21 Potential Organ Donor: Organ Donor Management

Pia Löwhagen Hendén

Recommendations

Level I

There are mostly insufficient data to support Level I recommendations for this topic. Randomized controlled trials on active lung treatment, including lung protective ventilation, have shown increased number of eligible and transplanted lungs with unchanged recipient survival rates.

Level II

Active donor management according to "bundle" protocols is associated with more organs transplanted per donor. Hormone replacement therapy (HRT) and strict blood glucose control are both associated with more organs transplanted per donor.

Level III

Active donor management according to "bundle" protocols is associated with more organs transplanted per donor.

21.1 Introduction

The primary aim in the critical care of severe TBI is to provide full neurointensive care until treatment is regarded futile. If all objective signs indicate complete loss of brain function, procedures leading to the diagnosis of death are initiated. For the potential organ donor, the critical care is changed toward maintenance of organ function and investigation of donation will. Potential organ donor, according to the terminology recommended by the WHO 2010, is "a person whose clinical condition is suspected to fulfill brain death criteria" (Dominguez-Gil et al. 2011).

Diagnosis of death is regulated in national legal documents and is subjected to modifications. The basis of diagnosis of death is, in most western countries, the irreversible cessation of all functions of the entire brain, including the brainstem (Citerio and Murphy 2015). We emphasize that organ donation from diseased persons is regulated by each country's legislation.

Death due to brain-related criteria leads to circulatory, pulmonary, renal, hepatic, and metabolic consequences that need attention in order to maintain sufficient organ function. The treatment strategies should aim at normalization of organ physiology as far as possible (Maciel and Greer 2016; Kotloff et al. 2015; McKeown and Ball 2014).

P. Löwhagen Hendén (✉)
Department of Anesthesiology and Intensive Care,
Sahlgrenska University Hospital,
Gothenburg, Sweden
e-mail: pia.lowhagen@vgregion.se

T. Sundstrøm et al. (eds.), *Management of Severe Traumatic Brain Injury*,
https://doi.org/10.1007/978-3-030-39383-0_21

21.2 Organ Donor Management Goals

Rigorous organ donor management is a major determinant of outcome after organ transplantation. The use of an organ donor management protocol with physiological goals is mandatory. Several studies have shown that achieving organ donor physiological goals before the organ donation surgery results in a higher number of available organs per donor and better organ outcomes (Patel et al. 2014, 2017; Abuanzeh et al. 2015; Marshall et al. 2014). Common organ donor physiological goals are presented in Table 21.1. However, management strategies for the treatment of the organ donor and preservation of organ function are based on sparse scientific evidence.

21.3 Pathophysiology of Brainstem Herniation and Death

With increasing intracranial pressure, the brainstem herniation into foramen magnum leads to pathophysiological changes explained by the rostral to caudal brainstem ischemia evolution. The faster the herniation process, the more aggravating pathophysiological signs are seen. Initial parasympathetic stimulation with profound bradycardia is followed by a sympathetic storm with hypertension and tachycardia. Finally, loss of sympathetic tone causes peripheral vasodilation and hypotension.

Both the hypertension and the hypotension have the potential to result in end-organ damage during and after the brainstem herniation process.

Table 21.1 Organ donor management goals

Parameter	Goal	Commentary
Systolic blood pressure Mean arterial pressure	>100 mmHg >60 mmHg	Maintain normovolemia with sufficient fluids and use vasopressor support
Cardiac output	>2.5 L/min/m^2	Maintain normovolemia with sufficient fluids and use vasopressor support Inotropic drugs as needed
Lactate	<2 mmol/L	Maintain normovolemia with sufficient fluids and use vasopressor support
Urinary output	>1 mL/kg/h	Maintain normovolemia with sufficient fluids and use vasopressor support
Hemoglobin	>70 g/L	Transfusion of red blood cells
PaO_2	>10 kPa	Use lung protective ventilation, avoid atelectasis and aspiration
$PaCO_2$	4.5–6.0 kPa	Normoventilation
Central venous pressure (CVP)	<10 mmHg	Maintain normovolemia. Too high PEEP will impede venous return
Body temperature	>35 °C	Warming blankets, warm fluids
Blood glucose	<5–10 mmol/L	Short-acting insulin
Sodium	<155 mmol/L	Desmopressin, restricted use of sodium-containing fluids
Potassium-magnesium-calcium	Normal	Electrolyte supplement
pH	7.35–7.45	Maintaining normovolemia, normoventilation, sodium bicarbonate
Platelet count	>50 × 10^9/L	Transfusion of platelets if hemorrhage
PT/INR[a]	>1.5	Transfusion of fresh frozen plasma if hemorrhage

[a]Prothrombin time/International Normalised Ratio

Cessation of the cerebral blood flow leads to hypothalamic and hypophysis insufficiency, resulting in lost thermoregulation, hypothermia, and lack of hypophysis hormones. The sympathetic storm triggers the inflammatory system as well as the coagulation system and leads to peripheral insulin resistance.

Not all patients experience all the described effects. Diabetes insipidus, for example, as a sign of posterior hypophysis insufficiency, is described in 65–90% of brain-dead persons (McKeown and Ball 2014; Essien et al. 2017; Smith 2004).

Tips, Tricks, and Pitfalls

Be prepared for the pathophysiological changes after brainstem herniation with the following:

- Vasopressor infusion
- Desmopressin
- Warming blankets

By these measures, the most common problems, i.e., profound hypotension, hypovolemia, hypernatremia, and hypothermia, can be avoided.

21.4 Circulatory Considerations

Hypertension during brainstem herniation is most often self-limiting. The sympathetic storm results in increased preload and afterload for the heart with an obvious risk of cardiac ischemia, arrhythmia, and pulmonary edema. Treatment with short-acting agents (i.e., esmolol, labetalol, metoprolol) might be necessary to protect the heart.

Bradycardia in this setting cannot be treated with atropine as the vagus nerve is not active. If bradycardia has to be treated, beta-receptor-stimulating drugs can be used (isoprenaline).

Subsequent hypotension, due to loss of vasomotor tone, is the major problem in the care of an organ donor. Hypotension caused by vasodilation can be aggravated by hypovolemia due to diabetes insipidus or pre-existing hypovolemia before herniation, caused by hemorrhage and cerebral edema treatment (i.e., mannitol and negative fluid balance).

To achieve the organ donor goals, blood pressure should be kept at an acceptable level using sufficient fluids, with balanced salt content to avoid hypernatremia, and in addition, most donors need vasopressor support. Fluid resuscitation should exclude hydroxyethyl starch solutions due to the possibility of negative effects on kidney function (Patel et al. 2015). No scientific evidence exists regarding the use of crystalloids versus albumin or plasma.

The preferable first-line vasopressor is, in most guidelines, arginine vasopressin (antidiuretic hormone). Another commonly used vasopressor is norepinephrine. Arginine vasopressin might be in favor of norepinephrine for hemodynamically instable patients and patients with cardiac failure, due to the lack of adrenergic receptor stimulation (Kotloff et al. 2015). The vasopressin analogue desmopressin has no significant vasopressor activity.

In case of increasing vasopressor support, hemodynamic monitoring (PICCO, PA catheter, repeated echocardiography) should be instituted to differ between vasoplegia, hypovolemia, and cardiac failure and to tailor the treatment and avoid coronary, renal, and splanchnic vasoconstriction.

Dopamine, milrinone, dobutamine, or epinephrine may be used in primary cardiac pump dysfunction. Hypothermal myocardial depression must be avoided. Repeated echocardiography examinations should be performed in assessment for heart donation, as myocardial hypokinesia occurring during brainstem herniation might be reversible.

Recommended doses for vasoactive drugs are as follows:

- Norepinephrine <0.2 mcg/kg/min
- Arginine vasopressin 0.5–4 U/h
- Dopamine <10 mcg/kg/min
- Dobutamine <10 mcg/kg/min

If recommended doses are exceeded, a combination of vasoactive drugs should be considered.

Bolus dose of methylprednisolone is included in most protocols for its effect on hemodynamic stabilization, although the scientific evidence is weak (D'Aragon et al. 2017; Dupuis et al. 2014). The recommendation is methylprednisolone 15 mg/kg IV as a bolus in conjunction with the brain death declaration.

In several protocols, a combined hormone replacement therapy (HRT) is recommended if hemodynamic goals are not met despite vasopressor treatment and/or if left ventricular ejection fraction remains less than 45% (Kotloff et al. 2015). HRT includes arginine vasopressin, thyroid hormone (T3 or T4), methylprednisolone, and insulin. HRT is in retrospective studies associated with improved number of organs transplanted per donor and improved graft function (Buchanan and Mehta 2018; Novitzky et al. 2014). Recommended doses for thyroid hormones are as follows: T3 bolus dose 4 mcg followed by infusion 3 mcg/h or T4 bolus dose 20 mcg followed by infusion 10–40 mcg/h (Buchanan and Mehta 2018). T4 is converted to T3 in target tissues.

Aggressive hemodynamic support prevents cardiovascular collapse before a planned organ donation operation. Without vigorous treatment, 25–40% of the organ donors will have a circulatory arrest within the first few days (McKeown and Ball 2014).

21.5 Central Diabetes Insipidus

Diabetes insipidus, caused by decreased secretion of antidiuretic hormone (ADH), leads to polyuria, and if left uncorrected, it will quickly lead to severe hypovolemia and hypernatremia. Clinically manifest diabetes insipidus (urinary output >300 mL/h, serum sodium >150 mmol/L, urinary sodium <20 mmol/L, urinary specific gravity ≤1.005) can threaten organ donation due to the profound hypovolemia.

Treatment is by bolus dose of the vasopressin analogue desmopressin (1-deamino-8-D-arginine vasopressin, DDAVP) or by infusion of arginine vasopressin (8-arginine vasopressin, AVP). Arginine vasopressin is an exact synthetic protein of antidiuretic hormone (ADH).

Recommended doses are as follows: for desmopressin titrated bolus doses of 0.25–1 mcg IV and for arginine vasopressin infusion 0.6–2.4 U/h (Kotloff et al. 2015). It is important to remember that the terminal half-life of desmopressin is around 3 h in patients without renal impairment. Administration of desmopressin and arginine vasopressin does not negatively affect the kidney graft.

Drug administration is most often combined with administration of intravenous fluids and/or pure water administration via the nasogastric tube. The urinary losses of magnesium, phosphate, and potassium must be replaced if profound polyuria persists.

21.6 Pulmonary Considerations

The lungs have the highest risk of being unsuitable for transplantation, and historically a low rate of suitable lungs has been identified among organ donors. Intensified lung donor management in the intensive care unit (ICU) increases the number of lungs recovered and transplanted (Minambres et al. 2014, 2013; Kirschbaum and Hudson 2010; Venkateswaran et al. 2008; Angel et al. 2006).

During the brainstem herniation, the sympathetic storm can result in both a neurogenic and a cardiogenic lung edema. The use of colloids together with meticulous fluid balance has shown to be beneficial in minimizing the development of pulmonary edema (Dictus et al. 2009).

The lungs are also most susceptible to the systemic inflammatory response caused by the sympathetic storm, and they might furthermore be harmed following blunt trauma and/or aspiration. There is also a risk of ventilator-associated pneumonia in the ICU. Every effort should be made to prevent further exacerbation of pre-existing lung injury. Antibiotics should be liberally administered after a bronchoscopy has been performed (to obtain material for bacterial examination and culture).

Most donor management protocols include administration of corticosteroids (methylprednisolone 15 mg/kg) moderating the release of pro-inflammatory molecules and, in animal models, improving alveolar fluid clearance (Folkesson et al. 2000). Clinically, improved donor oxygenation, lung utilization, and graft outcomes are described (Naik and Angel 2011; Follette et al. 1998).

The lung donor management protocols include:

- Methylprednisolone
- Lung protective ventilation
  - Low tidal volumes (6–8 mL/kg predicted body weight)
  - Normoventilation ($PaCO_2$ 4.5–6.0 kPa)
  - Plateau inspiratory pressure <30 cm H_2O
  - PEEP of (5–)10 cm H_2O

In one RCT, lung protective ventilation resulted in 54% of the lungs being utilized for transplantation compared to 27% in the control group (Mascia et al. 2010).

- Neutral fluid balance
- Avoiding atelectasis by
  - Adequate, individualized PEEP titration
  - Regularly turning the patient
  - Humidification of inspired air/oxygen
  - Appropriate bronchoscopies if necessary to avoid mucous plugs
  - Careful recruitment maneuvers with subsequent adequate PEEP setting
- Avoiding gastric aspiration by
  - Elevation of the head of the bed
  - Oral care
  - Assessing for a cuff leak

21.7 Renal and Hepatic Considerations

The kidneys and liver are affected both by the sympathetic storm and by the following hypotensive situation. Hemodynamic optimization is of uttermost importance for possible donation. The urinary output should be kept >1 mL/kg/h. This is primarily achieved by adequate fluid administration and vasopressor support. Expert opinions differ regarding which vasopressor agent should be first line in a kidney donor; both norepinephrine and vasopressin are used. As earlier mentioned, fluid resuscitation should exclude hydroxyethyl starch solutions due to the possibility of negative effects on kidney function (Patel et al. 2015). In a multicenter RCT, low-dose dopamine (4 mcg/kg/min) reduced the need for dialysis after kidney transplantation with no effect on graft survival (Schnuelle et al. 2017, 2018).

21.8 Metabolic Considerations

Hypophysis insufficiency includes hormones from both posterior and anterior hypophysis as vasopressin, oxytocin, ACTH, GH, LH, FSH, and TSH. Administration of the vasopressin analogue desmopressin, in order to treat diabetes insipidus, is considered standard procedure in organ donor management (Maciel and Greer 2016; Kotloff et al. 2015; McKeown and Ball 2014), and replacement with corticosteroids is included in most organ donor management protocols although the scientific evidence is scarce (D'Aragon et al. 2017; Dupuis et al. 2014).

Thyroid hormone replacement might be of benefit in therapy-resistant hemodynamic instability (Buchanan and Mehta 2018; Novitzky et al. 2014).

Hypothalamic insufficiency leads to dysregulation of body temperature, most often resulting in hypothermia. Hypothermia can cause numerous complications such as decreased cardiac contractility, cardiac arrhythmia, and coagulation disorders and must be prevented by warm blankets, external warming devices, and warm fluids. The body temperature should be kept >35 °C.

Hyperglycemia is considered to be a consequence of elevated levels of catecholamines, infusion of glucose, administration of corticosteroids, and peripheral insulin resistance. Blood glucose ≤180 mg/dL (10 mmol/L) was an independent predictor of number of organs transplanted per donor and better graft outcome in a retrospective study (Sally et al. 2014). Normoglycemia should be maintained and insulin infusion is most often needed.

Lingering respiratory alkalosis as a result of hyperventilation for treatment of imminent brainstem herniation should be corrected and results in normalization of arterial pH in order to promote tissue oxygen delivery. Hyperlactatemia and metabolic acidosis as a result of hypoperfusion must be avoided.

Coagulopathies, e.g., disseminated intravascular coagulation (DIC), as well as dilution coagulopathy and hypothermia are not uncommon after brain death. Appropriate blood components are transfused if clinically significant hemorrhage occurs.

21.9 Specific Pediatric Concerns

Scientific data concerning donor management strategies are limited in adults and even more limited when it comes to children (Mallory et al. 2009; Finfer et al. 1996). Pediatric organ donors are rare in most hospitals. The diagnosis of death due to brain-related criteria is the same in pediatric patients as in adults, although the confirmation of death in infants may require specially trained staff. Consultation of specific expertise for advice and support should be liberally used, both for diagnosis of death and for management of the organ donor. The level of physiological and laboratory parameters must be adjusted for age, especially levels for blood pressure. A cuffed endotracheal tube is recommended even in young children due to the risk of aspiration (Mallory et al. 2009).

References

Abuanzeh R, Hashmi F, Dimarakis I, Khasati N, Machaal A, Yonan N, et al. Early donor management increases the retrieval rate of hearts for transplantation in marginal donors. Eur J Cardiothorac Surg. 2015;47(1):72–7; discussion 7.

Angel LF, Levine DJ, Restrepo MI, Johnson S, Sako E, Carpenter A, et al. Impact of a lung transplantation donor-management protocol on lung donation and recipient outcomes. Am J Respir Crit Care Med. 2006;174(6):710–6.

Buchanan IA, Mehta VA. Thyroid hormone resuscitation after brain death in potential organ donors: a primer for neurocritical care providers and narrative review of the literature. Clin Neurol Neurosurg. 2018;165:96–102.

Citerio G, Murphy PG. Brain death: the European perspective. Semin Neurol. 2015;35(2):139–44.

D'Aragon F, Belley-Cote E, Agarwal A, Frenette AJ, Lamontagne F, Guyatt G, et al. Effect of corticosteroid administration on neurologically deceased organ donors and transplant recipients: a systematic review and meta-analysis. BMJ Open. 2017;7(6):e014436.

Dictus C, Vienenkoetter B, Esmaeilzadeh M, Unterberg A, Ahmadi R. Critical care management of potential organ donors: our current standard. Clin Transplant. 2009;23(Suppl 21):2–9.

Dominguez-Gil B, Delmonico FL, Shaheen FA, Matesanz R, O'Connor K, Minina M, et al. The critical pathway for deceased donation: reportable uniformity in the approach to deceased donation. Transpl Int. 2011;24(4):373–8.

Dupuis S, Amiel JA, Desgroseilliers M, Williamson DR, Thiboutot Z, Serri K, et al. Corticosteroids in the management of brain-dead potential organ donors: a systematic review. Br J Anaesth. 2014;113(3):346–59.

Essien EO, Fioretti K, Scalea TM, Stein DM. Physiologic features of brain death. Am Surg. 2017;83(8):850–4.

Finfer S, Bohn D, Colpitts D, Cox P, Fleming F, Barker G. Intensive care management of paediatric organ donors and its effect on post-transplant organ function. Intensive Care Med. 1996;22(12):1424–32.

Folkesson HG, Norlin A, Wang Y, Abedinpour P, Matthay MA. Dexamethasone and thyroid hormone pretreatment upregulate alveolar epithelial fluid clearance in adult rats. J Appl Physiol (Bethesda, Md: 1985). 2000;88(2):416–24.

Follette DM, Rudich SM, Babcock WD. Improved oxygenation and increased lung donor recovery with high-dose steroid administration after brain death. J Heart Lung Transplant. 1998;17(4):423–9.

Kirschbaum CE, Hudson S. Increasing organ yield through a lung management protocol. Prog Transplant (Aliso Viejo, Calif). 2010;20(1):28–32.

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. Crit Care Med. 2015;43(6):1291–325.

Maciel CB, Greer DM. ICU management of the potential organ donor: state of the art. Curr Neurol Neurosci Rep. 2016;16(9):86.

Mallory GB Jr, Schecter MG, Elidemir O. Management of the pediatric organ donor to optimize lung donation. Pediatr Pulmonol. 2009;44(6):536–46.

Marshall GR, Mangus RS, Powelson JA, Fridell JA, Kubal CA, Tector AJ. Donor management parameters and organ yield: single center results. J Surg Res. 2014;191(1):208–13.

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. 2010;304(23):2620–7.

McKeown DW, Ball J. Treating the donor. Curr Opin Organ Transplant. 2014;19(2):85–91.

Minambres E, Ballesteros MA, Rodrigo E, Garcia-Miguelez A, Llorca J, Ruiz JC, et al. Aggressive lung donor management increases graft procurement without increasing renal graft loss after transplantation. Clin Transplant. 2013;27(1):52–9.

Minambres E, Coll E, Duerto J, Suberviola B, Mons R, Cifrian JM, et al. Effect of an intensive lung donor-management protocol on lung transplantation outcomes. J Heart Lung Transplant. 2014;33(2):178–84.

Naik PM, Angel LF. Special issues in the management and selection of the donor for lung transplantation. Semin Immunopathol. 2011;33(2):201–10.

Novitzky D, Mi Z, Sun Q, Collins JF, Cooper DK. Thyroid hormone therapy in the management of 63,593 brain-dead organ donors: a retrospective analysis. Transplantation. 2014;98(10):1119–27.

Patel MS, Zatarain J, De La Cruz S, Sally MB, Ewing T, Crutchfield M, et al. The impact of meeting donor management goals on the number of organs transplanted per expanded criteria donor: a prospective study from the UNOS Region 5 Donor Management Goals Workgroup. JAMA Surg. 2014;149(9):969–75.

Patel MS, Niemann CU, Sally MB, De La Cruz S, Zatarain J, Ewing T, et al. The impact of hydroxyethyl starch use in deceased organ donors on the development of delayed graft function in kidney transplant recipients: a propensity-adjusted analysis. Am J Transplant. 2015;15(8):2152–8.

Patel MS, De La Cruz S, Sally MB, Groat T, Malinoski DJ. active donor management during the hospital phase of care is associated with more organs transplanted per donor. J Am Coll Surg. 2017;225(4):525–31.

Sally MB, Ewing T, Crutchfield M, Patel MS, Raza S, De La Cruz S, et al. Determining optimal threshold for glucose control in organ donors after neurologic determination of death: a United Network for Organ Sharing Region 5 Donor Management Goals Workgroup prospective analysis. J Trauma Acute Care Surg. 2014;76(1):62–8; discussion 8–9.

Schnuelle P, Schmitt WH, Weiss C, Habicht A, Renders L, Zeier M, et al. Effects of dopamine donor pretreatment on graft survival after kidney transplantation: a randomized trial. Clin J Am Soc Nephrol. 2017;12(3):493–501.

Schnuelle P, Benck U, Yard BA. Dopamine in transplantation: written off or comeback with novel indication? Clin Transplant. 2018;32(7):e13292.

Smith M. Physiologic changes during brain stem death—lessons for management of the organ donor. J Heart Lung Transplant. 2004;23(Suppl 9):S217–22.

Venkateswaran RV, Patchell VB, Wilson IC, Mascaro JG, Thompson RD, Quinn DW, et al. Early donor management increases the retrieval rate of lungs for transplantation. Ann Thorac Surg. 2008;85(1):278–86; discussion 86.