascular instability.
- Severe facial trauma, otorrhagia/otorrhea, eye agenesis preclude the performance of clinical examination.
- A panel of doctors who are in doubt or disagreement with the diagnosis.
- Establishment of a clear, irreversible cause of brain injury.
- Exclusion of confounders and persistent coma.

Ancillary Tests

1. Digital subtraction angiography (DSA): It is considered the gold standard in ancillary testing, with a sensitivity and specificity of 100%. The contrast fails to reach intracranial circulation, thus no contrast opacification is seen in four-vessel cerebral angiography, and intact extracranial circulation is seen.[32,33] This indicates a lack of perfusion to the brain indicating BD. In procedures (EVD or craniectomy) where blood flow dynamics are affected, the interpretation of DSA, computed tomographic angiography (CTA), magnetic resonance angiography (MRA), and TCD becomes complicated (Table 4).

The main drawback of DSA is it is time consuming, and the patient needs to be transferred to an angiography suite, there will be a need for technical skills, risk of vasospasm, and contrast nephropathy.

2. Transcranial Doppler: This is an attractive ancillary test for BD as it can be done bedside, inexpensive, and has the potential for visualization of the posterior circulation. Typically, two separate examinations, both anterior and posterior, separated by at least 30 minutes are required. It involves the use of acoustic temporal bone windows for analysis of the anterior circulation but also requires evaluation of the posterior circulation.

One of the following findings is detected at least 30 minutes apart on both sides:[34,35]

- Net zero oscillatory flow with near-equal flow in opposing directions in systole and diastole.
- Small sharp systolic spikes with velocity below 50 cm/second lasting less than 200 ms in duration.
- Absent intracranial flow with preserved extracranial blood flow.

The TCD findings have high specificity for cerebral circulatory arrest and are recommended as an ancillary test and are incorporated in BD certification rules in Latin America, China, Spain, and Germany.

3. Single photon emission computed tomography (SPECT): It is a radionuclide study; SPECT involves administering a radiotracer (usually technetium 99 compounds) into the peripheral circulation, and diffusion across the blood–brain barrier, uptake into the brain, and metabolic breakdown are seen in the images.[36] Sensitivity and specificity are similar to DSA.

Limitation includes potentially inadequate visualization of the posterior fossa which could lead to false-positive results.[37]

Table 4: Recommended ancillary test

Tests	*Procedure*	*Comments*	*Limitations*
DSA	Lack of contrast opacification indicates no blood flow in intracranial vessels while extracranial flow is present	The gold standard,100% sensitivity and specificity	Expertise required, cost, transfer hemodynamically unstable patient to catheterization laboratory is difficult
Radionuclide imaging	Lipophilic or lyophobic technetium produce signals as they move intracranial(lyophobic), or pass through the blood–brain barrier and are metabolized by metabolically active parenchyma	Sensitivity and specificity similar to DSA	The patient need to be transported to the scan department lyophobic compounds inadequately demonstrate flow through the posterior fossa, hence lipophilic compounds preferred
TCD	Measures dynamic blood flow to the brain and confirms circulatory arrests (anterior and posterior circulation)	Portable, easily performed bedside 2 examinations at least 30 minutes apart	Not suggested in pediatrics, 10% of patients have poor bone window procedures affecting flow dynamics interfere in the interpretation
CTA	Peripheral injection of iodinated contrast and evaluation after 25–40 seconds Absence of intracranial flow with persistence in extracranial carotid circulation	Ease of use, speed, and wide availability	"Stasis filling" transporting patient to radiology department
EEG	Detects only cortical activity	Portable bedside	Interference by bedside monitors, TTM or sedation lack of ability to assess posterior fossa/ brainstem

4. Computed tomographic angiography/MRA and angiography (MRA).

It involves peripheral (venous) injection of iodinated contrast and evaluation of blood flow to the distal cerebral vasculature after a specified period of 25–40 seconds.[38]

The absence of flow in the intracranial circulation with preserved extracranial carotid circulation is diagnostic of BD.

5. Electroencephalography and evoked potentials (EPs).

Electroencephalography has the ability to detect electrical activity.

Limitations: It has the ability to detect only cortical activity reliably, and is unable to assess the posterior fossa/brainstem. Routine bedside monitors may cause a number of artifacts, leading to potential false negatives. Electroencephalography activity may be suppressed by targeted temperature management (TTM) or sedation, leading to false positives.[39,40]

Also, EPs are proposed complement to EEG. It evaluates the integrity of the entire pathway, from periphery to cortical output, specifically brainstem circuits. It includes visual evoked potentials (VEPs), somatosensory evoked potentials (SSEP), and/ or auditory evoked potentials (AEPs). It is helpful in patients who have undergone decompressive surgery or in patients who have undergone procedures interfering with flow dynamics.

Limitations: For interpretation, skilled personnel are required and EP studies the integrity of only the specific pathway, hence it cannot be used to assess the integrity of other pathways.

Recommendations 8

- In patients who are on ECMO support detailed clinical examination mentioned above should be carried out and while performing AT sweep flow rate (CO_2 clearance rate) should be decreased to 0.5–1 L/minute.
- In patients treated with TTM, evaluation for brain death/death by neurologic criteria [(BD/donation after neurological criteria (DNC)] not be initiated until at least 24 hours following complete rewarming.

Justification

- Brain dead declaration in a patient on ECMO: With more and more positive studies on ECMO, the use of ECMO has increased.[41–43] Thus we come across BD patients on ECMO. The cause of BD can be either the underlying disease itself or it can occur as a complication of ECMO. It can also happen that a BD patient is put on ECMO to improve oxygenation. Thus, the need of the hour is to form and develop a protocolized approach for BD patients on ECMO. Venoarterial ECMO (V-A ECMO) bypasses the pulmonary and cardiac circuits; thus, preventing the arrest of cardiopulmonary function. This makes the assessment of BD/ DNC as the primary determination of death very important. The same clinical tests are carried out as in any critically ill BD patient.

  Steps for AT are described in the section "Troubleshooting" under the AT. An important step to remember involves minimizing the sweep gas flow rate (CO_2 clearance rate) to 0–1 L/minute to prevent the exchange of CO_2 for oxygen in the membrane oxygenator.[30] In V-A ECMO, the phenomenon of "mixing" occurs due to antegrade flow residual native circulation from through the left ventricle into the aorta and retrograde flow from the arterial cannula. The distal arterial measurements may be inconsistent with those from the membrane oxygenator circuit and should be collected simultaneously to avoid inconsistencies.[27,30] The targets for pH and CO_2 levels should be the same for both sites and are recommended to be pH < 7.3, and $PaCO_2 \geq 60$ mm Hg.
- Patient treated with TTM: Hypothermia is one of the confounders for diagnosis of BD/DNC. Hypothermia leads to blunting of brainstem reflexes, decreased clearance of medications (especially if there is a concomitant hepatic or renal injury), and false-positive "electrocerebral silence" on EEG.[19,20,27] In these patients, evaluation for BD/DNC not be initiated until at least 24 hours following complete rewarming to allow for normalization of existing brainstem reflexes. For sedatives and other medications that may interfere in the examination, it is recommended to wait for at least 5 half-lives until the start of clinical testing (longer if hepatic or renal insufficiency) and to collect serum levels of sedating medications to check they are at below therapeutic[6,17] If there are queries, an ancillary test involving a blood flow study can be performed.[28,38]

Recommendations 9

- The ISCCM recommends to strictly follow THOA amendment 2011 regulations and 2014 rules laid down for certification of brainstem death.

- The ISCCM recommends that certification of the brainstem death patient/deceased organ donor be done by the registered intensivist/medical practitioner/anesthetist/neurophysician/neurosurgeon (registered by the hospital in the organ donation program.
- Clinical examination (brainstem reflexes) and AT need to be done 2 times, 6 hours apart, by two doctors who do not belong to the retrieval and transplantation teams.
- Documentation should include the patient's identification, the potential cause of brainstem death, clinical/neurological examination findings, and ATs interpretation.
- All four doctors (members of the panel of the board of medical experts) should sign tests done to document the absence of brainstem function (Table 5).

Who can certify and how many doctors are required?

Registered medical practitioners with appropriate authority should do AT and can certify brainstem death. The diagnosis of BD is established and recorded by two doctors not belonging to the retrieval and transplantation teams. Out of the two doctors, one must be a specialist in neurology. The order of examination is irrelevant, that is, it does not matter whether the neurologist performs the first or the second examination.[16,18,20,31,43]

Certification of brainstem death requires a panel of four doctors:

- The doctor in-charge of the patient.
- The doctor in-charge of the hospital where the patient was treated.
- An independent specialist of unspecified specialty (physicians, surgeons, or intensivists) nominated from the panel of names approved by the appropriate authority.
- Neurologist or neurosurgeon.

Form 10 should be filled and signed by the medical experts certifying brainstem death. Amendments in the THOA – 2011 and THAO –2014 rules have allowed the selection of a surgeon/physician and an anesthetist/intensivist, in the event of the nonavailability of a neurosurgeon/neurologist (Table 6).

How many times does the clinical examination and test need to be done and what is the interval between two tests?

Table 5: Legal aspects for certification of BD

1.	Who can certify?
2.	How many doctors required?
3.	How many times tests should be done?
4.	What needs to be included in medical record documentation?
5.	What is the observation interval between the second set of tests?
6.	Consent/willingness for organ donation (who can give?).
7.	Approach the patient of BD who is not a potential organ donor.
8.	Communication with relatives.

Clinical examination and AT need to be done 2 times after an interval of 6 hours. After the second test, the team should start counseling the family regarding organ donation. The time of death is the end of the second AT.[16,21]

For BD in children, an observation period of 24 hours for full-term newborns to 30 days, and 12 hours for infants and children (from 30 days to 18 years) is recommended. Apnea test in children involves the documentation of an arterial $PaCO_2$ of 20 mm Hg above the baseline and more than 60 mm Hg with no respiratory effort.

What needs to be included in medical record documentation?[16,21]

All phases of the determination of BD should be clearly documented in the medical record:

- Etiology and irreversibility of coma/unresponsiveness.
- Absence of motor response to pain.
- Absence of brainstem reflexes during two separate examinations separated by at least 6 hours.
- Absence of respiration with $PCO_2 \geq 60$ mm Hg (AT).
- Justification for, and result of, confirmatory tests if used.

Recommendation 10

- The ISCCM recommends communication with the next of kin be carried out in a stepwise fashion regarding the severity of the illness of the patient and the brainstem death state.
- The transplant coordinator of the hospital plays a vital role in communication and obtaining consent for organ donation along with the intensivist.
- It is necessary to inform about organ donation consent to the station house officer or superintendent of police or deputy inspector general in case of a documented medicolegal case.

Justification for communication with relatives: The medical experts registered with appropriate authority need to have a dialogue with the relatives about carrying out the tests for the determination of brainstem death. Keeping in mind the situation and the sentiments of family members the doctor responsible for breaking news should be aware of the response and feelings of the family members.

The ICU physician should communicate the confirmation of brainstem death to the transplant coordinator who in turn can communicate with the family and make a request for the organ donation. Simultaneously, the administrators of the hospital should be communicated to stop further billing once the diagnosis of brainstem death is confirmed and the family has consented to the organ donation.

Opt-in consent is practiced in India. The opt-out system is not practiced in India. The process of consent for organ and tissue donation involves the following:[16,20,21]

- The deceased wishes/willingness.
- Next of kin.
- Coroners' consent (medicolegal cases).

Table 6: The THOA amendment – 2011, and rules – 2014

1.	Allows transplantation of organs and tissues from living donors and cadavers (after cardiac or BD).
2.	Appropriate authority (AA) approves the panel of RMPs and also provides certification for transplantation and retrieval. Regulatory as well.
3.	Any hospital with ICU facilities and requisite systems can register with AA as a retrieval center.
4.	Brain Death Committee consists of four physicians: The RMP in charge of the hospital, the RMP independent specialist, the neurologist/neurosurgeon, and the physician in charge of the case.
5.	In case of the nonavailability of a neurophysician or surgeon, any AA-approved surgeon, physician, anesthetist or ICU specialist can stand in.
6.	Testing is done by one of the members to be witnessed by the others and all four sign the document.
7.	Apnea test only if other clinical tests are negative. For adults two sets of tests with an observation period of 6 hours.

Deceased wishes: The deceased wishes must be ascertained through hospital staff/relatives/donor coordinator (driving license, etc., wherein the provision for donation may be incorporated after notification of the THOA rules). It is the responsibility of the concerned physician and transplant coordinator to ascertain the existence of such documented/informally conveyed willingness to donate. In India, even if the deceased wishes are known, the next of kin needs to formally consent and sign the consent form.[16,20] Any person can document a willingness to donate in writing witnessed by two—one of whom should be a near relative.

The NOTTO Organ Donor Registry is a computerized database that records the wishes of people who have pledged for organ and tissue donation and decided that, after their death, they want to leave a legacy of life for others. There are also many hospitals and organizations maintaining a list of persons who have pledged organ donation with them, all this will be a part of the NOTTO website for the National Registry.

Next of kin consent: The transplant coordinator of the hospital should speak to the next of kin or surrogate decision makers about organ donation on behalf of the deceased.

The surrogate decision-making authority includes the spouse, son, daughter (18 years or over), parents, grandparents, and grandchildren. In the absence of the above, consent of a near relative/person in legal possession of the body is required. In case of a dispute in the family or a difference of opinion in the family, an ample amount of time should be given to the family to discuss, settle, and give a final decision.

Form 8 needs to be filled and signed to record the status of the consent by a near relative or lawful possessor of a brainstem-dead person. A copy of consent should also be sent to the designated postmortem doctor. It shall be ensured that by retrieving organs the determination of the cause of death is not jeopardized. The medical report in respect of the organs or tissues retrieved and prepared by retrieving doctors shall be taken on record in postmortem notes.

Data protection and confidentiality of recipients have to be maintained. The donor's family cannot have access to the recipient's name.

Recommendation 11

The ISCCM mandates the certification and notification of all BDs irrespective of organ donation.

Justification

The concept of BD determination preceded the advent of organ transplantation.[44] The purpose of BD/DNC determination was to avoid the futile continuation of organ support and wherever feasible, enable deceased organ donation as per the dead donor rule. This was found on scientific and ethical considerations and in the interest of professional integrity and the maintenance of public trust.[44] Physicians in India find it difficult to determine and document BD in this context, fearing misunderstandings and legal liability.[45,46] Despite the equivalence to circulatory death accepted worldwide, and in the definition of death in THOA, such apprehensions have led to futile treatments, false expectations, emotional burdens, and loss of public trust.[38] There is no viable option but to accept the professional responsibility of determining BD and continue support only if consent for organ donation is received. The Government of Kerala in India was the first state in the country to mandate the certification and notification of BD irrespective of organ donation.[46,47] Early, open, and sensitive communication of BD/DNC is mandatory to achieve ethical and appropriate decision making. Counseling for organ donation should not be initiated by the treating or the organ retrieving team but by a transplant coordinator.[44] This is to avoid any perceived conflict of interest on the part of treating physicians.

Recommendation 12

The ISCCM recommends "a critical pathway for the sequential tasks in deceased organ donation program." This is to maintain the uniformity of organ donation programs in all institutes prevent potential conflicts of interest and help to run organ donation programs with public trust.

Sequential tasks for deceased organ donation. Organ donation is a complex process involving multiple teams located in varied geography and expertise. A critical pathway is advised to avoid delay.[48] Prevention of transmission of any disease from donor to immunosuppressed recipients is an important principle in the critical pathway. To avoid legal and medical risks, we should follow all steps in sequence right from death declaration and handing over the body to next of kin to avoid legal and medical risks (Fig. 6).[49]

The patient must be medically suitable to donate organs for transplantation. Criteria for suitability change over time and vary according to recipient circumstances. Early determination of the suitability for transplantation of specific organs facilitates the development of focused medical management strategies (e.g., more aggressive fluid therapy when lung donation is contraindicated).

Recommendation 13

The ISCCM recommends that an intensivist along with procurement team members evaluate the organ donor meticulously. Perform a detailed physical examination, detailed history (past and present) and finally perform investigation (biochemistry, radiological, and organ-specific investigations such as HRCT, bronchoscopy, transesophageal echocardiography) and necessary procedures (biopsy) to evaluate the quality of the donor.

Justification

For evaluation of a donor's fitness to donate organs, one needs to have a structured approach, from focused revisit to history to specific investigations. Table 7 enlists the elements in history as well as lab work. Certain lab values need to be as latest as possible and the desirable gap from sampling time to organ procurement is mentioned in parenthesis in the table. For patients resuscitated with a large volume (>2000 mL) of crystalloid (in the last 1 hour), 2000 mL colloid, and blood products combined (within 48 hours) is at risk of diluted sample. The United States Food and Drug Administration (US FDA) preretrieval sample dilution estimation tool is one structured way for screening and calculation.[50]

Recommendation 14

The ISCCM recommends the absolute contraindications of organ donation under headings of metastasis malignancy, infections, and organ-specific end-stage disease.

Justification

Once the labs are available, the treating team must rule out absolute contraindications for Organ donation.[8,9] Table 8 enlists such contraindications for organ donation divided into the following three headings: "Malignancies," "Infections," and "Organ-specific chronic end-stage diseases."

The risk of malignancy and its transmission to recipients need consideration. Brain tumors need special mention as a breach

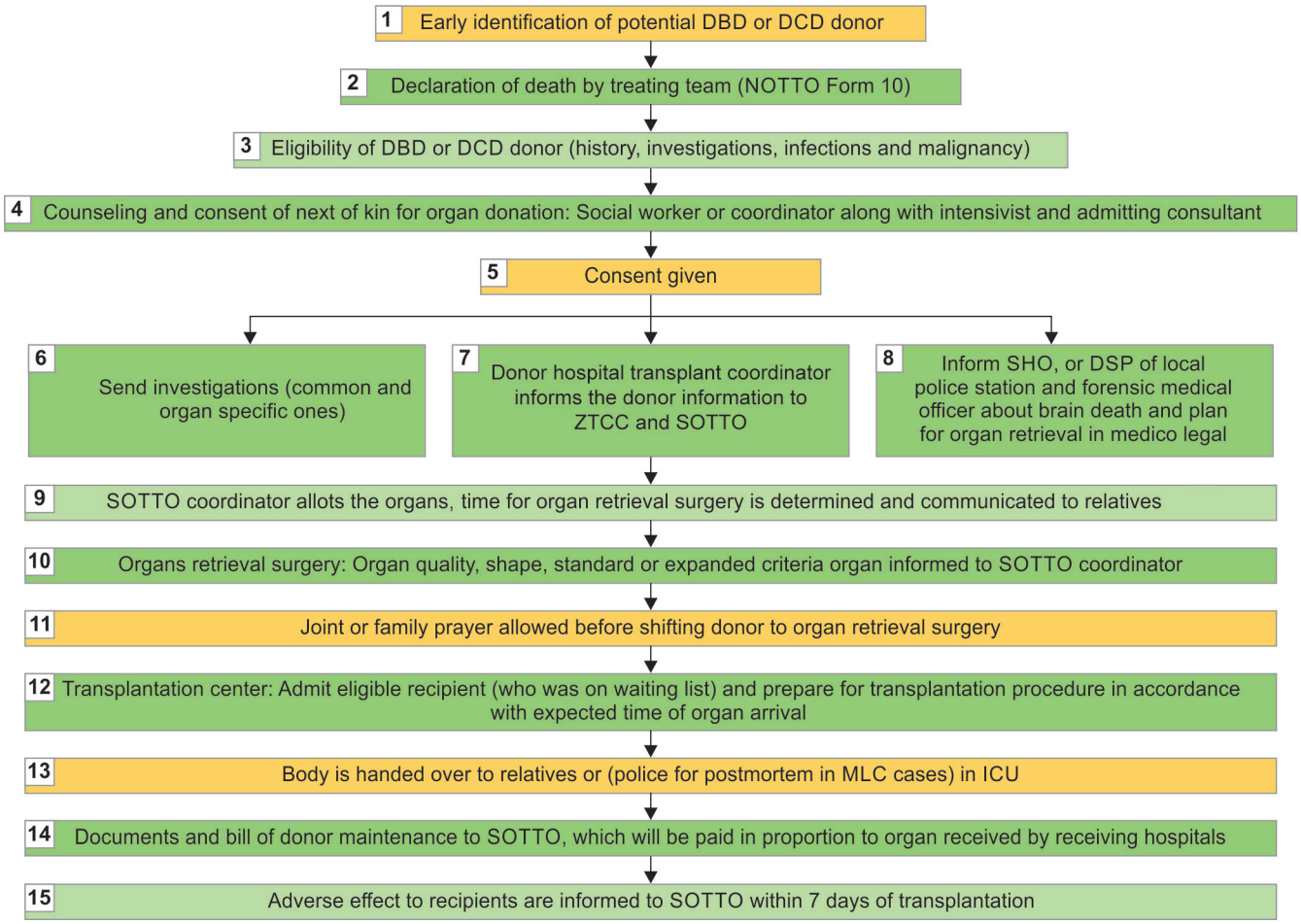


Fig. 6: Sequential steps for deceased organ donation

DSP, deputy superintendent of police; SHO, station house officer; SOTTO; state organ and tissue transplant organization; ZTCC, zonal organ transplant coordination center

Table 7: Special points in history and investigations required for preretrieval screening

Point in history before organ donation considered.	Infections in the current/recent admissions (any tropical infections such as dengue, malaria, chikungunya, and leptospira).
	Use of live vaccines (especially in pediatrics).
	Occupational exposures.
	Recent international or domestic travel history.
	Recent transfusions with blood or blood products.
	Any contact with people with HIV, HBV, HCV, or other transmissible diseases.
	Tattooing, ear piercing, or body piercing in (<6 months).
	Use of illicit drugs.
	Unsafe sexual practices.
	History of any malignancy—present or past, treated or untreated.
All donors	*Caution:* Collect undiluted blood sample (pre-resuscitation or dilution with banked blood) to avoid false negative serology (use USFDA method for dilution calculations).
	Complete blood count, electrolytes, and creatinine.
	Chest X-ray.
	ABO blood group and Rh typing, HLA typing.
	Infectious disease screen (when suspected): PSMP, dengue NS1, Salmonella PCR, Chikungunya PCR, Rickettsia PCR, tropical fever, multiplex PCR, blood, urine, and sputum culture.
	HIV1 and HIV2 antibodies, HCV antibody, HBsAG Antigen by ELISA or ECLIA (avoid rapid card test), VDRL, COVID-19 RT-PCR (follow local protocol) (<4 days).

(Contd...)

Table 7: *(Contd...)*

	NAT testing for HIV, HBsAG and HCV (in donors with high-risk sexual behavior within 30 days of organ procurement, as per USPHS 2020 Guidelines) to avoid "antibody window period of false negativity."
	Antibodies for CMV, EBV, and toxoplasma.
	A plasma and serum sample must be drawn within 24 hours of procurement and stored frozen for 10 years for detection of donor-derived infections and diseases retrospectively should they occur in the recipient.
Kidney	BUN, creatinine, urine analysis (<24 hours), urine culture, USG abdomen and pelvis, and biopsy if indicated.
	Human T-lymphotropic virus (HTLV-1) antibody (ELISA).
Liver	AST, ALT, alkaline phosphatase, total and direct bilirubin, γ-glutamyl transferase, S proteins, PT/INR, PTT, fibrinogen, TEG, and biopsy if indicated obese, HCV positive, alcoholism); USG abdomen and pelvis (LFT <12 hours).
Heart	12-lead ECG, 2D Echocardiography [With photo and video recordings on a disk] cardiac enzymes, NT pro-BNP.
	Coronary angiography if the donor age >40 or at risk of coronary artery disease.
Pancreas	Serum amylase, serum lipase, USG abdomen.
Lungs	Chest X-ray and ABG (<2–3 hours), sputum gram stain and culture, and bronchoscopy.

Caution: Collect an undiluted blood sample (preresuscitation or dilution with banked blood) to avoid false negative serology (use the USFDA method for dilution calculations), time interval in parenthesis indicates the time before retrieval of that organ. HBV, hepatitis B virus

ABG, arterial blood gas; ABO, blood grouping system; AST, aspartate aminotransferase; ALT, alanine transaminase; CMV, cytomegalovirus; DSP, deputy superintendent of police; EBV, Epstein-Barr virus; ECLIA, electro-chemiluminescent immune-assay; ECG, electrocardiogram; ELISA, enzyme linked immunoassay; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; HIV, Human immunodeficiency virus; HLA, human leucocyte antigens; INR, international normal ratio; LFT, liver function test; NOTTO, National organ and tissue transplant organization; NT pro-BNP, N-terminal pro-brain natriuretic peptide; NS1, nonstructural protein 1; PCR, polymerase chain reaction; PSMP, peripheral smear for malarial parasite; PT, prothrombin; PTT, partial thromboplastin time; RT PCR, real-time reverse transcriptase-polymerase chain reaction; SHO, Station house officer; TEG, thromboelastography; VDRL, venereal disease research laboratory; USPHS, U.S. public health service; USG, ultrasonography

Table 8: List of absolute contraindications for organ donation

1. *Malignancies: Exclude patients who are treated and free from malignancy more than 5 years*
- Metastatic malignant neoplasm.
- Acute leukemia in progress.
- Acute lymphoma.
- Melanoma with less than 5-year follow-up.
- Pulmonary microcytoma.
- Multiple myeloma in progress.

2. *Infections*
- Bacteremia not a contraindication but caution is advised.
  - Treat with appropriate antibiotics for 48 hours (wait) and 4–7 days antibiotics course in recipients of each organ.
- HIV infection (positive donor to positive recipient is in experimental stage).
- Severe systemic infections, intracellular pathogens such as Listeria and Trypanosoma.
- Untreated infection of unknown origin.
- Uncertain encephalitis of viral origin.
- Febrile meningoencephalitis of unknown origin.
- Active infection due to fungi or another opportunistic organism.
- Infection with no treatment options, like rabies or dengue within their infectious/transmissible period.

3. *Chronic end-stage diseases*
- Cirrhosis of the liver for liver donation.
- CKD for kidney donation.
- Cardiomyopathy (LVEF < 45%) or left main/triple vessel coronary artery disease for heart donation.
- Advanced COPD, ILD for lung donation.
- Pancreas: History of diabetes mellitus, history of chronic alcohol abuse (allowed for cell Islet transplant retrieval), history of pancreatitis, pseudocyst, pancreas surgery (allowed for Islet cell transplant retrieval).
- Intestine: Extensive atherosclerotic disease of aorta; SMA.

COPD, chronic obstructive disease; ILD, interstitial lung disease; LVEF, left ventricle ejection fraction; SMA, superior mesenteric artery

in blood–brain barrier by high-grade lesions of tumors, surgery, ventriculoperitoneal (VP) or ventriculoatrial (VA) shunt, systemic chemotherapy (transmission risk: 23%) and the possibility of missing a brain tumor in donors presenting as spontaneous intracerebral hemorrhage (actually tumor bleed) or misdiagnosis of brain metastasis of systemic malignancy has led to tumors in recipient in as high as 74%.[20,21,51,52] Risk categorizations for specific tumor types are narrated in Table 9.

Table 9: Classification of tumors in donors to estimate the risk of transmission to recipient (Adapted from SOTTO Maharashtra – 2021 guidelines)

Category	*Tumors*	*Recommendation*
Absolute contraindication.	• Primary cerebral lymphoma. • All secondary intracranial tumors. • Active cancer with spread outside the organ of origin. • Active hematological malignancy.	Contraindicated.
High risk (>10% risk of transmission).	• Malignant melanoma. • Breast carcinoma >stage 0 (active). • Colon carcinoma >stage 0 (active). • Choriocarcinoma. • Central nervous system (CNS) tumor (any) with VP or VA shunt, surgery (other than uncomplicated biopsy), irradiation, or extra-CNS metastasis. • CNS tumor WHO grade III or IV.	Use of these donors is discouraged except in rare and extreme circumstances.
Intermediate risk (1–10% risk of transmission).	• Breast carcinoma (stage 0, that is, carcinoma *in situ*). • Colon carcinoma (stage 0, that is, carcinoma *in situ*). • (Resected) solitary renal cell carcinoma T 1b (4–7 cm) well differentiated (Fuhrman 1–2) stage I. • History of treated non-CNS malignancy (≥5 years prior) with a probability of cure between 90 and 99%.	Use of organs from these donors is generally not recommended. It may be acceptable if the recipient's expected survival without lifesaving transplantation is short (e.g., a few days or less).
Low risk (0.1–1% risk of transmission).	• (Resected) solitary renal cell carcinoma, >1.0 cm ≤2.5 cm, well differentiated (Fuhrman 1–2). • Low-grade CNS tumor (WHO grade I or II). • Primary CNS mature teratoma. • Solitary papillary thyroid carcinoma, 0.5–2.0 cm. • Minimally invasive follicular carcinoma, thyroid, 1.0–2.0 cm. • History of treated non-CNS malignancy (≥5 years prior) with > 99% probability of cure.	Use in recipients at significant risk without transplant.
Minimal risk (<0.1% risk of transmission).	• Basal cell carcinoma, skin. • Squamous cell carcinoma, skin without metastases. • Carcinoma *in situ*, skin (nonmelanoma). • *In situ* cervical carcinoma. • *In situ* vocal cord carcinoma. • Superficial (noninvasive) papillary carcinoma of the bladder (T0N0M0 by TNM stage) (nonrenal transplant only). • Solitary papillary thyroid carcinoma, ≤0.5 cm. • Minimally invasive follicular carcinoma, thyroid, ≤ 1.0 cm. • (Resected) solitary renal cell carcinoma, ≤1.0 cm, well differentiated (Fuhrman 1–2).	Based on clinical judgment with informed consent.
No significant risk.	• Brain tumor from which malignancy is excluded by excision biopsy.	

TNM, tumor node metastasis; VA, ventriculoatrial; VP, ventriculoperitoneal shunt

Bacteremia or fungemia is not an absolute contraindication to organ donation.[53] Acute organ dysfunction, in particular acute renal injury, in a potential donor with prior renal function is not a contraindication to donation.

Recommendation 15

The ISCCM recommends standard and expanded criteria for organ donation (put forth by NOTTO). The ISCCM recommends initiating new approaches for screening and selection of donor.

Justification

Standard criteria (SCD) or expanded criteria donation (ECD): Once infections and malignancies are ruled out, the donor is deemed fit for organ donation, and consent from family member is obtained. The treating team maintains the donor in a way to maximize organ retrieval and documentation is shared with the SOTTO coordinator. To maximize the pool of organs available from such a donor, standard criteria are modified or expanded so that borderline organ conditions can be used without significant effect on the survival of the organ and recipient. This concept was introduced by Kuffman in 1997.[54] Organs (for which consent is available) are then evaluated as per elements in Table 10 to classify as Donated under the SCD or ECD for accepting organs for donation. With advances in methodology such as split liver and hypothermic mechanical perfusion methods, many organs deemed unfit for transplant are now considered usable and so the list of ECDs is getting longer. It is up to the retrieval team and informed transplant recipient, who ultimately, will decide whether to accept ECD organ or not. Furthermore, SOTTO has specific rules for listing and allotment of SCD and ECD organs which are binding by law for transplant teams as well as recipients.[8,55–60]

Table 10: Standard and expanded criteria for organ donation

Standard criteria organ donor (SCD) (routine consent from organ acceptance from recipient is enough)	*Expanded criteria donation (ECD) (additional consent taken from recipient along with consent to accept deceased organs under heading of "Organ accepted under Expanded Criteria")*
1. Kidney	
• Age <50-year, cause of death due to BD due to isolated head injury or medical condition like stroke. • Normal renal function. • No hypertension requiring treatment. • No diabetes mellitus. • No malignancy other than a primary brain tumor or treated superficial skin cancer. • No generalized viral or bacterial infection. • Acceptable urinalysis. • 7. Negative assays for syphilis, hepatitis, HIV, and human T-lymphotropic proliferative virus.	• Age <6 years. • Age >60 years with other parameters normal. • Age 50–59 years plus two of the following: 1. HT. 2. Cerebrovascular death. • Preretrieval creatinine <1.5 mg%. • Elevated creatinine (up to 3 mg/dL) is not a contraindication, especially if the creatinine level is falling and if the donor is known to have normal renal function in the recent past. (notto.gov.in/WriteReadData/Final_sop/Kidney/Kidney_Deceased_Donor_Criteria.pdf).
2. Liver	
• Macrosteatosis <30%. • Age <70 years. • Hemodynamically stable or on low-dose ionotropes. • No hypotension <60 mm Hg for >1 hr. • Transaminitis (raised AST/ALT) < 10 times ULN or < 5 times ULN and static. • Bilirubin < 5 mg/dL. • Negative blood culture within last 5 days. • Anti-HCV, HBsAg, HBcAb, HIV Negative. • Expected cold ischemia time (CIT) < 10 hours. • Last preretrieval serum sodium <160 mEq/L.	*SOTTO Maharashtra – 2021.* • Macrosteatosis >30%. • Age >70 years. • High ionotropes (single ionotrope at doses as below or 3 or more ionotropes at any doses), dopamine >15 μg/kg/minute, Noradrenaline > 0.3 μg/kg/minute. Adrenaline >0.3 μg/kg/minute, Vasopressin > 2.4 units/hour. • Transaminitis (raised AST/ALT) >10 times ULN or 5 times ULN and rising trend. • Cholestatic liver: Bilirubin >5 mg/dL. • Positive blood culture within last 5 days. • Anti-HCV, HBsAg, HBcAb, HIV positive. • Expected cold ischemia time (CIT) >10 hours. • Partial/split graft. • Last preretrieval sodium >160 mEq/L. Additional ECD points by *Sotiropoulos GC et book on Liver Transplant.* • Obesity (weight >100 kg or BMI >27 kg/m^2). • ICU stay >5 days. • Prolonged hypotensive (MAP <60 mm Hg) episodes >1 hour. • Cardiac arrest, CPR. • Cold ischemia time >12–14 hours. • Peak serum sodium >150–155 mEq/L. • Alcoholism. • Bilirubin level >2 mg/dL.
3. Heart (ISHLT, NOTP, and SOTTO – Maharashtra)	
• Hemodynamically stable with optimal ionotropic support (dopamine less than 10 μg/kg/minute; epinephrine, nor epinephrine <0.1 μg/kg/minute, dobutamine <10 μg/kg/minute). • Donor age <60 years. • No significant coronary artery disease (coronary angiography indicated for age >40 years). • No history of heart disease. • No significant structural heart disease on ECHO. • Ejection fraction >45% by ECHO. • Weight/size matching. • Cardiac arrest – donors revived after a brief cardiac arrest must be assessed extra carefully but can be considered if the cardiac function is normal.	• Age up to 65 years long-distance procurement. • Undersizing/oversizing >20% of body weight high-dose pressor requirement. • Prolonged hospitalization. • Significant but correctable valvular dysfunction by ECHO. • History of chest trauma. • Significant CAD or history of (myocardial infarction) but bypassable one- or two-vessel coronary artery disease. • Elevation of myocardial enzyme level prolonged CPR >5 minutes. • Transient hypotension. • Open cardiac massage. • Significant cardiac anomalies.

(Contd...)

Table 10: *(Contd...)*

Standard criteria organ donor (SCD) (routine consent from organ acceptance from recipient is enough)	*Expanded criteria donation (ECD) (additional consent taken from recipient along with consent to accept deceased organs under heading of "Organ accepted under Expanded Criteria")*
	• Refractory ventricular arrhythmias. • Ejection fraction <45% by ECHO. • Wall motion abnormality by echocardiography persistent conduction disturbance. • Cold ischemic time 4–5 hours.
4. Lung (NOTP and SOTTO – Maharashtra)	
• Age <55 years, ABO compatibility. • Clear chest radiogram. • PaO_2 >300 on FiO_2—1, PEEP—5 (SOTTO P/F ratio >400]. • Less than or equal to 20 pack-year smoking history. • Absence of chest trauma. • No previous surgery on the side of the harvest. • No active sepsis/malignancy in the lungs and outside. • No history of significant chronic obstructive pulmonary disease. • No aspiration or sepsis. • Absence of purulent secretions at bronchoscopy. • Sputum gram stain free of significant number of bacteria fungus and white blood cells (WBCs).	• Age >55 years healthy. • PaO_2 <140 on FiO_2—0.4 or <300 on FiO_2—1. • Smokers more than 20 pack-year. • Absence of history of lung disease. • Mild asthmatic donors. *Last moment rejections (ISHLT)* • Inability to recruit. • Unacceptable P/F ratio. • Unanticipated confirmation of primary or nonprimary malignancy. • Severe trauma not appreciated on CT. • New data on noncompatibility. • Demise of the original recipient during transit. • Withdrawal of consent from the donor's decision-maker.
5. Pancreas (SOTTO – Maharashtra)	
• Age ≤ 55 years. • BMI ≤ 28 kg/m^2. • No history of diabetes mellitus. • No history of alcohol abuse. • Donor hyperglycemia (high blood sugars) due to current acute illness (BD, dextrose infusions, steroids, CNS injury can lead to hyperglycemia in donor) may be acceptable. • HBA1C ≤7. Blood sugars, serum amylase, serum lipase, and HBA1C are required for all donors (no donor pancreas will be allocated without these tests).	
6. Intestine (SOTTO – Maharashtra)	
• Age <65 years. • BMI <30 kg/m^2.	
7. Hands (SOTTO – Maharashtra)	
• Weight/size matching. • No trauma to the limb being procured. • No neurological disease or deformities in the limb being procured. • No implant inside the limb being procured.	
Standard criteria donors (SCD) and expanded criteria donors (ECD)[7,23–27]	

AST/ALT, aspartate aminotransferase/Alanine transaminase; BD, brain death; BMI, body mass index; CAD, coronary artery disease; ECHO, echocardiography, HBsAG, hepatitis surface antigen; HBcAb, hepatitis core antibody; HCV, hepatitis C virus; HIV, human immunodeficiency virus; HT, hypertension; ISHLT, international society for heart and lung transplantation NOTP, National organ transplantation program; P/F, partial pressure of oxygen (arterial/venous)/fraction of inspiratory oxygen concentration); ULN, upper limit normal

Recommendation 16

The ISCCM recommends proper coordination between NTORC and transplant centers with the help of ROTTO, SOTTO, and NOTTO for proper allotment of organs to institutes and to prevent wastage of organs.

Justification

In India, registered NTORC and transplant centers may be located at distant geographical locations. So, optimal coordination between donor and transplant hospitals, minimizing warm ischemia time, storage and transportation with cold chain, and smooth and quick transportation between centers without any undue risk to the transporting team is a must. Keeping cold ischemia time within permitted limits such as kidney (<36 hours)], heart (<4 hours), lungs (<6 hours), liver and intestines (<12 hours), pancreas (<18 hours) to maintain the quality of organ and reduce failure.

What is the accepted age range for multiple organ and tissue donors?

There is no maximum age for donation; however, comorbidities that develop together with aging make donation less acceptable. Marginal or expanded criteria donors are those presenting with clinical conditions that might reduce graft survival, impair its function, or are at a high risk of disease transmission (Table 6).[8]

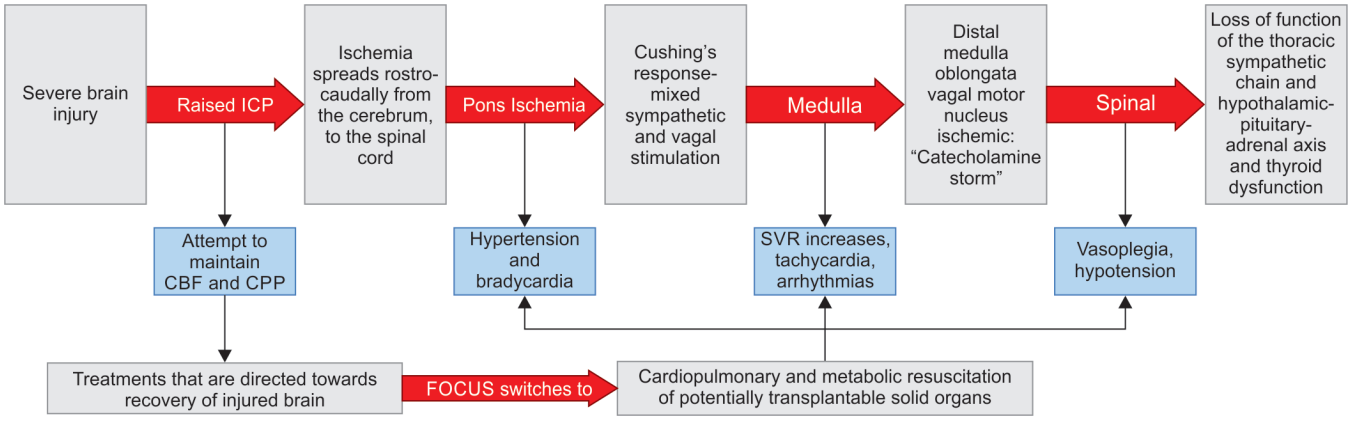


Fig. 7: Pathophysiological events in brainstem death and change in goals

CBF, cerebral blood flow; CPP, cerebral perfusion pressure; ICP, intracranial pressure; SVR, systemic vascular resistance

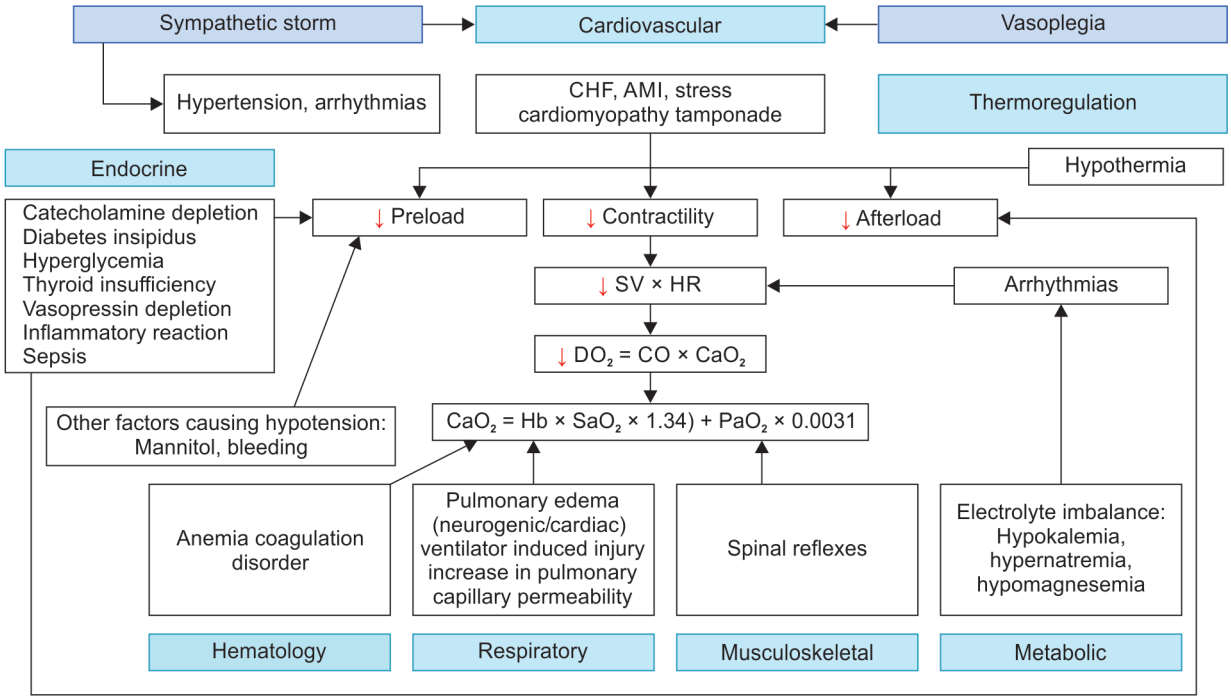


Fig. 8: Multisystemic effect of brainstem death

AMI, acute myocardial infarction; CaO_2, arterial oxygen content; CHF, congestive heart failure, DO_2, delivery of oxygen; HB, hemoglobin; HR, heart rate; PaO_2, partial pressure of oxygen, SaO_2, oxygen saturation; SV, stroke volume

The use of marginal donors is only justified when the life expectancy after transplantation is higher compared with conventional clinical treatment.[21]

Older persons (e.g., up to 80 years of age) and those with a history of hypertension and diabetes mellitus need to be worked up for individual organ function such as albumin: Creatinine ratio for kidney function of transplanted organs.[16] Even organ-specific biopsy is recommended before the organ retrieval decision or on the operation table during retrieval.

Recommendations 17

The ISCCM recommends multimodal management of potential organ donors to maximize the utility of the organs and improve the quality of organs.

Justification

Physiological and metabolic changes during brain death: See Figure 7; Pathophysiological events occurring following brainstem death and change in goals; (Fig. 8 and Table 11).[15,61–63] Brain death is a catastrophic event that not only affects the central nervous system but also causes significant changes in almost all the organs. Sometimes, the changes are so severe that despite the best medical efforts and support, it becomes difficult to maintain normal homeostasis. Changes occurring in distant organs may be attributed to the following two causes:

- Diffuse vascular regulation injury: This is due to massive sympathetic outflow and an increase in circulating catecholamines followed by a reduction of the sympathetic outflow (catecholamine toxicity).

Table 11: Common physiological changes in brainstem death patient

Variable	*Cause*	*Frequency (%)*
Hypothermia	Hypothalamic dysfunction; vasoplegia and heat loss; reduced metabolic rate.	100
Hypotension	Myocardial dysfunction, vasoplegia, hypovolemia.	81–97
DI	Posterior pituitary damage.	46–78
Arrhythmias	Catecholamine release, myocardial injury.	25–32
Pulmonary edema	Endothelial injury, blood volume diversion.	13–18
DIC	Tissue factor release, coagulopathy.	29–55

DI, diabetes insipidus; DIC, disseminated intravascular coagulation

Table 12: Primary targets for maintenance of potential organ donor (Adapted from Donation optimization extended care bundle)[24,86–88]

MAP	>60–65 mm Hg (if donor is hypertensive, MAP higher side 80–100 mm Hg).
Heart rate	60–120 bpm
Central venous pressure (CVP)	6–10 cm H_2O
Urine output	>0.5–2 mL/kg/hour
PaO_2 and pH (P/F ratio for lung donor)	>70–100 mm Hg, pH > 7.35–7.45, (>300 mm Hg on PEEP of 5 with FiO_2:100%).
Blood sugars	120–180 mg/dL
Hemoglobin	>70 gm/dL, higher trigger if hemodynamic instability, organ dysfunction, or hypoxia.
Target temperature range	36.5–37.5°C
Sodium (Na), potassium (K)	Na >135 mEq/dL and <155 mEq, K >4 and <5 mEq/dL
LV ejection fraction	>45%
Cardiac index	2.4 L/minute/m^2
$PaCO_2$ (partial pressure of carbon dioxide) level	34–44 mm Hg

BPM, beats per minute; LV, left ventricle; MAP, mean arterial pressure

- Diffuse cellular metabolic injury: This is due to a shift to anaerobic metabolism in almost all the major organs.[61]

Recommendation 18

The ISCCM recommends a list of general measures to be followed during the management of organ donors.

The general measures to be followed are listed as follows:

- Hand hygiene: As per standard medical/nursing care.
- Propped up position (30–45°).
- Eye care: Taping of eyelids, to prevent corneal ulcers, and facilitate corneal transplant.
- A nasogastric tube must be inserted for gastric decompression and prevention of aspiration.
- Stress ulcer prophylaxis.
- Prophylaxis for deep vein thrombosis – pneumatic compression device.
- Arterial and central venous lines should be inserted preferably into the upper extremities because femoral line readings can become inaccurate during surgical procedures for organ procurement.
- Frequent change of position for decubitus ulcer prophylaxis, skincare, and dressing changes.
- Bronchial toilet – improves elimination of secretion and therefore improves chances of lung donation.
- Urinary and intravascular catheter care must be handled with appropriate care to minimize the risk of infection.
- Warming blankets to maintain body temperature around 36.5°C.
- Broad spectrum antibiotics (to be prescribed as per hospital antibiotic stewardship program).
- Document the patient's height, weight, and chest circumference.

Recommendation 19

The ISCCM recommends close monitoring of hemodynamic and ventilation parameters. This is for ensuring adequate oxygenation and normocapnia.

Justification

There is very little consensus regarding the recommendation of hemodynamic monitoring use; thus, using standard tools as in critically ill patients is acceptable (central line and arterial line and markers for perfusion lactate, urine output, and venous oxygen saturation). Bedside echocardiography will guide us for fluid resuscitation. Real-time cardiac output measurement may be required in case of advanced monitoring. Monitoring is a crucial part of the medical management of potential organ donors. Routine monitoring includes ECG, BP, pulse oximetry, core temperature, hourly urine output, and central venous pressure (CVP).

Bedside echocardiography for the assessment of fluid deficit [inferior vena cava (IVC) distensibility, velocity time index (VTI), and calculation of cardiac output]. It can also be used to assess the fluid responsiveness, to rule out differential if any desaturation occurs. Use of Swan–Ganz catheter/cardiac output monitors should be reserved for unstable donors, who have persistent acidosis with evidence of tissue hypoperfusion (Table 12).

Central venous pressure measurement alone is a poor guide for directing resuscitation, and alternative techniques can be used to assess effective fluid administration responsiveness.[15,62,63]

- Repeat bedside echocardiography.
- Pulse pressure variation (PPV) is a method that has been used to determine optimal fluid status.

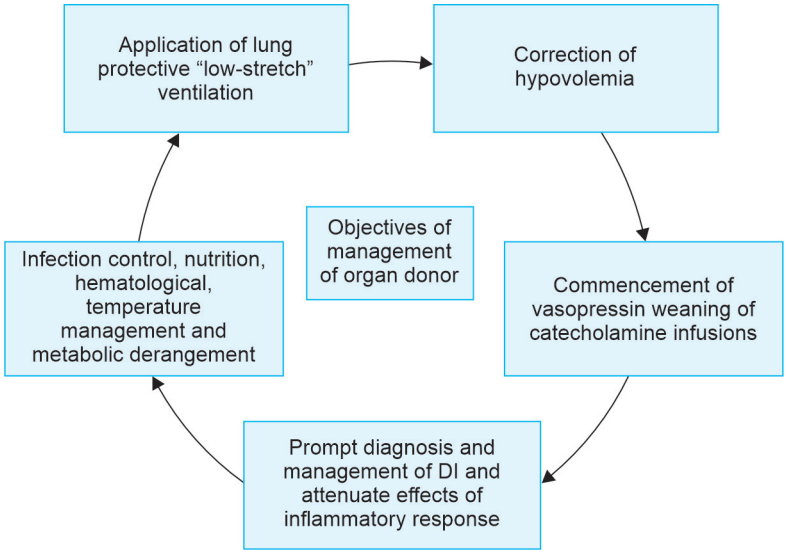


Fig. 9: Main objectives of organ donor management

- Urine output 1–3 mL/kg/hour (in the absence of polyuria due to DI or diuretics).
- Cardiac index above 2.5 (*Note:* High cardiac output state due to vasodilatory shock may be a confounder).
- Central venous oxygen saturation above 70% (*Note:* Low basal metabolism due to BD may be a confounder).

Recommendation 20

The ISCCM recommends monitoring metabolic parameters every 2–4 hours; for example, arterial blood gas, lactate, electrolytes, and blood sugar levels. It recommends sending blood urine and endotracheal secretions for culture from the deceased donor.

Justification

Against a background of autonomic dysfunction and hormonal disruption, a large amount of fluid is administered to the donor. Steroids and insulin resistance make sugar monitoring necessary. This also affects electrolytes. Parameters such as hemoglobin, hematocrit (Hct), complete blood count, blood glucose, urine analysis, blood urea nitrogen, serum creatinine, serum electrolytes, liver function tests, coagulation profile, blood group, and microbiological screening for hepatitis B and hepatitis C; hepatitis B core antigen; HIV; and immunoglobulin M (IgM) and IgG for cytomegalovirus are necessary.

Cultures of blood and urine may be required, if there is evidence of infection or if the patient is hospitalized for more than 72 hours. Organ-specific investigations need to be carried out as per requirements.

Recommendation 21

The ISCCM recommends adequate time should be given for organ optimization and brainstem death donors to come out of the autonomic storm injury.

Justification

Up to 20% of organs and a large number of potential brain-dead donors (PBDDs) are lost because of the challenging management of potential organ donors. The organ donation system requires early identification of PBDD and early appropriate evaluation and prevention of catastrophes occurring due to pathophysiology during the process of BD. This can be overcome with the use of bedside checklists to achieve cardiovascular, respiratory, and endocrine-metabolic targeted physiology. Injury caused by BD may differ between organs and thus the optimal time-point of organ procurement also differs for all organs. For lungs and heart, the procurement time as long as possible is better, and for kidneys 20–50 hours.[64,65] A median time of around 48 hours from autonomic storm to cardiac function recovery has been proven by serial echocardiographic screening. Ignacio–Martin–Loeches et al. have recommended that organ procurement should be done within 30 hours after brainstem death.[66,67] This prevents the loss of potential donors, and organs secondary to cardiac arrest.

Our aim should not only be to increase the number of donated organs but also to increase their quality and reduce cardiac arrests in PBDD. This will also preserve long-term graft function.

Objectives for management of organ donors: See Figure 9 for the diagrammatic representation of the main objectives in the management of organ donors.

Objectives in the management of organ donors can be broadly divided further as mentioned in the following:

- Management of hemodynamics.
- Management of metabolic derangement.
- Management of respiration application of lung protective "low-stretch" ventilation.
- Temperature management.
- Management of hematologic derangement hematological parameters.
- Nutrition management.
- Management of hormonal and metabolic derangement.

Recommendation 22

The ISCCM recommends aggressive management of the hemodynamic status of the donor. It recommends maintaining normovolemia, mean arterial pressure (MAP: From –60 to 65 mm Hg), and optimizing cardiac output.

Justification

Hemodynamic instability and cardiac dysfunction are almost always encountered in brain-dead patients. Myocardial and hemodynamic changes can be seen when the intracranial pressure (ICP) increases above the MAP and the body tries to maintain the cerebral blood flow and hence the cerebral perfusion pressure (CPP). Ischemia spreads rostro-caudally from the cerebrum to the spinal cord. Pontine ischemia is seen clinically as the Cushing's response-mixed sympathetic and vagal stimulation leads to hypertension and bradycardia. Ischemia progresses downward to the distal medulla oblongata, making the vagal motor nucleus ischemic. A catecholamine storm or a period of increased circulating catecholamines follows leading to intense vasoconstriction, raised systemic vascular resistance, tachycardia, or arrythmias. This results in visceral and myocardial ischemia, including myocardial and conduction system necrosis. The rate of rise in catecholamines and the extent of myocardial injury is directly proportional to the rate of rise of ICP. Catecholamine storm causes adenosine triphosphate (ATP) depletion in the cardiac myocyte. About 20–25% of brain-dead donors show evidence of myocardial ischemia and 40% have echocardiographic evidence of myocardial dysfunction. As ischemia progresses to the spinal cord there is a loss of function of the thoracic sympathetic chain, and loss of vascular tone leading to vasoplegia, hypotension, and vasodilatation. This correlates with low levels of circulating catecholamines, deficient cardiac inotropy, and chronotropy, causing poor tissue perfusion. As the aortic diastolic pressure decreases, it may compromise the coronary perfusion pressure to critical levels, resulting in myocardial ischemia. Another cause of reduction in coronary blood flow is endothelial dysfunction caused by BD, impairing endothelial-dependent vasodilatory mechanisms, loss of autoregulatory reserve in coronary vessels, and consequent hypoperfusion. Other factors contributing to hypotension may be the use of mannitol, hyperglycemia-induced osmotic diuresis, DI, hypothermic "cold" diuresis, inadequate fluid resuscitation, or ongoing blood loss due to trauma.[68–74]

Renal function is affected by vasoconstriction during the autonomic storm with poor renal perfusion. This may be further exacerbated by the hypotension seen in the brain-dead organ donor due to hypovolemia and vasoplegia.[75]

To maximize the organ donation number and also the quality it is necessary to maintain the perfusion pressure of all organs with the use of the least amount of vasoactive support.[15,76]

Recommendation 23

The ISCCM recommends that the use of antihypertensives should be avoided.

Justification

Due to the transient nature of autonomic storms, antihypertensives are usually not required.[58] If needed, short-acting antihypertensives such as esmolol, sodium nitroprusside, hydralazine, labetalol, or nitroglycerine should be used. Antihypertensive is not required for a long time.

Recommendation 24

The ISCCM recommends aggressive management of hypotension. Three recommended measures to keep donor hemodynamically stable are volume expansion, vasopressor and inotropes, and hormone replacement.

Recommendation 25

The ISCCM recommends the use of isotonic crystalloids with balanced salt content. It recommends avoiding colloids. It recommends transfusion of packed red blood cells (RBCs) to maintain Hct above >30%.

Recommendation 26

ISCCM recommends the use of vasopressors to maintain MAP >60–65 mm Hg and SBP >100 mm Hg after or during fluid resuscitation is done. The choice of vasopressor depends on the presence of DI and organ-specific requirements.

Recommendation 27

The ISCCM recommends that hormonal replacement therapy (HRT) with T4 and methylprednisolone can be considered in hemodynamically unstable patients who are adequately fluid resuscitated and are on vasopressor support.

Justification

Volume expansion/preload:[15,53] Hypovolemia is present in brainstem death patients. This should be addressed primarily before proceeding to other interventions. Simultaneously look for other causes of hypotension and initiate treatment accordingly. The initial approach to hypotension is fluid resuscitation to replenish the circulating volume.

To avoid hypernatremia (concurrent DI) and hyperchloremic acidosis (increases renal vascular resistance, confounds base excess) 0.9% normal saline should be avoided. Administration of excessive intravenous fluids containing 5% dextrose may further complicate hyperglycemia and hypothermia.[62,63,77]

- Avoid colloids – Hydroxyethyl starch is contraindicated in organ donors because it can damage renal epithelial cells and cause early graft dysfunction in the transplanted kidneys.[62,77]
- Albumin solutions (20%; 5%) may be considered to reduce the amount of volume of fluid or for rapid volume expansion. The high sodium content of albumin-based solutions needs to be taken into account.
- The most commonly used fluids are half-normal saline, Ringer's lactate, plasmalyte-A, and Ringer's acetate.
- Packed red cells should be transfused to achieve a Hct of ≥30% to maintain oxygen delivery.[15]

Vasopressors: Vasopressin up to 2.4 U/hour may reduce the requirement of other ionotropes.[63,77–79] The utility of low-dose vasopressin to treat DI, aid restoration of vascular tone, and reduce epinephrine requirement was first identified in brain-dead patients receiving long-term support. When the loss of vascular tone is preventing the achievement of donor goals, low-dose vasopressin may allow the reduction or elimination of catecholamine use, as in other ICU patients. Vasopressin has been associated with increased organ recovery and decreased graft refusal due to poor function.[62] The use of vasopressin in pressor dose (1–2 U/hour) plays an important role in stabilizing the hemodynamics of brain-dead patients.

Norepinephrine is also commonly used for maintaining MAP.[62,63,77] Norepinephrine is required in higher doses compared to epinephrine. As far as possible, high doses of norepinephrine >0.05 mg/kg/minute should be avoided.

Other agents and combinations: A study of brain-dead patients has shown that a pressor dose of vasopressin and epinephrine combination effectively increases the MAP with an increase in total peripheral resistance index and cardiac index. Dopamine can also be used but it has an increased incidence of arrhythmia.

Due to autonomic storm occurring in the brainstem death patient, few donors develop stress cardiomyopathy; thus results in a fall in cardiac output. This failing heart may require ionotropic support—dobutamine.

Hormonal Replacement

Justification

The anterior pituitary function is well preserved in most donors with normal values of thyroid-stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), and human growth hormone, indicating some residual function of the hypothalamic–pituitary neuroendocrine system. Thyroid hormone and TSH levels are typical for the "sick euthyroid syndrome" that often accompanies severe brain injury, rather than a result of TSH deficiency.

The posterior pituitary function is lost in almost 80% of brain-dead organ donors. Central DI due to a deficiency of antidiuretic hormone occurs characterized by polyuria, hyperosmolarity, and hypernatremia.[31,80–82]

Hormonal treatment is initiated in donors in whom volume resuscitation and vasopressors have failed to achieve hemodynamic stability. There are no clear recommendations regarding T3 administration for improving the hemodynamic status and cardiac function in potential donors.[15,62,63,77,78] Moreover, T3 administration is not easily available in India. Thyroxine (T4) 300–400 µg through the nasogastric route can be given in hemodynamically unstable patients, but absorption and clinical effects are not proven. Methylprednisolone 15 mg/kg immediately after diagnosis of BD and every 24 hours is recommended.

Ventilation, infusion, pharmacological (VIP) support approach: It is a simplified and systematic approach that can help us to guide the hemodynamic management of organ donors.[62] See Figure 10. It is also expanded to ventilation, infusion, pumping, pharmacological support, and specific intervention (VIPPS). Furthermore, VIP is a simultaneous approach to tackle the hemodynamic parameters along with ventilation parameters.

"Low-stretch" ventilator settings are to be set on a ventilator to take care of oxygenation. If MAP is below 65 mm Hg or urine output is below 1 mL/kg/hour and the PPV is above 15%, give the fluid challenge of 20–30 mL/kg of crystalloid. Check for fluid responsiveness (bedside echocardiography, IVC distensibility, and VTI). Fluid administration is continued to achieve MAP above 65 mm Hg and urine output (UOP) above 1 mL/kg.

Administration of vasoconstrictor may be needed to compensate for the loss of vascular tone (vasoplegia) seen in brainstem death patients. Start with vasopressin 0.5–2.4 U/hour plus norepinephrine infusion. If echocardiography reveals poor ejection fraction start dobutamine.

Despite fluid resuscitation and vasopressors, If MAP is not above 65, think of hormonal treatment. Administer methylprednisolone and T4.

Recommendation 28

The ISCCM recommends that arrhythmias in organ donors should be detected, prevented, and treated immediately.

Justification

Efforts should be made to prevent arrhythmia or to treat them promptly because it can affect cardiac output, and cause an imbalance between coronary supply and demand leading to cardiac dysfunction. It is more commonly seen in cases of longer lag between BD and organ removal. For the prevention of arrhythmia,

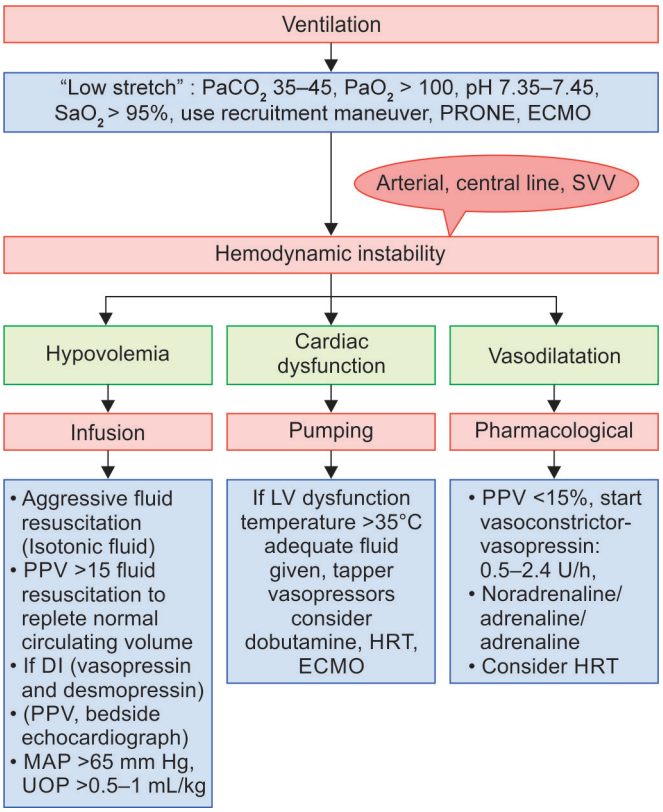


Fig. 10: Flow diagram of VIPP approach for hemodynamic management of brain-dead patient

DI, diabetes insipidus; ECMO, extracorporeal membrane oxygenation; HRT, hormonal replacement therapy; LV, left ventricle; MAP, mean arterial pressure; PaO_2, partial pressure of oxygen; $PaCO_2$, partial pressure of carbon dioxide; SVV, stroke volume variation; PPV, pulse pressure variation; UOP, urine output

electrolytes, BP, fluid volume, and body temperature should be carefully monitored and maintained within normal range.

If arrhythmia occurs, it can be treated with standard therapy such as amiodarone or cardioversion. Atropine is not useful in the management of bradycardia whereas adrenaline, isoprenaline, or pacing may be effective.

Recommendation 29

The ISCCM recommends aggressive correction of sodium. It recommends to maintain blood sugar levels between 80 and 150 mg/dL. Sodium values should be maintained below 160 mEq/L.

Justification

Brain-dead organ donors have a high incidence of hyperglycemia, due to insulin resistance and unsuppressed gluconeogenesis. Histological and immune histological examination of pancreatic tissue after organ procurement did not reveal endocrine pancreatic dysfunction. The elevated levels of glucose, C-peptide, and insulin appear to represent a peripheral resistance to insulin as seen after major trauma. Hyperglycemia may lead to osmotic diuresis, fluid depletion, electrolyte imbalance, and an increased risk of infection.[83]

For liver-deceased donors, serum sodium above 160 mEq/L was presumed to be associated with graft failure. Hypernatremia secondary to DI needs to be taken care of with water, 5% dextrose, and 0.45% normal saline. Serum sodium and potassium should

be monitored every 2–4 hours. Sodium should be kept below 155 mEq/dL and potassium between 4–5 mEq/dL. Insulin infusion may be required for the maintenance of blood glucose in the recommended range. Doses of insulin required for maintaining glucose control may be higher than normal. Blood sugars must be maintained in the range of 80–150 mg/dL.

Recommendation 30

The ISCCM recommends the use of lung-protective ventilation protocols using low tidal volume, plateau pressures below 30-cm H_2O (to prevent ventilator-associated lung injury), minimum oxygen requirement, and positive end-expiratory pressures of 5-cm H_2O or high as necessary adjusted to maintain PaO_2 above 70 mm Hg.

Justification

The BD-induced lung dysfunction is related to neurogenic pulmonary edema and inflammatory acute lung injury, sometimes causing a clinical picture resembling acute respiratory distress syndrome (ARDS). The sympathetic storm causes systemic vasoconstriction causing an increase in afterload and left heart pressures. Blood is redistributed to the central circulation causing an increase in pulmonary blood volume and pulmonary arterial pressures. The increase in hydrostatic pressure causes structural damage to the capillary endothelium. A combination of raised hydrostatic pressures and capillary damage in the pulmonary vascular bed unbalances Starling forces across the endothelium, causing leakage of plasma into the interstitium and alveolar space, and resulting in neurogenic pulmonary edema. Severe brain injury increases the vulnerability of the lungs to mechanical, inflammatory, or reperfusion injury, through increased release of inflammatory mediators, neutrophil infiltration, and activated macrophages in the alveolar space and alveolar hemorrhage. In addition, proinflammatory mediators that are released following BD may further contribute toward lung injury by promoting the infiltration of activated neutrophils into the lungs. Pulmonary dysfunction in the brain-dead organ donor may also be due to other causes such as aspiration, pneumonia, contusion, and ventilator-induced lung injury.[84]

A set of European critical care units observed that a low-stretch ventilation strategy doubled the number of lungs transplanted.[62] The ventilator goals of donor management are to maintain tissue oxygenation, to maintain the quality of another organ, and at the same time, to protect the lungs for transplant. The respiratory passage should be clear without any obstruction. To achieve this, routine measures such as suctioning, positioning, and change of position should be continued. Interstitial fluid overload should be avoided. Oxygen saturations within normal limits and normocapnia should be maintained.[62,63]

Lung recruitment maneuvers may be used if oxygenation goals are not met for donation. A closed circuit for tracheal suction, alveolar recruitment maneuvers after any disconnection, and the use of continuous positive airway pressure during the AT are advisable. If the P/F ratio is less than 150 mm Hg, we must think of prone ventilation; furthermore, if oxygenation does not improve, think of ECMO if available.

Recommendation 31

The ISCCM recommends the prevention of hypothermia in a potential organ donor and the maintenance of temperature between 35 and 36°C.

Justification

Temperature regulation in the hypothalamus is affected resulting initially in hyperthermia followed by hypothermia. Hypothermia is worsened by loss of protective mechanisms such as shivering or vasoconstriction, reduced metabolic rate, excessive heat loss, and peripheral vasodilation. Hypothermia can worsen acidosis and coagulopathy, increase the risk for arrhythmias, reduce myocardial contractility, induce diuresis, and cause a left shift in the oxygen dissociation curve affecting oxygen delivery to tissues.

Prevention of hypothermia is easier compared to its reversal. Niemann et al. showed that mild therapeutic hypothermia (34–35°C) led to a significant reduction in the rate of delayed graft function in kidney transplant recipients as compared to those donors maintained in normothermia (36.5–37.5°C).[62,85]

Active warming helps to prevent hypothermia as hypothermia causes impaired myocardial contractility, acidosis, and coagulopathy. Efforts should be made to maintain temperature above 35°C. Surface warming should be done in all patients with hypothermia. Patients with body temperature below 34°C should be given core warming. In such cases, inhaled gases should be warmed and humidified using a humidifier. Intravenous fluid should also be warmed if large volumes are to be administered.

Recommendation 32

The ISCCM recommends PRBCs transfusion if Hct is below 30% and continuation of low molecular weight heparin (LMWH) in patients with normal coagulation and platelets.

Justification

Brain death is associated with the activation of the coagulation cascade. The other changes seen are an increase in fibrin formation, hypofibrinolysis, higher platelet activation, and dysregulation of the von Willebrand factor production which promotes platelet attachment to damaged vasculature. This prothrombotic state may contribute to the formation of microthrombi in transplantable organs. In brain-dead donors due to traumatic brain injury (TBI), the incidence of disseminated intravascular coagulation (DIC) can be as high as 15–25% due to the release of tissue thromboplastin from necrotic brain tissue. Anemia seen in brain-dead patients could be due to traumatic bleeding, coagulopathy, and excessive fluid administration.[86] There is no conclusive evidence for the continuation of LMWH in organ donors. In a brainstem-dead donor with normal platelet and normal coagulation, it is reasonable to continue LMWH.

In case of active bleeding, the cause of bleeding should be corrected at the earliest. Recommendations from general ICU guidelines can be applied and hemoglobin trigger of less than 70 gm/L.[87] It is recommended to maintain the Hct above 30%. If the Hct drops below 30%, 2 units of PRBCs should be transfused. Coagulopathy should be treated with blood product. In case of worsening coagulopathy, organ removal should be expedited. Transfusion of blood or blood products should be done only if necessary.

Recommendation 33

The ISCCM recommends continuing enteral nutrition in the management of the potential of organ donors.

Justification

This enables to maintenance of intestinal flora intact and prevents their translocation thereby preventing infection. It also increases glycogen supply and helps in optimizing allograft function.[88]

Recommendation 34

The ISCCM recommends hormonal replacement therapy in the maintenance of potential organ donors:

- Vasopressin 1 U bolus followed by an infusion of 0.5–0.04 U/minute (desmopressin intranasal has a selective action on the V2 receptors and a half-life varying from 6 to 20 hours).
- Methylprednisolone – 15 mg/kg immediately after the diagnosis of BD and 24th hourly thereafter. Another option is 250 mg followed by 100 mg/hour till the organ retrieval.
- Insulin infusion to maintain blood glucose between 80 and 150 mg.
- A T4 20-μg bolus followed by infusions of 10 μg/hour; T3 given as a 4-μg bolus followed by an infusion of 3 μg/hour; T4 improves hemodynamics and prevents cardiovascular collapse in hemodynamically unstable organ donors. However, intravenous T3 is generally not available. So, T4 oral 300–400 μg/8 hourly is suggested instead of T3 (NOTTO).
- In hemodynamically stable patients, desmopressin dose—an initial dose of 1–4 μg followed by 1–2 μg every *6* hours monitoring the sodium and urine output. If the donor is hemodynamically unstable, then use vasopressin. Vasopressin – U bolus followed by an infusion of 0.5–4.0 U/hour.

Justification

Some studies have recommended its use in persistent hemodynamic instability and/or when ejection fraction is below 45% on echocardiography, and when heart donation is planned.[62,63,76] However, there is no strong evidence for the use of hormonal resuscitation. In 2014, Novitzky et al. in their retrospective analysis of 10-year brain-dead organ donors strongly favored the use of T3/T4 therapy, when combined with vasopressin and corticosteroids.[89] He recommended this combination should be considered for all brain-dead donors as it significantly increases the number of procured organs.[63] In 2005, Powner and Hernandez concluded that thyroid hormone administration along with steroids and vasopressin should be used in the protocol care for donors.[65] Thus, the evidence on anterior pituitary or thyroid dysfunction in BD is conflicting. In patients in whom lung transplant is distinctly possible, the use of methylprednisolone has shown some benefits.[62,63,76,90,91] The results of a retrospective analysis of 118 consecutive organ donors, of which 80 received high-dose methylprednisolone during donor management, demonstrated improved oxygenation at organ recovery.[63,90,91] With high-dose steroid treatment, a significant increase in the number of lung utilization was seen possibly because of the anti-inflammatory benefits of steroids.

Treatment of DI depends on whether the patient is hemodynamical stable or unstable. Desmopressin or vasopressin should be used early in the management of DI.[62] Early use of antidiuretic agents in suspected DI may prevent physiological instability due to hypovolemia and hypothermia. A large amount of fluid loss in the urine should be replaced by intravenous fluids using the balanced salt solution or fluids with low-sodium content (5% dextrose or 0.45% saline) to maintain a sodium level between 135 and 145 mEq/L. In hemodynamical stable donors, desmopressin is recommended as it predominantly exerts an antidiuretic response due to its strong affinity for V2 receptors in distal convoluted tubules.[62]

Recommendation 35

The ISCCM recommends adopting appropriate infection control measures to prevent infection in the donor.

Justification

A severe systemic inflammatory response occurs in a brain-dead donor. Increased blood levels of several cytokines such as tumor necrosis factor (TNF)-α, interleukin (IL)-6, IL-8, IL-1b, and IL-2R are seen after severe cerebral injury and BD, and there is an up-regulation of these cytokines in various organs. Activation of the cytokine system could be due to catecholamine storm, hemodynamic instability leading to hypoperfusion and ischemia in several organs, reperfusion injury, and inadequate volume resuscitation. Several cytokines have been found in brain tissue and cerebrospinal fluid after brain injury and through a defective blood–brain barrier, they may reach the circulation and stimulate target cells in the blood and somatic organs. Brain death-induced systemic inflammation is as high as that induced by sepsis and BD itself triggers the inflammatory cascade.[90–94]

Severe brain damage and cerebral death predisposes to infection, due to heavy impairment of the cellular immune system and hemodynamic instability, with consequent bacterial translocation from the bowel. Further, the invasive lines used for monitoring purposes, mechanical ventilation, inadequate nursing, and medical management (steroids administration) can increase the chances of infection. The presence of infection may complicate the donor organs and further the recipient. The actual rate of unexpected infection transmission from donor to receptor is low, occurring in less than 1–5% of solid organ transplant recipients. The infection screening protocols should be implemented and they vary as per geographical regions and transplant centers.

Recommendation 36

The ISCCM recommends that bacteremia or sepsis are not contraindications to donation, provided pathogen-specific antibiotics have been administered for at least 48 hours prior to procurement and the recipient receives pathogen-specific antibiotics for 7–10 days.[53]

Justification

Positive blood cultures in potential organ donors are not unusual and the documented rate is 20% in the literature.[53,55] The incidence of positive blood culture appears to be higher in older donors (>50 years) and in donors whose length of stay is more than 3 days.[13] In younger donors (<40 years) bacteremia is most likely due to gram-positive microbes (*Staphylococcus aureus*), while in older donors, it is due to Gram-negative bacteremia.

However, the rate of transmission of infection to the recipient is less,[53,95,96] provided donor organ procurement is delayed for 48 hours so that the donor receives antibiotics as per culture sensitivity for 48 hours. If the blood cultures of the donor come positive after the organ transplantation. This should be communicated with the transplant intensivist/transplant surgeon so that the recipient receives pathogen-specific antibiotics for 7–10 days.[53]

Can PBDD with Meningitis Donate Organs?

Potential organ donors with bacterial meningitis are considered suitable for organ procurement only if they receive pathogen-specific antibiotics or therapy against the probable pathogen.[97,98] The suggested duration of therapy is the same as above (48 hours) and the recipient should receive similar antibiotics for 5–10 days.[21] Furthermore, PBDD with undiagnosed febrile illness, encephalitis, meningitis, or flaccid paralysis of unknown cause and lymphocytic choriomeningitis virus and rabies are absolute contraindications for organ donation.

Recommendation 37

The ISCCM recommends that causes for refusal of organ donation need to be recorded and measures taken to overcome these hurdles should be taken.

Justification

An excellent review by Anjali, from the Faculty of Law, at the University of Delhi, New Delhi, India suggested many reforms to increase deceased organ donation in India.[99] Table 13 is a compilation and modification from her article and states the hurdles and advisory on overcoming the same to increase the deceased donor pool. Hurdles for low organ donation rate in India are low rate of BD declaration and delayed declaration, suboptimal donor maintenance, low consent rate by Next of Kin, legal hurdles, organ selection, delays in Retrieval and transplantation, incomplete Documentation, dissatisfaction among next of Kin and consequent disharmony and medical staff protection. Suggested measures to overcome these hurdles are depicted in Table 13.

Recommendation 38

The ISCCM recommends the implementation of donation after circulatory determination of death (DCDD).

Justification

Donation after circulatory determination of death (controlled DCDD) – THOTA recognizes the deceased state to be either irreversible circulatory or brainstem failure, yet it has prescribed protocol and procedure only for donation after neurological determination of death (DNDD) and not for DCDD. Therefore, in India, organ harvesting has only been possible for "heart-beating donors" and not for the "nonheart beating donors." Furthermore, DCDD has been increasing exponentially in the Global North expanding the opportunities for deceased organ.[100] This gap needs to be corrected to bring us up to date with the current practices. Recently a consensus position statement was published simultaneously in two journals to initiate a process for including a protocol for DCDD in THOTA.[10]

Moreover, DCDD is considered for patients in whom there is no hope of viable recovery (polytrauma, cardiac arrest, and malignant stroke), and the next of kin has made the decision to withdraw life-sustaining treatment and is willing for organ donation. These potential organ donors are expected to expire within a small interval (60 minutes) after discontinuation of life-sustaining supports. To make controlled DCDD possible in India, we need enabling legislations to facilitate the withdrawal (WD) of life support treatment (WLST) for those who refuse such interventions in terminal illness. A living will/advance medical directives (AD), WD), and withholding (WH) decisions were held to be lawful in the Supreme Court's judgment, Common Cause vs The Union of India.[101] However, the procedure prescribed by the court was unworkable. In Jan 2023, in a path-breaking judgment, an appeal for simplification by the ISCCM represented by the Vidhi Centre for Legal Policy was upheld by the Supreme Court.[102] The precise process of controlled DCCDD is described in the consensus statement.

Once a WLST decision is made *via* due process described in the ISCCM position statement on end-of-life care (EOLC), the critical care team should notify the regional/hospital transplant coordinator/trained requester to broach the subject of transplant opportunity with the family. Following initial agreement by the patient/family the treating team should be available for clarifications, answering queries, and for emotional support. At no point at this stage, a member of the transplant team or caregivers involved in the care of a potential recipient should be involved in the discussions with the donor family.

This strategy will be important in the context of a continuing shortage of DNC organ donors. This technique may increase the number of donors by 220,007 per year in the USA.[27]

Furthermore, DCD can be controlled or uncontrolled. In unexpected cardiac arrest cases when CPR has failed, it is described as an uncontrolled DCD and if the WD of care is planned it is called controlled DCD.[10,27,102,103]

Controlled DCD: Organ procuring teams should be kept ready to reduce the warm ischemic time. The procuring teams enter only when the patient is declared dead and the family members are out of the operating room.[30]

Step 1: First step, once the decision on the end of life/WD of life support has been taken (independently from organ donation), the patient is evaluated as a potential candidate.

Step 2: From local legislation, the authorization for donation is obtained from the patient, who could have previously authorized donation in case of death, or from the family.

Step 3: The patient's medical history and conditions for DCD potential should be made, including donor screening for compatibility and organ allocation.

Step 4: End-of-life care plan is decided and WD of care is planned. Withdrawal of life support is best done near (the recovery room) or in the operation room by the primary team. Friends and family members may wish to wait inside the room. Heparin is administered at the time of WD of life support to prevent thrombosis in transplantable organs.

Step 5: Diagnosis of death is made with a variable "no-touch" observation period of 5–20 minutes (each as per the respective country's law). Determination of death is done by the permanent absence of respiration, responsiveness, and circulation (standard cardiopulmonary criteria). Italy practices a very long no-touch period thus the prolongation of warm ischemia will require *ex vivo* perfusion for a better organ function evaluation.

Step 6: Transport the donor to the operating room and the organ retrieved suggested recovery of organs can proceed within 2 minutes and should not extend beyond 5 minutes.

Warm ischemia time can be calculated from the time of onset of hypoxia or hypotension to the time the organs procured and cooling initiated. Some centers calculate the ischemic time from the time of WD of support.

If the patient does not expire after 60 minutes, the patient is transported back to critical care. This is informed to relatives.[27]

Uncontrolled donation after circulatory death:

Step 1: Recognize patients with certain characteristics and cardiac arrest with unsuccessful CPR.

Step 2: The patient is then considered a potential donor and is transferred to the hospital maintaining ventilation and cardiac compression.

Step 3: At the hospital, a declaration of death is made and the "no-touch" period starts.

Step 4: After certifying death extracorporeal support is restored to maintain organ perfusion. ECMO or other modalities of

Table 13: Hurdles in deceased organ donation in India

Hurdles in deceased organ donation in India	*What can be done to overcome the same?*
Low rate of BD declaration and delayed declaration	Brain death declaration made mandatory in many states of India. NOTTO has form 10, as standardized fill in the blank format to facilitate step wise BD declaration and certification.
Suboptimal donor maintenance	Follow donor optimization care bundle (NHS-BT).
Low consent rate by next of kin	Increase awareness by govt and nongovernmental organizations. NOTTO has 24 × 7 helpline and organ donor card. Many NGOs facilitate MOHAN foundation, donate life, etc. Organ donor card. The government made mandatory to have cocoordinators or social workers in organ retrieval and transplant centers. They develop rapport and educate next of kin about donation process. Religious leaders discussing this topic in their discourses that it is permitted in each religion.
Legal hurdles	• NOTTO website has free access to 21 standardized formats for documentation and consent for organ donation under THOA – 2011, and THOA rules – 2014 NOTTO Forms. • State and regional organ and tissue transplantation organizations formed in each state or region, respectively (SOTTO and ROTTO) has 24 × 7 help from transplant coordinator to guide in organ donation and allocation process. • NGOs working in this field has volunteers to help the clinical team to facilitate the same. • Police officers and forensic expert's awareness and training for facilitation of permission for organ retrieval. • NOTP guidelines for period from 2021–2022 to 2025–2026 to facilitate organ donation and transplantation. – Tissue donation, tissue transplantation, and tissue banking included. – Mandatory transplant coordinators in transplant and retrieval hospitals. – Registration of retrieval only centers. – Mandatory request for donations from potential donors in ICU. – ICU. – Brainstem death certification permitted by anesthetist/intensivist if neurological experts are not available. – National networking between retrieval centers, transplant centers, tissue banks, networking organizations at the state, regional, and national levels to establish an efficient organ procurement and distribution system in the country (mandate given to central government). – National Registry for organ donation and transplantation. – Eye/cornea retrieval permitted from trained technicians.
Organ selection	National association to have standardized criteria for fitness of organ retrieval so as to avoid last-minute hurdles to bedside team. Organ retrieval units to follow preretrieval check lists.
Delays in retrieval and transplantation	NTORC and transplant center coordinators must have a close liaison to avoid delay and timely retrieval and transplantation. Next of kin or family must be updated if any unexpected delay is forthcoming. ICU and operating room at the donor and transplant center must be kept in the loop so that routine care of other patients is not compromised. Creating "green corridor" for transporting organs by local municipal and police authorities"
Incomplete documentation	Have standardized formats downloaded and available as ready-to-use organ donation resource files/ folder on ICU and OR desktop? Hospital administrators must maintain zero tolerance toward missing documentation. It must be part of duty of the transplant coordinator to ensure all the duly signed documents are filed before the task is completed.
Dissatisfaction among next of kin and consequent disharmony	Lack of timely updates is the key reason; coordinators must give a timely update. Transparency about organ procurement plans including refusal with reasons.
Medical staff protection	ICU and operating room staff must be acknowledged for the humanitarian act of walking these extra miles to make organ donation possible. Appreciation letter with or without monetary compensation is one such option. Strict mob control strategies including police protection back up desirable in India.

organ preservation (such as *ex vivo* perfusion) can be taken into consideration as an organ preservation measure. Some centers were able to transplant organs without ECMO, by ventilating the lung without circulation, using a careful *ex vivo* lung perfusion phase.

The outcome of organ transplantation after DCD: It is observed long-term outcomes are better in uncontrolled DCD where the function of grafts is preserved by normothermic recirculation.

Summary of all recommendations of position statement for organ donation by ISCCM (See Table 14).

Table 14: Recommendations for management of potential organ donation

	Recommendation number	*Recommendations*
Role of intensivist	Recommendation 1	ISCCM recommends that a trained critical care personnel be involved in the management of potential organ donor.
		ISCCM recommends early identification, assessment, and maintenance of potential organ donors.
		ISCCM recommends that an intensivist plays a vital role in evaluating the deceased donor.
BD criteria	Recommendation 2	ISCCM recommends that for declaration of brainstem death, there should be a potential irreversible cause of catastrophic brain injury, supported by imaging evidence, confounding factors ruled out and precondition criteria are strictly checked.
NOTTO, SOTTO and ROTTO	Recommendation 3	ISCCM describes about national organ transplantation program and its network (SOTTO and ROTTO).
Clinical evaluation	Recommendation 4	ISCCM recommends thorough evaluation of potential/deceased organ donors which includes ensuring the potential cause of devastating brain injury, detailed medical history of the patient, clinical/neurological examination, and AT.
Apnea tests	Recommendation 5	ISCCM recommends AT is mandatory in confirming the diagnosis of brainstem death and AT should be performed only after prerequisites are met and thorough clinical examination and examination of brainstem reflexes are done.
		STEPS for AT should be strictly followed to avoid failure and complications.
		Apnea test can be performed with an oxygen insufflation catheter, PEEP valve, T-piece, Bains circuit, and CPAP on a ventilator.
Incompatible and compatible observation an organ donor	Recommendation 6	ISCCM recommends that intensivists be aware of compatible and incompatible observations seen in brainstem death patients
Ancillary therapy	Recommendations 7	ISCCM recommends that ancillary test are not mandatory in diagnosing brainstem death ISCCM recommends to conduct ancillary test only if panel of doctors who are in doubt or disagreement of the diagnosis, to establish a clear, irreversible cause of brain injury or if any contraindication to carry clinical examination is present.
Special cases (ECMO; TTM)	Recommendations 8 for special cases	In these special cases, all clinical examinations mention above should be carried.
		While performing AT the sweep gas flow rate (CO_2 clearance rate) to 0–1 L/minute should be decreased.
		In patients treated with TTM evaluation for BD/DNC not be initiated until at least 24 hours following complete rewarming.
THOA amendment	Recommendations 9	ISCCM recommends strictly following THOA amendment 2011 regulations and rules 2014 laid down for the certification of brainstem death.
		ISCCM recommends certification of brainstem death patient/deceased organ donor should be done by the registered intensivist/medical practitioner/anesthetist/neurophysician/ neurosurgeon (registered by the hospital in the organ donation program).
		Clinical examination and AT need to be done 2 times, 6 hours apart/by two doctors not belonging to the retrieval and transplantation teams. Documentation should include patient's identification, potential cause of brainstem death, clinical/neurological examination findings, and AT interpretation.
		All four doctors (members from the panel of the board of medical experts) should sign tests done to document the absence of brainstem function.
Communication for organ donation	Recommendation 10	ISCCM recommends communication with the next akin be carried out in a stepwise fashion regarding the severity of the condition of the patient, about BD state.
		Transplant coordinator of the hospital plays vital role in communication and obtaining consent for organ donation along with the intensivist.
		It is necessary to inform police about organ donation consent to the station house officer or superintendent of police or deputy inspector general if it is a documented medicolegal case.

(Contd...)

Table 14: *(Contd...)*

	Recommendation number	*Recommendations*
Certification of all brain-dead patients	Recommendation 11	ISCCM mandates the certification and notification of BD irrespective of organ donation.
Critical pathway for sequential tasks	Recommendation 12	ISCCM recommends a "critical pathway for the sequential tasks in deceased organ donation." This is to maintain the uniformity of organ donation programs in all institutes prevent potential conflicts of interest and help to run organ donation program with public trust.
Evaluation of organ donor	Recommendation 13	ISCCM recommends intensivists along with procurement team members evaluate the organ donor meticulously. Perform a detailed physical examination, detailed history (past and present) and finally perform investigation (biochemistry, radiologically, organ-specific investigation such as HRCT, bronchoscopy, transesophageal echocardiography) and necessary procedures (biopsy) to evaluate the quality of donor.
Absolute contraindication	Recommendation 14	ISCCM recommends the absolute contraindications of organ donation under headings of metastatic malignancy, unknown source of infections, and organ-specific end-stage disease.
Standard and extended criteria	Recommendation 15	ISCCM recommends standard and expanded criteria for organ donation (put forth by NOTTO). With increased awareness on organ donation and evidences ISCCM recommends to initiate new approaches for screening and selection of donor.
NTORC and transplant coordination	Recommendation 16	ISCCM recommends proper coordination between NTORC and transplant centers with help of ROTTO, SOTTO and NOTTO for proper allotment of organs to institutes and to prevent wastage of organs.
Multimodal management	Recommendation 17	ISCCM recommends multimodal management of potential organ donors to maximize the utility of the organs and improve the quality of organs.
General measures	Recommendation 18	ISCCM recommends the bundle of general measures to be followed during the management of organ donor.
Monitoring	Recommendation 19	ISCCM recommends close monitoring of hemodynamic parameters, and ventilation for adequate oxygenation, urine output, and temperature.
	Recommendation 20	ISCCM recommends monitoring metabolic parameters every 2–4 hours: Arterial blood gas, lactate, electrolytes, and blood sugar levels. It recommends sending blood urine and endotracheal secretions for culture from the deceased donor.
Adequate time for optimization	Recommendations 21	ISCCM recommends adequate time should be given for organ optimization and to come out of the autonomic storm injury.
Management of organ donor	Recommendation 22	ISCCM recommends aggressive management of the hemodynamic status of the donor. It recommends maintaining normovolemia, MAP from 60 to 65 mm Hg), and to optimize cardiac output.
For hypertension	Recommendations 23	ISCCM recommends that the use of antihypertensives should be avoided.
For hypotension (VIPP approach)	Recommendation 24	ISCCM recommends aggressive management of hypotension. The recommended three measures to keep donor hemodynamically stable are volume expansion; vasopressor and inotropes; and hormone replacement.
Fluid for resuscitation	Recommendation 25	ISCCM recommends the use of isotonic crystalloids with balanced salt content. It recommends avoiding colloids.
Vasopressors	Recommendation 26	ISCCM recommends the use of vasopressors to maintain MAP > 60–65 mm Hg and SBP >100 mm Hg after or during fluid resuscitation is done. The choice of vasopressor depends on the presence of DI and organ-specific requirement.
Hormonal replacement	Recommendation 27	We recommend that hormonal replacement with T4 and methylprednisolone can be considered in hemodynamically unstable patients who are adequately fluid resuscitated and are on vasopressor support.
Arrhythmias	Recommendations 28	ISCCM recommends that arrhythmias in organ donors should be detected, prevented, and treated immediately.
Correction of sodium and sugars	Recommendations 29	ISCCM recommends aggressive correction of sodium. It recommends maintaining sugars and sugar levels between 80 and 150 mg/dL. Sodium values should be maintained <160 mEq/L.
Ventilation	Recommendation 30	ISCCM recommends the use of lung-protective ventilation protocols using low tidal volume (6–8 mL/kg), plateau pressures <30 cm H_2O (to prevent ventilator-associated lung injury), driving pressure minimum oxygen requirement, and positive end-expiratory pressures of 5 cm H_2O or high as necessary adjusted to maintain PaO_2 >70 mm Hg
Temperature	Recommendation 31	ISCCM recommends prevention of hypothermia in potential organ donors and maintenance of temperature between 35 and 36°C.

(Contd...)

Table 14: *(Contd...)*

	Recommendation number	*Recommendations*
Blood transfusion trigger	Recommendation 32	ISCCM recommends PRBCs transfusion if Hct <30%.
Nutrition	Recommendation 33	ISCCM recommends continuing enteral nutrition in the management of the potential of organ donors.
Hormonal replacement	Recommendation 34	ISCCM recommends hormonal replacement therapy.
Infection control	Recommendation 35	ISCCM recommends adopting appropriate infection control measures to prevent infection in donor.
Positive blood cultures	Recommendation 36	ISCCM recommends that bacteremia or sepsis are not contraindications to donation, provided pathogen-specific antibiotics have been administered for at least 48 hours prior to procurement and the recipient receives pathogen specific antibiotics for 7–10 days.
Hurdles in organ donation	Recommendation 37	ISCCM recommends that causes for refusal of organ donation need to be recorded and measures taken to overcome these hurdles should be taken.

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