Organ Donation in Ontario: A Guide for Critical Care Residents

1st Edition

Trillium Gift of Life Network

Organ Donation in Ontario: A Guide for Critical Care Residents

1st. Edition

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Produced by the Trillium Gift of Life Network and the Practice Performance and Innovation Unit of the Royal College of Physicians and Surgeons of Canada

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Contributors

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Content

Design Note

Unlike a traditional printed publication, this eBook was designed to be experienced in a non-linear manner with the thought that clinicians can use the material as reference or at the bedside.

Within the material you will see several conceptual maps that represent expert consensus on how to approach a particular treatment goal. These maps, allow you to jump around the book content quickly.

The book also includes a set of icons that provide access to layers of information that we hope you will find useful.


Tap this shape to jump to an overview map for the current chapter


Tap this shape to jump to an overview map for a different chapter


Tap this symbol to jump to a sub-map within the chapter


Tap this symbol to play multimedia content


Tap this symbol to access material that supports the map

Underlined text indicates that a short definition is available on tap.

Ellipses like these... indicate that tapping the item reveals additional text

Neurological Declaration of Death

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Introduction

Brain death is defined as the irreversible loss of consciousness combined with the irreversible loss of all brainstem functions, including the capacity to breathe. For patients who die as a result of severe brain injury, standard end-of-life care should include offering the option of organ and tissue donation. All patients who are suspected of being brain dead should have an assessment to document death by neurologic criteria and to establish donor eligibility. This chapter reviews the concept of brain death, pathophysiology, and diagnostic criteria for declaration including minimum clinical criteria and ancillary testing. In addition, it presents a clinical approach to the declaration of neurological death which is supported by evidence for each task performed during the process (refer to the interactive map under Clinical Approach).

Brain Death Concept

In Canada, brain death is defined as the irreversible loss of the capacity for consciousness combined with the irreversible loss of all brainstem functions, including the capacity to breathe. The concept of brain death served to address 2 major issues that arose as a result of advances in health care in the 1960's:[1] practical issues that arose with the advent of intensive care units with artificial airways and mechanical ventilators regarding the treatment of apneic patients and ethical concerns associated with organ donation arising from the then-new discipline of transplant surgery [2]. The clinical appearance of brain death was first described in seminal work by the French in 1959 and termed "coma dépassé" meaning "a state beyond coma". In 1968, the Ad Hoc Committee of the Harvard Medical School defined irreversible coma and brain death and the definition of irreversible loss of brainstem function in brain death was formally adopted in the UK in 1995[3] In the United States, the Uniform Determination of Death Act states than "an individual who has sustained irreversible cessation of all functions of the entire brain, including the brainstem, is dead." It is important to understand that the clinical bedside evaluation assesses the complete loss of brainstem function, but it does not distinguish between brainstem death, as may be seen in isolated brainstem infarction, or whole brain death that involves the cerebrum and the brainstem[4].

Brain death is a term and a concept that remains a source of misunderstanding for many practitioners, casual observers, and the public. From a physiological perspective, it is better understood as irreversible brain arrest or complete and irreversible cessation of clinical functions of the brain. Neurological determination of death is the process and procedure to determine death in the context of a ventilated patient with irreversible brain failure. It should never be confused with other forms of severe brain injury, such as unconsciousness, reversible coma, persistent vegetative state, cortical death or anencephaly[5,6].

Pathophysiology

Regardless of the primary etiology of brain injury, tissue edema or mass effect leads to the final common pathway characterized by increasing intracranial pressure, which progressively impairs cerebral blood flow. As pressure rises inside the rigid intracranial vault, it may do so heterogeneously throughout the brain or selectively within compartments. Pressure-related ischemia ensues leading to further neuronal/glial injury, abnormal vascular autoregulation, and edema[7]. This contributes to a continued rise in ICP until intracranial pressure

1 Mollaret P, Goulon M. Le coma dépassé. Rev Neurol (Paris). 1959;101:3-15

2 A definition of irreversible coma: Report of the Ad Hoc Committee of the Harvard Medical School to Examine the Definition of Brain death. JAMA. 1968;205:337-40

3 Diagnosis of brain death: Statement issued by the honorary secretary of the Conference of Medical Royal Colleges and Their Faculties in the United Kingdom on 11 October 1976. BMJ. 1976;2:1187-8

4 The President's Council on Bioethics: Controversies in the determination of death: a white paper by the President's Council on Bioethics 2008. http://bioethicsprint.bioethics.gov/reports/death/Controversies%20in%20the%20Determination%20of%20Death%20for%20the%20Web%20(2)

5 Wijdicks EF, "Brain death worldwide: Accepted fact but no global consensus in diagnostic criteria", Neurology, 2002;58;20-25

6 Bernat JL.Contemporary controversies in the definition of death. Prog Brain Res. 2009;177:21-31.

7 Shemie SD, Doig C, Belitsky P. Advancing towards a modern death: The path from severe brain injury to neurological determination of death. CMAJ. 2003 Apr 15;168(8):993-5.

exceeds arterial inflow pressure and irreversible brain arrest/failure occurs. In response to rising intracranial pressure, the brain herniates through paths of least resistance, most commonly seen as downward descent of the brainstem and cerebellum through the foramen magnum. Cellular disruption and herniation triggers an inflammatory cascade that affects cardiorespiratory function and hormonal regulation. This cascade affects pituitary and hypothalamic function, and the brainstem resulting in catecholamine, thyroid, and vasopressin abnormalities. The duration of time from injury to brain death may vary, depending on mechanism and severity of initial injury and the response to neuroprotective therapies[8].

Clinical Approach (Map 1)

Neurologic Determination of Death is a detailed clinical examination that documents the complete and irreversible loss of consciousness and absence of brainstem function including the capacity to breathe. In accordance with the Trillium Gift of Life Network Act, Trillium Gift of Life Network (TGLN) endorses recommendations from the Canadian Council for Donation and Transplantation (CCDT) 2003 Forum on Severe Brain Injury to Neurological Determination of Death, and 2007 Forum on Brain Blood Flow in the Neurological Determination of Death. Adaptations have been made based on other newer recommendations[9,10,11].

The physician must work in accordance with provincial standards (Map2) to identify irreversible proximate cause for death and account for conditions capable of mimicking neurologic death (Map 3). Once potential confounding conditions are identified and corrected, the physician with appropriate skills and knowledge must perform a clinical neurologic exam confirming neurologic death (Map 4). Once the exam is completed and is consistent with neurologic death, the pronouncement of death with specific documentation is completed. A second exam is necessary for the purposes of organ donation, consistent with existing provincial laws.

If conditions capable of mimicking neurological death cannot be corrected or if any part of the neurological exam cannot be reliably interpreted or fully performed, then the appropriate use of ancillary testing, where specifically indicated, is required. Even with the addition of ancillary testing, all feasible components of the clinical neurological exam should be completed by two physicians. Once ancillary testing confirms the findings of the clinical exam, then the pronouncement of neurologic death is complete. Contacting the TGLN Donation Support Physician may be appropriate to discuss best practices for management of neurological determination of death and organ donation.

8 Dhanani S and Shemie SD. “Brain Death”. Pediatric Critical Care Medicine: Basic Science and Clinical Evidence, 2nd Edition. Eds Derek S. Wheeler, Hector R. Wong, Thomas P. Shanley, Springer, 2014

9 Shemie SD, Doig C, Dickens B, Byrne P et al. Severe brain injury to neurological determination of death: Canadian Council for Donation and Transplantation Forum recommendations. CMAJ. 2006 Mar 14;174(6):S1-13.

10 Shemie SD, Lee D, Sharpe M, Tampieri D, Young B; Canadian Critical Care Society. Brain blood flow in the neurological determination of death: Canadian expert report. Can J Neurol Sci. 2008 May;35(2):140-5.

11 Wijdicks EF, Varelas PN, Gronseth GS, Greer DM; American Academy of Neurology.Evidence-based guideline update: determining brain death in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2010 Jun 8;74(23):1911-8.

Conclusion

The neurologic determination of death is currently the standard of practice as one of the prerequisites to organ donation in ventilated patients with irreversible cessation of all clinical functions of the brain. It is being used to initiate withdrawal of mechanical support discussions and is a prerequisite to organ donation. Its concept has been internationally accepted as a medical and legal definition of death in many countries with advanced health care systems. Brain death is defined as the irreversible loss of the capacity for consciousness combined with the irreversible loss of all brainstem functions, including the capacity to breathe. NDD remains a fundamentally clinical examination establishing a clear mechanism for catastrophic brain injury in the absence of confounding or reversible factors. Ancillary radiologic testing is only recommended when a full clinical exam cannot be reliably completed or when mimickers of neurological death cannot be rapidly and completely reversed. Stringent legal and clinical criteria exist to ensure transparency, safety and trust in the process.

Return to Chapter

Declaring Neurological Death

ensure

Work process in accordance with Provincial Standards

identify

Proximate cause

identify and correct

Conditions capable of mimimicking neurologcal death

if it is anticipated that

Findings from neurological examination cannot be completed or reliably interpreted
OR
Conditions capable of mimicking death cannot be completely and rapidly corrected

still need to perform

All feasible components of neurological examination

contact

Donation Support Physician

to advise on need for

Ancillary tests

and confirm

Death

once conditions have been corrected, complete

Clinical examination of neurological death

if completed and consistent with death, declare

Return to Chapter

Declaring Neurological Death

Working in Accordance with Provincial Standards

which specify

Physicians

with

No association to
the proposed recipient
AND
Full and current licensure for independent
medical practice in the relevant Canadian jurisdiction
AND
Skill and knowledge in the management of patients
with severe brain injury and in NDD in the patient's
age group

Minimum of two determinations

if performed in

Neonates (less than 30 days)

done

At different times with a minimum of 24 hours between determinations

Infants (30 days to less than 1 year)

done

At different times with no specified time interval between determinations

Children (1 year or older), adolescents, and adults

either done

Simultaneously or at different times with no specified time interval between determinations

Return to Chapter

Declaring Neurological Death

Identifying Conditions Capable of Mimicking Neurological Death

consider

Defined as: Core temperature < 34⁰ C in infants, children and adults: core temperature < 36⁰ C in newborn

- Hypothermia
- Electrolyte abnormalities
- Neuromuscular blockade
- Unresuscitated shock
- Peripheral nerve or muscle dysfunction
- Inborn errors of metabolism, severe liver and/or renal dysfunction
- Clinically significant drug intoxications, liver and renal dysfucntion - hypothermia
- Hypoxic brain damage secondary to cardiac arrest

wait for

24 hours following return of spontaneous circulation

then proceed to

Clinical Examinaition of Neurological Death

correct, then proceed to

if deemed uncorrectable

Consult the Donation Support Physician

if unsure

either

Wait until medication has been metabolized/excreted, or give antidotes

Return to Chapter

Declaring Neurological Death

Clinical Examination of Neurological Death

perform

Assessment

confirm

Deep unresponsive coma

perform

assess

Apnea test

recognize

Chronic respiratory insufficiency and responsiveness to only supranormal levels of carbon dioxide
OR
Patients dependent on hypoxic drive

consult

Donation Support Physician

Brainstem reflexes

if performed in

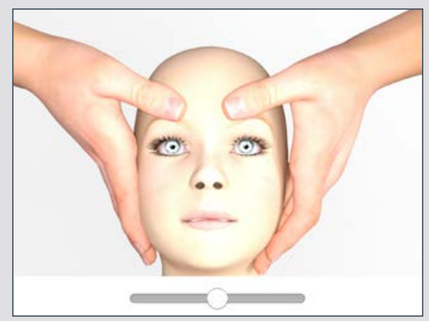
Neonates (less than 30 days and minimum time from birth of 48h, and correct gestational age of 36 weeks)
add both oculocephalic and suck reflex assessment. Minimum core temperature 36 degrees C

Infants
(30 days to less than 1 year)
add oculocephalic reflex assessment

Adults, adolescents, and children (1 year or older)

Cough and Gag Reflexes
Corneal Reflexes
Vestibulo Ocular Response

Select image to see a demonstration of oculocephalic relex. Requires internet connection.



Identifying Proximate Cause

Kim Bowman

Description

Identification of a proximate cause of death is a prerequisite to NDD. There must be definite clinical or neuroimaging evidence of an acute central nervous system (CNS) event consistent with the irreversible loss of neurological function[1].

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Rationale

In order for NDD to be declared, a definitive cause of death must be identified and conditions mimicking neurological death must be ruled out. The identified proximate cause of death must be consistent with irreversible loss of neurological function[1].

Examples of conditions leading to neurological death may include (but are not limited to) the following:

- Acute brain injury - e.g. cerebrovascular accidents, head trauma, intracranial tumors, intracranial hemorrhage or acute hydrocephalus
- Hypoxic-ischemic injury - e.g. resuscitated cardiac arrest, near drowning asphyxia, hypovolemic shock
- CNS infection - e.g. meningitis, encephalitis
- Miscellaneous - e.g. Metabolic encephalopathy from liver disease, diabetic ketoacidosis, metabolic disorders, acute hyponatremia or vasculitis[2].

However these conditions must also be associated evidence of increased intracranial pressure or cerebral edema in order to lead to irreversible neuronal injury. In the clinical judgement of the treating physician, the proximate cause of death must be confirmed by a clinical presentation (e.g. prolonged circulatory arrest) or neuroimaging (e.g. cerebral edema on CT head) that fully explain neurological death1. NDD for the purposes of donation cannot take place unless a proximate cause has been established.

1 Shemie SD, Doig C, Dickens B, et al. Severe brain injury to neurological determination of death: Canadian forum recommendations. CMAJ : Canadian Medical Association Journal. 2006;174(6):S1-S12. doi:10.1503/cmaj.045142.

2 "Determination of Death". Donation Resource Manual: A Tool To Assist Hospitals With The Process Of Organ And Tissue Donation. 6th ed. Toronto: Queen's Printer, 2014. Print.

Findings from the Neurological Examination Cannot be Completed or Reliably Interpreted

Louise Pope-Rhoden, Janice Beitel

Description

When findings from the clinical Neurological Examination cannot be completed or reliably interpreted

- Consider consultation with an expert opinion, (i.e. TGLN donation support physician or local expert)
- When any component of the clinical neurological examination cannot be performed, consider performing an ancillary test demonstrating the global absence of intracranial blood flow[1].

Return to Overview Map

Rationale

Certain injuries or preexisting diseases, especially when very severe, can make the clinical exam unreliable. It is preferable to complete the Neurological Exam including the apnea test and to then seek an expert opinion, (i.e. TGLN donation support physician or local expert) before proceeding to ancillary testing. A neurological exam must be conducted that establishes compatibility with death as ancillary testing is considered supportive, not confirmatory of neurological death[1].

At a minimum, two particular clinical criteria must be met before ancillary tests are performed:

- An established etiology capable of causing neurological death in the absence of reversible conditions capable of mimicking neurological death.
- Deep unresponsive coma.

If a patient is unstable or becomes too unstable to complete any portion of the clinical exam (including apnea testing), or the clinical components of the exam cannot be completed, ancillary testing may be required to determine death by neurological criteria. Examples of situations where this occurs include:

- High cervical cord injury-- the efferent pathway for the cough/gag reflex are the phrenic nerve and the innervation of the thoracic and abdominal musculature which cannot be assessed in patients with high cervical injury[2].
- The use of anticholinergic drugs such as atropine that can cause pupillary dilatation[2].
- Fractures to base of skull or petrous temporal bone that may obliterate reflex responses on the side of the fracture[2].
- Severe lung disease: Caution must be exercised in considering the validity of the apnea test if, in the physician's judgment, there is a history suggestive of chronic respiratory insufficiency and responsiveness to only supranormal levels of carbon dioxide, or if the patient is dependent on hypoxic drive. If the physician cannot be sure of the validity of the apnea test, an a ncillary test should be administered[1]. Consider seeking an expert opinion (e.g.TGLN Donation Support Physician or local expert) before proceeding to ancillary testing.

1 Shemie SD, Doig C, Dickens B, et al. Severe brain injury to neurological determination of death: Canadian forum recommendations. CMAJ : Canadian Medical Association Journal. 2006;174(6):S2,3. doi:10.1503/cmaj.045142.

2 Australian and New Zealand Intensive Care Society (ANZICS) THE ANZICS STATEMENT ON DEATH AND ORGAN DONATION (pgs 20,21) Edition 3.2 2013

Conditions Capable of Mimicking Death Cannot be Completely or Rapidly Corrected

Kim Bowman

Description

May include but are not limited to factors such as hypothermia, electrolyte abnormalities, neuromuscular blockage etc.

- If such conditions cannot be completely or rapidly corrected, a clinical exam should still be conducted to the extent possible.
- An ancillary test should be considered[1].
- Consult with the donation support physician (DSP) or local expert should be considered before ordering any ancillary tests to ensure that all efforts have been made to perform neurological declaration of death (NDD) using clinical criteria including the apnea test.

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Rationale

Conditions capable of mimicking neurological death have been well cited in numerous donation related documents [1,2]. In order to determine neurological declaration of death for the purposes of donation, conditions capable of mimicking neurological death[3] should be identified and corrected. Ancillary testing should be considered if in the physician's judgement some of these conditions cannot be fully corrected or if correction of a mimicker of neurological death (e.g. a serum sodium of >160), would unduly prolong the time period before donation as perceived by the donor's family. Because ancillary testing is considered supportive, not confirmatory of neurological death, a neurological exam must be conducted that establishes (to the extent possible) compatibility with death[2]. Consider seeking an expert opinion (e.g. TGLN Donation Support Physician or local expert) before proceeding to ancillary testing.

1 Shemie SD, Doig C, Dickens B, et al. Severe brain injury to neurological determination of death: Canadian forum recommendations. CMAJ : Canadian Medical Association Journal. 2006;174(6):S1-S12. doi:10.1503/cmaj.045142.

2 "Determination Of Death". Donation Resource Manual: A Tool To Assist Hospitals With The Process Of Organ And Tissue Donation. 6th ed. Toronto: Queen's Printer, 2014. Print.

3 Shemie, Sam D. et al. "International Guideline Development For The Determination Of Death". Intensive Care Med 40.6 (2014): 788-797. Web.

Contact Donation Support Physician

Eli Malus, Sonny Dhanani

Description

Contact Donation Support Physician (DSP) or local expert: TGLN 1-877-363-8456

Rationale

The Donation Support Physician (DSP) is an intensivist on-call and available by phone 24/7 within Ontario. Their main role is to support and advise the provincial resource centre, the organ and tissue donation coordinator, and the most responsible physician. Discussions might include donor identification, declaration of death, organ suitability, and donation logistics.

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Consultation with a physician expert from TGLN prior to declaration of death may appear to represent a conflict of interest. However, it is well recognized that appropriate expertise and experience for NDD is greatest at the OPO with the organ and tissue donation coordinator and the donation support physician. This is an important mechanism to support this process and physicians invested in the donation system will be committed to the integrity of this system. A consultation to the DSP is always done with acknowledgements of ethical practice standards and with the utmost professionalism

When findings from neurological examination cannot performed or reliably interpreted OR conditions mimicking neurological death cannot be corrected, it is important to consider contacting either the DSP or a local expert to discuss concerns or performing ancillary tests. Even though TGLN documents suggest that ancillary tests may be performed in these situations, these tests should only be ordered during appropriate situations while considering risks and benefits of the chosen ancillary test The DSP or local expert can help determine their appropriateness given the clinical context. If examination according to the minimum clinical criteria (to the extent possible) is compatible with death, an ancillary test demonstrating the global absence of intracranial blood flow supports the declaration of death[1]. Any ancillary test is considered supportive, not confirmatory, of neurologic death.

Contacting the DSP or local expert should be considered before ordering any ancillary tests to ensure that all efforts have been made to perform NDD using clinical criteria including the apnea test. It is our experience that on occasion, with advice from a DSP or local expert, it still may be possible to perform NDD using clinical criteria obviating the need for ancillary tests. If after consultation with the DSP or local expert it is deemed that an ancillary test is required, the DSP/local expert can also help guide the selection of the most appropriate ancillary test given the clinical situation and local expertise.

1 Shemie SD, Doig C, Dickens B, et al. Severe brain injury to neurological determination of death: Canadian forum recommendations. CMAJ : Canadian Medical Association Journal. 2006;174(6):S1-S12. doi:10.1503/cmaj.045142.

Determining Neurological Death in Neonates According to Provincial Standards

Louise Pope-Rhoden

Description

The brainstem examination is different in neonates (36 weeks, gestation to 29 days old (corrected for gestational age)[1]:

- Minimum clinical criteria include absence of oculocephalic reflex and suck reflex.
- Minimum temperature must be a core temperature 36°C[1].
- Minimum time from birth to first determination is 48 h[1].
- Two examinations are required, by two different physicians, at a minimum time interval of 24 hours between each examination is required[1].
- Ancillary testing, as defined by demonstration of the absence of intracranial blood flow, should be performed when any of the minimum clinical criteria cannot be established or confounding factors remain unresolved[2].
- The physicians performing NDD should have special expertise in the patient's age group. The minimum level of physician qualifications should be understood as specialists with skill and knowledge in the management of newborns/infants/children and/or adolescents, respectively with brain injury and the determination of death based on neurological criteria[1].

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Rationale

It is prudent to have an independent examination because of the lack of collective experience and research on brain death in this age group a repeat examination no less than 24 hours apart is recommended to ensure independent confirmation by another qualified physician, regardless of the primary mechanism of the brain injury. Accuracy of gestational age should be supported by clinical history (e.g., dates and prenatal ultrasound) and physical examination. Inability to confirm a gestational age > 36 weeks should preclude NDD.

Should uncertainty or confounding issues arise that cannot be resolved, the time interval may be extended according to physician judgement, or an ancillary test demonstrating absence of intracranial blood flow may be used[2]. The 48 hour recommendation from injury to first determination reflects a reduced certainty of neurological prognostication in the newborn[1].

1 Shemie SD, Doig C, Dickens B, et al. Severe brain injury to neurological determination of death: Canadian forum recommendations. CMAJ : Canadian Medical Association Journal. 2006;174(6):S2,3. doi:10.1503/cmaj.045142.

2 CCDT 2003 Severe brain injury to neurological determination of death Canadian Forum Report and Recommendations

Determining Neurological Death in Infants According to Provincial Standards

Janice Beitel, Pierre Cardinal

Description

For infants (30 days to 1 year, corrected for gestational age)[1]:

- Two examinations are required that should be performed at different times by two different physicians
- There is no recommended minimum time interval between examinations
- The physicians performing NDD should have special expertise in the patient's age group.

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- The minimum level of physician qualifications should be understood as specialists with skill and knowledge in the management of newborns/infants/children and/or adolescents, respectively.

Rationale

Given less widespread experience with NDD for infants, a repeat examination at a different point in time is recommended to ensure independent confirmation by another qualified physician, regardless of the primary mechanism of the brain injury. It is prudent to have an independent examination because of the lack of collective experience and research on brain death in this age group. There is no recommended minimal time interval between determinations. Should uncertainty or confounding issues arise that cannot be resolved, the time interval may be extended according to physician judgement, or an ancillary test demonstrating absence of intracranial blood flow may be used[2].

1 Shemie SD, Doig C, Dickens B, et al. Severe brain injury to neurological determination of death: Canadian forum recommendations. CMAJ : Canadian Medical Association Journal. 2006;174(6):S1-S12. doi:10.1503/cmaj.045142.

2 CCDT 2003 Severe brain injury to neurological determination of death Canadian Forum Report and Recommendations

Hypothermia as a Mimicker of Neurological Death

Louise Pope-Rhoden, Janice Beitel

Description

- Core temperature should be obtained through central blood, rectal or esophageal–gastric measurement[1].
- The core body temperature required to apply the minimum clinical criteria should be 34°C in infants, children, and adults[2].
- The brainstem examination is different in neonates, for newborns aged 36 weeks gestation to 29 days old (corrected for gestational age) minimal core body temperature should be 36°C[1].

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Rationale

When body temperature is below normal, hypothermia should be considered as a confounding factor which might prevent the observation of neurologic responses and/or mimic neurological death. Confounding conditions that may invalidate testing for cessation of brain function include naturally occurring and/or therapeutic hypothermia[3]. There is little evidence to inform the threshold temperature below which NDD becomes unreliable. Given the lack of evidence, a consensus decision was made to adopt 36°C and 34°C as rational, safe and attainable standards in neonates and in any patients older than 1 month, respectively. Ideally, temperature should be as close to normal as possible as these threshold temperatures are the minimal temperature at which the test is considered valid. Raising a patient's temperature to 34°C (or to 36°C in neonates) is also easy to achieve[1].

In neonates, it is also important to ensure the accuracy of gestational age based on clinical history (e.g. dates and prenatal ultrasound) and physical examination. Inability to confirm a gestational age >36 weeks should preclude NDD[1]. The higher recommended temperature threshold in neonates reflects uncertainty about hypothermic effects on neurological function in the newborn and the fact that normothermia is an easily attainable standard[1].

1 Shemie SD, Doig C, Dickens B, et al. Severe brain injury to neurological determination of death: Canadian forum recommendations. CMAJ : Canadian Medical Association Journal. 2006;174(6):S2-4. doi:10.1503/cmaj.045142.

2 Trillium Gift of Life Network (TGLN), Guidelines for the neurological determination of death (NDD) for the purposes of organ donation in ontario: adult and paediatric patients 1 year and older

3 S. D. Shemie, L. Hornby, A. Baker, et al. International guideline development for the determination of brain death Intensive Care Med (2014) 40:791 DOI 10.1007/s00134-014-3242-7

Electrolyte Abnormalities as Mimickers of Neurological Death

Lindsay Wilson, Louise Pope-Rhoden, Sonny Dhanani

Description

Before completing the neurological examination or apnea test:

- Recognize and correct any severe electrolyte abnormality including:[1,2]
  - Hypophosphatemia (< 0.4mmol/L)[1]
  - Hypocalcemia (<1.0 mmol/L ionized)
  - Hypomagnesemia (<0.8 mmol/L)
  - Hypernatremia (>160 mmol/L)[1]
  - Hyponatremia (<125 mmol/L)[1]

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- Recognize and correct hypoglycemia (<4 mmol/L)

Rationale

Certain metabolic abnormalities, including severe hypophosphatemia, hypocalcemia, hypomagnesemia, hypernatremia, hyponatremia, and hypoglycemia may impact the ability to declare death based on neurological criteria. The effect of electrolyte abnormalities resulting in a condition capable of mimicking neurologic death is theoretical in that there are no specific reports of cases of misdiagnosis resulting from electrolyte abnormalities alone and no reported guidance on actual thresholds for appropriate electrolyte targets. However, correction of electrolyte levels are based on established clinical standards and accepted physiological normals levels[1]. All metabolic abnormalities should be corrected before completing NDD if it is believed that they might interfere with the interpretation of the clinical examination or apnea test results[2].

1 "Determination Of Death". Donation Resource Manual: A Tool To Assist Hospitals With The Process Of Organ And Tissue Donation. 6th ed. Toronto: Queen's Printer, 2014. Print.

2 Shemie SD, Doig C, Dickens B, et al. Severe brain injury to neurological determination of death: Canadian forum recommendations. CMAJ : Canadian Medical Association Journal. 2006;174(6):S2,3. doi:10.1503/cmaj.045142.

Neuromuscular Blockade as a Mimicker of Neurological Death

Kim Bowman, Janice Beitel

Description

Stop any neuromuscular blockade agent before performing the clinical examination or apnea test for NDD[1].

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Rationale

Neuromuscular blocking agents inhibit the action of acetylcholine by blocking neuromuscular transmission and thus causing paralysis of all skeletal muscles. Common agents include vecuronium, pancuronium, cisatracurium and rocuronium. Depolarizing agents such as succinylcholine are short acting and often not a consideration in the ICU patient but should also be recognized. Neuromuscular blockade will affect all striated muscles including the diaphragm and therefore will mimic unresponsiveness and lead to absence of breathing during apnea tests[1,2]. Cranial nerve functions are also affected with the exception of the pupillary light reflex which is preserved in normal patients on neuromuscular blocking agents. Thus, any neuromuscular blockade agent should be stopped before performing the clinical examination or apnea test for NDD[2]. If any concerns about persisting pharmacologic neuromuscular blockade, train of four testing to confirm reversal of paralysis should be conducted.

1 Shemie SD, Doig C, Dickens B, et al. Severe brain injury to neurological determination of death: Canadian forum recommendations. CMAJ : Canadian Medical Association Journal. 2006;174(6):S1-S12. doi:10.1503/cmaj.045142.

2. International guideline development for the determination of death Intensive Care Med (2014) 40:788–797 DOI 10.1007/s00134-014-3242-7

Unresuscitated Shock as a Mimicker of Neurological Death

Kim Bowman, Janice Beitel

Description

Recognize and treat unresuscitated shock:

- Persistent hypotension despite fluid resuscitation and vasopressors

AND/OR

- Persistent hypoperfusion despite fluid resuscitation or inotropes[1].
- In the presence of shock refractory to resuscitative measures, contact the donation support physician (DSP) or local expert before proceeding with NDD or ordering ancillary tests.

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Rationale

Shock is associated with inadequate oxygenated circulation to the brain[2]. In the presence of unresuscitated shock (i.e. persistent hypotension despite fluid resuscitation and vasopressors or persistent hypoperfusion despite fluid resuscitation or inotropes), the motor response, cranial nerve examination and apnea test may be falsely positive mimicking neurological death. It is important to assess for both hypotension and hypoperfusion and to correct the shock state prior to proceeding with a diagnosis of brain death for the purposes of donation. In the presence of shock refractory to all resuscitative measures, a consultation with the DSP or local expert should be considered before ordering ancillary tests[2].

1 "Determination Of Death". Donation Resource Manual: A Tool To Assist Hospitals With The Process Of Organ And Tissue Donation. 6th ed. Toronto: Queen's Printer, 2014. Print.

2 International guideline development for the determination of death Intensive Care Med (2014) 40:788–797 DOI 10.1007/s00134-014-3242-7

Peripheral Nerve or Muscle Dysfunction as a Mimicker of Neurological Death

Karim Soliman

Description

Consider peripheral nerve or muscle dysfunction as mimickers of neurological death especially in the presence of diseases that may lead to severe neuromuscular dysfunction such as:

- Myasthenia gravis
- Guillain-Barre Syndrome
- Botulism

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Rationale

Certain peripheral nerve and muscle diseases, especially when very severe, can make it difficult to interpret the result of the neurological exam especially the apnea test. In the presence of severe neuromuscular diseases, the motor response, cranial nerve examination and apnea test may be falsely positive mimicking neurological death. In such cases, it is preferable to complete the clinical neurological examination, including the apnea test, and to then seek a second opinion or consultation with neurology. Ancillary testing may be warranted to confirm absence of brain blood flow. An expert opinion (e.g. TGLN donation support physician or a local expert) before proceeding to ancillary testing should also be considered[1].

1 Shemie SD, Doig C, Dickens B, et al. Severe brain injury to neurological determination of death: Canadian forum recommendations. CMAJ : Canadian Medical Association Journal. 2006;174(6):S1-S12. doi:10.1503/cmaj.045142.

Inborn Errors of Metabolism as Mimickers of Neurological Death

Kim Bowman, Janice Beitel

Description

Always perform a detailed review of the past medical history to exclude inborn errors of metabolism (IEM).

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Rationale

Inborn errors of metabolism (IEM) may result in unresponsiveness and preclude the diagnosis of neurological determination of death. IEM typically present in the neonatal period or infancy but can occur at any time, even in adulthood[1]. Potential symptoms include: hypoglycemia, metabolic acidosis, and electrolyte imbalances. Diagnoses include fructose intolerance, galactosemia, phenylketonuria (PKU)[2]. As a minimum consideration, a thorough review of the patient's medical history should be conducted to exclude IEM.

Severe metabolic disorders may appear as part of the primary presentation. Symptoms and signs can complicate management for the physician and thus may impact the ability to declare death based on neurological criteria[3]. Attempts should be made to correct any metabolic abnormality that might play interfere with the neurological declaration of death. If the metabolic abnormalities cannot be corrected, it is preferable to complete the neurological examination, including the apnea test, and then consider consultation with an expert (e.g.TGLN Donation Support Physician or a local expert) before proceeding to ancillary testing.

1 Emedicine.medscape.com,. "Inborn Errors Of Metabolism: Background, Pathophysiology, Epidemiology". N.p., 2016. Web. 2 Mar. 2016.

2 Updated by: Chad Haldeman-Englert, and the A.D.A.M. Editorial team. "Inborn Errors Of Metabolism: Medlineplus Medical Encyclopedia". Nlm.nih.gov. N.p., 2016. Web. 3 Mar. 2016.

3 Shemie SD, Doig C, Dickens B, et al. Severe brain injury to neurological determination of death: Canadian forum recommendations. CMAJ : Canadian Medical Association Journal. 2006;174(6):S1-S12. doi:10.1503/cmaj.045142.

Clinically Significant Drug Intoxications as Mimickers of Neurological Death

Ian Ball, Pierre Cardinal

Description

Many drugs can affect neurological function and may even mimic neurological death. Given the disastrous consequences of a false positive NDD, it is essential to always consider drugs as potential confounders especially in the absence of a clear proximate cause of death. This can be very challenging given that a complete drug history is often missing and that current screening tests are notoriously inaccurate. In addition, patients considered for NDD may have hepatic and renal dysfunction or be hypothermic which may influence the metabolism and action of various drugs in unpredictable ways. It is important to distinguish drugs that may have played a role in the primary presentation of coma (i.e. overdose) versus drugs that are used in routine ICU care. For lingering effects of therapeutic narcotics or sedatives that may impair appropriate neurologic examination, delaying the testing for neurologic death or considering ancillary test is warranted. A consultation with a DSP or local expert should be considered.

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Rationale

A negative urine "drug screen" is completely inadequate for ruling out the presence of confounding agents because most hospital urine 'drug screens' only test for five or six classes of drugs. Even when the drug belongs to one of these classes, a negative result does not necessarily exclude an intoxication given the poor performance of these tests (low sensitivity and specificity)[1,2,3]. Positive test results do not necessarily confound the interpretation of the clinical examination for NDD. For example, patients who overdose on sympathomimetic agents (e.g. cocaine) may sustain intracranial hemorrhages and irreversible neurological injury as a result of the overdose, yet these agents could never confound the clinical NDD given their short half-lives. Opioids and sedative hypnotics are the agents most likely to confound the NDD examination, particularly when administered at high doses, for long durations, or in patients with compromised hepatic and/or renal function. Clinicians should be proactive at stopping these agents as early as possible when they are not required clinically (i.e. for ICP control), in anticipation of an NDD assessment. When agents are required therapeutically, clinicians are well advised to use short acting agents that are less reliant on hepatic metabolism, such as propofol. In addition, antidotes (particularly naloxone and flumazenil) are not recommended as they may precipitate acute withdrawal, leading to catecholamine surges that may be injurious to vulnerable organs.

Clinicians should consider consultation with local poison centers when drug intoxication may be affecting the NDD assessment. Consider seeking an expert opinion (e.g.TGLN Donation Support Physician or local expert).

1 Hammett-Stabler CA, Pesce AJ, Cannon DJ: Urine drug screening in the medical setting. Clin Chim Acta 2002;315:125-135.

2 Hepler BR, Sutheimer CA, SUnshine I: The role of the toxicology laboratory in emergency medicine.II. Study of an integrated approach. J Toxicol Clin Toxicol 1984-85;22:503-528.

3 Kellerman AL, Fihn SD, Logerfro JP, et al: Impact of drug screening in suspected overdose. Ann Emerg Med 1987;16:1206-1216.

Hypoxic Brain Damage Secondary to Cardiac Arrest as a Mimicker of Neurological Death

Karim Soliman

Description

Consider hypoxic-ischemic brain damage secondary to cardiac arrest as mimicker of neurological death. In particular the first 24 hours post arrest where the clinical exam may be confounded.

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Rationale

Hypoxic-ischemic injury post cardiac arrest can mimic neurological death especially in the first 24 hours post arrest. Canadian guidelines require a minimum of 24 hours between cardiac arrest and clinical declarations[1]. Several other national neurological death declaration guidelines carry an observation period between anoxic-ischemic brain injury and neurological declarations[2]. Current recommendation in Ontario is to delay declaration testing until 24 hours after the time of the hypoxic-ischemic event. Clinical context is important and consultation with the DSP or local expert should be considered.

When hypothermia is used post arrest, the prolonged effect of sedatives due to altered drug metabolism may warrant further consideration to ensure that they too are not potential mimickers of neurological death[3,4]. Testing should be delayed until the patient has been rewarmed.

1 Shemie SD, Doig C, Dickens B, et al. Severe brain injury to neurological determination of death: Canadian forum recommendations. CMAJ : Canadian Medical Association Journal. 2006;174(6):S1-S12. doi:10.1503/cmaj.045142.

2 Wijdicks EF. Brain death worldwide: Accepted fact but no global consensus in diagnostic criteria. Neurology 2002;58;20-25

3 Wijdicks EF, Determining Brain Death. Continuum: Lifelong Learning in Neurology 2015;21:1419

4 Greer DM, Busl KM. Pitfalls in the Diagnosis of Brain Death. Neurocritical Care 2009; 11:276–287

Apnea Testing During Clinical Examination of Neurological Death

Lindsay Wilson, Edwin Poon

Description

An apnea test is typically the last of the clinical tests performed for purposes of declaring NDD and involves the following steps[1]:

- Attempt to achieve normal baseline arterial gases: pH 7.35-7.45, $PaCO_2$ 35-45 mmHg, PaO_2 > 100 mmHg[2].
- Preoxygenate with 100% O2 for 10 minutes[2].
- Apply one of either open-circuit technique or closed-circuit technique as described below:

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Open-circuit technique ("Flow" apnea testing):

- Disconnect ETT from ventilator and insert catheter into ETT to deliver O_2 at 1-4 L/minute (alternatively set ventilator to achieve this effect)[2].
- For patients with high FiO2 or PEEP requirements, the following may be prepared for use to maintain optimal oxygenation:
  - Connect a BVM system with a complete seal (reusable bags are suggested for their air tight qualities) to the in-line O_2 flow meter.
  - Attach appropriate PEEP valve and swivel ETT adapter for patient support.
  - Inflate the BVM system with inline O_2 to the minimal setting required for adequate inflation of the BVM system; suggest using O_2 flow greater than or equal to 10 l/minute[3].

Closed-circuit technique ("CPAP" apnea testing):

- The patient remains on mechanical ventilation for the duration of the apnea test
- Ensure the following conditions on the ventilator:
  - Ventilator circuit is free of water or condensation
  - Ventilator circuit is not resting on patient's body
  - Ventilator Trigger Sensitivity setting within reasonable range
  - Ventilator Apnea Alarm is off or at most lenient allowable setting
  - Ventilator Apnea Backup Ventilation setting is off or at most lenient allowable setting
  - FiO2 = 1
  - Change ventilator mode to CPAP / PEEP-only
  - Set CPAP level to PEEP level of ventilation settings prior to apnea test
- For monitoring during the apnea test:

  a) If using O_2 tubing:
  - Draw patient's gown to umbilicus level to facilitate the observation of the thorax and abdomen and confirm the lack of respiratory effort

  b) If using BVM with PEEP:
  - Observe as above
  - Provide one breath after bag-valve-mask set-up has been attached
  - At completion of spontaneous exhalation and bag-valve-mask refill, the apnea test begins[3].

1 Shemie SD, Ross H, Pagliarello J, Baker AJ, Greig PD, Brand T, et al. Organ donor management in Canada: recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ : Canadian Medical Association Journal 2006;174(6):S13-32.

2 "Determination Of Death". Donation Resource Manual: A Tool To Assist Hospitals With The Process Of Organ And Tissue Donation. 6th ed. Toronto: Queen's Printer, 2014. Print.

3 Trillium Gift of Life Network (TGLN), Neurological Determination of Death Policy and Procedure. 2014.

c) If using closed-circuit technique:
  - Observe for apnea as described in section (a)
  - Also observe ventilator waveform and rate
- Verify apnea for a period of 5-15 minutes. A physician must be present to observe the chest and abdomen continuously to ensure the absence of respiratory effort while the patient is not being ventilated. Ensure cardiovascular status and oxygen saturations remain stable[2].
- Draw arterial blood gases after 5, 10, and

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15 minutes, then reconnect ventilator[4].

Absence of capacity to breathe is confirmed if all three of the following thresholds (documented by arterial gas measurement) have been met:

- PaCO2 ≥ 60 mmHg, and
- PaCO2 ≥ 20 mmHg rise above baseline,
- and pH ≤ 7.282

Notes:

- If the patient becomes unstable at any time, it is recommended to draw arterial blood gases before putting the patient back on the ventilator, as they may have met the requirements outlined above[4].
- If the test fails to meet the criteria listed above or an apnea test cannot be completed due to patient instability, a repeat exam, ancillary testing, or both may be required. Discussion with TGLN is recommended[4].
- For patients over one year, a single apnea test may be performed if both physicians are present at the time of the test[5].
- For neonates (36 weeks gestation to <30 days), two neurological death determinations (including apnea testing) are required, with a minimum interval of 24 hours between examinations. Physician qualifications should be understood as specialists with skill and knowledge in the management of newborns[5].
- For infants (30 days to 1 year, corrected for gestational age), two neurological death determinations (including apnea testing) are required, though there is no recommended minimum time interval between determinations. Physician qualifications should be understood as specialists with skill and knowledge in the management of infants[5].

Rationale

The minimum clinical criteria as a Canadian medical standard for neurological death include absent respiratory effort based on an apnea test. Apnea testing involves driving up pCO_2 levels to a maximum point to elicit respiratory response (while supporting oxygenation). Cooler body temperature may impact clinical testing for neurological death, and can prolong the time required for apnea tests due to decreased production of CO_2. Caution must be exercised in considering the validity of the apnea test in cases of chronic respiratory insufficiency or dependence on hypoxic respiratory drive[4]. If the physician cannot be sure of the validity of the apnea test, an ancillary test should be administered. Consider consultation with an expert opinion (e.g.TGLN Donation Support Physician or local expert) before proceeding to ancillary testing.

4 Trillium Gift of Life Network (TGLN), Guidelines for the neurological determination of death (NDD) for the purposes of organ donation in ontario: adult and paediatric patients 1 year and older.

5 Shemie SD, Doig C, Dickens B, et al. Severe brain injury to neurological determination of death: Canadian forum recommendations. CMAJ : Canadian Medical Association Journal. 2006;174(6):S2,3. doi:10.1503/cmaj.045142.

Recognition of Chronic Respiratory Insufficiency and Response to Supranormal Levels of Carbon Dioxide During Apnea Testing

Karim Soliman

Description

Recognize chronic respiratory insufficiency and response to only supranormal levels of carbon dioxide as special consideration when undergoing apnea testing in setting of neurological test.

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Rationale

The main objective of apnea testing is to test respiratory drive via a carbon dioxide challenge. In patients with chronic carbon dioxide retention due to COPD or other diseases, central and peripheral chemoreceptors have been reset to the new baseline carbon dioxide levels and the kidneys compensate for the chronic respiratory acidosis[1,2]. Special consideration should be given to these patients so that their pre-apnea exam arterial blood gas is normalized to their baseline. This will prevent the apnea testing from being unnecessarily prolonged and hence is safer for the patient.

The guidelines also suggest that in patients with chronic respiratory insufficiency who only respond to supranormal levels of carbon dioxide, the validity of the apnea exam must be considered with caution[3]. In these cases, consultation with expert opinion should be considered (e.g. TGLN donation support physician or a local expert) to discuss the use of ancillary testing based on this clinical context.

1 Acid-Base Response to Chronic Hypercapnia in Man. Newton C. Brackett, Jr., M.D., Charles F. Wingo, M.D., Orhan Muren, M.D., and Jose T. Solano, M.D. N Engl J Med 1969; 280:124-130

2 Lumb, BL. Nunn's Applied Respiratory Physiology. 7th edition. Churchill Livingston, c2016. Chapter 5: Control of Breathing.

3 Shemie SD, Doig C, Dickens B, et al. Severe brain injury to neurological determination of death: Canadian forum recommendations. CMAJ : Canadian Medical Association Journal. 2006;174(6):S1-S12. doi:10.1503/cmaj.045142.

Recognition of Patients Dependant on Hypoxic Drive During Apnea Testing

Karim Soliman, Pierre Cardinal

Description

Recognize patients with central hypoventilation as a contraindication to interpreting the apnea test for neurological death declarations[1].

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Rationale

The Canadian guideline recommends the identification of patients who are dependent on their hypoxic drive to breathe[1]. Such patients usually suffer from either congenital or acquired central hypoventilation. Recently, congenital central hypoventilation syndrome has been to be linked to mutations of the PHOX2B gene[2]. Acquired hypoventilation is associated with traumatic, ischemic, and inflammatory processes affecting the brainstem[3]. Congenital disorders such as myelomeningocele associated with Arnold Chiari Type II malformation may also lead to central hypoventilation. The pathogenesis of hypoventilation in these patients is usually multifactorial denoting conditions resulting from underlying neurologic disorders affecting the sensors (i.e. peripheral and central chemoreceptors, and mechanoreceptors) and/or the central controller that receive input and integrate the response from sensors[3,4]. Most patients not only have an impaired response to hypercarbia but also to hypoxemia. Such patients would not be adequately challenged with rising carbon dioxide levels thus any concerns with the performance or interpretation of apnea testing warrants ancillary testing. In these cases, it is important that consultation with expert opinion should be considered (e.g. TGLN donation support physician or a local expert) to discuss the use of ancillary testing.

1 Shemie SD, Doig C, Dickens B, et al. Severe brain injury to neurological determination of death: Canadian forum recommendations. CMAJ : Canadian Medical Association Journal. 2006;174(6):S1-S12. doi:10.1503/cmaj.045142.

2 Amiel J, Laudier B, Attie-Bitach T, et al. Polyalanine expansion and frameshift mutations of the paired like homeobox gene PHOX2B in congenital central hypoventilation syndrome. Nat Genet 2003;33(4): 459–61.

3 Muzumdar H, Arens R. Central Alveolar Hypoventilation Syndromes. Sleep Medicine Clinics. 2008;3:601-615.

4 Ramanantsoa N, Gallego J. Congenital central hypoventilation syndrome. Respiratory Physiology & Neurobiology. 2013;189:272-279.

Confirming Deep Unresponsive Coma During Clinical Examination of Neurological Death

Lindsay Wilson

Description

- Assess level of consciousness (Glasgow Coma Scale = 3)[1].
- By definition, "deep unresponsive coma includes the absence of any centrally mediated motor responses to pain or centrally mediated spontaneous movements. Any CNS-mediated motor response to pain in any distribution, seizures, decorticate and decerebrate responses are not consistent with NDD. Spinal reflexive movements confined to spinal distribution may persist." [1]
- Test CNS-mediated motor response to pain on all extremities and above the clavicles. Any centrally mediated response to painful stimulation excludes neurological death. Movements should be examined closely to be distinguished from intact spinal reflexive movements. If there is difficulty distinguishing between spinal reflexive movements and centrally mediated motor responses, consider consulttion with TGLN or a local expert to determine whether an ancillary test should be performed.

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Rationale

The minimum clinical criteria as a Canadian medical standard for neurological death includes deep unresponsive coma with absence of bilateral motor responses, excluding spinal reflexive movements. Spinal reflexive movements can be either spontaneous or elicited by stimulation, including painful stimuli applied to limbs or sternum, tactile stimulation applied to palmar or plantar areas, neck flexion, limb elevation or hypoxia (as may occur during ventilation disconnection). Spinal reflexes are not to be confused with a pathological flexion or extension response. Spinal reflexive movements are only observed in a spinal (i.e. not cranial nerve) distribution. They may be triggered by stimulating spinal nerves (e.g. sternal or nail bed pressure) but not by stimulating cranial nerves (e.g. pressure on eyebrow). Spinal reflexive movements may include: extension-pronation movements of the upper limbs or non-specific flexion of the lower limbs; undulating toe reflex (plantar flexion of great toe, followed by brief plantar flexion sequentially of second to fifth toes); Lazarus sign (bilateral arm flexion, shoulder adduction, hand raising to above the chest, and may include flexion of trunk, hips and knees); deep tendon reflexes; plantar responses, either flexor or extensor; respiratory-like movements (shoulder elevation and adduction, back arching or intercostal expansion) without significant tidal volume; and head turning."[2] If there are any questions about spinal reflexes, it is preferable to complete the neurological examination, including the apnea test, and consider consultation with an expert opinion (e.g.TGLN Donation Support Physician) before proceeding to ancillary testing.

1 Shemie SD, Doig C, Dickens B, et al. Severe brain injury to neurological determination of death: Canadian forum recommendations. CMAJ : Canadian Medical Association Journal. 2006;174(6):S1-S12. doi:10.1503/cmaj.045142.

2 Australian and New Zealand Intensive Care Society. The ANZICS Statement on Death and Organ Donation (Edition 3.2). Melbourne: ANZICS, 2013.

Assessing Brainstem Reflexes in Adults, Adolescents and Children when Examining Neurological Death

Lindsay Wilson

Description[1,2]

Assess corneal reflex:

- Stimulate the cornea above and below the pupil with a tissue and observe both eyelids for any response.
- Any response, such as blinking or tearing excludes neurological determination of death.

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Assess cough reflex:

- Insert a suction catheter into the endotracheal tube and stimulate the trachea.
- Any effort to cough excludes neurological death.

Assess gag reflex:

- Insert a yankauer or tongue depressor to stimulate the back of the pharynx.
- Any effort to gag excludes neurological death[1].

Assess pupillary response:

- In a darkened room, shine a light into each eye and observe change in pupil size.
- Absent reflex involves fixed and dilated pupils that are unreactive to light. Pupils smaller than 3 mm in diameter in adults or any direct or consensual reaction exclude neurological death[1].

Assess caloric/vestibulo-ocular response:

- Position head at 30° from horizontal
- Using an otoscope, confirm that the external auditory canals are not obstructed
- Irrigate the auditory canal with at least 50 ml of ice water, and observe both eyes.
- Any eye movement excludes neurological death.
- Five minutes should be observed before the other auditory canal is irrigated.
- Halt the cold caloric testing if the tympanic membrane is perforated.

Consider contacting the TGLN donation support physician or a local expert if the neurological exam cannot be completed or there is doubt regarding the interpretation of some neurological findings.

Rationale

The minimum clinical criteria as a Canadian medical standard for neurological death include absent brainstem reflexes as defined by absent gag and cough reflexes and the bilateral absence of corneal responses, pupillary responses to light, with pupils at mid-size or greater, and vestibulo-ocular responses. Although the mechanism that moderates the vestibular ocular response is independent of the presence of an intact tympanic membrane, many guidelines including the Trillium Gift of Life Guidelines currently recommends to halt the cold caloric testing and perform ancillary testing if the tympanic membrane is perforated[2]. In other jurisdictions practice differs. For example, the Australian guidelines state that the presence of a ruptured tympanic membrane does not inval-

1 Step-by step overview of the clinical practice guidelines for declaring neurological death in adults and children. Video available at http://www.organsandtissues.ca/s/english-expert/leading-practices-public-awareness-and-education-2 Canadian Council for Donation and Transplantation (CCDT); 2007.

2 "Determination Of Death". Donation Resource Manual: A Tool To Assist Hospitals With The Process Of Organ And Tissue Donation. 6th ed. Toronto: Queen's Printer, 2014. Print.

idate the test[2,3]. In such cases that the brainstem assessment cannot be completed (i.e. a glass eye), ancillary testing may be recommended[4]. Consider seeking an expert opinion (e.g.TGLN Donation Support Physician or local expert) before proceeding to ancillary testing[5].

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3 Australian and New Zealand Intensive Care Society. The ANZICS Statement on Death and Organ Donation (Edition 3.2). Melbourne: ANZICS, 2013.

4 Trillium Gift of Life Network (TGLN), Guidelines for the neurological determination of death (NDD) for the purposes of organ donation in ontario: adult and paediatric patients 1 year and older

5 Shemie SD, Doig C, Dickens B, et al. Severe brain injury to neurological determination of death: Canadian forum recommendations. CMAJ : Canadian Medical Association Journal. 2006;174(6):S1-S12. doi:10.1503/cmaj.045142.

Assessing Brainstem Reflexes in Infants When Examining Neurological Death

Louise Pope-Rhoden, Janice Beitel, Sonny Dhanani

Description[1,2]

Assess corneal reflex:

- Stimulate the cornea with a tissue and observe both eyelids for any response.
- Any response, such as blinking, excludes neurological determination of death.

Assess cough reflex:

- Insert a suction catheter into the endotracheal tube and stimulate the trachea.
- Any effort to cough excludes neurological death.

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Assess gag reflex:

- Insert a yankauer or tongue depressor to stimulate the back of the pharynx.
- Any effort to gag excludes neurological death.

Assess pupillary response:

- In a darkened room, shine a light into each eye and observe change in pupil size.
- Absent reflex involves fixed and dilated pupils that are unreactive to light. Pupils smaller than 3 mm in diameter or any direct or consensual reaction exclude neurological death.

Assess oculocephalic reflex:

- Should only be performed if there is no suspicion of cervical spinal cord injury
- Turn head both left and right looking at the position of the eyes
- With brain death, the eyes remain mid-positioned as the head is turned
- Any eye movement excludes neurological death

Assess caloric/vestibulo-ocular response:

- Position head at 30° horizontally
- Using an otoscope, confirm that the external auditory canals are not obstructed
- Irrigate the auditory canal with at least 50 ml of ice water, and observe both eyes.
- Any eye movement excludes neurological death
- Five minutes should be observed before the other auditory canal is irrigated.
- Halt the cold caloric testing if the tympanic membrane is perforated.

Consider contacting the TGLN donation support physician or a local expert if the neurological exam cannot be completed or there is doubt regarding the interpretation of some neurological findings.

Rationale

In infants (aged 30 days to 1 year (corrected for gestational age), clinical examination of neurological death is the same as in adults, except that oculocephalic reflex should also be absent. This test may be more reliable than the vestibulo ocular reflex in infants due to the unique anatomy of the external auditory canal[2]. Although the mechanism that moderates the vestibular ocular response is independent of the

1 Step-by step overview of the clinical practice guidelines for declaring neurological death in adults and children. Video available at http://www.organsandtissues.ca/s/english-expert/leading-practices-public-awareness-and-education-2 Canadian Council for Donation and Transplantation (CCDT); 2007.

2 Shemie SD, Doig C, Dickens B, et al. Severe brain injury to neurological determination of death: Canadian forum recommendations. CMAJ : Canadian Medical Association Journal. 2006;174(6):S2-4. doi:10.1503/cmaj.045142.

presence of an intact tympanic membrane, many guidelines including the Trillium Gift of Life Guidelines currently recommends to halt the cold caloric testing and perform ancillary testing if the tympanic membrane is perforated[3]. In other jurisdictions practice differs. For example, the Australian guidelines state that the presence of a ruptured tympanic membrane does not invalidate the test[3,4].

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3 "Determination Of Death". Donation Resource Manual: A Tool To Assist Hospitals With The Process Of Organ And Tissue Donation. 6th ed. Toronto: Queen's Printer, 2014. Print.

4 Australian and New Zealand Intensive Care Society. The ANZICS Statement on Death and Organ Donation (Edition 3.2). Melbourne: ANZICS, 2013.

Assessing Brainstem Reflexes in Neonates when Examining Neurological Death

Louise Pope-Rhoden, Janice Beitel, Sonny Dhanani

Description[1]

Assess corneal reflex:

- Stimulate the cornea with a tissue and observe both eyelids for any response.
- Any response, such as blinking, excludes neurological determination of death.

Assess cough reflex:

- Insert a suction catheter into the endotracheal tube and stimulate the trachea.
- Any effort to cough excludes neurological death.

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Assess gag reflex:

- Insert a yankauer or tongue depressor to stimulate the back of the pharynx.
- Any effort to gag excludes neurological death.

Assess pupillary response:

- In a darkened room, shine a light into each eye and observe change in pupil size.
- Absent reflex involves fixed and dilated pupils that are unreactive to light. Pupils smaller than 3 mm in diameter or any direct or consensual reaction exclude neurological death

Assess suck reflex:

- Place and lightly press the pad of the small finger against the roof of the mouth to determine if a response (movement of the tongue, mouth or pharynx) is elicited
- Any sucking action excludes the diagnosis of neurological death

Assess oculocephalic reflex:

- Should only be performed if there is no suspicion of cervical spinal cord injury
- Turn head both left and right looking at the position of the eyes
- With brain death, the eyes remain mid-positioned as the head is turned
- Any eye movement excludes neurological death

Assess caloric/vestibulo-ocular response:

- Position head at 30° horizontally
- Using an otoscope, confirm that the external auditory canals are not obstructed
- Irrigate the auditory canal with at least 50 ml of ice water, and observe both eyes.
- Any eye movement excludes neurological death
- Five minutes should be observed before the other auditory canal is irrigated.
- Halt the cold caloric testing if the tympanic membrane is perforated.

Consider contacting the TGLN donation support physician or a local expert if the neurological exam cannot be completed or there is doubt regarding the interpretation of some neurological findings.

Rationale

In neonates 36 weeks gestation to 29 days old (corrected for gestational age), the clinical examination of Neurological Death is the same as in adults, except that both oculocephalic reflex and suck reflex should also be absent, and the minimum temperature must be a core temperature of 36°C. The accuracy of gestational age should be supported by clinical history (e.g. dates and prenatal ultrasound) and physical examination. Inability to confirm a gestational

1 Step-by step overview of the clinical practice guidelines for declaring neurological death in adults and children. Video available at http://www.organsandtissues.ca/s/english-expert/leading-practices-public-awareness-and-education-2 Canadian Council for Donation and Transplantation (CCDT); 2007.

age >36 weeks should preclude NDD[2].

Although the mechanism that moderates the vestibular ocular response is independent of the presence of an intact tympanic membrane, many guidelines including the Trillium Gift of Life Guidelines currently recommends to halt the cold caloric testing and perform ancillary testing if the tympanic membrane is perforated[3]. In other jurisdictions practice differs. For example, the Australian guidelines state that the presence of a ruptured tympanic membrane does not invalidate the test[3,4].

Return to overview map

Return to sub map

A call to the TGLN donation support physician or local expert is warranted to discuss individual cases.

2 Shemie SD, Doig C, Dickens B, et al. Severe brain injury to neurological determination of death: Canadian forum recommendations. CMAJ : Canadian Medical Association Journal. 2006;174(6):S2-4. doi:10.1503/cmaj.045142.

3 "Determination Of Death". Donation Resource Manual: A Tool To Assist Hospitals With The Process Of Organ And Tissue Donation. 6th ed. Toronto: Queen's Printer, 2014. Print.

4 Australian and New Zealand Intensive Care Society. The ANZICS Statement on Death and Organ Donation (Edition 3.2). Melbourne: ANZICS, 2013.

Donor Management

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Collaborators: Louise Pope-Rhoden RN, Kim Bowman RN BScN MEd, Lindsay Wilson MHA(c) BA

Introduction

For the purposes of this chapter, donor management begins at the time of the declaration of neurological death and ends at the time of organ retrieval. This chapter will not address the management of Donation After Cardiac Death donors. Medical management is critical to actualizing the individual or family's intent to donate and maximizing the benefit of that intent. Attentive patient care during this period is of paramount importance, as it ensures consented donors are actually able to donate and affects both the number and quality of organs available for transplantation. The brain dead donor may experience autonomic dysfunction that results in precipitous changes in vital signs, potentially compromising transplantable organs, with consequences on graft function, graft survival, and overall transplantability.

Donor Management

Until recently, the donor management literature was underdeveloped, and physicians were compelled to rely on physiology, and extrapolations from related research. Fortunately, there is an increasing body of literature available to guide physicians through donor management decisions, and this trend is expected to increase in the coming years.

In the past, organ donors were sometimes relegated to a less important status than other critically ill patients. We encourage clinicians to view donors not just as patients deserving of the highest quality end of life care, but also for their ability to save and enhance the lives of recipients. This requires attention and vigilance to principles of multi-organ support and resuscitation.

Key Concepts

The process of organ transplantation is often lengthy, and the physiologic changes prior to and after neurologic death can lead to irreversible end-organ dysfunction preventing organ donation. Missed opportunities to donate have obvious ramifications on the number of transplants, but more importantly, may have detrimental effects on families of consented donors. A review of 1,554 organ donors revealed that the average time from neurologic declaration of death to organ procurement was 34 hours, and that in 15% of cases, procurement took place greater than 48 hours after declaration[1]. During this time period, the potential donor must be aggressively managed in order to minimize end-organ dysfunction, increase the number of organs available for surgical recovery, and optimize the post-transplant graft function. This is important as it has been shown that almost one-quarter of potential donors were unable to donate due to pre-procurement instability[2]. In addition, meeting organ donor management goals (normal cardiac, pulmonary, renal and endocrine parameters) increases rates of organ procurement (≥ 4 organs)[3]. The delay between declaration of neurologic death and organ retrieval can be advantageous. With appropriate management of fluids and vasoactive agents, it is not uncommon for cardiac function to improve over the first 24-36 hours, particularly after a cardiac arrest.

Canadian guidelines have been created to standardize the multisystem management[4]. These have been used to create Trillium Gift of Life Network and hospital specific order sets for the management of the potential organ donor after neurological determination of death. A close collaborative relationship and excellent communication between the ICU team and the organ and tissue donation coordinators is paramount for optimal organ donor management.

1 Inaba K, Branco BC, Lam L, et al. Organ donation and time to procurement: Late is not too late. J Trauma - Inj Infect Crit Care. 2010;68(6):1362-1366. doi:10.1097/TA.0b013e3181db30d3\r00005373-201006000-00014 [pii].

2 Malinoski DJ, Patel MS, Daly MC, Oley-Graybill C, Salim A. The impact of meeting donor management goals on the number of organs transplanted per donor. Crit Care Med. 2012;40(10):2773-2780. doi:10.1097/CCM.0b013e31825b252a.

3 Kotloff RM, Blosser S, Fulda GJ, et al. Management of the Potential Organ Donor in the ICU. Crit Care Med. 2015;43(6):1291-1325. doi:10.1097/CCM.0000000000000958.

4 Shemie SD, Ross H, Pagliarello J, et al. Organ donor management in Canada: Recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ. 2006;174:S13-S30. doi:10.1503/cmaj.045131.

Clinical Approach (Map 1)

The multisystem management of the potential donor starts with the neurologic determination of death, consent for donation, and the institution of standardized order sets outlining the necessary monitoring and investigations required. In essence, the intensive care is optimized as per any other patient, and should not be considered as different or unique. The optimization of oxygenation and hemodynamic parameters are considered. In addition, the unique physiology including autonomic instability and hormonal dysregulation should be attended to.

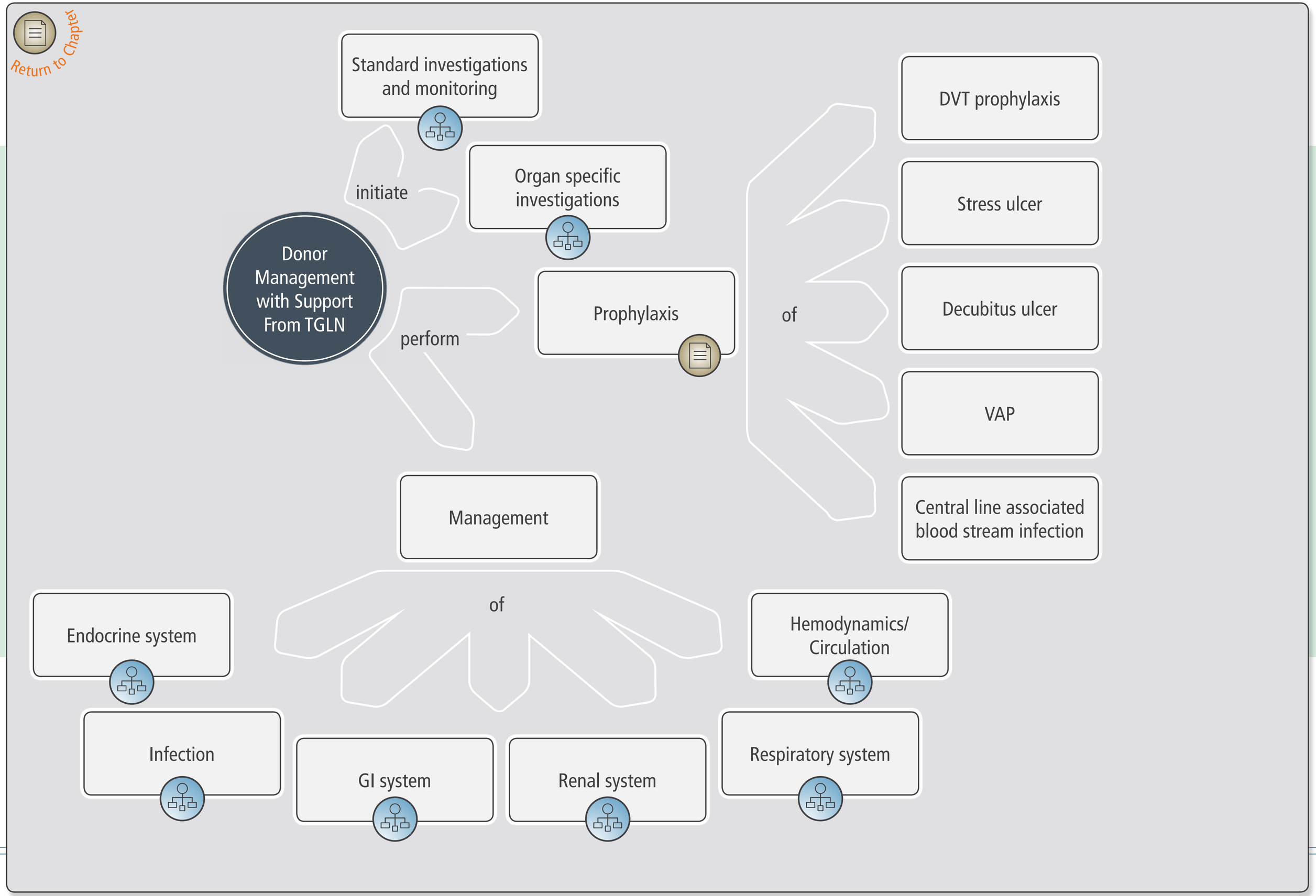
Standard monitoring and investigation (Map 2) to ensure appropriate oxygen delivery to end organs should continue. Organ specific investigations (Map 3) may also be needed to ensure suitability for eventual transplantation. This may include additional and repeated laboratory samples as well as specific testing for function such as bronchoscopy, echocardiography, and ultrasound. Routine prophylaxis measures such as for DVT, ulcers, VAP should be continued.

Normalization of hemodynamics with appropriate fluid, vasopressors, and inotropes may be necessary based on the clinical situation (Map 9,10). Aggressive treatment of arrhythmias is warranted. Neurogenic pulmonary edema may occur requiring increased support. More aggressive standard strategies should be instituted if ARDS is present. A balanced approach is needed for fluid resuscitation to optimize renal perfusion but minimize pulmonary edema. Infections, both isolated and systemic, do not preclude donation and should be treated. One of the most common physiologic complications of neurologic death includes abnormalities in hormonal regulation. Diabetes insipidus is common and should be identified early to prevent hypovolemia and hypernatremia. Triple hormonal therapy with methylprednisolone, thyroxine, and insulin has shown to improve potential for donation and improve organ utilization (Maps 4-8).

Summary/Conclusion

Successful medical management of the organ donor is critical to actualizing the individual or family's intent to donate and maximizing the benefit of that intent. After brain death, the time needed to obtain consent, assess suitability, and organize transplant recovery teams may be prolonged. During this phase, risks for hemodynamic instability and compromise of end organ function are high necessitating aggressive, and standardized donor management strategies to improve the opportunity to donate and increase the number and quality of transplants.

Return to Chapter



Map 2 - Standard Investigations and Monitoring

Return to Chapter

Donor Management with Support From TGLN

Standard Invetigations and Monitoring

initiate

Investigations to meet targets (when applicable)

including

Monitoring to meet targets

including

Monitor	Interval	Target
ECG Monitoring, Pulse oximetry	hourly	MAP > 70 SBP >100 HR 60-120 O2 sats >95%
Urine output via catheter and urometer	q1h	0.5-3 ml/kg/h
ABG	q4h	pH 7.35 - 7.45 PaCO2 35-45 mmHg PaO2 > 80mmHg

Investigation	Interval	Target
CBC	q4h	Hg > 70g/L
INR and PT	q6h	
Biochemistry		
Electrolytes	q4h	Serum Na <150, normal K,P04, Ca, Mg
BUN, Cr	q6h	
Blood Glucose	q4h	BG <= 10
AST, ALT, GGT, Bilirubin (total, direct), LDH, total protien, albumin, amylase, lipase	q4h	
Microbiology		
Blood, urine, and ETT culture	daily	
Organ matching and suitability Microbiologic testing, HLA subtype, Blood type	TGLN will arrange	

Map 3 - Organ Specific Investigations

Return to Chapter

Baseline ECG, 2D echo, TnI or TnT

if

Hemodynamically unstable

consider

Serial echo

if

perform

One of:
1) male > 55, female > 60
2) Two risk factors AND male >40, female >45
3) >Three risk factors
4) History of cocaine use
5) Upon transplant program request

request

Coronary angiogram

Heart Donor

if possible

perform initial

Bronchoscopy with bronchial washing sent for culture, gram stain

Lung Donor

if possible

perform daily

CXR

Donor Management with Support From TGLN

Organ Specific Investigations

if possible

Kidney Donor

perform

if

Urinalysis

Requested by transplant program

perform

Ultrasound or other investigations

if possible

Liver Donor

if

Weight > 100kg or BMI > 30 or HCVAb positive or request by the transplant program

perform

Ultrasound

consult

Transplant program

Map 4 - Management of Endocrine Deficiency

Return to Chapter

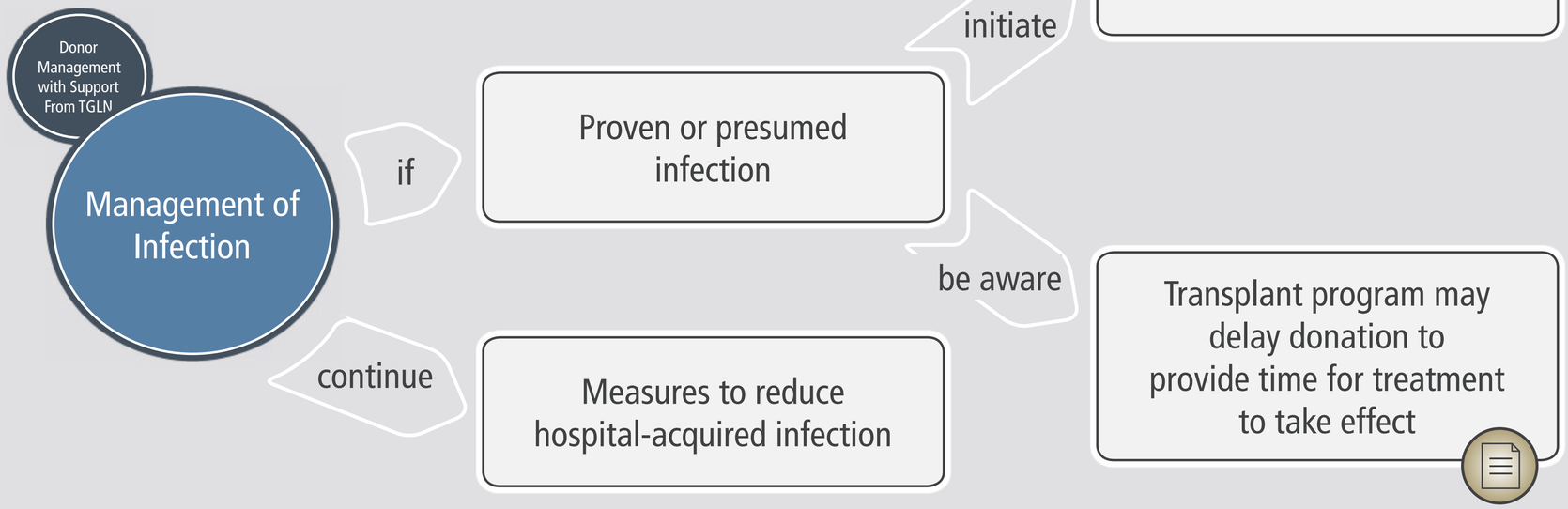
Donor Management with Support From TGLN

Management of Endocrine Deficiency

anticipate

- **Diabetes insipidus**
  - administer
  - **Vasopressin in all patients**
    - if
      - **Elevated urine output**
      - **Elevated serum [Na]**
        - administer
        - **Free water (IV or enterally)**
      - add
        - **Intermittent DDAVP**
          - targeting
          - **Urine output 0.5-3 mL/kg/h, Serum sodium 130-150 mmol/L**
- **LV dysfunction secondary to thyroid hormone deficiency**
  - administer
  - **Thyroid hormone replacement in all patients**
- **Lung donation**
  - administer
  - **High dose steroids**

Return to Chapter



Map 6 - Management of the Gastrointestinal System

Return to Chapter

Donor Management with Support From TGI *

Management of the GI System

- continue
  - Enternal nutrition only
  - Glycemic control → with → Insulin infusion → target → BG <=10
- consider
  - Possible liver donation → avoid → Hyponatremia/ Hypernatremia
- if small bowel donation considered, consult
  - Donation Support Physician

Map 7 - Management of the Renal System

Return to Chapter

Donor Management with Support From TGI

Management of the Renal System

- ensure → Pre-defined BP and perfusion targets
- avoid → Nephrotoxic agent
- administer → Fluid bolus prior to contrast administration
  - consider → Administering isotonic fluid solution prior to contrast administration
- consider → Mild hypothermia (temp 34-35C)

Map 8 - Management of the Respiratory System

Return to Chapter

Donor Management with Support From TGLN

Management of the Resiratory System

- administer
  - Steroids in all patients
- consider if
  - Patient does not meet ARDS criteria
    - institute or continue
      - Lung protective ventilatory strategy (non ARDS patients)
        - PEEP of 8-10 cm H2O
        - Apnea tests performed by using continuous positive airway pressure
        - Closed circuit for airway suction
        - Recruitment maneuvers after disconnect from the ventilator
        - Tidal volumes of 6-8 mL/kg of predicted body weight
        - monitor
          - PF ratio, PIP, Pplat, $PaCO_2$
        - verify
          - Tidal volume appropriate for ideal body weight
  - Patient meets ARDS criteria
    - institute or continue
      - Lung protective ventilation strategy (ARDS patients)
        - monitor
          - PF ratio, PIP, Pplat, $PaCO_2$
        - verify
          - Tidal volume appropriate for ideal body weight
        - if refractory hypoxemia
          - Rescue measures to optimize oxygenation
            - consider
              - Recruitment manouevers

Map 9 - Management of Hemodynamic Abnormalities

Return to Chapter

Donor Management with Support From TGLN

Management of Hemodynamic Abnormalities

recognize and manage

- Shock
- Hypertension
- Arrhythmia

perform

Systematic data collection

to challenge

Current hypotheses and management plan

Map 10 - Management of Hemodynamic Abnormalities - Shock

Donor Management with Support From TGLN

Management of Hemodynamic Abnormalities

Management of Hemodynamic Abnormalities; Shock

anticipate

Catecholamine induced myocardial dysfunction

verify

Thyroid replacement

consider

First choice Norepinephrine then Dobutamine

titrate to

Predefined BP and perfusion targets

monitor

Adverse effects (e.g. arrhythmia)

anticipate

Distributive type shock

verify

Vasopressin instituted

Steroid administration

consider

Other vasopressors (first choice norepinephrine)

titrate to

monitor

Adverse effects (Ischemic events)

consider

verify

Hypovolemia secondary to DI or other causes

institute

Fluid resuscitation

monitor

Adverse effects (pulmonary edema)

Vasopressin instituted

if high urine output or [Na] high

Fluid resuscitation

titrate to

monitor

Adverse effects (pulmonary edema)

Administer DDAVP in addition to vasopression

select

Type of crystalloid (based on serum Na)

titrate to

Performing Prophylaxis for Organ Donors

Louise Pope-Rhoden

Description

Start or continue measures to prevent:

- Deep vein thrombosis
- Stress ulcers
- Decubitus ulcers
- Ventilator-associated pneumonia
- Central line-associated bloodstream infection

Return to Overview map

Rationale

As intensivists become increasingly involved in donor management, it is imperative that the same rigor that is applied to the care of living patients be employed in the care of organ Donors[1]. Through provision of meticulous and aggressive care, and in collaboration with the TGLN and transplant teams, the intensivist has the opportunity to both preserve the option of organ donation for patients and their families and provide the gift of life to others.

1 Kotloff RM, Blosser S, Fulda GJ, et al. Management of the Potential Organ Donor in the ICU. Crit Care Med. 2015;43(6):1291-1325. doi:10.1097/CCM.0000000000000958.

Standard Monitoring to Meet Targets

Janice Beitel

Description

Standard monitoring of potential donors includes[1,2]:

- Vital signs q1h
- Core temperature q4h
- Continuous electrocardiogram (EKG) monitoring
- Continuous pulse oximetry
- Arterial blood pressure q1h
- Continuous central venous pressure (CVP) monitoring
- Urine output q1h
- Infectious disease assessment (via q24h blood, urine & sputum cultures)[1]
- Optional pulmonary artery catheter in situ or central venous line (central venous oximetry)[1,2,3]

Rationale

Close monitoring of hemodynamic and ventilatory function is required to optimize resuscitation and maintain optimal organ function at the time of surgical recovery [1, 2,3,4]. Monitoring for possible sources of infections is also recommended.

Return to Overview map

Return to Standard Investigations and Monitoring map

1 "Donor Screening and Testing". Donation Resource Manual: A Tool To Assist Hospitals With The Process Of Organ And Tissue Donation. 6th ed. Toronto: Queen's Printer, 2014. Print.

2 Shemie SD, Ross H, Pagliarello J, Baker AJ, Greig PD, Brand T, et al. Organ donor management in Canada: recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ : Canadian Medical Association Journal 2006;174(6):S13-32.

3 Menza R. Evaluation and Assessment of Organ Donors. In: Dianne LaPointe R, Linda O, Teresa S, ed. by. A Clinician's Guide to Donation and Transplantation. 1st ed. Lenexa: NATCO, The Organization for Transplant Professionals; 2016.

4 Kotloff RM, Blosser S, Fulda GJ, et al. Management of the Potential Organ Donor in the ICU. Crit Care Med. 2015;43(6):1291-1325. doi:10.1097/CCM.0000000000000958.

Standard Investigations to Meet Targets

Janice Beitel

Description

Standard investigations for all potential donors include[1,2]:

- ABO - Blood Group (Cross and Type)
- Arterial Blood Gases (ABGs)on positive end expiratory pressure (PEEP) 8-10 cm H_2O q2-4h. Contact the transplant team for patients on higher PEEP who may become hypoxemic with lower PEEP levels.
- CBC q4h
- Serum Lactate q 2-4h
- Mixed venous blood gases or central venous oxygen saturation q6h through either pulmonary artery catheter in situ or central venous line, respectively
- Liver profile – Bilirubin (total and direct), AST, ALT, ALP, LDH, Total Protein, Albumin, Amylase, Lipase, GGT q4h
- PT/INR, PTT q6h
- Electrolytes, Creatinine, Urea, Glucose, Ca, PO4, Mg, Lactate q4h
- CK, CK-MB q4-8h
- Troponin (I or T) q8h
- Urinalysis q24h
- C & S – sputum, urine and blood (include gram stain) q24h
- 12 lead EKG
- CXR q4h

Note:

Please see organ specific investigations for lung and heart serological tests for infectious diseases are requested by TGLN and sent to be processed in central laboratories in Ontario

Return to Overview map

Return to Standard Investigations and Monitoring map

Rationale

Standard investigations provide baseline information on organ function and physiological homeostasis[3]. Potential organ donors may be hemodynamically unstable with electrolyte disturbances related to the underlying cause of death, disease process or treatments[2, 3]. Standard investigations are well accepted in practice and serial testing provides trending information on organ function for the early identification and correction of electrolyte imbalances and/or the implementation of other interventions to meet targets[2].

1 "Donor Screening and Testing". Donation Resource Manual: A Tool To Assist Hospitals With The Process Of Organ And Tissue Donation. 6th ed. Toronto: Queen's Printer, 2014. Print.

2 Shemie SD, Ross H, Pagliarello J, Baker AJ, Greig PD, Brand T, et al. Organ donor management in Canada: recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ : Canadian Medical Association Journal 2006;174(6):S13-32.

3 Menza R. Evaluation and Assessment of Organ Donors. In: Dianne LaPointe R, Linda O, Teresa S, ed. by. A Clinician's Guide to Donation and Transplantation. 1st ed. Lenexa: NATCO, The Organization for Transplant Professionals; 2016.

Investigations for Heart Donors

Andrew Healey

Description

- EKG
- Troponin I or T q12h
- Baseline echocardiography
- If hemodynamically unstable,or reduced ejection fraction on baseline echo, perform serial echocardiogram
- In patients with risk factors, request coronary angiography

Return to Overview map

Return to Organ Specific Investigations map

Rationale

In evaluating the heart donor, three critical key concepts should be considered:

1. With the advent of expertly managed ventricular assist devices, the quality of the donor heart must be sufficient that transplantation of the donor heart results in mortality reduction compared to ongoing circulatory support.
2. (Serial examinations of the heart by EKG, biochemistry, and echocardiography significantly increases the number of hearts suitable for transplantation as the often severe myocardial dysfunction resolve with time and hormonal replacement therapy (T4) [1,2,3,4,5]. The heart is rarely ruled out for transplantation based on the initial echocardiogram [5]. Therefore, medical support and re-evaluation by serial echocardiogram should be performed prior to decisions about transplantability.
3. Knowledge of the data supporting improvement will assist intensivists in discussing the need for serial evaluation with colleagues and the healthcare team.

The EKG and Troponin are useful to assess for conduction abnormalities and ongoing ischemia[6]. In Canada, Health Canada requires these investigations of all donors where possible. When initially abnormal, serial ECGs and Troponins assist transplanters assess suitability as commonly the abnormalities are transient.

The hemodynamic assessment of all donors begins with a surface echocardiogram[7]. This begins the assessment of the suitability of the heart for transplant but also critically informs the hemodynamic management of patients who are not heart donors. The time following herniation is associated with an initial excess of sympathetic outflow, followed by loss of sympathetic tone and systemic vascular resistance. These result in often dramatic changes in the ECG, Troponin and the echocardiogram. Both left ventricular dysfunction and vasodilation often lead to hypotension. In the most hemodynamically unstable potential donors, echocar-

1 Casartelli M, Bombardini T, Simion D, Gaspari MG, Procaccio F. Wait, treat and see: echocardiographic monitoring of brain-dead potential donors with stunned heart. Cardiovasc Ultrasound. 2012;10:25.

2 Zaroff JG, Babcock WD, Shiboski SC. The impact of left ventricular dysfunction on cardiac donor transplant rates. J Heart Lung Transplant. 2003;22(3):334-7.

3 Mascia L, Mastromauro I, Viberti S, Vincenzi M, Zanello M. Management to optimize organ procurement in brain dead donors. Minerva Anestesiol. 2009;75(3):125-33.

4 Borbely XI, Krishnamoorthy V, Modi S, et al. Temporal Changes in Left Ventricular Systolic Function and Use of Echocardiography in Adult Heart Donors. Neurocrit Care. 2015;23(1):66-71.

5 Sopko N, Shea KJ, Ludrosky K, et al. Survival is not compromised in donor hearts with echocardiographic abnormalities. J Surg Res. 2007;143(1):141-4.

6 Shemie SD, Ross H, Pagliarello J, et al. Organ donor management in Canada: recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ. 2006;174(6):S13-32.

7 Venkateswaran RV, Townend JN, Wilson IC, Mascaro JG, Bonser RS, Steeds RP. Echocardiography in the potential heart donor. Transplantation. 2010;89(7):894-901.

diography can provide information on causes of instability (e.g. stress cardiomyopathy) and guide a goal-directed resuscitation and choice of initial vasopressors [7]. While early echocardiography may assist the physician with management of the hemodynamics, an abnormal echocardiogram should not be seen as an exclusion to potential heart donation [5]. There is a significant body of literature that cites the marked effects of time and hormonal treatment, resulting in the resolution of both regional and

Return to Overview map

Return to Organ Specific Investigations map

global left ventricular dysfunction to complete recovery [1,2,3,4,5] In special circumstances, transesophageal echocardiography may be required at the request of the transplant teams or in the event transthoracic echocardiography does not produce adequate imaging windows.

Coronary angiography is an essential and often final step in the assessment of the donor heart suitability. In perfect circumstances, angiography is not required but this is rare. It behoves intensivists to remember that coronary artery disease in an allograft progresses rapidly and is one of the main causes of graft loss after transplantation. The CCDT guidelines[6] suggest if one of the following are present, coronary angiography should be performed:

1. male > 55 or female > 60
2. two cardiac risk factors* AND male > 40 or female >45
3. > three risk factors
4. history of cocaine use
5. transplant program request

*Risk Factors include: smoking, hypertension, diabetes, hyperlipidemia, body mass index > 32, family history of the disease, prior history of coronary artery disease, ischemia on electrocardiogram, anterolateral regional wall motion abnormalities on echocardiogram, 2-dimensional echocardiographic assessment of ejection fraction of ≤ 40%.

The authors recommend contact with the organ donor organization with all other data prior to proceeding to coronary angiography to ensure potential suitability as there is risk associated with both the contrast load and the transfer of donors.

The use of the pulmonary artery catheter is often found within algorithms for donor management[6]. Experience over time with CVP monitoring, targeted therapy to address deficits in organ perfusion and serial echocardiography has diminished the need for PA catheters. In special circumstances in the donor or recipient, a pulmonary artery catheter might be requested to evaluate a specific parameter of donor heart function. This is almost exclusively performed at the request of the accepting transplant program and after all other testing suggests suitability of the organ.

Investigations for Lung Donors

Janice Beitel, Pierre Cardinal, Andrew Healey, Kim Bowman

Description

For any potential donors when lungs are being considered for transplantation, perform:

- Arterial Blood Gases q 4h on 100% O_2 (challenge gases)
- Chest radiography q4[1,2]
- Bronchoscopy [1,2] a second bronchoscopy is performed in recovery surgery[1]
- Bronchoalveolar lavage (BAL) [2]
- BAL gram stain, culture and sensitivity

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Return to Organ Specific Investigations map

Rationale

Ongoing assessment for oxygenation occurs throughout management and organ specific investigation of the potential donor.

ABG's (challenge gases) are routinely drawn after 20 min on a FiO_2 of 1 to assess the PaO_2:-FiO_2 ratio. Chest radiography is used to assess atelectasis, infiltrates, or infection in combination with other clinical findings[3]. Although not supported by strong evidence, investigations (CXR/ABGs) are requested every four hours to monitor lung function. The role of bedside ultrasound to evaluate lung volume status and cardiac function is evolving, but is not considered standard at this time. Bronchoscopy is required to investigate any CXR findings, identify aspiration, infection and to clear airway secretions as needed [3]. Bronchoscopy is also performed to exclude any endobronchial lesions and to define anatomy. A bronchial lavage for gram stain and sensitivity may help confirm infection and refine treatment that will often need to continue in the immunocompromised recipient [2,3]. A second bronchoscopy is almost universally repeated in the OR by the transplant team prior to lung recovery [1,3].

1 "Donor Screening and Testing". Donation Resource Manual: A Tool To Assist Hospitals With The Process Of Organ And Tissue Donation. 6th ed. Toronto: Queen's Printer, 2014. Print.

2 Shemie SD, Ross H, Pagliarello J, Baker AJ, Greig PD, Brand T, et al. Organ donor management in Canada: recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ : Canadian Medical Association Journal 2006;174(6):S13-32.

3 Menza R. Evaluation and Assessment of Organ Donors. In: Dianne LaPointe R, Linda O, Teresa S, ed. by. A Clinician's Guide to Donation and Transplantation. 1st ed. Lenexa: NATCO, The Organization for Transplant Professionals; 2016.

Investigations for Liver Donors

Janice Beitel, Pierre Cardinal, Andrew Healey, Kim Bowman

Description

For any potential donors when liver is being considered for potential transplantation, biochemical tests should include: [1,2,3]

- Bilirubin (total and direct), AST, ALT, ALP, LDH, Total Protein, Albumin, Amylase, Lipase, GGT q 4 h
- INR, PTT q6
- Serum sodium levels should be maintained within normal ranges of 135 - 145 mmol/L

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Return to Organ Specific Investigations map

- Liver ultrasound may be requested by transplant team, especially if the donor weighs over 100 kg or has a body mass index greater than 30.
- Uncommonly, intraoperative liver biopsy

Note:
Serologic testing is requested by TGLN and sent to be processed in in central laboratories in Ontario

Rationale

Assessment of liver enzymes through biochemical testing provides information to assess for acute ischemia related to events either preceding or surrounding neurological death [2,3,4]. Repeated testing provides the opportunity to see a trend in liver enzymes as an indication that the insult is over and the liver is showing signs of recovery. Since the bile ducts have only one blood supply (hepatic artery), they are most susceptible to ischemic injury placing the potential recipient at risk for bile duct complications.

Donor serum sodium greater than 155 has been weakly associated with primary liver dysfunction in transplant recipients but reversible if hypernatremia is corrected[4].

While the use of ultrasound to assess for fatty liver remains controversial, the test may be requested by the transplant program when donor characteristics are associated with an increased risk of graft failure in the recipient. Ultrasounds are also requested to assist with assessment especially when the donor is located in a geographically remote area[3]. The transplant team will very rarely perform liver biopsies intraoperatively at the time of procurement in donors who weigh over 100 kg or have a body mass index greater than 30 [3].

1 "Donor Screening and Testing". Donation Resource Manual: A Tool To Assist Hospitals With The Process Of Organ And Tissue Donation. 6th ed. Toronto: Queen's Printer, 2014. Print.

2 Shemie SD, Ross H, Pagliarello J, Baker AJ, Greig PD, Brand T, et al. Organ donor management in Canada: recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ : Canadian Medical Association Journal 2006;174(6):S13-32.

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4 Kotloff RM, Blosser S, Fulda GJ, et al. Management of the Potential Organ Donor in the ICU. Crit Care Med. 2015;43(6):1291-1325. doi:10.1097/CCM.0000000000000958.

Investigations for Kidney Donors

Alissa Visram, Sabira Valiani, Pierre Cardinal

Description

In addition to the standard investigations needed for all NDD donors, investigations for renal donors should include:

- Urinalysis daily
- Serum creatinine and urea every 6 hours
- Uncommonly, intraoperative kidney biopsy (if age >65, or age <65 with a history of hypertension, diabetes, abnormal urinalysis, or serum creatinine >133µmol/L) - this decision is made in concert with the transplant team and the procedure usually carried out intraoperatively at the time of procurement.
- Consider radiographic imaging of kidneys if requested by the transplant teams. Indications for radiographic imaging include donors with a family history of polycystic kidney disease, renal stones or other urologic abnormalities.

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Return to Organ Specific Investigations map

Rationale

A urinalysis is a useful screening tool to assess for microscopic hematuria and proteinuria, both of which can be markers of glomerular pathology and may affect the decision to transplant the kidney[1]. Persistent microscopic hematuria should prompt a workup to exclude urologic causes such as urinary tract infections or nephrolithiasis. If the microscopic hematuria persists, consultation with the transplant physician is warranted in order to determine if a kidney biopsy is required. Urinalysis and urine culture are Health Canada requirements of all organ donors.

Routine evaluation of the donor's creatinine and urea is used to monitor for objective signs of end organ dysfunction and acute kidney injury. Serial measurements can document improvement (or deterioration) with time and treatment.

The Canadian guidelines recommend kidney biopsies for patients older than 65, or those younger than 65 with a creatinine of 133µmol/L or greater, an abnormal urinalysis, or a history of hypertension or diabetes[2]. If a kidney biopsy is warranted, it is usually performed intraoperatively at the time of procurement, and not in the intensive care unit[2]. A kidney biopsy in a potential extended criteria donor can identify conditions such as glomerulosclerosis, vascular abnormalities, or interstitial fibrosis that may affect the decision of the team to transplant the kidney[3]. Expanded criteria donors are those who are at increased risk of graft failure, and include donors older than 60 years, or those 50-59 years with at least two comorbidities (cerebrovascular cause of death, renal insufficiency, or hypertension)[4].

The Society of Critical Care Medicine

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2 Shemie SD, Ross H, Pagliarello J, et al. Organ donor management in Canada: Recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ. 2006;174:S13-S30. doi:10.1503/cmaj.045131.

3 Kotloff RM, Blosser S, Fulda GJ, et al. Management of the Potential Organ Donor in the ICU. Crit Care Med. 2015;43(6):1291-1325. doi:10.1097/CCM.0000000000000958.

4 Port F, Bragg-Gresham J, Metzger R, Dykstra D, Gillespie B, Young E, Delmonico F, Wynn J, Merion R, Wolfe R, Held P. Donor characteristics associated with reduced graft survival: an approach to expanding the pool of kidney donors. Transplantation. 2002;74:1281-1286.

suggests that radiographic imaging of the kidneys may be warranted in donors who have a family history of polycystic kidney disease, or a history of renal stones or urologic abnormalities[3]. Renal imaging in Canada is currently performed only on the request of the transplant teams.

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Anticipating Diabetes Insipidus in the Organ Donor

Michael Hartwick, Sonny Dhanani

Description

- Anticipate that diabetes insipidus (DI) is common in patients who are dead by neurological criteria.
- Insert a foley catheter and monitor fluid inputs and outputs.
- Recognize dilute urine (< 200 mOsm/kg•H_2O), polyuria (> 4mL/kg/h), as well as hypernatremia (> 145mmol/L) as signs of diabetes insipidus in the potential NDD donor.

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Rationale

Arginine vasopressin (AVP) is a peptide that is formed in the hypothalamus and then stored in as well as secreted from the posterior pituitary. Its anti-diuretic effect on the V2 receptors within the renal collecting system promotes the reabsorption of free water. AVP regulates extracellular fluid volume by the reabsorption of water from the kidneys. After brain death, a lack of AVP leads to unregulated renal losses of free water resulting in a state of diabetes insipidus[1]. Diabetes insipidus is confirmed if urine output remains excessive (> 4mL/kg/h) as well as dilute (< 200 mOsm/kg•H_2O) and associated with hypernatremia (> 145mmol/L) and an increased serum osmolality (> 300mOsm/kg•H_2O)[2]. In the context of brain death, diabetes insipidus should be presumed even if all criteria are not met, especially in the context of clinical hypovolemia.

1 Loh JA, Verbalis JG. Disorders of water and salt metabolism associated with pituitary disease. Endocrinol Metab Clin North Am 2008; 37:213–234

2 Trillium Gift of Life Network. Donation Resource Manual: A tool to assist hospitals with the process of organ and tissue Donation. Queen's Printer for Ontario: 2010.

Anticipating LV Dysfunction Secondary to Thyroid Hormone Deficiency

Sonny Dhanani

Description

To anticipate the transient left ventricular cardiac dysfunction after brain death that may be responsive to empiric thyroid hormone replacement.

Rationale

Thyroid hormone plays a part in cardiovascular regulation by improving both contractility and chronotropy, as well as by decreasing systemic vascular resistance. The damage to the hypothalamic-pituitary axis that ensues with herniation triggers hormonal dysregulation and may lead to clinical hypothyroidism[1]. However, in some patients, the clinical picture is more consistent with sick euthyroid syndrome rather than true hypothyroidism. Animal models demonstrate significant decline in triiodothyronine (T3) and free thyroxine (T4) levels after brain death. This results in a depletion of myocardial energy stores, a shift from aerobic to anaerobic metabolism, and a reduction in cardiac function. In addition, thyroid replacement has been shown to exert a positive effect on myocardial gene expression[2]. In animal models, the transition to anaerobic metabolism is reversed with T3 replacement and is accompanied by a return of myocardial function[3],[4].

The evidence supports starting thyroxine in the presence of LV dysfunction. However, in light of minimal harm, the recommendation is to start thyroid replacement even without confirmed LV dysfunction as part of empiric triple hormonal therapy regimens (vasopressin, and corticosteroids)[5].

Return to Overview map

Return to Endocrine Deficiency map

1 1. Chen EP, Bittner HB, Kendall SW, et al: Hormonal and hemodynamic changes in a validated animal model of brain death. Crit Care Med 1996; 24:1352–1359

2 James SR, Ranasinghe AM, Venkateswaran R, McCabe CJ, Franklyn JA, Bonser RS.The effects of acute triiodothyronine therapy on myocardial gene expression in brain stem dead cardiac donors. J Clin Endocrinol Metab. 2010 Mar;95(3):1338-43. 159.

3 Novitzky D, Cooper DK, Rosendale JD, et al: Hormonal therapy of the brain-dead organ donor: Experimental and clinical studies.Transplantation 2006; 82:1396–1401

4 Cooper DK, Novitzky D, Wicomb WN: The pathophysiological effects of brain death on potential donor organs, with particular reference to the heart. Ann R Coll Surg Engl 1989; 71:261–266

5. Kutsogiannis DJ, Pagliarello G, Doig C, Ross H, Shemie SD. Medical management to optimize donor organ potential: review of the literature. Can J Anaesth. 2006 Aug;53(8):820-30.

Administering Intermittent DDAVP when Managing Donors

Sonny Dhanani, Ronish Gupta, Pierre Cardinal, Andrew Healey

Description

To administer vasopressin and or intermittent DDAVP in most potential donors after brain death.

Rationale

Although the mechanism has not been established, diabetes insipidus has the potential to impair organ function beyond that simply resulting from diuresis, hypovolemia, and hemodynamic instability. Potential organ donors with diabetes insipidus may be managed with an intravenous AVP infusion or intermittent desmopressin. An AVP infusion is the preferred agent for patients with concomitant hypotension. Given that it provides the dual benefits of anti-diuresis as well as hemodynamic support, it is administered in most NDD patients who are not hypertensive. In hypertensive patients, AVP is best avoided given concerns around possible interference with end-organ perfusion based on animal models of splanchnic blood flow[1].

Diabetes insipidus without hypotension may also be managed with desmopressin (1-desamino-8-d-arginine vasopressin, or DDAVP). Desmopressin is an AVP analogue whose mechanism of action is highly specific for the V2 vasopressin receptors in the renal collecting system. This property allows desmopressin to inhibit diuresis with virtually no vasopressor side effect. Multiple routes of administration are available, but the intravenous route is preferred in the organ donor[2]. Although concerns for potential thrombogenic complications have been raised with desmopressin use, it does not seem to impair graft survival. One trial of 97 adult organ donors randomized to receive desmopressin or nothing for diabetes insipidus demonstrated no impairment in pre-procurement renal function or post-transplant need for dialysis in those who received desmopressin[3]. A more recent retrospective analysis of 458 neurologically deceased adult kidney donors suggested that those treated with desmopressin actually had improved pre-recovery renal function (creatinine 97 ± 44 vs 124 ± 106 μmol/L; $p < 0.001$)[4].

In either case, AVP infusions or desmopressin boluses should be titrated to target serum sodium levels 130 – 155 mmol/L and urine output 0.5 – 3 mL/kg/h. If needed, AVP and desmopressin may also be used simultaneously for patients who continue to have a high urine output despite treatment with AVP alone. Intermittent intravenous DDAVP 4 micrograms every 6 hours is a common regimen. Intravenous AVP can be titrated between 0.5 units/h and maximum of 2.4 units/h. Intravenous maintenance fluids to maintain blood pressure and perfusion and the administration of free water (either through the enteral route (free water flushes) or intravenously (D5W)) should be considered to aggressively correct hypernatremia[5].

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Return to Endocrine Deficiency map

1 Chen JM, Cullinane S, Spanier TB, Artrip JH, John R, Edwards NM, Oz MC, Landry DW. Vasopressin deficiency and pressor hypersensitivity in hemodynamically unstable organ donors. Circulation 1999; 100 (suppl II):II-246.

2 Pennefather SH, Bullock RE, Mantle D, Dark JH. Use of low dose arginine vasopressin to support brain-dead organ donors. Transplantation 1995; 59(1):58-62.

3 Nakagawa K, Tang JF. Physiologic response of human brain death and the use of vasopressin for successful organ transplantation. J Clin Anesth. 2011 Mar;23(2):145-8.

4 Dunser MW, Mayr AJ, Ulmer H, Knotzer H, Sumann G, Pajk W, Friesenecker B, Hasibeder WR. Arginine vasopressin in advanced vasodilatory shock: a prospective, randomized,controlled study. Circulation. 2003 May 13;107(18):2313-9.

5 Kutsogiannis DJ, Pagliarello G, Doig C, Ross H, Shemie SD. Medical management to optimize donor organ potential: review of the literature. Can J Anaesth. 2006 Aug;53(8):820-30.

Administering Free Water in the Organ Donor

Sonny Dhanani, Pierre Cardinal, Andrew Healey

Description

If euvolemic with serum Na between 135-145 mmol/L:

- Initial maintenance intravenous fluids should be administered to achieve euvolemia with 0.9%NS or Ringer's Lactate

If euvolemic with serum Na>145mmol/L:

- Administer a IV bolus of 250 mL of D5W or free water enterally
- and immediately assess for diabetes insipidus

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- Change maintenance fluids to D5W.

If clinically hypovolemic and hypernatremic:

- Administer Ringer's Lactate bolus of 500 mL IV
- Once fluid resuscitated administer free water (intravenously or enterally)

Rationale

Hypernatremia (serum sodium > 155 mmol/L) secondary to excessive sodium administration during resuscitation or diabetes insipidus may lead to the accumulation of compensatory idiogenic osmoles in donor organs. Once transplanted, significant intracellular fluid shifts may develop as these organs are exposed to the recipient normal serum; the different osmolalities resulting in a water influx into the transplanted organs.

Traditionally, hypernatremia was considered to be independently associated with hepatic and renal dysfunction or graft loss after transplantation. However, more recent evidence suggests that this effect may be less significant than once believed and that detrimental effects of hypernatremia are reversible if serum sodium levels are corrected [1,2,3].

Given that avoiding or treating hypernatremia is easily achieved using inexpensive management strategies, it is recommended to target normal serum sodium levels by selecting appropriate maintenance intravenous fluids, the early recognition of diabetes insipidus and hypovolemia, and the aggressive correction of hypernatremia.

1 Bloom MB, Raza S, Bhakta A, et al. Impact of Deceased Organ Donor Demographics and Critical Care End Points on Liver Transplantation and Graft Survival Rates. J Am Coll Surg. 2015;220(1):38-47. doi:10.1016/j.jamcollsurg.2014.09.020.

2 Kazemeyni SM, Esfahani F. Influence of hypernatremia and polyuria of brain-dead donors before organ procurement on kidney allograft function. Urol J. 2008 Summer;5(3):173-7.

3 Mangus RS, Fridell JA, Vianna RM, Milgrom ML, Chestovich P, Vandenboom C,Tector AJ. Severe hypernatremia in deceased liver donors does not impact early transplant outcome. Transplantation. 2010 Aug 27;90(4):438-43.

Donation Delays Due to Infection Treatment

Alissa Visram, Sabira Valiani, Pierre Cardinal, Andrew Healey

Description

- Invasive bacterial infection may not be a contraindication to organ donation.
- In the presence of proven or suspected bacterial infection, organ procurement may be delayed to ensure that donors are treated with appropriate targeted antibiotics and to reduce the risk of transmission to the recipient.
- Consult with transplant team and infectious diseases specialists to determine the appropriate duration of therapy.

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Rationale

It is important to appreciate that bacterial infections are not necessarily contraindications to organ donation[1,2]. Donors in the intensive care unit are at increased risk of bacterial infections from sources such as indwelling catheters/ indwelling monitoring devices[3], bronchopneumonia or other sites as observed in all critically ill patients. On occasion, the event leading to NDD may be infectious in origin (e.g. bacterial meningitis). However, bacteremic donors who receive pathogen-directed antibiotic therapy for 24 to 48 hours prior to organ procurement transmit few, if any, infections to the recipients[4]. Therefore, bacteremic donors should be promptly treated with pathogen-directed antibiotic therapy. Empiric antibiotic therapy may be considered in those NDD donors at risk of bronchopneumonia. Similarly, NDD donors with bacterial meningitis may also be suitable organ donors assuming that they receive antibiotic therapy directed at the presumed pathogen. Of note, a similar antibiotic regimen is often continued for a 5-10 day duration in recipients whose organs are retrieved from donors with proven or suspected infections[2]. The risks associated with organ procurement from fungemic donors has not been clearly established but this too does not represent a contraindication to transplantation. Expert consultation is advised in the event of fungemia.

Consultation with infectious disease specialists may be beneficial in order to provide recommendations regarding the choice of antibiotic. In addition, the transplant team should be informed of any proven or suspected infections (whether bacterial, fungal, or viral) as this will influence the decision to transplant or its timing[1].

1 Shemie SD, Ross H, Pagliarello J, et al. Organ donor management in Canada: Recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ. 2006;174:S13-S30. doi:10.1503/cmaj.045131.

2 Kotloff RM, Blosser S, Fulda GJ, et al. Management of the Potential Organ Donor in the ICU. Crit Care Med. 2015;43(6):1291-1325. doi:10.1097/CCM.0000000000000958.

3 Cerutti E, Stratta C, Romagnoli R, Serra R, Lepore M, Fop F, Mascia L, Lupo F, Franchello A, Panio A, Salizzoni M. Bacterial- and fungal-positive cultures in organ donors: Clinical impact in liver transplantation. Liver Transpl. 2006;12:1253-1259.

4 Cohen J, Michowiz R, Ashkenazi T, Pitlik S, Singer P. Successful Organ Transplantation from Donors with Acinetobacter Baumannii Septic Shock. Transplantation. 2006;81:853-855.

Enternal Nutrition in the Organ Donor

Kim Bowman

Description

- Medical management of the donor is similar to the management of critically ill patients
- Routine enteral feedings should be initiated and continued in donors[1]
- If initiated, parenteral nutrition should be continued[1]

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Rationale

The influence of donor nutrition on graft survival has been previously studied in several small animal studies but not formally in humans[2]. Tube feedings may be beneficial for small bowel donors due to a perceived protective effect on mucosal structure[3]. It is recommended that nutrition in donors be continued. Feedings should be discontinued on call to the operating room prior to organ recovery. Earlier discontinuation may be requested if lung retrieval is being considered[1].

1 Shemie SD, Ross H, Pagliarello J, et al. Organ donor management in Canada: Recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ. 2006;174:S13-S30. doi:10.1503/cmaj.045131.

2 Kutsogiannis, D.J., Shemie, S.D., Doig, C. Donor Organ Management: Literature Review (short version). Edmonton: The Canadian Council for Donation and Transplantation, 2004.

3 Kotloff RM, Blosser S, Fulda GJ, et al. Management of the Potential Organ Donor in the ICU. Crit Care Med. 2015;43(6):1291-1325. doi:10.1097/CCM.0000000000000958.

Glycemic Control in the Organ Donor

Kim Bowman, Sonny Dhanani, Andrew Healey

Description

- Loss of glycemic control part of hormonal changes accompanying brain death[1]
- Hyperglycemia is not uncommon in brain dead donors
- Glucose level should be assessed q4h[2] and normal parameters maintained
- Standard management includes maintaining glucose level of 6-10 mmol/L[3]

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Rationale

The goals of donor management are similar to those used to treat other patients in the ICU. Hemodynamic stability, normovolemia and normothermia should be preserved. Endocrine disorders (including changes in glycemic control) are commonly observed in brain dead donors[1].

Several factors may impact glucose levels, including underlying diabetes mellitus, pancreatic insufficiency, and hypotonic dextrose solutions used for the treatment of free water replacement in patients with hypernatremia. Traditionally, protocols have recommended to initiate and titrate insulin infusion to maintain serum glucose level at 6-10 mmol/L[3]. Without specific evidence in NDD patients, more recent guidelines recommend that glucose should be maintained within normal parameters, as per current practice in the ICU[3].

1 Kutsogiannis, D.J., Shemie, Sam D., Doig, Christopher. Donor Organ Management: Literature Review (short version). Edmonton: The Canadian Council for Donation and Transplantation, 2004.

2 "Donor Screening and Testing". Donation Resource Manual: A Tool to Assist Hospitals with The Process Of Organ And Tissue Donation. 6th ed. Toronto: Queen's Printer, 2014. Print.

3 Kotloff RM, Blosser S, Fulda GJ, et al. Management of the Potential Organ Donor in the ICU. Crit Care Med. 2015;43(6):1291-1325. doi:10.1097/CCM.0000000000000958.

Avoid Hyponatremia or Hypernatremia

Janice Beitel, Andrew Healey

Description

Serum sodium levels should be maintained within normal ranges of 135 - 145 mmol/L to enable pronouncement of neurological death[1], promote optimal donor organ function[2], and improve liver outcomes for transplant recipients [2,3,4].

Interventions associated with donor care to avoid hyper/hyponatremia include[1,3,4]:

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- Standard investigation to manage targets (frequent electrolyte monitoring)
- Assessment of underlying causes (free water diuresis, diabetes insipidus, osmotic diuresis (e.g. glucosuria))
- Treating diabetes insipidus with v asopressin infusions or desmopressin
- Administering vasopressin infusions in patients who are at high risk of death by neurological criteria and hypotensive
- Appropriate fluid resuscitation and sodium based IV fluids (Ringer Lactate, Normal Saline) for hyponatremia
- Use of hypotonic IV fluids (e.g. D5W) and enteral free water replacement for hypernatremia

Rationale

The most common electrolyte disturbances in patients who have been pronounced dead by neurological criteria or who are at risk for progressing to death are sodium disturbances, usually hypernatremia.

Severe electrolyte abnormalities are considered a confounding factor which might rarely prevent the observation of neurological responses and/or mimic neurological death[1,2], specifically hypernatremia (> 160 mmol/L) is of concern. Further, donor serum sodium greater than 155 has been weakly associated with primary liver dysfunction in transplant recipients but reversible if hypernatremia is corrected[2,3]. Given the potential impact of serum sodium abnormalities on pronouncement of death by neurological criteria and possibly liver graft outcomes, it is necessary to proactively manage levels and address imbalances.

1 Shemie SD, Doig C, Dickens B, et al. Severe brain injury to neurological determination of death: Canadian forum recommendations. CMAJ : Canadian Medical Association Journal. 2006;174(6):S2,3. doi:10.1503/cmaj.045142.

2 Shemie SD, Ross H, Pagliarello J, et al. Organ donor management in Canada: Recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ. 2006;174:S13-S30. doi:10.1503/cmaj.045131.

3 Kotloff RM, Blosser S, Fulda GJ, et al. Management of the Potential Organ Donor in the ICU. Crit Care Med. 2015;43(6):1291-1325. doi:10.1097/CCM.0000000000000958.

4 Totsuka E, Dodson F, Urakami A, Moras N, Ishii T, Lee MC, et al. Influence of high donor serum sodium levels on early postoperative graft function in human liver transplantation: Effect of correction of donor hypernatremia. Liver Transplantation and Surgery 1999;5:421-8

Consulting the Donation Support Physician when Small Bowel Donation is Considered

Louise Pope-Rhoden, Andrew Healey

Description

Small bowel transplant is the rarest form of organ transplantation. If small bowel donation is being considered, consultation with TGLN is recommended. Should it be determined there is potential for small bowel donation:

- Hemodynamics should be optimized (blood pressure, pressor requirements, and lactate clearance) to ensure normal perfusion of the bowel[1]
- Administration of oral and/or intravenous antibiotics to reduce infection and bacterial translocation following transplant may be requested[1]
- Bowel preparation to remove stool from the colon may be requested

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Rationale

The selection of small bowel donors varies somewhat from donor selection for other organ allografts. The organs procured for intestine transplantation include the small bowel alone or with the some or all of the stomach, duodenum, liver, large bowel, and kidneys. While awaiting the organ recovery surgery, it is important that the donor is well oxygenated and well perfused with normal electrolyte levels. High dose vasopressors should be avoided or minimized because they can cause splanchnic vasoconstriction which leads to intestinal ischemia. Excessive intravenous fluids and/or a low sodium should be avoided because they can cause bowel edema. Enteral feeds should be stopped for at least six hours prior to organ retrieval.

The unique consequences of intestinal ischemic injury could result in bacterial translocation or intestinal perforation, so donors with excessive vasopressor requirements or prolonged arrest are generally avoided. Intestinal decontamination with enteral antibiotic mixtures is aimed at decreasing the bacterial content of the intestinal allograft and may be requested by the transplant team. In some circumstances, intravenous antibiotics will also be requested. Some centers may ask for a CT with intravenous and oral contrast to define the intra-abdominal anatomy. If the latter request is made, consider the potential for acute kidney injury and discuss with the donation physician if you are concerned.

1 Kotloff RM, Blosser S, Fulda GJ, et al. Management of the Potential Organ Donor in the ICU. Crit Care Med. 2015;43(6):1291-1325. doi:10.1097/CCM.0000000000000958.

BP and Perfusion Targets when Managing the Renal System for NDD Donors

Alissa Visram, Sabira Valiani, Pierre Cardinal, Andrew Healey

Description

- Target a default MAP of ≥ 70 mmHg in adult donors[1], which can be adjusted based on the patient's baseline blood pressure
- Monitor perfusion and cardiac output using the following targets:
  - Clinical surrogates - no mottling, capillary refill less than 4 seconds, and warm extremities
  - Laboratory surrogates - a normal or decreasing lactate, and a central venous oxygen saturation ≥ 60%
  - Noninvasive means - normal stroke olume by echocardiography, or non-invasive cardiac output monitors
- Monitor fluid balance as fluid deficit and fluid overload may both adversely affect the function of kidneys

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Rationale

It is essential to closely monitor both blood pressure and perfusion in NDD patients to ensure the early identification of patients in need of further resuscitation. Achieving the targeted pressures and perfusion parameters increases the likelihood of successful multi-organ donation. Frequent reassessments are necessary to ensure that therapeutic interventions meet their goals and do not result in unintended adverse effects.

Both the 2006 Canadian[1] and the 2015 SCCM[2] guidelines recommend that fluid replacement should be administered to maintain euvolemia as defined by central venous pressure (CVP) and pulmonary artery occlusion pressure (PAOP) measurements. However, using CVP to assess volume is no longer supported by recent work. A systematic review has demonstrated that the CVP is not a reliable measure of blood volume and cannot be used to predict the hemodynamic response to a fluid challenge[3]. Given that assessment of volume status is difficult, we suggest focusing on blood pressure and perfusion monitoring. In the presence of shock (poor pressure and/or perfusion), bedside echocardiography[4] or other tests to assess fluid responsiveness (e.g. respiratory variation of systolic pressure, pulse pressure, stroke index, passive straight leg raising) may help identify patients who require fluid administration.

In patients with normal pressure and perfusion, fluid should not be administered to 'protect' the kidneys. In the absence of hypotension or hypoperfusion excessive fluid administration may also impair renal function as it may lead to renal venous congestion[5]. While there are no

1 Shemie S. Organ donor management in Canada: recommendations of the forum on Medical Management to Optimize Donor Organ Potential. Canadian Medical Association Journal. 2006;174:S13-S30.

2 Kotloff RM, Blosser S, Fulda GJ, et al. Management of the Potential Organ Donor in the ICU. Crit Care Med. 2015;43(6):1291-1325. doi:10.1097/CCM.0000000000000958.

3 Marik P, Baram M, Vahid B. Does Central Venous Pressure Predict Fluid Responsiveness?*: A Systematic Review of the Literature and the Tale of Seven Mares. Chest. 2008;134:172-178.

4 Kumar A, Anel R, Bunnell E, Habet K, Zanotti S, Marshall S, Neumann A, Ali A, Cheang M, Kavinsky C, Parrillo J. Pulmonary artery occlusion pressure and central venous pressure fail to predict ventricular filling volume, cardiac performance, or the response to volume infusion in normal subjects. Critical Care Medicine. 2004;32:691-699.

5 Prowle J, Echeverri J, Ligabo E, Ronco C, Bellomo R. Fluid balance and acute kidney injury. Nat Rev Nephrol. 2009;6:107-115.

randomized control trials comparing a liberal fluid strategy to a restricted one, two retrospective studies in NDD donors suggest that a liberal fluid strategy does not improve renal function[6,7] and possibly decreases heart, lung, and kidney procurement for transplantation[6].

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6 Abdelnour T, Rieke S: Relationship of hormonal resuscitation therapy and central venous pressure on increasing organs for transplant. J Heart Lung Transplant 2009; 28:480–485.

7 Miñambres E, Rodrigo E, Ballesteros MA, et al: Impact of restrictive fluid balance focused to increase lung procurement on renal function after kidney transplantation. Nephrol Dial Transplant 2010; 25:2352–2356.

Avoiding Nephrotoxic Agents when Managing the Renal System

Alissa Visram, Sabira Valiani, Pierre Cardinal

Description

Avoid the use of nephrotoxic agents when caring for NDD donors, in order to prevent renal injury.

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Rationale

Much like the care of standard ICU patients, it is recommended that nephrotoxic agents (ie: contrast agents, nephrotoxic antibiotics) be avoided if possible when caring for NDD donors, in order to prevent renal injury[1].

If aminoglycoside antibiotics are required, once daily dosing is preferred to maximize concentration dependent bactericidal activity and limit aminoglycoside induced acute kidney injury. Additionally, monitoring of aminoglycoside levels is recommended when administration is required beyond single doses[2]. When vancomycin is used, careful monitoring of levels is important to avoid nephrotoxicity. Appropriate fluid replacement should be considered in order to optimize renal clearance.

1 Shemie SD, Ross H, Pagliarello J, et al. Organ donor management in Canada: Recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ. 2006;174:S13-S30. doi:10.1503/cmaj.045131.

2 Khwaja A. KDIGO Clinical Practice Guidelines for Acute Kidney Injury. Nephron Clinical Practice. 2012;120:179-184.

Consider Mild Hypothermia when Managing the Renal System

Alissa Visram, Pierre Cardinal

Description

Consider targeting a body temperature between 34-35°C in NDD renal donors in order to reduce the rate of delayed renal graft function

Rationale

Currently there are no national or provincial guidelines that recommend altering temperature targets based on the organ to be transplanted. The Trillium Gift of Life Network guidelines recommend NDD donor temperature should be maintained between 35.5 and 37°C in order to avoid deleterious effects of hypothermia, such as myocardial suppression, hypoxemia, and acidosis[1] (see 'Standard Investigations and Monitoring'). However, hypothermia also has potential beneficial effects as it may reduce ischemia-reperfusion injury thereby improving allograft function post-transplantation.

A study published by Malinoski et al. in 2015 showed that, in NDD renal donors, targeting a body temperature of 34-35°C (hypothermia) compared to 36.5-37.5°C (normothermia) significantly reduced the rate of delayed graft function (the need for kidney recipients to undergo dialysis within 7 days of transplant). The beneficial effects of hypothermia on reducing the rate of delayed graft function was more pronounced when kidneys were transplanted from expanded criteria donors (i.e. older than 60 years, or those 50-59 years with at least two comorbidities - cerebrovascular cause of death, renal insufficiency, or hypertension) when compared to standard donors[2,3]. There was also no significant difference in the number of organs transplanted from donors in the hypothermia group as compared to the normothermia group which suggests that hypothermia does not significantly alter the transplant potential of other organs (specifically heart, lung, liver, or pancreas donation)[2]. In addition, the rate of adverse events was similar in the experimental and control groups. The results of this study cannot be applied to coagulopathic NDD donors (INR >2.5, PTT > 3 times normal, platelets <50,000/mcl) or hemodynamically unstable donors (>1 vasopressor or one agent at high dose, dopamine >10mcg/kg/min, norepinephrine >10mcg/min, or phenylephrine >60mcg/min) as they were excluded from the study. Though this study did not address the effects of donor hypothermia on long term renal outcomes, the findings present a compelling argument that hypothermia should be considered in hemodynamically stable renal NDD donors.

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1 Trillium Gift of Life Network. Donation Resource Manual: A tool to assist hospitals with the process of organ and tissue Donation. Queen's Printer for Ontario: 2010.

2 Niemann CU, Feiner J, Swain S, Bunting S, Friedman M, Crutchfield M, Broglio K, Hirose R, Roberts JP, Malinoski D. Therapeutic hypothermia in deceased organ donors and kidney-graft function. New England Journal of Medicine. 2015 Jul 30;373(5):405-14.

3 Port F, Bragg-Gresham J, Metzger R, Dykstra D, Gillespie B, Young E, Delmonico F, Wynn J, Merion R, Wolfe R, Held P. Donor characteristics associated with reduced graft survival: an approach to expanding the pool of kidney donors. Transplantation. 2002;74:1281-1286.

Consider Saline to Prevent Contrast Induced Nephropathy

Alissa Visram, Sabira Valiani, Pierre Cardinal, Sonny Dhanani, Andrew Healey

Description

For prophylaxis against contrast induced nephropathy in patients with an abnormal creatinine or acute kidney injury, consider administering isotonic crystalloid solutions to ensure normovolemia.

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Rationale

In NDD donors with acute kidney injury or an abnormal creatinine who are scheduled to receive intravenous contrast, the donor should be adequately hydrated with intravenous isotonic crystalloid solutions[1,2,3]. Fluids should be started three hours prior to contrast administration where possible, and should be continued three to six hours after contrast exposure. Fluids should be titrated to achieve a urine output of >150 mL/hour for the first six hours after contrast exposure[4], acknowledging that the presence of diabetes insipidus may confound the urine output assessment. The fluid regimen suggested above may need to be increased if volume contraction is suspected.

The use of N-acetyl-cysteine (NAC) has also been previously recommended to prevent contrast induced nephropathy (CIN)[1,3]. The mechanism by which NAC prevents renal injury has not been clearly established, however its vasodilatory and antioxidant effects are thought to play a role in renal protection[4].

In a recent systematic review of various strategies[5], none was shown to be clearly effective for contrast induced nephropathy prevention. Crystalloid therapy should be instituted first, with NAC administration left to the discretion of the care team.

1 Shemie SD, Ross H, Pagliarello J, Baker AJ, Greig PD, Brand T, et al. Organ donor management in Canada: recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 2006;174(6):S13-32. doi: 10.1503/cmaj.045131. PubMed PMID: 16534070; PubMed Central PMCID: PMCPMC1402396.

2 Kotloff RM, Blosser S, Fulda GJ, Malinoski D, Ahya VN, Angel L, et al. Management of the Potential Organ Donor in the ICU: Society of Critical Care Medicine/American College of Chest Physicians/Association of Organ Procurement Organizations Consensus Statement. Critical care medicine. 2015;43(6):1291-325. doi: 10.1097/CCM.0000000000000958. PubMed PMID: 25978154.

3 Khwaja A. KDIGO Clinical Practice Guidelines for Acute Kidney Injury. Nephron Clinical Practice. 2012;120:179-184.

4 Trillium Gift of Life Network. Donation Resource Manual: A tool to assist hospitals with the process of organ and tissue Donation. Queen's Printer for Ontario: 2010.

5 Subramaniam RM, Suarez-Cuervo C, Wilson RF,Turban S, Zhang A, Sherrod C, Aboagye J, Eng J, Choi MJ, Hutfless S, Bass EB, Effectiveness of Prevention Strategies for Contrast-Induced Nephropathy: A Systematic Review and Meta-analysis Ann Intern Med. 2016;164:406-416

Administering Steroids when Managing the Respiratory System

Sabira Valiani, Alissa Visram, Pierre Cardinal

Description

- High-dose methylprednisolone should be administered to all NDD donors[1].
- The recommended dose of methylprednisolone is 15mg/kg IV daily (to a maximum of 1000mg IV daily)[2].

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Rationale

High-dose methylprednisolone is recommended in all patients for respiratory optimization and protection following the neurologic declaration of death (NDD)[1]. The administration of high-dose methylprednisolone is believed to mitigate the effects of the inflammatory cascade on organ donor function[3]. The recommendation for high dose steroid administration is based on a systematic review of nonrandomized studies demonstrating that steroid administration may improve donor lung PaO2/FiO2 ratios and lung retrieval rates[4]. Although the evidence is limited, methylprednisolone administration is recommended for steroid replacement therapy in all NDD patients unless their lungs are not considered suitable for donation. In these patients, stress dose steroids may be still be required to manage shock (see 'Steroid Administration in Patients with Distributive Shock').

1 Shemie SD, Ross H, Pagliarello J, et al. Organ donor management in Canada: Recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ. 2006;174:S13-S30. doi:10.1503/cmaj.045131.

2 Trillium Gift of Life Network. Donation Resource Manual: A tool to assist hospitals with the process of organ and tissue Donation. Queen's Printer for Ontario: 2010.

3 Kotloff RM, Blosser S, Fulda GJ, et al. Management of the Potential Organ Donor in the ICU. Crit Care Med. 2015;43(6):1291-1325. doi:10.1097/CCM.0000000000000958.

4 Dupuis, S., Amiel, J., Desgroseilliers, M., Williamson, D., Thiboutot, Z., & Serri, K. et al. (2014). Corticosteroids in the management of brain-dead potential organ donors: a systematic review. British Journal Of Anaesthesia, 113(3), 346-359. http://dx.doi.org/10.1093/bja/aeu154

Lung Protective Ventilation Strategy in NDD Donors - Non ARDS

Sabira Valiani, Ian Ball, Alissa Visram, Pierre Cardinal

Description

- Institute a lung protective ventilation strategy for NDD donors not meeting ARDS criteria with the following initial settings[1]:
  - Tidal volume 6-8mL/kg of ideal body weight for both adult and pediatric donors
  - PEEP of 8-10 cm H20

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- Avoid derecruitment in NDD patients by[1]:
  - Performing closed-circuit suctioning
  - Providing recruitment maneuvers after any disconnection from the ventilator
  - Performing the apnea test using continuous positive airway pressure
- Institute chest physiotherapy, therapeutic bronchoscopy, routine suctioning and repositioning as required
- Utilize a judicious fluid management strategy

Rationale

In NDD donors not meeting ARDS criteria, lung protective ventilation strategies aim to minimize ventilator induced lung injury which is postulated to be mediated, in part, by damage caused by overdistention of alveoli (volutrauma), and ventilation at low lung volumes (atelectrauma)[2]. Such strategies generally consist of some combination of low tidal volume ventilation, the use of higher PEEP, recruitment manoeuvres, and a limitation of plateau airway pressures[2,3].

The Ranieri protocol, which includes low tidal volume ventilation, is the lung protective ventilation strategy of choice in NDD donors who do not meet ARDS criteria (see "Patient meets ARDS criteria" for details). This protocol was tested in a randomized controlled trial of 118 NDD donors, and may increase the number of lungs available for transplant[1]. Potential donors with a history of smoking, asthma, COPD, purulent secretions, aspiration, or infiltrates on chest x-ray were excluded from the study. NDD donors in the lung protective ventilation (intervention) arm were ventilated with tidal volumes of 6-8mL/kg of ideal body weight and a PEEP of 8-10 cm H_2O. Additionally, the intervention arm included closed circuit suctioning, recruitment after any disconnect from the ventilator, and apnea testing performed with continuous positive airway pressure. This was compared to a conventional ventilation strategy, consisting of tidal volumes of 10-12mL/kg of ideal body weight and PEEP of 3-5 cm H_2O. The control group had open circuit suctioning, no recruitment maneuvers, and apnea testing performed with high flow oxygen alone. The study demonstrated that a lung protective strategy in potential NDD donors increased the number of lungs eligible for transplant (from 54% in the conventional strategy to 95% in the protective strategy, $p<0.01$) and harvested lungs

1 Mascia L, Pasero D, Slutsky AS, et al. Effect of a lung protective strategy for organ donors on eligibility and availability of lungs for transplantation: a randomized controlled trial. JAMA. 2010;304(23):2620-7. doi: 10.1001/jama.2010.1796.

2 Slutsky AS, Ranieri VM. Ventilator-induced lung injury. NEJM. 2013;369(22):2126-36. doi: 10.1056/NEJMra1208707.

3 Kotloff RM, Blosser S, Fulda GJ, Malinoski D, Ahya VN, Angel L, et al. Management of the Potential Organ Donor in the ICU: Society of Critical Care Medicine/American College of Chest Physicians/Association of Organ Procurement Organizations Consensus Statement. Critical care medicine. 2015;43(6):1291-325. doi: 10.1097/CCM.0000000000000958.

(from 27% in the conventional strategy to 54% in the protective strategy, p=0.04). Six-month survival rates did not differ between recipients who received lungs from donors ventilated with the conventional strategy compared with the protective strategy (69% vs 75%, respectively).

The SCCM and Canadian guidelines also recommend further adjuncts to the above lung protective ventilation strategy[3,4] These adjuncts include chest physiotherapy, therapeutic bronchoscopy, routine suctioning and repositioning. Finally, judicious fluid management is

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recommended to prevent volume overload which may lead to pulmonary edema, while ensuring adequate volume resuscitation[3,4].

4 Shemie SD, Ross H, Pagliarello J, et al. Organ donor management in Canada: Recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ. 2006;174:S13-S30. doi:10.1503/cmaj.045131.

Monitoring Oxygenation when Managing the Respiratory System - ARDS

Sabira Valiani, Alissa Visram, Pierre Cardinal

Description

- In NDD patients who meet ARDS criteria, monitor ventilatory management and adjust initial settings to meet the following targets:
  - PaO2 55-80 mmHg or oxygen saturation 88-95%
  - Peak inspiratory pressure (PIP) < 35 cm H2O
  - Plateau pressure (Pplat) < 30 cm H_20
  - pH 7.30-7.45, with permissive hypercapnea

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Rationale

ARDS is defined clinically by an acute onset (less than 7 days) of bilateral infiltrates on chest x-ray or computed tomography (CT) scan, with a PaO2/FiO_2 ratio of < 300, which cannot be fully explained by cardiac failure or fluid overload[1]. Pathophysiologically, ARDS is characterized by increased shunt and dead space fraction, as well as poor lung compliance[2]. In NDD patients with ARDS, implementation of a lung protective ventilation strategy based on the ARDSnet protocol is recommended (see 'Lung Protective Ventilation Strategy for ARDS')[3]. Initial tidal volumes should be set at 6mL/kg of ideal body weight. Plateau pressure (Pplat) should then be measured, and tidal volumes can be decreased to a minimum of 4mL/kg until Pplat is < 30 cm H_2O.

The oxygenation target for NDD patients with ARDS is not well defined. Given the lack of randomized controlled trials in the NDD donors specifically meeting ARDS criteria, the 2006 Canadian guidelines suggest an oxygen saturation >95% in all NDD donors[4]. However, consideration should be made to adhering to the ARDSnet goal PaO_2 is 55-80 mmHg or oxygen saturation 88-95%, with PEEP titration based on FiO_2. Discussion with TGLN and the donation support physician to best optimize respiratory management for these cases may be warranted. In cases of refractory hypoxemia, rescue measures can be used (see 'Instituting Rescue Measures for Refractory Hypoxemia').

Due to the increased dead space in ARDS, hypercapnia is common, and the pH goal has been liberalized to 7.30-7.45. In the ARDSnet protocol, patients who were difficult to ventilate due to increased dead space were managed with bicarbonate infusions, or had their Pplat goals liberalized if their pH was less than 7.15[3]. Local protocols should be followed in these extreme cases.

1 Force ADT, Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, et al. Acute respiratory distress syndrome: the Berlin Definition. JAMA : the journal of the American Medical Association. 2012;307(23):2526-33. doi: 10.1001/jama.2012.5669.

2 Ware LB, Matthay MA. The Acute Respiratory Distress Syndrome. New England Journal of Medicine. 2000;342(18):1334-49. doi:10.1056/NEJM200005043421806.

3 ARDS Network. Ventilation with Lower Tidal Volumes as Compared with Traditional Tidal Volumes for Acute Lung Injury and the Acute Respiratory Distress Syndrome. New England Journal of Medicine. 2000;342(18):1301-8. doi:10.1056/NEJM200005043421801.

4 Shemie SD, Ross H, Pagliarello J, et al. Organ donor management in Canada: Recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ. 2006;174:S13-S30. doi:10.1503/cmaj.045131.

Considering if Patients Meet ARDS Criteria

Sabira Valiani, Ian Ball, Alissa Visram, Pierre Cardinal

Description

Recognize ARDS in NDD donors, as defined by an acute onset (less than 7 days) of bilateral infiltrates on chest x-ray or computed tomography (CT) scan, with a PaO_2/FiO_2 ratio of < 300, which cannot be fully explained by cardiac failure or fluid overload[1].

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Rationale

Potential donors that have been declared dead by neurological criteria remain at risk for the Acute Respiratory Distress Syndrome (ARDS), as any other patient who has sustained a similar physiologic insult. The incidence of ARDS in severe traumatic brain injury is approximately 20-30%[2,3]. ARDS is defined by the Berlin Criteria as an acute (<7 days) impairment in oxygenation that is not fully explained by cardiac failure or volume overload, with bilateral infiltrates on chest x-ray or CT. The impairment in oxygenation is quantified by the ratio of PaO_2 to FiO_2 (PF ratio), measured at a PEEP of > 5 cm H_2O. ARDS is subdivided into mild (PF ratio < 300), moderate (PF ratio < 200), and severe (PF ratio < 100)[1]. One should distinguish ARDS from neurogenic pulmonary edema that may accompany brain herniation. Neurogenic pulmonary edema often presents with rapid onset infiltrates, which responds well to high levels of PEEP and is generally reversible over hours.

1 Force ADT, Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, et al. Acute respiratory distress syndrome: the Berlin Definition. JAMA. 2012;307(23):2526-33. doi: 10.1001/jama.2012.5669.

2 Hendrickson CM, Howard BM, Kornblith LZ, Conroy AS, Nelson MF, Zhuo H, et al. The acute respiratory distress syndrome following isolated severe traumatic brain injury. The journal of trauma and acute care surgery. 2016. Epub 2016/02/18. doi: 10.1097/ta.0000000000000982.

3 Aisiku IP, Yamal JM, Doshi P, Rubin ML, Benoit JS, Hannay J, et al. The incidence of ARDS and associated mortality in severe TBI using the Berlin definition. The journal of trauma and acute care surgery. 2016;80(2):308-12. doi: 10.1097/TA.0000000000000903.

Monitoring PF Ratios, Peak and Plateau Pressures, and PaCO2 – Non ARDS

Sabira Valiani, Alissa Visram, Pierre Cardinal

Description

In patients who do not meet ARDS criteria, monitor ventilatory management, and adjust initial settings to ensure that the following are targets are met[1,2]:

- $PaCO_2$ of 35-45 mmHg and pH 7.35-7.45
- PaO_2 > 90 mmHg or oxygen saturation > 95%
- Peak inspiratory pressure (PIP) < 35 cm H_2O
- Plateau pressure (Pplat) < 30 cm H_2O

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Rationale

In patients who do not meet ARDS criteria, ventilation strategies must be monitored to ensure that adequate ventilation and oxygenation are being provided, while limiting the effects of ventilator induced lung injury. As the patient's clinical status changes, ventilator settings should be adjusted to address changing lung compliance, resistance, dead space, shunt, and acid-base status. The 2006 Canadian guidelines suggest a target pH of 7.35-7.45 and $PaCO_2$ of 35-45 mmHg[2]. The recommended lung protective ventilation strategy is based on the Ranieri protocol , which uses a target PaO_2 of >90 mmHg (see 'Lung Protective Ventilation Strategy')[1]. Finally, recommended peak inspiratory pressure (PIP) <35 cm H_2O and plateau pressure < 30 cm H_2O were targets used in the ARDSnet protocol[3].

1 Mascia L, Pasero D, Slutsky A, et al., Effect of a Lung Protective Strategy for Organ Donors on Eligibility and Availability of Lungs for Transplantation. JAMA. 2010;304:2620.

2 Shemie SD, Ross H, Pagliarello J, et al. Organ donor management in Canada: Recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ. 2006;174:S13-S30. doi:10.1503/cmaj.045131.

3 ARDS Network. Ventilation with Lower Tidal Volumes as Compared with Traditional Tidal Volumes for Acute Lung Injury and the Acute Respiratory Distress Syndrome. New England Journal of Medicine. 2000;342(18):1301-8. Doi: 0.1056/NEJM200005043421801.

Lung Protective Ventilation Strategy in NDD Donors - ARDS

Sabira Valiani, Ian Ball, Alissa Visram, Pierre Cardinal

Description

If the NDD donor meets ARDS criteria, initiate lung protective ventilation strategies according to the ARDSnet protocol and local practice protocols, including:

- Low tidal volume ventilation of 4-6mL/kg of ideal body weight
- Goal plateau pressures (Pplat) < 30 cm H_2O
- PEEP titration based on FiO_2

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Rationale

NDD donors meeting ARDS criteria should be ventilated according to local practice protocols that implement low tidal volume ventilation based on the ARDSnet protocol[1]. Low tidal volume ventilation has been shown to reduce absolute mortality and increase ventilator free days in living patients with ARDS[1]. In NDD patients, this ventilation strategy is suggested in order to optimize oxygenation and prevent further pulmonary deterioration, thereby preserving the transplant potential of other organs.

In the ARDSnet protocol, patients in the low tidal volume strategy were ventilated with target tidal volumes of 4-6mL/kg of ideal body weight, and maximal plateau pressures of 30 cm H_2O, compared to conventional ventilation with tidal volumes of 12mL/kg of ideal body weight and maximal plateau pressures of 50 cm H_2O. PEEP was titrated based on FiO_2 requirements, and this or similar titration protocols are generally also included in local practice protocols.

1 ARDS Network. Ventilation with Lower Tidal Volumes as Compared with Traditional Tidal Volumes for Acute Lung Injury and the Acute Respiratory Distress Syndrome. New England Journal of Medicine. 2000;342(18):1301-8. doi:10.1056/NEJM200005043421801.

Instituting Rescue Measures to Optimize Oxygenation in NDD Donors with ARDS and Refractory Hypoxemia

Ian Ball, Sonny Dhanani

Description

In the donor patient with refractory hypoxemia, several evidence based strategies from the non-organ donation literature should be implemented:

- Neuromuscular blockade[1]
- Prone positioning[2]
- Recruitment maneuvers with increase in peak airway pressure to 30 cm H_2O for 30-60 seconds

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Rationale

Potential donors that have been declared dead by neurologic criteria remain at risk for the Acute Respiratory Distress Syndrome (ARDS), in the same way that any other non-NDD patient who had sustained the same physiologic insult would be. Current evidence for ARDS management, not specifically for NDD, support the use of neuromuscular blockade to improve compliance, reduce respiratory work, and lessen metabolic demand[1]. Individual agents are not recommended over others, and local preference should be instituted. Prone positioning has also shown success in ARDS[2], but also has not been specifically studied in the NDD patient. Local ARDS protocols for prone positioning should be instituted[2].

There is no high level evidence for nitric oxide, epoprostenol, or oscillation in potential lung donors, and recent evidence has failed to show a survival benefit in the general literature[3,4]. However, both nitric oxide and epoprostenol may transiently improve systemic oxygenation, thereby improving oxygen delivery prior to organ donation. They should be considered second line therapies for cases refractory to more evidence based treatments.

Routine recruitment maneuvers have also not shown survival benefit in patients with refractory hypoxemia; however, a systematic review published in 2008[5] and a subsequent Cochrane Review in 2009[6] demonstrated that the use of recruitment maneuvers results in transient increases in oxygenation by PaO_2 and P:F measurements. This may be requested by lung recovery teams. The target pressure and time for recruitment maneuvers varies by centre; however, the Canadian recommendations are for an increase in pressure to 30 cm H_2O for 30-60 seconds[7,8].

1 Neuromuscular Blockers in Early Acute Respiratory Distress Syndrome Papazian L, Forel J-M, Gacouin A, et al. N Engl J Med 2010; 363:1107-1116

2 Prone Positioning in Severe Acute Respiratory Distress Syndrome. Guérin, C, Reignier J, Richard J-C, et al. N Engl J Med 2013; 368:2159-2168

3 Adhikari NK et al. Inhaled nitric oxide does not reduce mortality in patients with acute respiratory distress syndrome regardless of severity: systematic review and meta-analysis. Crit Care Med. 2014 Feb;42(2):404-12.

4 High-Frequency Oscillation in Early Acute Respiratory Distress Syndrome Ferguson ND, Cook DJ, Guyat GH, et al. N Engl J Med 2013; 368:795-805

5 Fan E, Wilcox M, Brower R, Stewart T, Mehta S, Lapinsky S, Meade M, Ferguson N. Recruitment Maneuvers for Acute Lung Injury. Am J Respir Crit Care Med. 2008;178:1156-1163.

6 Hodgson C, Keating JL, Holland AE, Davies AR, Smirneos L, Bradley SJ, Tuxen D. Recruitment manoeuvres for adults with acute lung injury receiving mechanical ventilation. Cochrane Database Syst Rev. 2009 Jan 1;2(2).

7 Shemie SD, Ross H, Pagliarello J, et al. Organ donor management in Canada: Recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ. 2006;174:S13-S30. doi:10.1503/cmaj.045131.,

8 Trillium Gift of Life Network. Donation Resource Manual: A tool to assist hospitals with the process of organ and tissue Donation. Queen's Printer for Ontario: 2010.

Consider Recruitment Manoeuvres

Sabira Valiani, Alissa Visram, Pierre Cardinal

Description

- Perform routine recruitment maneuvers in all NDD patients, regardless of PaO_2/FiO_2 ratio[1]
- In NDD patients with refractory hypoxemia, perform recruitment maneuvers as a rescue intervention to improve oxygenation[1,2]

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- Recruitment maneuvers done on an FiO_2 of 1 should be performed with a sustained inflation to a pressure of 30 cm H_2O for 30-60 seconds[1,3].

Rationale

Recruitment maneuvers improve oxygenation by re-inflating collapsed alveoli[4]. These recruitment maneuvers consist of a sustained inflation to a target pressure, which may result in unintended deleterious effects of hypotension or pneumothorax[4]. The target pressure and time for recruitment maneuvers varies by centre; however, the Canadian recommendations are for an increase in pressure to 30 cm H2O for 30-60 seconds[1,3]. In the Ranieri protocol, which implemented a lung protective ventilation strategy for potential lung donors, recruitments were performed by doubling of target tidal volumes (target tidal volumes in this study were 6-8mL/kg of ideal body weight) for 10 respiratory cycles[5].

Routine recruitment maneuvers are recommended by the 2006 Canadian guidelines as part of the management of all NDD donors and continue to be used despite weak evidence[1]. The recommended frequency of these recruitment maneuvers has not been specified.

Rescue recruitment maneuvers are recommended by the SCCM and Canadian guidelines to potentially improve lung procurement in NDD donors whose PaO_2 to FiO_2 ratio is < 300[1,2]. These recruitment maneuvers are part of an aggressive lung donor management protocol that includes chest physiotherapy, therapeutic bronchoscopy, routine suctioning and repositioning, and maintenance of euvolemia[1,2,3].

1 Shemie SD, Ross H, Pagliarello J, et al. Organ donor management in Canada: Recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ. 2006;174:S13-S30. doi:10.1503/cmaj.045131. Shemie SD, Ross H, Pagliarello J, et al. Organ donor management in Canada: Recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ. 2006;174:S13-S30. doi:10.1503/cmaj.045131.

2 Kotloff RM, Blosser S, Fulda GJ, et al. Management of the Potential Organ Donor in the ICU. Crit Care Med. 2015;43(6):1291-1325. doi:10.1097/CCM.0000000000000958.

3 Trillium Gift of Life Network. Donation Resource Manual: A tool to assist hospitals with the process of organ and tissue Donation. Queen's Printer for Ontario: 2010.

4 Slutsky AS, Ranieri VM. Ventilator-induced lung injury. The New England journal of medicine. 2013;369(22):2126-36. doi: 10.1056/NEJMra1208707. PubMed PMID: 24283226

5 Mascia L, Pasero D, Slutsky AS, Arguis MJ, Berardino M, Grasso S, et al. Effect of a lung protective strategy for organ donors on eligibility and availability of lungs for transplantation: a randomized controlled trial. JAMA : the journal of the American Medical Association. 2010;304(23):2620-7. Epub 2010/12/16. doi: 10.1001/jama.2010.1796. PubMed PMID: 21156950.

Recognize and Manage Hypertension in an Organ Donor

Ian Ball, Sonny Dhanani, Andrew Healey

Description

Appropriate agents to manage acute hypertension secondary to neurologic herniation include Hydralazine, phentolamine, and nitroprusside.

Rationale

Potential donors that have been declared dead by neurologic criteria are at risk of malignant hypertension secondary to a catecholamine release resulting from medullary ischemia[1,2]. This is the brain's effort to maintain an adequate cerebral perfusion pressure. Human autopsy evidence and baboon models of brain death demonstrate an association between brainstem ischemia and left ventricular subendocardial ischemia[3,4]. Despite the lack of supporting high level evidence, medical management of brain death induced hypertension is physiologically justified, to optimize transplanted organ outcomes.

The ideal antihypertensive agent needs to have predominantly peripheral effects, with minimal inotropy or chronotropy. It needs to be titratable and shorter acting. Hypotension subsequent to spinal cord ischemia with resultant peripheral vasodilation, decrease in serum catecholamines, and decreased beta receptor activity[5,6] is likely to follow the hypertensive emergency and will be worsened by antihypertensive therapy.

Ideal agents include:

1. Hydralazine
2. Phentolamine
3. *Nitroprusside

All should be administered as intravenous infusions in a monitored setting. It is not unusual for some patients to require multiple antihypertensive agents. Clinicians should be prepared to administer vasopressors at a moment's notice in case of hypotension from evolving brainstem ischemia.

*Caution with infusions administered for greater than 48 hours due to the accumulation of toxic metabolites

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1 Wilhelm MJ, Pratschke J, Laskowski IA, Paz DM, Tilney NL. Brain death and its impact on the donor heart — lessons from animal models. J Heart Lung Transplant 2000;19:414-8.

2 Baroldi G, Di Pasquale G, Silver MD, Pinelli G, Lusa AM, Fineschi V. Type and extent of myocardial injury related to brain damage and its significance in heart trans- plantation: a morphometric study. J Heart Lung Transplant 1997;16:994-1000.

3 Novitzky D, Horak A, Cooper DK, Rose AG. Electrocardiographic and histopatho- logic changes developing during experi- mental brain death in the baboon. Transplant Proc 1989;21:2567-9.

4 Kolin A, Norris JW. Myocardial damage from acute cerebral lesions. Stroke 1984;15: 990-3.

5 Shivalkar B, Van Loon J, Wieland W, et al. Variable effects of explosive or gradual increase of intracranial pressure on myocardial structure and function. Circulation 1993; 87:230-9.

6 Wood KE, Becker BN, McCartney JG, et al., Care of the Potential Organ Donor. N Engl J Med 2004;351:2730-9.

Anticipate Catecholamine Induced Myocardial Injury

Sonny Dhanani

Description

Anticipate catecholamine induced myocardial dysfunction after typical sympathetic storm following brain death.

Rationale

Myocardial dysfunction may be related to many different mechanisms including contusion, anoxic-ischemic injuries, or underlying comorbidities. However, myocardial injury following brain death is often related to catecholamine release. Neurological insults that cause progressive and sustained rise in intracranial pressure produce ischemia of the brainstem. When extension into the medulla oblongata occurs, the vagal cardiomotor nucleus becomes ischemic, preventing tonic vagal stimuli resulting in unopposed sympathetic stimulation. The result is a massive release of catecholamines which may last for minutes to hours and clinically presents as arterial hypertension with the potential for tachydysrhythmias[1,2,3]. This often referred the "autonomic" or "sympathetic storm" during which time significant cardiac damage can occur secondary to changes in oxygen consumption and delivery[3,4]. The release of endogenous catecholamines results in increased peripheral resistance causing a sudden increase in myocardial work and oxygen consumption possibly leading to myocardial ischemia or infarction. In animals, the rise of epinephrine after brain death and the extent of myocardial damage have been shown to depend on the rate of rise in ICP[5,6]. This culminates in the commonly seen, and often reversible, stress cardiomyopathy following herniation.

Interestingly, when studied in patients with subarachnoid hemorrhages, autopsies have shown scattered foci of transmural myocardial injury that are not seen in patients dying of non-neurogenic causes[7,8]. Brain dead patients with elevations in cardiac troponin I and T have been shown to have diffuse subendocardial myocytolysis and coagulative necrosis. Echocardiographic systolic myocardial dysfunction is present in 42% of adult brain death and associated with ventricular dysrhythmias. More of-

Return to Management of Hemodynamics map

Return to Management of Shock map

1 Novitzky D, Wicomb WN, Cooper DKC, Rose AG, Fraser RC, Barnard CW. Electrocardiographic, hemodynamic and endocrine changes occurring during experimental brain death in the chacma baboon. Heart Transplantation 1984; 4:63-9.

2 Ferrera R, Hadour G, Tamion F, Henry JP, Mulder P, Richard V, Thuillez C,Ovize M, Derumeaux G. Brain death provokes very acute alteration in myocardial morphology detected by echocardiography: preventive effect of beta-blockers. Transpl Int. 2011 Mar;24(3):300-6.

3 Li J, Konstantinov IE, Cai S, Shimizu M, Redington AN. Systemic and myocardial oxygen transport responses to brain death in pigs. Transplant Proc. 2007 Jan-Feb;39(1):21-6

4 Pérez López S, Otero Hernández J, Vázquez Moreno N, et al: Brain death effects on catecholamine levels and subsequent cardiac damage assessed in organ donors. J Heart Lung Transplant 2009; 28(8):815-820.

5 Kono T, Morita H, Kuroiwa T, Onaka H, Takatsuka H, Fujiwara A. Left ventricular wall motion abnormalities in patients with subarachnoid hemorrhage: neurogenic stunned myocardium. J Am Coll Cardiol 1994; 24:636-40.

6 Temes RE, Tessitore E, Schmidt JM, Naidech AM, Fernandez A, Ostapkovich ND,Frontera JA, Wartenberg KE, Di Tullio MR, Badjatia N, Connolly ES, Mayer SA,Parra A. Left ventricular dysfunction and cerebral infarction from vasospasm after subarachnoid hemorrhage. Neurocrit Care. 2010 Dec;13(3):359-65.

7 Macmillan CSA, Grant IS, Andrews PJD. Pulmonary and cardiac sequelae of subarachnoid haemorrhage: time for active management? Intensive Care Med 2002; 28:1012-23.

8 Tung P, Kopelnik A, Banki N, Ong K, Ko N, Lawton MT, Gress D, Drew B, Foster E, Parmley W, Zaroff J. Predictors of neurocardiogenic injury after subarachnoid hemorrhage. Stroke. 2004 Feb;35(2):548-51. Epub 2004 Jan 22.

ten, the myocardial injury resulting from the sympathetic storm is transient and potentially reversible and has been defined as the "neurogenically stunned myocardium". With temporary support, this often resolves even to the point where the heart may be suitable for transplantation despite a brief period of severe systolic dysfunction[9].

Return to Management of Hemodynamics map

Return to Management of Shock map

9 Dujardin KS, McCully RB, Wijdicks EF, Tazelaar HD, Seward JB, McGregor CG, Olson LJ. Myocardial dysfunction associated with brain death: clinical, echocardiographic, and pathologic features. J Heart Lung Transplant 2001; 20:350-7.

Verifying Thyroid Replacement

Sonny Dhanani, Ronish Gupta, Pierre Cardinal, Andrew Healey

Description

Thyroid replacement should be considered in all NDD patients as part of triple-hormonal replacement therapy.

- Administer T4/ L-thyroxine 100 micrograms IV bolus, then 50 micrograms IV every 12 hours.

OR

- Administer T4/ L-thyroxine 20 micrograms IV bolus followed by 10µg/hr IV infusion

Return to Management of Hemodynamics map

Return to Management of Shock map

Rationale

The benefit of using thyroid hormone replacement therapy in brain dead donors is based on conflicting weak evidence, though evidence in animal models is supportive. Alone, T3 replacement has been shown to reduce vasopressor use and improve cardiac function on echocardiography. Studies that also include the co-administration of steroids, and vasopressin have been more impressive. These have shown that routine use may improve the chance of heart transplantation. However, studies on thyroid replacement in the brain dead donor are of low quality with poor study design, limiting objective analysis[1,2].

Given the limited evidence, some have suggested restricting the use of thyroid replacement to patients with documented hypothyroidism, identified cardiac dysfunction, or hemodynamic instability. Because of minimal side effects, many donor management protocols advocate for its empiric use in all NDD patients. Empiric thyroid hormone administration with vasopressin and methylprednisolone (so called triple hormone therapy) has been shown to increase the number of transplanted organs, especially the heart[3,4].

Two forms of thyroid replacement are available. There are advantages of parenteral T3 over T4 (stability for intravenous infusion, rapid onset as T3 does not require peripheral tissue conversion), but T3 is extremely expensive in comparison to intravenous T4 and may not be commercially available in many countries[5]. There has not been evidence of benefit of one form over the other. Thus, most sites continue to use T4 more commonly[6]. While there is some evidence for an oral route[7], we continue to advocate for intravenous use until larger studies of equivalence have been completed.

1 Klein I, Ojamaak K. Thyroid hormone and the cardiovascular system. NEJM 2001; 344(7): 501.

2 Sazontseva IE, Kozlov IA, Moisuc YG, Ermolenko AE, Afonin VV, Illnitskiy VV. Hormonal response to brain death. Transplantation Proceedings 1991; 23(5):2467.

3 James SR, Ranasinghe AM, Venkateswaran R, McCabe CJ, Franklyn JA, Bonser RS.The effects of acute triiodothyronine therapy on myocardial gene expression in brain stem dead cardiac donors. J Clin Endocrinol Metab. 2010 Mar;95(3):1338-43.

4 Roels L, Pirenne J, Delooz H, Lauwers P, Vandermeersch E. Effect of triiodothyronine replacement therapy on maintenance characteristics and organ availability in hemodynamically unstable donors. Transplantation Proceedings 2000; 32:1564-6.

5 Zuppa AF, Nadkarni V, Davis L, Adamson PC, Helfaer MA, Elliott MR, Abrams J,Durbin D. The effect of a thyroid hormone infusion on vasopressor support in critically ill children with cessation of neurologic function. Crit Care Med.2004 Nov;32(11):2318-22.

6 Kutsogiannis DJ, Pagliarello G, Doig C, Ross H, Shemie SD. Medical management to optimize donor organ potential: review of the literature. Can J Anaesth. 2006 Aug;53(8):820-30.

7 Sharpe MD, van Rassel B, Haddara W. Oral and intravenous thyroxine (T4) achieve comparable serum levels for hormonal resuscitation protocol in organ donors: a randomized double-blinded study.Can J Anaesth. 2013 Oct;60(10):998-1002.

Consider First Choice Norepinephrine then Dobutamine

Sabira Valiani, Alissa Visram, Pierre Cardinal

Description

- Institute norepinephrine as the vasopressor of choice in patients who are suspected to have shock secondary to catecholamine induced myocardial dysfunction
  - The maximal dose recommended is 20mcg/minute or 0.2mcg/kg/minute[1], [2]
- If the targets are not met, the addition of dobutamine may be considered
  - Recognize and monitor for tachyarrhythmias and hypotension as the most common adverse effects of dobutamine administration[3]
  - Milrinone and epinephrine may also be considered as inotropic support.
- The above vasopressors and inotropes should be instituted along thyroid hormone replacement (see 'Verifying Thyroid Replacement').

Return to Management of Hemodynamics map

Return to Management of Shock map

Rationale

In NDD patients presenting with cardiogenic shock, the initial step is to verify that thyroid hormone therapy has been instituted. Thyroid hormone therapy with intravenous T3 may reduce cardiac dysfunction in NDD patients[3]. However, patients may remain in shock despite thyroid hormone replacement. In these cases, vasopressors and inotropes should be added based on physiologic rationale[1]. Norepinephrine is often the first vasopressor of choice because it provides both vasoconstrictor activity via α1-adrenergic stimulation, and inotropy via ß1-adrenergic stimulation. This results in an improvement in MAP and a small increase in cardiac output and stroke volume[3]. If the administration of norepinephrine fails to improve perfusion and surrogate markers for cardiac output, an inotrope, such as dobutamine can be added. Dobutamine has primarily ß1-adrenergic activity, which increases myocardial contractility and heart rate. Its effects are limited by the development of tachyarrythmias and vasodilation resulting in hypotension[3]. Other vasoactive agents, such as dopamine, milrinone or epinephrine could also be considered in these situations[4]. Although dopamine is traditionally considered first line for the management of shock in NDD donors, there is limited evidence to recommend its use over other vasopressor agents, and there are concerns that it may lead to increased arrhythmia[5].

In NDD patients who are potential heart donors, catecholamines should be used with caution. The Canadian guidelines state that downregulation of ß-receptors and depletion of ATP occurs with the use of catecholamines[1]. The SCCM guidelines also caution about the use of α–agonists, as stimulation of this receptor predisposes to increased pulmonary

1 Shemie SD, Ross H, Pagliarello J, et al. Organ donor management in Canada: Recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ. 2006;174:S13-S30. doi:10.1503/cmaj.045131.

2 Trillium Gift of Life Network. Donation Resource Manual: A tool to assist hospitals with the process of organ and tissue Donation. Queen's Printer for Ontario: 2010.

3 Hollenberg SM. Vasoactive drugs in circulatory shock. American journal of respiratory and critical care medicine. 2011;183(7):847-55. doi: 10.1164/rccm.201006-0972CI.

4 Kotloff RM, Blosser S, Fulda GJ, et al. Management of the Potential Organ Donor in the ICU. Crit Care Med. 2015;43(6):1291-1325. doi:10.1097/CCM.0000000000000958.

5 De Backer D, Biston P, Devriendt J, Madl C, Chochrad D, Aldecoa C, et al. Comparison of dopamine and norepinephrine in the treatment of shock. NEJM. 2010;362(9):779-89. doi: 10.1056/NEJMoa0907118.

capillary permeability, and may result in coronary vasoconstriction[4].

Due to the potential harms of catecholamine administration to NDD patients who are potential heart donors, optimization with thyroid hormone administration should be performed first. If a shock state is persistent, the minimal doses of vasopressors and inotropes required to meet blood pressure and perfusion targets should be instituted.

Return to Management of Hemodynamics map

Return to Management of Shock map

Anticipate Distributive Shock

Sonny Dhanani, Pierre Cardinal, Andrew Healey

Description

Anticipate distributive shock given its high prevalence in NDD patients.

Rationale

The etiology of hypotension in brain dead patients is characterized by low preload due to vascular volume depletion, neurogenically-mediated contractile myocardial dysfunction, and a fall in the systemic vascular resistance resulting from a catecholamine and sympathetic hormone depletion.

Return to Management of Hemodynamics map

Return to Management of Shock map

During the process of brainstem ischemia and herniation, the regulation of sympathetic and parasympathetic activity becomes unbalanced. Periods of unopposed sympathetic activity known as "sympathetic storm" occur within minutes of marked increases in intracranial pressure, and coincide with elevated levels of circulating catecholamines. Within hours of this initial phase, a state of catecholamine depletion ensues leading to decreased systemic vascular resistance and profound vasodilation[1].

From a hormonal perspective, the combination of increased intracranial pressure, ischemia and inflammatory mediated damage in neurologic death interfere with hypothalamus and pituitary functioning. As a result, several hormonal axes begin to fail. Secretion of arginine vasopressin from the posterior pituitary is impaired in over three-quarters of potential organ donors[2,3]. A reduction in vasopressin (a direct vasoconstrictor), as well as ACTH (cortisol stimulation) result in decreased vascular tone and hypotension. The decreased vascular tone of the venous capacitance vessels often lowers the mean systemic venous pressure reducing venous return, hence cardiac output[4,5].

Overall, sympathetic arrest due to catecholamine and sympathetic hormone depletion and consequent reduced systemic vascular resistance underly hypotension and distributive shock in the potential donor. Other etiologies of distributive shock (e.g. sepsis) should always be considered but are far less common. Aggressive management of hypotension during the interval from admission to procurement is essential to prevent the development of multiple organ failure and possibly cardiac arrest[5].

1 Salim A., Martin M., Brown C., et al: Complications of brain death: frequency and impact on organ retrieval. Am Surg 2006; 72(5):377-381.

2 Huang J, Trinkaus K, Huddleston CB, Mendeloff EN, Spray TL, Canter CE. Risk factors for primary graft failure after pediatric cardiac transplantation: importance of recipient and donor characteristics. J Heart Lung Transplant. 2004 Jun;23(6):716-22.

3 Nakagawa K, Tang JF. Physiologic response of human brain death and the use of vasopressin for successful organ transplantation. J Clin Anesth. 2011 Mar;23(2):145-8.

4 Shah VR. Aggressive management of multiorgan donor. Transplant Proc. 2008 May;40(4):1087-90.

5 Zaroff JG, Rosengard BR, Armstrong WF, et al., Consensus conference report Maximizing use of organs recovered from the cadaver donor: cardiac recommendations. Circulation 2002; 106:836-41.

Verifing Vasopressin Administration for Distributive Shock

Sonny Dhanani, Ronish Gupta, Pierre Cardinal

Description

Adults

- Administer vasopressin at a rate of 2.4 units/hour (0.04 units/min) in all adult patients unless hypertensive

Rationale

Brain death and hypotension are often associated with vasopressin deficiency[1]. Arginine Vasopressin (AVP) is a peptide that is formed in the hypothalamus and then stored in as well as secreted from the posterior pituitary. Its activity upon the V1 receptors of vascular smooth muscle leads to vasoconstriction (i.e. its "vasopressor" effect); and its activity upon the V2 receptors within the renal collecting system promote the reabsorption of free water (i.e. its "antidiuretic" effect).

Return to Management of Hemodynamics map

Return to Management of Shock map

Given that the sequence of brainstem ischemia and herniation typically results in diminished sympathetic activity as well as AVP deficiency, optimizing vascular tone becomes a priority. Secretion of AVP from the posterior pituitary is impaired in over three-quarters of potential organ donors. Low-dose AVP infusions have been shown to improve hemodynamic stability and spare catecholamine use[2,3]. Prolonged hemodynamic stability can be maintained after brain death with low-dose AVP (1–2 units/hour), permitting a significant decrease in epinephrine and extended preservation of renal function[4,5]. This finding is considered advantageous as it may limit excessive catecholamine driven demands on an already compromised heart. Supporting this idea, an analysis of 12,322 donors demonstrated that AVP use was associated with higher numbers of organs retrieved per donor (3.75 vs 3.33; $p < 0.001$)[6].

Caution should still be maintained when administering AVP as reductions in splanchnic blood flow have been demonstrated when compared to dopamine[2]. Additional benefit may be conferred to hemodynamically unstable patients when AVP is used in combination with other hormone therapies. Intravenous AVP/vasopressin infusion can be titrated from minimum of 0.5 units/h and maximum of 2.4 units/h to obtain a systolic blood pressure of 100 mmHg or mean arterial pressure of 70 mmHg.

1 Chen JM, Cullinane S, Spanier TB, Artrip JH, John R, Edwards NM, Oz MC, Landry DW. Vasopressin deficiency and pressor hypersensitivity in hemodynamically unstable organ donors. Circulation 1999; 100 (suppl II):II-246.

2 Pennefather SH, Bullock RE, Mantle D, Dark JH. Use of low dose arginine vasopressin to support brain-dead organ donors. Transplantation 1995; 59(1):58-62.

3 Holmes CL, Patel BM, Russell JA, Walley KR. Physiology of vasopressin relevant to management of septic shock. Chest 2001; 120:989-1002.

4 Nakagawa K, Tang JF. Physiologic response of human brain death and the use of vasopressin for successful organ transplantation. J Clin Anesth. 2011 Mar;23(2):145-8.

5 Dunser MW, Mayr AJ, Ulmer H, Knotzer H, Sumann G, Pajk W, Friesenecker B, Hasibeder WR. Arginine vasopressin in advanced vasodilatory shock: a prospective, randomized,controlled study. Circulation. 2003 May 13;107(18):2313-9.

6 Plurad DS, Bricker S, Neville A, Bongard F, Putnam B. Arginine vasopressin significantly increases the rate of successful organ procurement in potential donors. Am J Surg. 2012;204(6):856-861. doi:10.1016/j.amjsurg.2012.05.011.

Steroid Administration in Patients with Distributive Shock

Sonny Dhanani, Ronish Gupta, Pierre Cardinal

Description

- Verify if donor is already receiving high-dose steroid (e.g. methylprednisolone) as an immune modulator in preparation for potential lung donation
- In presence of shock for patients who are not on high-dose steroid, administer intravenous steroids (e.g. hydrocortisone) for maintenance of hemodynamic targets

Return to Management of Hemodynamics map

Return to Management of Shock map

Rationale

The anterior pituitary secretes adrenocorticotropic hormone (ACTH) which stimulates cortisol release from the adrenal glands. Cortisol has numerous functions in healthy individuals, but its most relevant roles in the organ donor are maintaining hemodynamic stability and modulating the body's immune system.

It is unclear whether potential organ donors develop a state of adrenal insufficiency and/or suppression that is unique to the brain death process or similar to critically ill patients in general[1]. A study of 37 adults with severe traumatic brain injury revealed that compared to matched non-neurologically deceased patients, the 17 neurologically deceased individuals had significantly lower circulating cortisol levels (234 ± 171 vs 469 ± 182 nmol/L; $p < 0.001$) and significantly reduced peak cortisol response to ACTH administration (466 ± 174 vs 659 ± 157 nmol/L; $p = 0.001$)[1].

Steroid replacement for the maintenance of hemodynamic targets in the management of distributive shock has been recommended. This is in addition to the recommendation of high-dose steroid administration for the anti-inflammatory benefits shown for lung transplantation. Note that patient receiving high-dose steroids in preparation for lung donation do not need to receive stress-dose steroids. A prospective multi-centre cluster study of 208 neurologically deceased adults has studied the effect of steroid replacement therapy (50 milligram bolus of hydrocortisone, followed by 10 milligram per hour continuous infusion). In this study, the group receiving steroid replacement had reduced need for norepinephrine (mean 1.18 ± 0.92 vs 1.49 ± 1.29 milligrams per hour; $p = 0.03$), shorter time on norepinephrine (median 874 vs 1,160 minutes; $p < 0.0001$) and a greater likelihood of being weaned off norepinephrine support (33.8% vs 9.5%; $p < 0.0001$). Steroid use however, was not associated with higher organ procurement or improved graft function[2].

Therefore, in patients who are not on high-dose steroids (administered in preparation for lung transplantation) and present with cardiovascular instability requiring inotrope/pressor, routine administration of low dose steroids should be considered to address the possibility of adrenal insufficiency.

1 Callahan DS, Kim D, Bricker S, et al. Trends in Organ Donor Management: 2002 to 2012. J Am Coll Surg. 2014;219(4):752-756. doi:10.1016/j.jamcollsurg.2014.04.017.

2 Pinsard M, Ragot S, Mertes PM, et al. Interest of l ow-dose hydrocortisone therapy during brain-dead organ donor resuscitation : the CORTICOME study. Crit Care. 2014;18(R158):1-8.

Considering Other Vasopressor Use in Donors with Distributive Shock

Sonny Dhanani, Pierre Cardinal, Andrew Healey

Description

- Initiate Norepinephrine (0-1.3 mcg/kg/min) and titrate to effect
- Select default MAP target of 65 mmHg. Target MAP may be readjusted based on the patient's baseline BP
- Monitor for hypoperfusion using clinical examination (prolonged capillary refill, cold extremities, presence of mottling); rising serum lactate; decrease in central venous oxygen saturation; or invasive or noninvasive means to identify any decrease in cardiac output
- Monitor for ischemic events (extremities, bowel, kidneys, and heart)

Return to Management of Hemodynamics map

Return to Management of Shock map

Rationale

In NDD patients presenting with distributive shock, vasopressin is often the first vasopressor of choice because it not only increases vasomotor tone but may also treat or prevent the development of diabetes insipidus (see 'Verifying Vasopressin Instituted'). Given the abnormal pituitary-adrenal axis (see 'Verifying Steroid Administration') of NDD patients, it is important to verify that all patients in distributive shock also be receiving corticosteroids to maintain a normal vasopressor response to catecholamine. However, many NDD patients remain hypotensive despite adequate volume resuscitation and the administration of vasopressin and corticosteroids and thus may require the addition of other vasopressors.

The 2006 Canadian guidelines recommend the use of norepinephrine, epinephrine and/or phenylephrine for hemodynamic support with dosing titrated to achieve clinical effect, but with no predetermined upper limit[1]. The guidelines also distinguish between pure vasopressors (vasopressin, phenylephrine) and vasopressors with beta-agonist inotropic action (norepinephrine, epinephrine). They recommend cautious use of vasopressors with beta-agonist action in potential heart donors, given concerns about myocardial adenosine triphosphate (ATP) depletion and downregulation of beta-receptors. In potential cardiac donors, the guidelines recommend limiting the maximal infusion rate (e.g. for dopamine, limiting to a rate no higher than 10 µg/kg per minute). The recent American guidelines note that dopamine has traditionally been the first-line vasoactive agent for management of cardiovascular collapse following brainstem death, but there remain insufficient data to preferentially recommend this drug over other vasopressor agents[2]. The guidelines also note that norepinephrine or phenylephrine are recommended in the predominantly vasodilatory component of shock (low systemic vascular resistance). In other causes of shock states with low SVR (e.g. septic patients), norepinephrine as compared to dopamine, was demonstrated to increase mean perfusion pressures without adverse effects to renal and splanchnic blood flow[3]. In addition, the rate of complications, in particular arrhythmia, was lower in patients

1 Shemie SD, Ross H, Pagliarello J, et al. Organ donor management in Canada: Recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ. 2006;174:S13-S30. doi:10.1503/cmaj.045131.

2 Kotloff RM, Blosser S, Fulda GJ, et al. Management of the Potential Organ Donor in the ICU. Crit Care Med. 2015;43(6):1291-1325. doi:10.1097/CCM.0000000000000958.88.

3 De Backer D, Creteur J, Silva E, Vincent JL. Effects of dopamine,norepinephrine, and epinephrine on the splanchnic circulation in septic shock:which is best? Crit Care Med. 2003 Jun;31(6):1659-67.

treated with norepinephrine compared to those treated with dopamine[4].

It is therefore recommended that norepinephrine be administered in NDD patients with distributive shock and persistent hypotension despite adequate fluid resuscitation and administration of vasopressin and corticosteroids.

Return to Management of Hemodynamics map

Return to Management of Shock map

4 De Backer, D, Biston P, et al. Comparison of Dopamine and Norepinephrine in the Treatment of ShockN Engl J Med 2010; 362:779-789

Fluid Resuscitation in Distributive Shock

Alissa Visram, Sabira Valiani, Pierre Cardinal, Andrew Healey

Description

- Recognize the need for fluid bolus administration in distributive and hypovolemic shock.
- Administer fluid boluses to improve hemodynamic stability and reach pre-defined blood pressure and perfusion targets.
- Choose fluid resuscitation based on the composition and physiologic properties of the fluid, as well as the patient's electrolyte and acid-base status.

Return to Management of Hemodynamics map

Return to Management of Shock map

- Recognize that there is no strong evidence to suggest the preferential use of colloids versus crystalloids when resuscitating NDD donors in shock.
- Avoid hydroxyethyl starch during resuscitative efforts given the risk of renal injury (both AKI and delayed renal graft function)

Rationale

The overall goal of donor management is to ensure adequate end organ perfusion in order to preserve organ function for donation. The principles of fluid resuscitation in an NDD donor are the same as living patients.

Fluid resuscitation is indicated in NDD donors who have hypovolemic or distributive type shock. The purpose of fluid resuscitation is to increase preload and thereby cardiac output[1]. The decision to administer a fluid bolus should be based on a clinical assessment suggestive of hypovolemia. Hypovolemia can be assessed by using static and dynamic indices, and a full discussion of the predictive value and limitations of these indices is beyond the scope of this chapter. However, common indicators of hypovolemia include significant stroke volume variation or significant pulse pressure variation[1].

The TGLN guidelines suggest fluid boluses to be administered in 250-500mL aliquots over 10 minutes, with frequent reassessment of response to fluid boluses[2]. A positive response to a fluid challenge could consist of an increase in blood pressure (or a decreased need for vasopressor support), increased urine output, a decrease in heart rate, or an improvement in peripheral perfusion (e.g. mottling, cool extremities) or other markers of hypoperfusion (serum lactate, pulse pressure variation, etc). Fluid should not be administered when there is a lack of a response to the previous fluid bolus, or if pulmonary edema develops[2].

Isotonic crystalloids or colloids may be chosen for initial fluid resuscitation in NDD donors[3]. There is limited evidence to guide the choice of crystalloid or colloid fluid for initial resuscitation in NDD patients[3]. In living patients with shock, the administration of 4% albumin, as compared to normal saline, for fluid resuscitation did not show any mortality benefit, and there were no differences in rates of organ failure or days of renal replacement thera-

1 Bendjelid K, Romand JA. Fluid responsiveness in mechanically ventilated patients: a review of indices used in intensive care. Intensive care medicine. 2003;29(3):352-60. doi: 10.1007/s00134-002-1615-9.

2 Trillium Gift of Life Network. Donation Resource Manual: A tool to assist hospitals with the process of organ and tissue Donation. Queen's Printer for Ontario: 2010.

3 Kotloff RM, Blosser S, Fulda GJ, et al. Management of the Potential Organ Donor in the ICU. Crit Care Med. 2015;43(6):1291-1325. doi:10.1097/CCM.0000000000000958.

py[4]. The lack of benefit for colloid resuscitation in critically ill patients was also confirmed in a Cochrane review in 2013[5]. It should be noted that colloids are more expensive than crystalloids[6].

Ringer's lactate and 0.9% saline are the recommended isotonic crystalloid solutions used in the resuscitation of critically ill patients[3]. Their use should be guided by the patient's electrolyte and acid-base status. Excessive use of 0.9% saline can lead to hypernatremia or a hyperchloremic metabolic acidosis. In NDD donors with hypernatremia and hypovolemia secondary to diabetes insipidus, first correct the patient's hypovolemia with an isotonic crystalloid (preferentially ringer's lactate given its lower sodium content) and then correct the hypernatremia with D5W intravenously or free water enterally. If the patient is euvolemic, correct the patient's hypernatremia with D5W or free water, as outlined in the "Endocrine - diabetes insipidus management" sections (see 'Anticipating Diabetes Insipidus')

When using colloids for fluid resuscitation, the primary options are starches or blood products (ie: albumin or packed red blood cells). The Society of Critical Care Medicine and TGLN guidelines recommend that hydroxyethyl starch (HES) should NOT be used given its association with delayed graft function and renal failure [3,7].

Fluid resuscitation alone may be unsuccessful in optimizing blood pressure and perfusion in the NDD donor. Given the abnormal pituitary-adrenal axis (see 'Verifying Steroid Administration') of NDD patients, it is important to verify that all patients in distributive shock also be receiving corticosteroids to maintain a normal vasopressor response to catecholamine. In patients suspected to be hypovolemic from diabetes insipidus, administration of vasopressin is important to limit further fluid loss, and must accompany fluid resuscitation. Many NDD patients remain hypotensive despite fluid resuscitation and commonly require the addition of other vasopressors or inotropes.

Return to Management of Hemodynamics map

Return to Management of Shock map

4 Finfer S, Bellomo R, Boyce N, French J, Myburgh J, Norton R. A comparison of albumin and saline for fluid resuscitation in the intensive care unit. The New England journal of medicine. 2004;350(22):2247-56. doi: 10.1056/NEJMoa040232.

5 Perel P, Roberts I, Ker K. Colloids versus crystalloids for fluid resuscitation in critically ill patients. The Cochrane database of systematic reviews. 2013;2:Cd000567. Epub 2013/03/02. doi: 10.1002/14651858.CD000567.pub6.

6 Vassalos A, Rooney K. Surviving Sepsis Guidelines 2012. Critical Care Medicine. 2013;41:e485-e486.

7 Shemie SD, Ross H, Pagliarello J, et al. Organ donor management in Canada: Recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ. 2006;174:S13-S30. doi:10.1503/cmaj.045131.

Anticipate Hypovolemia Secondary to DI or Other Causes

Sonny Dhanani, Pierre Cardinal, Andrew Healey

Description

- To anticipate hypovolemia in brain dead patient
- To identify that diabetes insipidus (DI) is a common cause of hypovolemia in brain dead patient
- To recognize other causes of hypovolemia

Return to Management of Hemodynamics map

Return to Management of Shock map

Rationale

Hypovolemia is frequently observed in brain dead patient. Fluid restriction and the administration of diuretics and mannitol to treat increased intracranial pressure, hidden blood loss in trauma patients, are but some of the many causes of hypovolemia in potential NDD donors. However, diabetes insipidus is so frequent that it should be expected in all NDD donors. Arginine vasopressin (AVP) is a peptide that is formed in the hypothalamus and then stored in as well as secreted from the posterior pituitary. Its anti-diuretic effect on the V2 receptors within the renal collecting system promotes the reabsorption of free water. AVP regulates extracellular fluid volume by the reabsorption of water from the kidneys. After brain death, a lack of AVP leads to unregulated renal losses of free water resulting in a state of diabetes insipidus. This almost universally leads to free water deficit and hypovolemia[1]. Diabetes insipidus is confirmed if urine output remains excessive (> 4mL/kg/h) as well as dilute (< 200 mOsm/kg•H2O) and associated with hypernatremia (> 145mmol/L) and an increased serum osmolality (> 300mOsm/kg•H2O). In the context of brain death, diabetes insipidus should be presumed even if all criteria not met, especially in the context of clinical hypovolemia[2,3].

1 Loh JA, Verbalis JG: Disorders of water and salt metabolism associated with pituitary disease. Endocrinol Metab Clin North Am 2008; 37:213–234

2 Ball SG: Vasopressin and disorders of water balance: The physiology and pathophysiology of vasopressin. Ann Clin Biochem 2007;44:417–431

3 Kutsogiannis DJ, Pagliarello G, Doig C, Ross H, Shemie SD. Medical management to optimize donor organ potential: review of the literature. Can J Anaesth. 2006 Aug;53(8):820-30.

Verifying Vasopressin Administration in the Context of DI

Sonny Dhanani, Ronish Gupta, Pierre Cardinal

Description

Titrate vasopressin intravenous infusion (0 to a maximal dose of 2.4 units/hr) targeting a systolic blood pressure above 100 mmHg, serum sodium levels between 130 – 155 mmol/L, and urine output 0.5 – 3 mL/kg/h

Return to Management of Hemodynamics map

Return to Management of Shock map

Rationale

Although the mechanism has not been established, diabetes insipidus has the potential to impair organ function beyond that simply resulting from diuresis, hypovolemia, and hemodynamic instability. Potential organ donors with diabetes insipidus often present with hypotension from excessive fluid losses. This may be managed with fluid replacement but more importantly needs to be managed for ongoing losses. A vasopressin (AVP) infusion is the preferred agent for patients with concomitant hypotension. It provides the dual benefits of anti-diuresis as well as hemodynamic support[1]. However, concerns around possible interference with end-organ perfusion exist based on animal models of splanchnic blood flow. For this reason, in hypertensive patients, high-doses of AVP might be avoided[2]. Vasopressin intravenous infusion should be started at 0-2.4 units/hr for systolic blood pressure < 100 mmHg or mean arterial pressure < 70 mmHg[3,4].

In situations, where signs of diabetes insipidus persist despite vasopressin infusion, intermittent desmopressin may be added to vasopressin. Desmopressin inhibits diuresis but has virtually no vasopressor side effect, so is not helpful in the context of hypotension.

In either case, AVP infusions should be titrated to target systolic blood pressure above 100 mmHg, serum sodium levels 130 – 155 mmol/L and urine output 0.5 – 3 mL/kg/h.

1 Chen JM, Cullinane S, Spanier TB, Artrip JH, John R, Edwards NM, Oz MC, Landry DW. Vasopressin deficiency and pressor hypersensitivity in hemodynamically unstable organ donors. Circulation 1999; 100 (suppl II):II-246.

2 Holmes CL, Patel BM, Russell JA, Walley KR. Physiology of vasopressin relevant to management of septic shock. Chest 2001; 120:989-1002.

3 Nakagawa K, Tang JF. Physiologic response of human brain death and the use of vasopressin for successful organ transplantation. J Clin Anesth. 2011 Mar;23(2):145-8.

4 Dunser MW, Mayr AJ, Ulmer H, Knotzer H, Sumann G, Pajk W, Friesenecker B, Hasibeder WR. Arginine vasopressin in advanced vasodilatory shock: a prospective, randomized,controlled study. Circulation. 2003 May 13;107(18):2313-9.

Administer Infusion of DDAVP in Addition to Vasopressin

Sonny Dhanani, Ronish Gupta, Pierre Cardinal, Andrew Healey

Description

In patients in shock and diabetes insipidus (DI) treated with vasopressin but with persistently high urine output

- Start desmopressin (DDAVP) 4 micrograms IV every 6 hours and titrate to urine output 0.5 - 3 mL/kg/hr with close monitoring of serum sodium levels (target 130-150 mmol)

Return to Management of Hemodynamics map

Return to Management of Shock map

Rationale

An AVP infusion is the preferred agent for patients with both shock and diabetes insipidus (DI) because vasopressin provides the dual benefits of anti-diuresis as well as weak vasopressor support. However, some patients may continue to have high water losses resulting in hypernatremia despite a vasopressin infusion. In such patients, desmopressin (1-desamino-8-d-arginine vasopressin, or DDAVP) is often added to vasopressin because of its highly specific affinity for the V2 vasopressin receptors in the renal collecting system[1]. This property allows desmopressin to inhibit diuresis but without any vasopressor effect. Multiple routes of administration are available, but the intravenous route is preferred in the organ donor. Although concerns for potential thrombogenic complications have been raised with desmopressin use, it does not seem to impair graft survival[2]. One trial of 97 adult organ donors randomized to receive desmopressin or nothing for diabetes insipidus demonstrated no impairment in pre-procurement renal function or post-transplant need for dialysis in those who received desmopressin. A more recent retrospective analysis of 458 neurologically deceased adult kidney donors suggested that those treated with desmopressin actually had improved renal function (creatinine 97 ± 44 vs 124 ± 106 μmol/L; $p < 0.001$)[3,4].

Desmopressin boluses should be titrated to target urine output 0.5 – 3 mL/kg/h with close monitoring of the serum sodium levels (target 130 – 155 mmol/L). Intermittent intravenous DDAVP 4 micrograms every 6 hours is a common regiment. Intravenous maintenance fluids to maintain blood pressure and perfusion and the administration of free water (either through the enteral route or intravenously) should be considered to correct hypernatremia[5].

1 Chen JM, Cullinane S, Spanier TB, Artrip JH, John R, Edwards NM, Oz MC, Landry DW. Vasopressin deficiency and pressor hypersensitivity in hemodynamically unstable organ donors. Circulation 1999; 100 (suppl II):II-246.

2 Pennefather SH, Bullock RE, Mantle D, Dark JH. Use of low dose arginine vasopressin to support brain-dead organ donors. Transplantation 1995; 59(1):58-62.

3 Nakagawa K, Tang JF. Physiologic response of human brain death and the use of vasopressin for successful organ transplantation. J Clin Anesth. 2011 Mar;23(2):145-8.

4 Dunser MW, Mayr AJ, Ulmer H, Knotzer H, Sumann G, Pajk W, Friesenecker B, Hasibeder WR. Arginine vasopressin in advanced vasodilatory shock: a prospective, randomized,controlled study. Circulation. 2003 May 13;107(18):2313-9. Epub 2003 May 5.

5 Kutsogiannis DJ, Pagliarello G, Doig C, Ross H, Shemie SD. Medical management to optimize donor organ potential: review of the literature. Can J Anaesth. 2006 Aug;53(8):820-30.

Select Type of Crystalloid Based on Serum Na in a DI Context

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Description

- Recognize the need for fluid bolus administration in hypovolemic shock.
- Administer fluid boluses to improve hemodynamic stability and reach predefined blood pressure and perfusion targets.
- If clinically hypovolemic and hyponatremic (serum Na < 135 mmol/L)
  - Administer 0.9%NS 500 mL IV and repeat until fluid resuscitated.

Return to Management of Hemodynamics map

Return to Management of Shock map

- If clinically hypovolemic and serum Na between 135-145 mmol/L
  - Administer 0.9%NS or Ringer's Lactate bolus of 500 mL IV repeat until fluid resuscitated.
- If clinically hypovolemic and hypernatremic (serum Na>145mmol/L)
  - Administer Ringer's Lactate bolus of 500 mL IV
  - Once fluid resuscitated administer free water (intravenously or enterally)
  - Administer a IV bolus of 250 mL of D5W or free water enterally.
  - Change maintenance fluids to D5W.

Rationale

The principles of fluid resuscitation in an NDD donor are the same as in living patients. Fluid resuscitation is indicated in NDD donors who have hypovolemic shock. The purpose of fluid resuscitation is to increase preload and thereby cardiac output[1]. The decision to administer a fluid bolus should be based on a clinical assessment suggestive of hypovolemia. Hypovolemia can be assessed by using static and dynamic indices, and a full discussion of the predictive value and limitations of these indices is beyond the scope of this chapter. However, common indicators of hypovolemia include significant stroke volume variation or significant pulse pressure variation[1].

The fluid selection is guided by the serum sodium level. In the presence of a normal serum sodium, either Ringer's lactate or 0.9% saline are recommended. For patients with hyponatremia, 0.9%NS solution is preferred, whereas RL is preferred in the patients with hypernatremia given its lower sodium content[2]. Once the patient becomes euvolemic, Ringer's lactate should be discontinued and the hypernatremia corrected with either D5W or free water[2].

Hypernatremia (serum sodium > 155 mmol/L) secondary to excessive sodium administration during resuscitation or diabetes insipidus may lead to the accumulation of compensatory idiogenic osmoles in donor organs. Once transplanted, significant intracellular fluid shifts may develop as these organs are exposed to the recipient normal serum; the different osmolalities resulting in a water influx into the transplanted organs[3,4].

1 Bendjelid K, Romand JA. Fluid responsiveness in mechanically ventilated patients: a review of indices used in intensive care. Intensive care medicine. 2003;29(3):352-60. doi: 10.1007/s00134-002-1615-9.

2 Trillium Gift of Life Network. Donation Resource Manual: A tool to assist hospitals with the process of organ and tissue Donation. Queen's Printer for Ontario: 2010.

3 Bloom MB, Raza S, Bhakta A, et al. Impact of Deceased Organ Donor Demographics and Critical Care End Points on Liver Transplantation and Graft Survival Rates. J Am Coll Surg. 2015;220(1):38-47. doi:10.1016/j.jamcollsurg.2014.09.020.

4 Kazemeyni SM, Esfahani F. Influence of hypernatremia and polyuria of brain-dead donors before organ procurement on kidney allograft function. Urol J. 2008 Summer;5(3):173-7.

Traditionally, hypernatremia was thought to be independently associated with hepatic and renal dysfunction or graft loss after transplantation[4]. However, more recent evidence suggests that this effect may be less significant than once believed[4,5]. Given that avoiding or treating hypernatremia is easily achieved using inexpensive management strategies, it is recommended to target normal serum sodium levels by selecting with appropriate maintenance intravenous fluids, and the aggressive correction of hypernatremia.

Return to Management of Hemodynamics map

Return to Management of Shock map

5 Mangus RS, Fridell JA, Vianna RM, Milgrom ML, Chestovich P, Vandenboom C,Tector AJ. Severe hypernatremia in deceased liver donors does not impact early transplant outcome. Transplantation. 2010 Aug 27;90(4):438-43.

Titrate to Pre-Defined Targets

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Description

- Titrate first line agent to pre-defined blood pressure and perfusion targets[1,2]
  - A default target MAP should be ≥ 70mmHg[1], which can be adjusted based on the patient's baseline blood pressure
  - Monitor perfusion and cardiac output using the following targets:
    - Clinical surrogates: No mottling, capillary refill less than 4 seconds, and warm extremities
    - Laboratory surrogates: a normal or decreasing lactate, and a central venous oxygen saturation ≥ 60%
    - Noninvasive means if skills and expertise: normal stroke volume by echocardiography, or non-invasive cardiac output monitors
- If the above targets are not met, the addition of second line agents should be considered
  - Recognize and monitor for common adverse effect of high dose vasopressor and inotrope administration

Return to Management of Hemodynamics map

Return to Management of Shock map

Rationale

It is essential to closely monitor both blood pressure and perfusion in NDD patients to ensure the early identification of patients in need of further resuscitation. Achieving the targeted pressures and perfusion parameters increases the likelihood of successful multi-organ donation and the likelihood of maintaining a donor to successful procurement[3]. The response to therapeutic interventions should also be closely monitored and should encompass not only the intended effect (e.g. a rising blood pressure with vasopressors) but also unintended effects (e.g. a reduction in perfusion due to arteriolar constriction) as well as adverse effects. Note that there is little clinical evidence to support the proposed targets for both blood pressure and perfusion.

1 Shemie SD, Ross H, Pagliarello J, et al. Organ donor management in Canada: Recommendations of the forum on Medical Management to Optimize Donor Organ Potential. CMAJ. 2006;174(6 SUPPL.):S13-S30. doi:10.1503/cmaj.045131.

2 Trillium Gift of Life Network. Donation Resource Manual: A tool to assist hospitals with the process of organ and tissue Donation. Queen's Printer for Ontario: 2010.

3 Malinoski DJ, Patel MS, Daly MC, Oley-Graybill C, Salim A. The impact of meeting donor management goals on the number of organs transplanted per donor. Crit Care Med. 2012;40(10):2773-2780. doi:10.1097/CCM.0b013e31825b252a.