Donor Optimization in Deceased Donor Organ Transplantation: kidney



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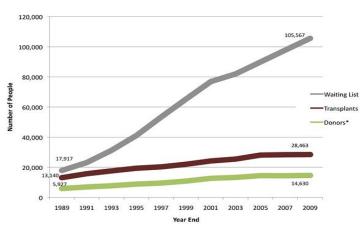


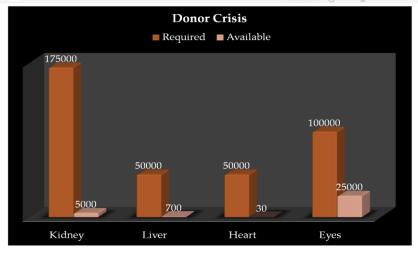
Jeevandan Cadaver Transplantation Programme Donating Life



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But the constraints are....

- Lack of public awareness regarding organ donation
- Lack of ICU protocols regarding donor optimization
- Many potential donors succumb to hemodynamic instability after brain death
- Less transplantable organs, even if consent is obtained

Key steps involved

Critical pathways for organ donation

Possible deceased organ donor

A patient with a devastating brain injury or lesion or a patient with circulatory failure and apparently medically suitable for organ donation

Donation after circulatory death (DCD)

Treating physician to identify/refer a potential donor

Potential DCD donor

 A person whose circulatory and respiratory functions have ceased and resuscitative measures are not to be attempted or continued.

A person in whom the cessation of circulatory and respiratory functions is anticipated to occur within a time frame that will enable organ recovery.

Eligible DCD donor

A medically suitable person who has been declared dead based on the irreversible absence of circulatory and respiratory functions as stipulated by the law of the relevant jurisdiction, within a time frame that enables organ recovery.

Actual DCD donor

A consented eligible donor:

In whom an operative incision was made with the intent of organ recovery for the purpose of transplantation.

From whom at least one organ was recovered for the purpose of transplantation.

Utilized DCD donor

An actual donor from whom at least one organ was transplanted.

Reasons why a potential donor does not become a utilized donor

System

- Failure to identify/refer a potential or eligible donor
- Brain death diagnosis not confirmed (e.g. does not fulfill criteria) or completed (e.g. lack of technical resources or clinician to make diagnosis or perform confirmatory tests)
- Circulatory death not declared within the appropriate time frame.
- Logistical problems (e.g. no recovery team)
- · Lack of appropriate recipient (e.g. child, blood type, serology positive)

Donor/Organ

- Medical unsuitability (e.g. serology positive, neoplasia)
- Haemodynamic instability/unanticipated cardiac
- · Anatomical, histological and/or functional abnormalities of organs
- Organs damaged during recovery
- Inadequate perfusion of organs or thrombosis

Permission

- Expressed intent of deceased not to be donor
- · Relative's refusal of permission for organ donation
- Refusal by coroner or other judicial officer to allow donation for forensic reasons

Donation after braindeath (DBD)

Potential DBD donor

A person whose clinical condition is suspected to fulfill brain death criteria.

Eligible DBD donor

A medically suitable person who has been declared dead based on neurologic criteria as stipulated by the law of the relevant jurisdiction.

Actual DBD donor

A consented eligible donor:

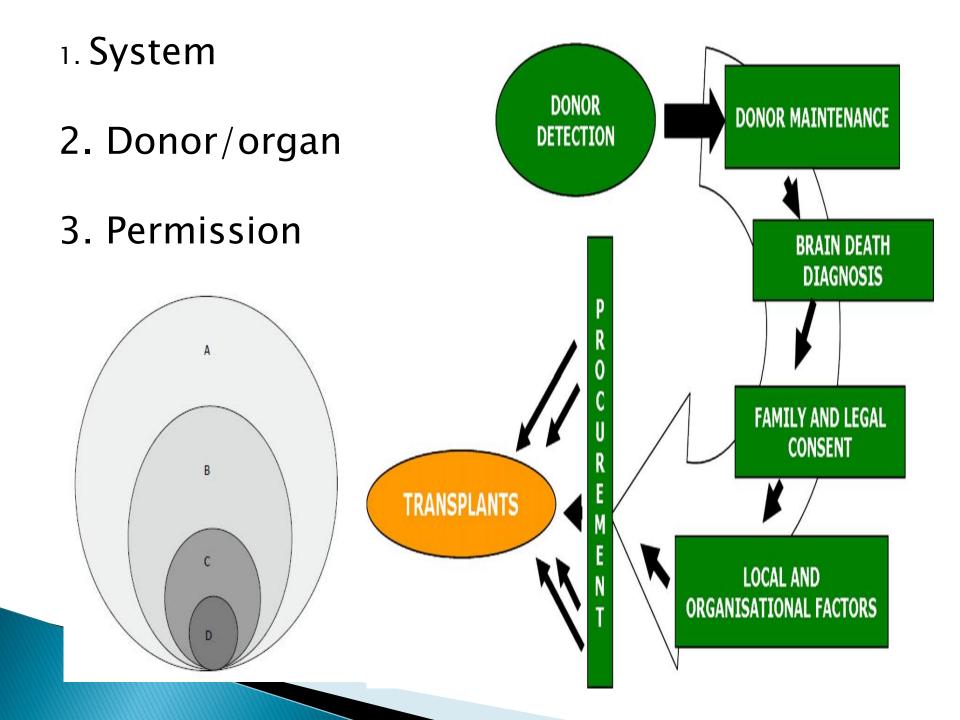
In whom an operative incision was made with the intent of organ recovery for the purpose of transplantation.

From whom at least one organ was recovered for the purpose of transplantation.

Utilized DBD donor

An actual donor from whom at least one organ was transplanted.

The "dead donor rule" must be respected That is, patients may only become donors after death, and the recovery of organs must not cause a donor's death



Brain Death Declaration

11.2. Declaration of brain death:

- (a) The procedure prescribed under Section(3) & (4) of the APTHOA Act, 1995 shall be strictly followed;
- (b) The medical board comprising of the following members shall be constituted by the NTOHC or OTC as the case may be for the declaration of brain death, in each case:
 - (i) Medical Superintendent of the Hospital
 - (ii) An independent Registered Medical Practitioner, i.e. Post graduate with 5 years post PG experience (Physician / Surgeon / Intensivist) (specialist to be nominated by the Medical Superintendent of the Hospital from the panel of names approved by the AACT)
 - (iii) A Neurologist or Neurosurgeon (to be nominated by the Medical Superintendent of the Hospital from the panel of names approved by the AACT)
 - (iv) The doctor on-duty treating the patient

Identification of the potential organ donor

- Donors should usually be<75 yr of age</p>
- No medical or social risk factors for HIV or hepatitis B/C infection
- No evidence of untreated sepsis or malignancy (apart from primary tumours of the central nervous system)

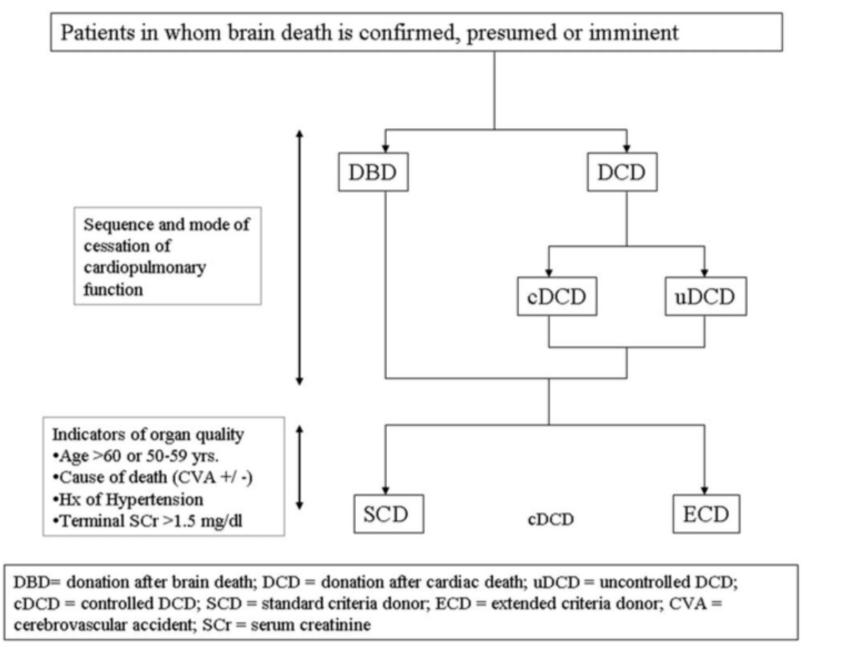
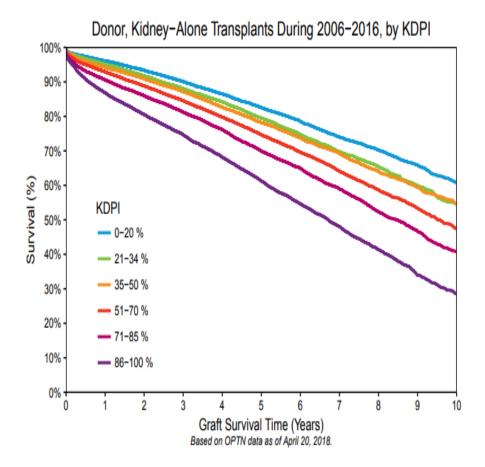


Figure 1. Categories of deceased kidney donors.

KDPI & KDRI

- The following donor characteristics are used to calculate the KDRI:
- ! Age
- ! Height
- ! Weight
- ! Ethnicity
- ! History of Hypertension
- ! History of Diabetes
- ! Cause of Death
- ! Serum Creatinine
- ! Hepatitis C Virus (HCV) Status, from serological or NAT testing
- ! Donation after Circulatory Death (DCD) Status

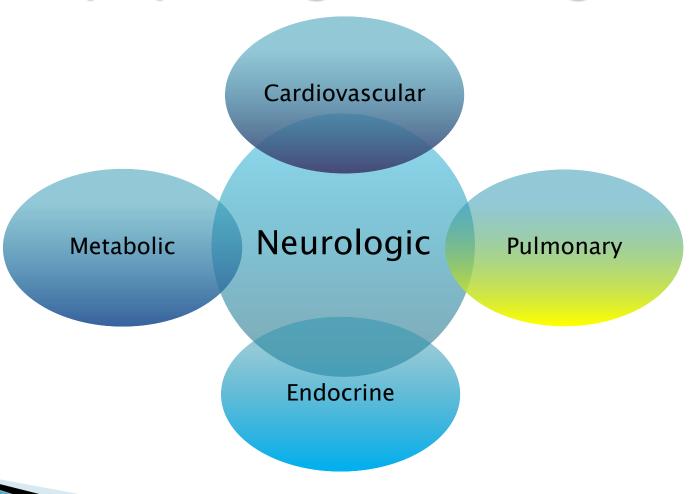
Figure 1. Kaplan-Meier Graft Survival Estimates for Adult, Deceased



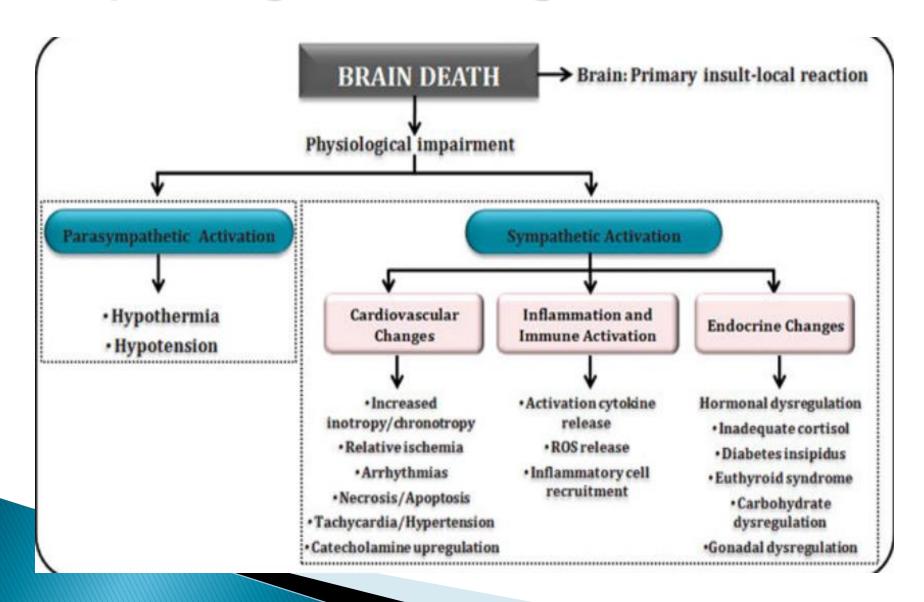
Age: (years)	
Height:	Weight:
ft in	lbs
cm	kg
Ethnicity/Race:	
History of Hypertension:	
History of Diabetes:	
Cause of Death:	
Serum Creatinine:(mg/dl)	
HCV Status	
Donor meets DCD Criteria?	

Domor optimization optimization protocols

Brain death: Pathophysiological changes



Physiological changes

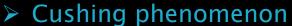


Negative feed back through Carotid and aortic sinuses

Vagal activation

Entire cerebrum Ischemic

Compression of brain stem



- Activation of Cardioaccelaratory Fibres
- Sympathetic nervous outflow
- Unopposed sympathetic stimulation
- > Autonomic storm

Hypertension/ Bradycardia

Tachycardia/ Hypertension

Tonsillar herniation
Outflow of the
cardioaccelerating and
vasomotor neurons to
the spinal cord ceases
Vagal cardiomotor nucleus
became ischemic

Loss of sympathetic tone

Myocardial dysfunction

Decreased SVR

 \downarrow HR

 $\sqrt{\mathsf{MAP}}$

↓ co

Vasomotor and cardio-accelerating neurons of spinal cord obtain automaticity



BP returns to normal

Neurogenic Pulmonary Edema



- Brain death is associated with numerous pulmonary problems
- The lungs are highly susceptible to injury resulting from the rapid changes that occur during the catecholamine storm
- Left-sided heart pressures exceed pulmonary pressure, temporarily halting pulmonary blood flow

The exposed lung tissue is severely injured, resulting in interstitial edema and alveolar hemorrhage, a state community referred to as neurogenic pulmonary edema

Endocrine

Pituitary Dysfunction

↓ Vasopressin↓ T3, T4↓ Insulin

- Diabetes insipidus
 - > Polyuria, Dehydration, Hyperosmolality
 - > Hypernatremia, Hypokalemia
- Euthyroid sick syndrome
- Hyperglycemia

Immune System

Increased levels of inflammatory mediators
Cytokines (IL-1β, IL-6, TNF-α)
Adhesion molecules
(E-selectin, ICAM-1, VCAM-1

Endocrine and acutephase reactant abnormalities



Changes in Temperature Regulation

Loss of Neural connection between the temperature-regulating center and peripheral body tissues

Reduction in metabolic rate and muscle activity and peripheral vasodilatation

Patient becomes poikilothermic

- Unwarmed IV Fluids
- > Hypothermic

Hypothermia

- ODC shifted to the left
 - Tissue oxygen delivery decreases
- ➤ 32°C -Release of tissue fibrinolytic agent from the necrotic brain
- > < 28°C VF
- No fever even if infection occurs

Coagulation

Necrotic brain

Release of Tissue thromboplastin

Disseminated Intravascular Coagulation

Incidence of common physiological derangements in brain-dead donors

Derangement	Approximate incidence
Hypothermia	Invariable if not prevented
Hypotension	81-97%
Diabetes insipidus	46-78%
Disseminated Intravascular Coagulation	29-59%
Arrhythmias	25-32%
Pulmonary oedema	13-18%

Management of the heart beating brain-dead organ donor, BJA 2012

Recommendations for treatment

Society of Critical Care Medicine/American College of Chest Physicians/Association of Organ Procurement Organizations Consensus Statement)

June 2015 · Volume 43 · Number 6

Physiological optimisation of the potential DBD donor

- Donor optimisation is an active process
- Require escalation of monitoring and therapies
- In principle it requires a switch in focus from therapies that are directed towards resuscitation of the injured brain (which is dead) to those that focus upon restoration of physiological and metabolic homeostasis of the transplantable somatic organs and tissues.
- It is particularly important to make every effort to improve cardiac and pulmonary function.
- The immediate objectives of donor optimisation should be achieved as soon as possible after consent / authorisation for organ retrieval has been established,
- Should not be delayed until the arrival of the Specialist Nurse
 Organ Donation.

Effective Donor Management

- Requires clinical expertise, vigilance, flexibility, and the ability to address multiple complex clinical issues simultaneously and effectively.
- Requires collaboration among the OPO, donor hospital critical care staff and consultants, and transplant program staff.

Effective Donor Management

It is appropriate to collaborate prior to brain death, consent, etc, to prevent death and keep the option of organ donation open.

Maximize the number of potentially transplantable organs per donor

·Optimum organ function before retrieval

British Journal of Anaesthesia 108 (S1): i96-i107 (2012)

Donor management : general considerations

- Continue ICU nursing care
- Care of indwelling catheters so as to prevent systemic sepsis
- Stop the following drugs :

Analgesics

Sedatives

Laxatives / Gastrointestinal motility agents

Antihypertensive

Mannitol

Diuretics.

Cardiovascular Management

Goal : Shift from CEREBRAL PERFUSION



ORGAN PERFUSION

- Targets:
- CVP 6–10mmHg
- HR<120bpm,</p>
- MAP 60-80mmHg.

Investigation	Interval
EGG	Baseline
CXR	Baseline
Bloods:	Daily
	Daily
FBC	Daily
Coagulation	6 hourly
Liver function	6 hourly
Electrolytes	6 hourly
Urea & Creatinine	Baseline
ABG	Once
Blood grouping and cross	Once
matching	
Viral markers	
	Once
Cultures	Once
Blood	Once
Urine	
Sputum (from ETT)	

Special Investigations	Indications
ECHO	Review functionality and structure of heart for all heart donors
PA catheter and PICO	As per unit protocol
Bronchoscopy	Selected lung donor
Coronary angiography	 Selected heart donors – extended criteria category with risk factors for CAD consultation with heart transplant team
Renal or hepatic ultrasound	As alinically indicated following
	As clinically indicated following consultation with transplant team

Points of Debate

Should Autonomic storm be treated?

How should they be monitored?

What should be the fluid therapy?

Type of Fluid

Amount of Fluid

What is the ideal vasoactive agent?

What is the optimal haemoglobin?- when is

transfusion indicated?

Treatment of Autonomic Storm

- Short-acting β-blocker drugs or nitroprusside
- Attenuate myocardial dysfunction
- Increase the number and success rate of heart procurements and cardiac transplantations

PA, Grégoire H, Devaux Y *et al.* Improvement of donor myocardial function after treatment of autonomic storm during brain death. Transplantation 2006;

Fluid Therapy: Recommendations

- Hypovolemia frequently is present at brain death and must be addressed promptly.
- Hemodynamic monitoring tools aid in assessment of volume status and response to therapy.
 - Pulmonary artery or central venous catheter insertion
- > Fluid replacement using hemodynamic parameters, particularly CVP or PAOP, and targeted at maintaining euvolemia of the donor, is recommended during the entire donor management phase of care.

Preferred Resuscitation Fluid for Organ Preservation

- > **Volume expansion**: Initial intravascular volume replacement with crystalloids or colloids is acceptable.
- The recommended isotonic crystalloids are 0.9% saline and lactated Ringer solution.
- HES(hydroxyethyl starch) should not be used routinely for colloidal resuscitation in organ donors
- Balanced crystalloids to avoid hypernatraemia and hyperchloremic acidosis

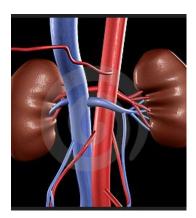
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RL / Plasmalyte A
0.45% NS / 5% Dextrose (if Na > 150 meq/l)
Avoid HES
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- PRBC transfusion, if Hb < 7 gm/dl (stable donors) or < 9 gm/dl (unstable donor)</p>
- Monitors: CVP, IVC dimensions (USG), Echo, PPV.

Competing physiologic needs



Heart: Balanced Fluids, Vasopressin

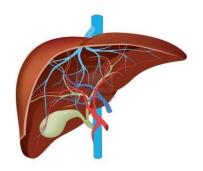


Kidney: Liberal Fluids, Dopamine



Community Elling

Lungs: Conservative Fluids, less pressors



Liver: Isotonic fluids

Vasoactive Drugs for Organ Preservation in the Donor

Dopamine

- Attenuates Inflammatory Response
- Improved renal graft function

Vasopressin

- Reduces use of nor-epinephrine
- Increased organ recovery
- · (1-2.4 u /hr)
- Norepinephrine, phenylephrine, and other vasoactive agents (e.g., dobutamine and epinephrine) may be used in severe shock
- Noradrenaline
 - Reduced one year graft survival (preferably < 0.2 mcg/kg/min)
 - If hemodynamic goals are not met and/or left ventricular ejection fraction remains less than 45%, HRT may be undertaken

Endocrine replacement

- DDAVP -treatment of Diabetes insipidus
- ▶ *I.V. triiodothyronine (T3*) improves cardiovascular stability in the donor
- High dose methylprednisolone attenuate the effects of proinflammatory cytokines, improving oxygenation and increasing lung donor recovery; it may be indicated if lung transplantation is planned or 'hormone resuscitation' considered
- Insulin- Treatment of hyperglycemia
 - Three-drug 'hormone resuscitation' is included in the standardized management protocol of the United Network for Organ Sharing (UNOS), which led to a 22% increase in numbers of organs recovered

AVP: Recommendations

- Treatment for AVP deficiency should be considered when hypotension persists despite adequate volume resuscitation.
- Treatment for AVP deficiency should be considered in the presence of DI, which is likely to be present if one or more of the following criteria are identified in the absence of other causes of these abnormalities:
 - Polyuria (urine output > 3-4 L/d or 2.5-3.0 mL/kg/hr).
 - Normal or increased serum osmolality.
 - Inappropriately dilute urine (specific gravity < 1.005,
 - Urine osmolality < 200 mOsm/kg H2O).
 - Hypernatremia (Na+ > 145 mmol/L).

Recommendations

- Hypotension,

start IV AVP at 0.01-0.04 IU/min.

For DI with significant hypernatremia (sodium, > 145-150 mmol/L) without hypotension, desmopressin IV 1-4 μg,

an additional 1 or 2 µg every 6 hours

- Both AVP and desmopressin can be used concurrently in the hemodynamically unstable donor with severe hypernatremia.
- Electrolytes should be monitored closely as urinary losses associated with DI can lead to hypokalemia, hypophosphatemia, and hypomagnesemia. These electrolytes should be replenished.

Cortisol therapy: Recommendation

- High-dose corticosteroid administration methylprednisolone 1,000 mg IV, 15 mg/kg IV, or 250 mg IV bolus followed by infusion at 100 mg/hr) reduces the potential deleterious effects of the inflammatory cascade on donor organ function following brain death.
- Ideally it should be administered after blood has been collected for tissue typing as it has the potential to suppress human leukocyte antigen expression

Recommendations for Thyoroid Hormone replacement Therapy

- Thyroid replacement therapy—either alone or as part of a combination hormone therapy with IV AVP, corticosteroids, and insulin—should be considered for hemodynamically unstable donors or for potential cardiac donors with abnormal (< 45%) left ventricular ejection fraction.
- Both T3 and T4 are acceptable for use as a component of HRT.
- Commonly utilized protocol
 - Administer T4 IV with a 20- μ g bolus, followed by an infusion at 10 μ g/hr
 - Or Administer T3 IV with a 4.0- μ g bolus, followed by an infusion at 3 μ g/hr.

(Crit Care Med 2015; 43:1291-1325)

Endocrine Management

Clinical problem	Management
Diabetes Insipidus	Maintain Na+ = 155 mmol.l-1 with 5% dextrose Maintain urine output about 1 - 2 ml.kg-1.h -1 with vasopressin 1 U bolus and 0.5-4.0 U.h-1 infusion. If vasopressin fails to control diuresis, intermittent desmopressin (DDAVP)
Hyperglycaemia	Insulin infusion to maintain plasma glucose 4-9 mmol.l-1 Maintain K >4.0 mmol.l-1
Hypothyroidism	Tri-iodothyronine (T3) 4 μg bolus then infusion at 3 $\mu g.h-1$

Hyperglycemia

- Brain death causes major hormonal alterations that result in insulin resistance and gluconeogenesis.
- 72% of the donors had terminal glucose concentrations more than 200 mg/dL and 39% had glucose concentrations more than 250 mg/dL
- Osmotic diuresis may lead to volume depletion and electrolyte abnormalities and perhaps increase the risk of donor organ dysfunction

Recommendation

- Hyperglycemic organ donors should be managed according to institutional guidelines for other critically ill patients.
- Routine use of IV fluids containing dextrose should be avoided.

Infection control measures

General measures:

- Hand Hygiene
- Bronchial toilet improves elimination of secretions and therefore improves chances of lung donation.
- Eye care to ensure no corneal abrasions or ulcers and improves chances of corneal donation.
- Antibiotics

Temperature Management

- Keep the donor's temperature above 34° C
 - Warm IV fluids
 - Increase the environmental temperature .
 - A convectional warming device
 - Bair Hugger/Warm Touch

Suggested goals for the active management of potential organ donors

Parameter	Target
Heart rate	60-120 beats min ⁻¹
Arterial pressure	Systolic pressure >100 mm Hg
	Mean pressure ≥70 mm Hg
Central venous pressure	6–10 mm Hg
Urine output	$0.5-3 \text{ ml kg}^{-1} \text{ h}^{-1}$
Electrolytes	Serum sodium 130–150 mmol litre ⁻¹
	Normal potassium, calcium, magnesium, phosphate
	Glucose 4-8 mmol litre ⁻¹
Blood gases	pH: 7.35-7.45
	Pa _{CO₂} : 4.7-6 kPa
	<i>P</i> a _{O2} : ≥10.7 kPa
	Sp_{O_2} saturation \geq 95%
If pulmonary artery catheter inserted	
Pulmonary capillary wedge pressure	6–10 mm Hg
Cardiac index	2.4 litre min ⁻¹ m ⁻²
Systemic vascular resistance	800–1200 dyn s cm ⁻⁵

Shemie et al. Organ donor management in Canada: recommendations of the forum on medical management to optimize donor organ potential. Can Med Assoc J 2006

Goals of Donor Management

- Rule of 100
 - >Systolic arterial pressure- 100 mm hg
 - ➤ Urine output -100 ml/ h
 - \geq Pao₂-100 mm hg
 - ➤ Haemoglobin concentration -100 g/l
 - ➤ Blood sugar –100% normal

(Gelb AW 2011)

Brain death – Declaration of brain death made mandatory in Government Medical College Hospitals in Chennai – Orders Issued. Health & Family Welfare (Z1) Department G.O.(Ms) No.6 – 2038, Sarvajith, Margazhi Matham –1) Dated: 08.01.2008

Chennai that could have been utilized by other patients who are not in a similar state and have a better chance of recovery. It is also known that failure to declare brain death even when all the conditions are evident has led to prolonged anxiety for all family members and friends of the patients.

- 2. Due to the lack of clarity on this issue and the optional nature of the current situation, it is necessary to issue orders making it mandatory to declare "Brain death" and certify it accordingly.
 - 3. The following orders are therefore issued in the matter:-

It is now made mandatory that whenever the medical condition (clinical and medical criteria have been met for) of a patient has reached a brain death stage, brain death certification is to be done by the authorized medical personnel.

4. The above order shall come into force in the three Government Medical College Hospitals in Chennai, viz., Government General Hospital, Government Stanley Hospital, and Government Kilpauk Medical College Hospital (Inclusive of Government Royapettah Hospital) with immediate

Dedicated Deceased Donor Maintenance Unit



Organ-specific optimisation concerns

kidneys

goal – Euvolemia CVP 4–10 mm Hg UOP > 1 mL/kg/hr

Resuscitate with crystalloids or colloids

Avoid HES

Single, low-dose pressor use preferred

Liver

Avoid and treat hypernatremia

Donor Na > 155 meq/l
Increased need for re-transplantation at 30d
Increased allograft failure at 90d

lungs

Goals

Arterial pH 7.3 - 7.45

 $PaO_2/FiO_2 > 300$

Avoid excessive fluid resuscitation and vasopressors

Early bronchoscopy

To obtain culture

To clear atelectasis

Chest physiotherapy every 4hrs

HOB elevation >30 degrees

Critical care support during retreival

- The multi-organ retrieval procedure laparotomy extended by a median sternotomy.
- Steps taken in the ICU to optimize organ function should continue.
- Anaesthesia low concentrations of volatile agents – treat hypertension
- Full paralysis is required, as spinal reflexes will persist, but histamine release after atracurium administration can cause unexpected hypotension.

Other - antibiotics and heparin

Organ Allocation Registry

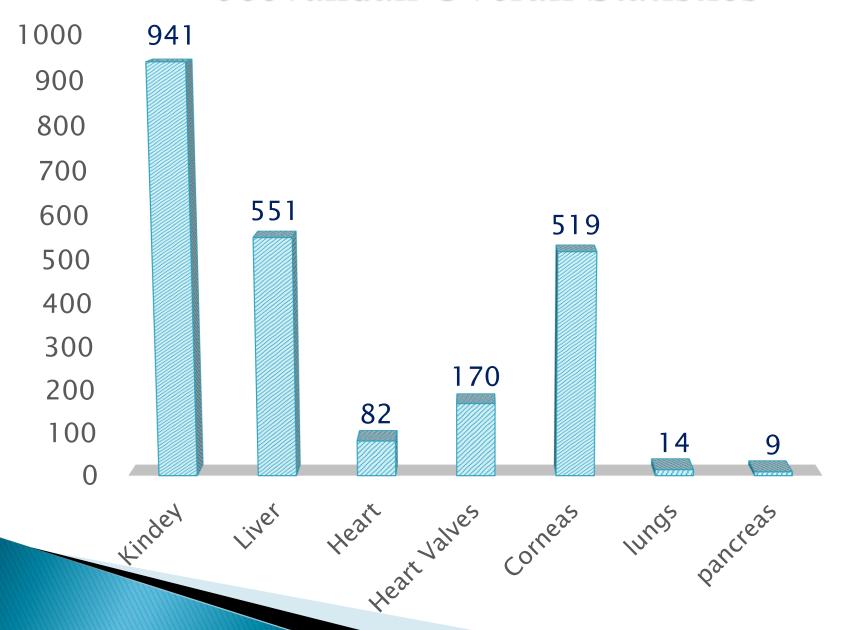
www.jeevandan.gov.in



https://twitter.com/Jeevanda



Jeevandan Overall Statistics

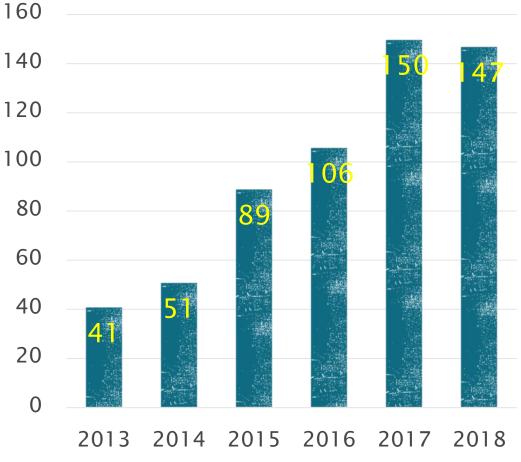


Registration Statistics

Organ Name	Total
Liver	2022
Kidney	2288
Heart	124
Lungs	28
Pancreas	13
Total	4475

Year Wise donations

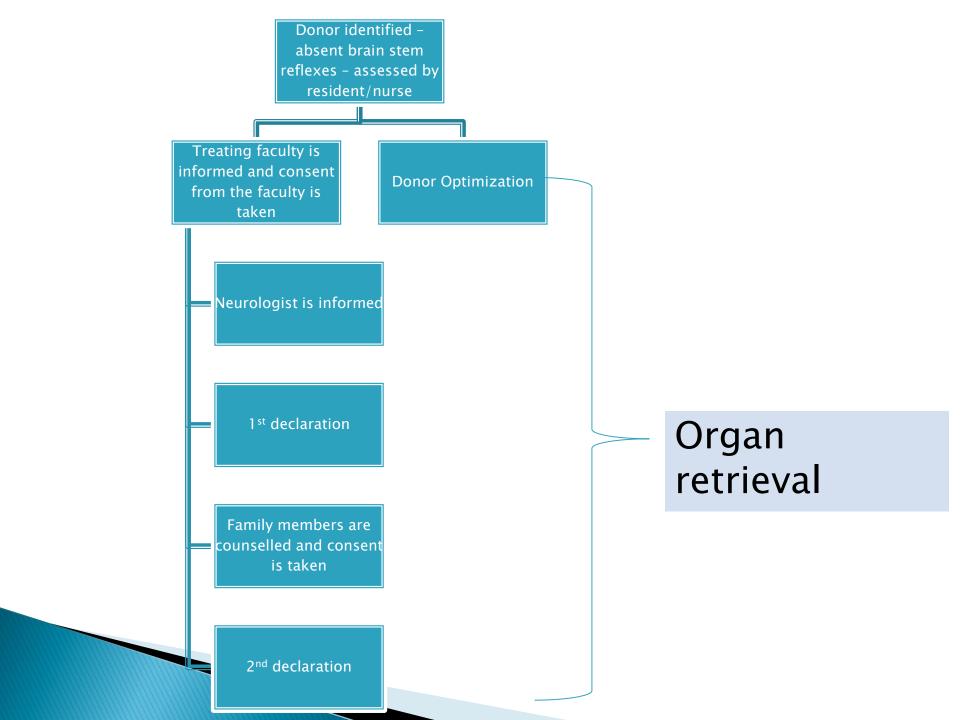
Year	Donations
2013	41
2014	51
2015	89
2016	106
2017	150
2018	147
Total	584



Donation rate of Jeevandan in 2016: 3.01 Donation/million Donation rate of Jeevandan in 2017: 4.26 Donation/million

Donation rate of Jeevandan in 2018 up to date: 4.87

Donation/million



Donor Optimization

· Vasopressors and thyroxine 300mcg 8th hourly

HR 60-120/min

- Dec vasopressors NA/vasopressin 1 2.5 U/hr
- Inc esmolol 0.1 0.3 mcg/kg/min, Na nitroprusside 1–5 mcg/kg/min

SBP - > 100 mm HgMAP - > 70 mm Hg

Hydration

CVP - 6-10 mm Hg

Na - 130 - 150 meq/L

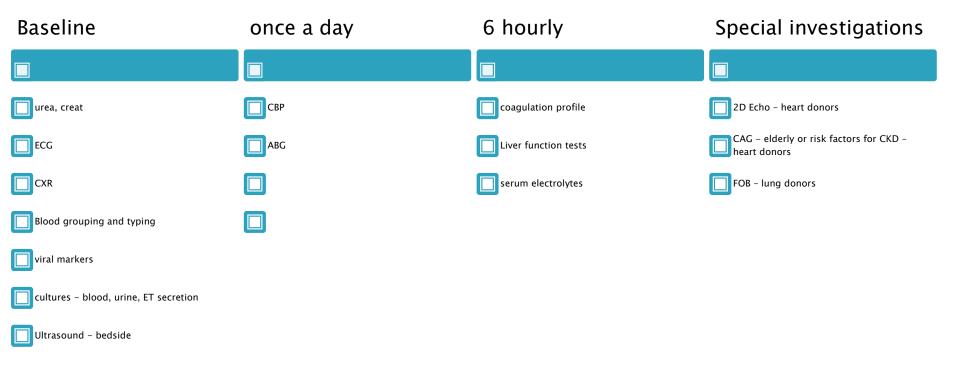
- $\cdot > 150 \text{ meg/L} 5\%D \text{ or } 0.45 \% \text{ NS}$
- Osmotic diuresis with 5% D, further increase in hypernatremia
 should be taken care

UOP - 0.5 - 3 ml/kg/hr

- $\cdot > 3 \text{ ml/kg/hr} DI$
- Vasopressin 2.2 U/hr
- DDAVP 2 4mcg 2-6 hrly

spO2 - >95% pH - 7.35 - 7.45 PaO2 - 80 mm Hg PaCO2 - 36 - 47 mm Hq Ventilatory settings

Donor Optimization – investigations



Summery

- >Brain stem death is frequently followed by a predictable pattern of complex multiple organ failure.
- Appropriate support before and after brain death can improve the number and quality of donor organs.
- > Such support is intensive and time-consuming.
- Increasing numbers of marginal donors are now being accepted as potential donors.
- ➤Organizational aspects of donor management (e.g.skilled retrieval teams) are important but have not been implemented fully

Summery

Aggressive donor management

- Early identification of potential organ donors
- Dedicated team providing medical management
- Targeted resuscitation with fluids, avoidance of both hypo & hypervolemia, vesopressors and hormonal therapy along with antiinflamatory therapies.

Success of Cadaver Transplantati Programme team work



JEEVANDAN CADAVER TRANSPLANTATION PROGRAMME



State Government of Telangana



The Loss of one Life could be the Begining of another....

Become an "ORGAN DONOR"

Thank You

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website: www.jeevandan.gov.in

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