Intensive care for organ preservation: A four-stage pathway

Dale Gardiner¹, David M Shaw^{2,3}, Jack K Kilcullen⁴ and
Anne L Dalle Ave⁵

Abstract

Objective: Intensive care for organ preservation (ICOP) is defined as the initiation or pursuit of intensive care not to save the patient's life, but to protect and optimize organs for transplantation.

Analysis: When a patient has devastating brain injury that might progress to organ donation this can be conceptualized as evolving through four consecutive stages: (1) instability, (2) stability, (3) futility and (4) finality. ICOP might be applied at any of these stages, raising different ethical issues. Only in the stage of *finality* is the switch from neurointensive care to ICOP ethically justified.

Conclusion: The difference between the stages is that during instability, stability and futility the focus must be neurointensive care which seeks the patient's recovery or an accurate neurological prognostication, while finality focuses on withdrawal of life-sustaining therapy and commencement of comfort care, which may include ICOP for deceased donation.

Keywords

Transplantation, ethics, brain death, intensive care, organ preservation, organ donation

Introduction

In deceased organ donation, the ethical divide between intensive care treatment before and after death is not always clear. Many intensive care interventions and technologies are continued unchanged or even escalated after the declaration of death. This can make the transition from the therapeutic goal of saving the patient's life to the goal of facilitating organ donation ambiguous, leading to potential or perceived conflicts of interest.

We define the initiation or pursuit of intensive care not to save the life of the patient but to protect and optimize organs for transplantation, as intensive care for organ preservation (ICOP), which may occur before, during or after the determination of death. Every organ donor in the context of donation after brain death (DBD) is managed with ICOP at some point. At the very least, ICOP is continued after death to optimize organ perfusion until organ recovery occurs.¹ Sometimes, however, ICOP is initiated and pursued before death, to allow time for brain death to develop or be confirmed.^{2,3} In uncontrolled donation after circulatory death programs (DCD), donation would not be possible without the use of ICOP after

death, for example in situ normothermic regional perfusion.⁴ This procedure is based on extra-corporeal membrane oxygenation technology, an advanced type of resuscitation technology potentially only provided to the patient after death, which raises additional ethical issues.⁵ In controlled DCD, like is practised in the UK, following consent for organ donation, life-sustaining therapy is not withdrawn until the surgical organ retrieval team is available and prepared in theatre, often resulting in the use of ICOP for several hours.⁶ In situ normothermic regional perfusion after death in controlled DCD is also seeing an increase.⁷

¹Adult Intensive Care Unit, Nottingham University Hospitals NHS Trust, Nottingham, UK

²Institute for Biomedical Ethics, University of Basel, Basel, Switzerland

³Care and Public Health Research Institute, Maastricht University, Maastricht, Netherlands

⁴Medical Critical Care Services, Inova Fairfax Hospital, Falls Church, VA, USA

⁵Ethics Unit, University Hospital of Lausanne, Lausanne, Switzerland

Corresponding author:

Anne L Dalle Ave, Ethics Unit, University Hospital of Lausanne, Rue du Bugnon 21, 1011 Lausanne, Switzerland.

Email: Anne.Dalle-Ave@chuv.ch

In this article, we conduct a detailed ethical analysis of ICOP and we suggest criteria under which ICOP is ethically acceptable.

Definitions and terms

Neurointensive care is defined as intensive care therapy specifically applied to patients with brain injury in order to achieve the best neurological outcome. Therapies are designed to support brain recovery and decrease intracranial pressure, and usually includes mechanical ventilation and blood pressure control, but can include increasing the salt concentration in the blood stream,^{8,9} deep sedation¹⁰ and intracranial pressure and oxygen monitoring. Neurointensive care is best understood as a therapeutic goal, which is to support neurologic recovery, rather than a place of treatment, as it can occur in resuscitation areas of emergency departments or small hospitals, not just in neurointensive care units.

In contrast, ICOP involves efforts to optimize organs, other than the brain, for transplantation purposes. ICOP can include the initiation or pursuit of mechanical ventilation, the use of fluids, vasopressors, drugs such as hormonal therapy, cardiopulmonary resuscitation in case of cardiac arrest¹¹ or extracorporeal membrane oxygenation in case of haemodynamic instability.¹² Importantly, just as neurointensive care is best understood as a therapeutic goal, ICOP is best understood not in terms of its treatment modalities but rather in terms of its intention. If the therapeutic goal is to optimize organs for transplantation, this is ICOP.

A change from neurointensive care to ICOP may or may not lead to immediate changes to the physical care of the patient. It will, however, always impact on the intentions and goals of treatment. This should, as we will detail, lead to altered communication within the multi-disciplinary team and with the patient's family.

ICOP would not include procedures that have the primary intention to hasten death, such as cranioplasty with bandaging¹³ or euthanasia, where the primary goal is death and any possible benefit for organ donation a secondary outcome.

We have avoided wherever possible terminology such as *elective* or *non-therapeutic* ventilation/intensive care as these terms have often been understood as purely the initiation of mechanical ventilation for donation purposes^{2,14–18} and we regard the scope of ICOP as broader.

While uncontrolled DCD can have ICOP elements as stated above, the patient population is sufficiently different (cardiac rather than brain injured) that we have not explored this issue further in this paper.

Choosing between neurointensive care and ICOP

When a patient has a devastating brain injury that eventuates in deceased organ donation, this can be conceptualized as having progressed through four consecutive stages: (1) instability, (2) stability, (3) futility and (4) finality. ICOP might be applied at any of these stages raising different ethical issues. Table 1 summarizes the stages and our recommendations.

Instability

During the first stage of instability, the patient is usually unconscious, unable to breathe independently, and in dire need of life-saving procedures in order to stabilize and allow further observation over time and/or appropriate diagnostic tests or treatments. During the stage of instability, the cause of coma and prognosis may not be fully known. While initiation of ICOP during the stage of instability might be technically possible the patient's own need for

Table 1. Recommendations.

Stages	Recommendations
1. The stage of reversing instability	As neurological outcome is uncertain, admit the patient to the ICU for neurointensive care
2. The stage of maintaining stability	Evaluate the patient, with diagnostic procedures and clinical evaluation, continuing with neurointensive care
3. The stage of establishing futility	The establishment of futility should be based solely on the conviction that everything that should be done to achieve the best outcome for the patient, consistent with his or her values, wishes and beliefs, has been done. Neurointensive care is continued until futility is established either through confirmation and acceptance of brain death or through a period of observed prognostication, medical consensus and taking account of the opinion of those closest to the patient
4. The stage of providing finality	The therapeutic goal shifts to focus on withdrawal of mechanical ventilation and other intensive care treatments and may include ICOP for deceased donation with patient/family consent

survival should remain the exclusive concern for the medical team. It would be difficult for the medical team to claim that the patient could not be saved without having performed appropriate diagnostic tests and without having devoted enough time to evaluating the patient.¹⁹

Stability

Once the patient has been stabilized by neurointensive care, often (but not always) a period of stability follows; this is usually characterized by prognostic uncertainty, with ongoing clinical investigations and observation.²⁰ Neurointensive care efforts at this stage will support neurological recovery, if any is possible, and simultaneously maintain organ function.

Recent guidance from the US Neurocritical Care Society has recommended maintaining physiologic stability in the early stages of patients with devastating brain injury, even when early limitation of aggressive care is being considered. The use of neurointensive care prevents unwarranted deterioration and allows for sufficient opportunity for prognostic evaluation.²¹ If this recommendation is accepted, this would in and of itself preclude ICOP at the stability stage.¹⁹ Other medical societies have made similar recommendations, for example in hypoxic cardiac arrest,²² strongly recommending that enough time of neurointensive care is given to allow better and safer prognostication.

However, the Neurocritical Care Society also suggested that the achievement of physiologic stability at this point also allows for care planning and consideration of organ donation. This consideration of organ donation could involve ICOP.^{23,24}

We believe that ICOP should not be commenced at this stage if there is any chance of the patient surviving in a state that would be compatible with their values, wishes and beliefs. Instead, efforts should remain focused on attempting to save the patient's life and improving future neurological functioning by use of appropriate neurointensive care. To achieve such prognostic certainty a period of stability allowing observed prognostication over time will be required. This should be the default therapy of choice, unless the patient has additional comorbidities that make intensive care non-beneficial or therapy is against the patient's wishes.

Futility

We are aware there is a movement away from the use of the term futility.²⁵ However, it is a commonly used word in intensive care to describe a patient's journey. When there is a belief that continuing neurointensive care may offer no prognostic benefit for the patient, we consider that the stage of futility has commenced. Establishing futility is usually part of a process rather than an event and remains one of the hardest areas in neurointensive care. After a careful medical evaluation,

futility can be established based on neurological prognosis and family input on the patient's values wishes and beliefs. The establishment and acceptance of futility is the final end point of this stage.

Futility should be based solely on the conviction that everything that should be done to achieve the best outcome for the patient, consistent with his or her values, wishes and beliefs, has been done.²⁶ When necessary, multiple disciplines can be brought to bear to assist the intensive care physicians, including neurologists, neurosurgeons and radiologists and, if making any decision regarding quality of future life, involve any advanced expressed wishes and those family and friends closest to the patient.

In patients with devastating brain injury, the establishment of futility may occur either by confirmation of brain death or through a period of observed prognostication, medical consensus and taking account of the opinion of those closest to the patient. During this stage, clinicians may stop some neurointensive care therapies but continue standard intensive care. For example, cessation of sedation and the acceptance that physiological targets typically pursued during neurointensive care (e.g. intracranial pressure control) may not be achievable. This is done to allow clinicians to accurately establish the neurological prognosis and confirm or refute futility.

Diagnosing death using neurological criteria (brain death) can be considered the gold standard for futility. Establishing if a patient is alive or dead is of benefit to the family, hospital staff and society, because it eradicates doubt.^{27,28} We do not consider the use of neurointensive care to achieve the diagnostic certainty of brain death as ICOP, if it is done to confirm prognostication.

If the establishment of brain death permits prognostic certainty, this benefit should be balanced against the burdens on families, the perceived wishes of the patient and the ICU resources available. If the benefits of diagnosing death before the withdrawal of mechanical ventilation are outweighed by the burdens, then it may be necessary to accept that futility has been reached without confirmation of brain death. Further exploration can be found in the case scenarios in Table 2.

Without the specificity achieved through a diagnosis of brain death there is always an element of uncertainty in prognostication. It is well recognized that a small percentage of intensive care patients who have their life-sustaining treatment withdrawn will not die but will be discharged alive.²⁹ The risk of harm for the patient who is incorrectly assessed as futile is therefore considerable, as it may 'deny patients with survivable injuries the chance of recovery'.³⁰ This risk can be exacerbated by prematurely declaring futility during the instability and stability phases.³¹

If futility is established either through confirmation and acceptance of brain death or through a period of observed prognostication, medical

Table 2. Scenarios related to brain death diagnosis and confirmation.

Scenario	Conceptual stage/s	Recommendation
The patient has been determined brain dead	Finality	ICOP will be necessary to support organ perfusion while the family considers donation. If the family agrees to donation, ICOP will need to be continued or even escalated until organ recovery.
The patient is believed to be brain dead but has yet to be formerly confirmed	Futility	Intensive care is continued with the goal of confirming the gold standard of futility which is brain death. If the burdens of intensive care are great, then a decision to withdraw life-sustaining treatment based on medical consensus and family agreement could be considered.
The patient is not yet believed to be brain dead but it is considered likely will evolve into brain death	Instability Stability Futility	The benefit of waiting to achieve prognostic certainty, i.e. brain death needs to be more carefully balanced against the burdens of pursuing this goal. The options should be openly discussed with the family
The patient is not brain dead and is believed to have low likelihood of evolving into brain death, but has a neurological outcome not consistent with the patient's values, wishes or beliefs	Futility Finality	Here, the options of withdrawal of life-sustaining therapy and DCD should be discussed with the family. If DCD is chosen, ICOP will be needed until organ recovery.

consensus and taking account of the opinion of those closest to the patient, then the finality stage can be commenced.

Finality

The finality stage can include the care of a living or deceased patient. In living patients, this is the time for end of life care and for deceased patients the time for post-mortem care. This stage includes, but is not limited to, the options of withdrawal of life-sustaining therapy (WLST), DCD or DBD.²⁶

It is only now that ICOP, in the finality stage, can be appropriately considered and discussed with the patient's family. If the patient is a consented organ donor (e.g. is on an Organ Donor Register) and/or if the family agree to organ donation, ICOP has commenced.

Switching from neurointensive care to ICOP without having first disclosed the reasons and implications of the switch to the family denies them the opportunity to bring information regarding the values, wishes and beliefs of the patient to the decision-making process. Communication and transparency is particularly crucial as the switch from neurointensive care to ICOP might not be noticeable by the family at the bedside. This period remains a delicate time of communication between the medical team and the family where end of life options have to be transparently discussed.³⁰

Discussion and recommendations

Notwithstanding issues of accurate prognostication, some patients may have ICOP initiated very early in

their hospital admission, even before receiving any neurointensive care. One example is elective ventilation, where intubation and ventilation is performed for the express purpose of facilitating donation. After an intense debate on elective or non-therapeutic ventilation in the 1990s,^{2,3,14–16} the UK Department of Health guidance was that, 'where the clinician's intention in referring the patient to intensive care is not for the patient's own benefit but is to ensure his or her organs can be retrieved for transplantation the practice would be unlawful'.³² Recently, the UK Donation Ethics Committee has stated that, 'the legal context has changed so dramatically since 1994 that the legal advice generated in that different era is no longer reliable'.³³ There is now some recognition in the UK that a desire to donate can give authority for clinicians to take actions to facilitate donation. While we do not reject this line of defence for elective ventilation, we see a potential risk that not enough will have been done to ensure accurate prognostication and would caution against policies encouraging elective ventilation before the stage of finality outside unique case by case circumstances.³⁴

In Switzerland, ICOP is acceptable if it has been established that the patient wanted to be an organ donor (either by first-person consent or surrogate consent), that a WLST has been decided and that there is a high probability that death will occur.³⁵ The Australian and New Zealand Intensive Care Society (ANZICS²⁰) has stated that

if the intensivist recommends that treatment be withdrawn and the family accepts and agrees with this, it may also be appropriate to discuss the possibility of maintaining physiological support for some hours, to

provide time to discuss and consider organ donation (DCD or DBD), or to allow the patient to deteriorate to brain death. (p. 36)

Likewise, in patients already mechanically ventilated the National Institute for Health and Care Excellence (NICE) advised that, ‘life-sustaining treatments should not be withdrawn or limited until the patient’s wishes around organ donation have been explored’.³⁶ Similarly, in the USA the Revised Uniform Anatomical Gift Act of 2009 has been widely adopted and provides that ‘measures necessary to ensure the medical suitability of the part [i.e. organs] may not be withdrawn unless the hospital . . . knows that the individual expressed a contrary intent’.³⁷

We interpret these recommendations as saying that achieving agreement on futility is a process and that continuing neurointensive care at this stage is acceptable as this helps achieve this decision end point. This should not be considered ICOP. However, once the futility stage is concluded the finality stage commences. This transition can occur quite quickly and even be part of the same family discussion. ICOP is appropriate here while options in the finality stage are explored.

The key difference between the stages is that during the instability, stability and futility stages the focus must be neurointensive care which seeks the patient’s recovery or achieving accurate neurological prognostication. Only in the finality stage should the therapeutic goal shift to focus on comfort care, the withdrawal of mechanical ventilation and other intensive care treatments for ICOP for deceased donation.

During the four stages, there is an additional risk of real or perceived conflicts of interest. This is a powerful reminder why a conclusion of futility should not be biased by organ donation considerations and why initiation of ICOP should not be considered during the instability, stability or futility stages but only in the finality stage, to avoid denying, or be perceived to be denying, neurointensive care to a saveable patient. By conceptualizing neurologically injured patient care using the four stages, as we have outlined in this paper, clinicians can better avoid real or perceived conflicts of interest. We consider that pursuing and maintaining trustworthiness, through transparent policies and shared decision making in each of the four stages, is the best way to mitigate these potential conflicts.

We would also recommend that a change in management, from neurointensive care to ICOP, should be documented in the patient’s chart, after a discussion and an agreement with the family, in order for any healthcare professionals taking care of the patient to be fully aware of the goals and intentions of treatment.

Conclusion

The switch from neurointensive care to ICOP carries a risk of denying treatment to a patient that will benefit

from it. We have suggested that the care of a patient with a devastating brain injury that eventuates in deceased donation can be conceptually understood as proceeding through four stages: instability, stability, futility and finality. During the first three stages, the focus must be neurointensive care which seeks the patient’s recovery or achieving accurate neurological prognostication. Only in the finality stage should the therapeutic goal shift to ICOP if organ donation is consented.

Our hope is that clinicians who conceptualize neurologically injured patient care in the four stages, we have outlined in this paper, will be better able to navigate the ethical challenges in this fraught area of clinical practice, which may otherwise defeat the good intentions of all involved.

Disclaimer

The opinions expressed are the views of the authors and do not reflect the policy of their belonging institutions, NHS Blood and Transplant, the Swiss National Medical Associations or the Swiss Public Health Service.

Declaration of conflicting interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Dale Gardiner is national clinical lead for organ donation in the UK for NHS Blood and Transplant.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. Rosendale JD, Chabalewski FL, et al. Increased transplanted organs from the use of a standardized donor management protocol. *Am J Transplant* 2002; 2: 761–768.
2. Feest TG, Riad HN, et al. Protocol for increasing organ donation after cerebrovascular deaths in a district general hospital. *Lancet* 1990; 335: 1133–1135.
3. Monette M. The ethics of elective ventilation. *CMAJ* 2012; 184: E841–E842.
4. Antoine C, and Tenaillon A. Conditions à respecter pour réaliser des prélèvements de reins sur des donneurs à Coeur arrêté dans un établissement de santé autorisé aux prélèvements d’organes. Agence de la biomédecine, www.urgences-serveur.fr/IMG/pdf/DVprotocole_V12_avril_2007.pdf (2007, accessed 14 March 2019).
5. Dalle Ave AL, Shaw DM, and Gardiner D. Extracorporeal membrane oxygenation (ECMO) assisted cardiopulmonary resuscitation or uncontrolled donation after the circulatory determination of death following out-of-hospital refractory cardiac arrest – an ethical analysis of an unresolved clinical dilemma. *Resuscitation* 2016; 108: 87–94.
6. Dalle Ave A, and Shaw D. Controlled donation after circulatory determination of death: ethical issues in withdrawing life-sustaining therapy. *J Intensive Care Med* 2017; 32: 179–186.

7. Oniscu GC, Randle LV, Muiesan P, et al. In situ normothermic regional perfusion for controlled donation after circulatory death – the United Kingdom experience. *Am J Transplant* 2014; 14: 2846–2854.
8. Levine JM and Kumar MA. Traumatic brain injury. Neurocritical care society practice update, www.neurocriticalcare.org/sites/default/files/pdfs/08.TBI.final.pdf (2013, accessed 2017).
9. Wijdevicks EF, Sheth KN, Carter BS, et al. Recommendations for the management of cerebral and cerebellar infarction with swelling: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2014; 45: 1222–1238.
10. Brain Trauma Foundation (BTS). Guidelines for the management of severe traumatic brain injury. 3rd ed. *Journal of Neurotrauma* 2007; 24(Suppl 1): S1–106.
11. Dalle Ave AL, Gardiner D, and Shaw DM. Cardiopulmonary resuscitation of brain-dead organ donors: a literature review and suggestions for practice. *Transpl Int* 2016; 29: 12–19.
12. Dalle Ave AL, Gardiner D, and Shaw DM. The ethics of extracorporeal membrane oxygenation in brain-dead potential organ donors. *Transpl Int* 2016; 29: 612–618.
13. Escudero D, Cofiño L, Gracia D, et al. Cranioplasty with bandaging. New forms of limitation of life support and organ donation. *Med Intensiva* 2013; 37: 180–184.
14. Shaw AB. Non-therapeutic (elective) ventilation of potential organ donors: the ethical basis for changing the law. *J Med Ethics* 1996; 22: 72–77.
15. Riad H, and Nicholls A. Elective ventilation of potential organ donors. *BMJ* 1995; 310: 714–718.
16. Price DPT. Organ transplant initiatives: the twilight zone. *J Med Ethics* 1997; 23: 170–175.
17. McGee AJ, and White BP. Is providing elective ventilation in the best interests of potential donors? *J Med Ethics* 2013; 39: 135–139.
18. Gillet G. Honouring the donor: in death and in life. *J Med Ethics* 2013; 39: 149–152.
19. Harvey D, Butler J, Groves J, et al. Management of perceived devastating brain injury after hospital admission: a consensus statement from stakeholder professional organizations. *Br J Anaesth* 2018; 120: 138–145.
20. Australian and New Zealand Intensive Care Society. The ANZICS Statement on Death and Organ Donation (Edition 3.2). Melbourne: ANZICS, 2013.
21. Souter MJ, Blissitt PA, Blosser S, et al. Recommendations for the critical care management of devastating brain injury: prognostication, psychosocial, and ethical management. A position statement for healthcare professionals from the Neurocritical Care Society. *Neurocrit Care* 2015; 23: 4–13.
22. Samaniego EA, Persoon S, and Wijman CAC. Prognosis after cardiac arrest and hypothermia: a new paradigm. *Curr Neurol Neurosci Rep* 2011; 11: 111–119.
23. Watkinson P, McKechnie S, Wilkinson K, et al. Actively delaying death to increase organ donation. *BMJ* 2012; 344: e1179.
24. Bauman A, Audibert G, et al. Elective non-therapeutic intensive care and the four principles of medical ethics. *J Med Ethics* 2013; 39: 139–142.
25. Bosslet GT, Pope TM, Rubenfeld GD, et al. An official ATS/AACN/ACCP/ESICM/SCCM policy statement: responding to requests for potentially inappropriate treatments in intensive care units. *Am J Respir Crit Care Med* 2015; 191: 1318–1330.
26. Bernat JL. The boundaries of organ donation after circulatory death. *N Engl J Med* 2008; 359: 669–671.
27. Clarke MJ, Remtema MS, and Swetz KM. Beyond transplantation: considering brain death as a hard clinical endpoint. *Am J Bioeth* 2014; 14: 43–35.
28. UK Donation Ethics Committee. An ethical framework for donation after confirmation of death using neurological criteria (DBD), www.aomrc.org.uk/wp-content/uploads/2016/07/Ethical_framework_donation_after_confirmation_death_using_neurological_criteria-2.pdf (2016, accessed 14 March 2019).
29. Nolin T, and Andersson R. Withdrawal of medical treatment in the ICU. A cohort study of 318 cases during 1994–2000. *Acta Anaesthesiol Scand* 2003; 47: 501–507.
30. Rady MY, Verheijde JL, et al. Scientific, legal, and ethical challenges of end-of-life organ procurement in emergency medicine. *Resuscitation* 2010; 81: 1069–1078.
31. Manara A, Thomas I, and Harding R. A case for stopping the early withdrawal of life sustaining therapies in patients with devastating brain injuries. *J Intensive Care Society* 2016; 17: 295–301.
32. National Health Service, Acute Services Policy Unit. Identification of potential donors of organs for transplantation. NHS Executive HSG(94)41. London: National Health Service, 1994.
33. UK Donation Ethics Committee. Nontherapeutic elective ventilation, www.aomrc.org.uk/wp-content/uploads/2016/07/Nontherapeutic_elective_ventilation_0416-2.pdf (2016, accessed 14 March 2019).
34. Patel UJ. Advance statement of consent from patients with primary CNS tumors to organ donation and elective ventilation. *J Med Ethics* 2013; 39: 143–144.
35. The Swiss Donation Pathway. Module 2: prise en charge des donneurs d'organes adultes: soins intensifs, www.swisstransplant.org/fr/info-materiel/professionnels/swiss-donation-pathway/ (2014, accessed 14 March 2019).
36. National Institute for Health and Clinical Excellence. Organ donation for transplantation: improving donor identification and consent rates for deceased organ donation, <http://guidance.nice.org.uk/CG135/NICEGuidance/pdf/English> (2011, accessed January 2016).
37. The National Conference of Commissioners on Uniform State Laws. Revised Uniform Anatomical Gift Act, www.uniformlaws.org/shared/docs/anatomical_gift/uaga_final_aug09.pdf (2006, accessed 2017).