

*Editorial***The Use of Normothermic Regional Perfusion Increases The Burden of Organ Donation After Euthanasia**Jadranka Buturovic Ponikvar^{1,2} and Zeljka Buturovic³¹University Medical Centre Ljubljana, Ljubljana, Slovenia, ²Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia, ³Institute of Social Sciences, Belgrade, Serbia**Abstract**

Post-mortem introduction of normothermic regional perfusion (NRP) is increasingly used in organ donation. In this procedure, after declaration of death according to circulatory-criteria and "no touch" time of 5 minutes, organ donors' circulation is restored by extracorporeal membrane oxygenation (ECMO). Before restoring circulation during NRP, surgeons block arteries perfusing brain to avoid regaining of brain functions. The mechanics and set-up of NRP may difficult understand for patients and medical professionals alike. In addition, restoration of circulation puts permanence of circulatory death into question, especially in the context where blocking of arteries perfusing brain after death is already declared is considered necessary. An outsized role that autonomy and consent play for a growing number of euthanasia patients considering organ donation exacerbates these already significant issues. A planned nature of euthanasia donors' death invites numerous perimortem interventions to optimize organ quality, with NRP joining an already long list of pre-mortem donor interventions. The growing burden of donation in euthanasia patients increases the odds that patients and their families do not fully understand this process, and raises significant ethical and potentially legal questions.

Keywords: organ donation, euthanasia, normothermic regional perfusion, donation after circulatory death, organ donation euthanasia, heart donation after euthanasia

Introduction

Post-mortem introduction of normothermic regional perfusion (NRP) is increasingly used in organ donation [1,2] and already celebrated as a "cost-effective alternative in donation after circulatory death in heart transplantation" [1]. In this procedure, after declaration of death according to circulatory-criteria and "no touch" time of usually 5 minutes (to avoid spontaneous resus-

citation), organ donors' circulation is restored by extracorporeal membrane oxygenation (ECMO). ECMO may reduce ischemic injury of organs to be transplanted and may enable heart transplantation, which is often not possible after circulatory determination of death. During one such recent heart transplantation from euthanised donor in Belgium, that followed NRP protocol, regular heartbeat during NRP was also restored. Diagnosis of amyotrophic lateral sclerosis was basis for euthanasia in this patient [3]. Importantly, during NRP, surgeons block the blood flow to the brain through clamping, intravascular balloons or ligation of arteries perfusing brain, thus ensuring brain death.

ECMO is not a new procedure-it has been routinely used during open heart surgery for decades (for short time during surgery or, in a modified version, for days and weeks to support lung and heart function and give them time to heal). However, it has now been repurposed from saving the life of the patient, to procuring their organs more efficiently while pursuing additional steps (i.e. blocking the blood flow to the brain) to make sure that an already dead patient (by determination of circulatory death) remains dead after circulation is restored, and that their brain function is not regained.

Bioethicists have already brought attention to some of the difficulties that this procedure presents for organ donation [4] and interventional research [5]. As Moorlock and Draper explain, "because the organ donation process has become more complex, it is not obvious that a willingness to donate some or all of one's organs necessarily translates into a willingness to undergo... all of the steps and interventions that may be... a part of donation". Meanwhile, a 2015 study [6] that randomly assigned brain dead to be organ donors to normothermia (standard approach) vs. hypothermia has faced challenges from a US-based consumer group, despite getting the approval of an Institutional Review Board [5] (the complaint argued that kidney graft recipients were involved in the trial without being with aware of it). Here we want to draw attention to ethical problems that the use of NRP may pose for organ donation in

euthanasia patients, including informed consent of to-be-donors and recipients.

The Burden of Organ Donation In Euthanasia Patients Keeps Growing

Euthanized patients are increasingly important source of organs in countries where euthanasia is legal (The Netherlands, Belgium, Luxemburg, Canada and Spain), representing 14% of recipients from donors after circulatory determination of death as of 2021 [7]. This was entirely predictable and, in fact, predicted [8,9]. Early on, beneficence was the prime justification for euthanasia and euthanasia laws were meant to be limited to terminal somatic patients experiencing unbearable suffering. Majority of these patients were cancer patients whose organs are not suitable for transplantation, nor are organs from other terminally ill patients or old patients. However, since then, autonomy became the overriding motivation for euthanasia and criteria for euthanasia have expanded, to non-terminal somatic patients, psychiatric patients, people with disabilities [10] and children. As a result, growing proportion of a growing number of euthanasia patients have or may become organ donor candidates in future. From the perspective of organ quality and a potential for a transplanted organ longevity, physically healthy and relatively young donors (for example those euthanized for psychiatric disorder) are likely to become the preferred donors to transplant physicians and recipients. According to recent report about the experience of organ donation from psychiatric patients (2012-2022, the Netherlands) patients euthanized for psychiatric disorder represented 28.9% of all organ donors after euthanasia in this period, the youngest being 21 years old [11].

Due to the planned and intentional nature of their deaths, organ donation in euthanasia patients (whose life is terminated in a hospital by a lethal injection), invites numerous interventions aimed at increasing quality of organs, effectively combining the burden of pre-mortals and post-mortals interventions. Thus, according to a recent review of the practices, "depending on which pre-mortals interventions the country's legislation permits"... pre-mortals donor interventions..." may include imaging, blood tests, invasive arterial blood pressure monitoring, heparin administration, and changing the setting where death takes place" ([7]). Relatively new are post-mortals regional perfusion procedures.

Heart transplantation from euthanized donors

The heart is the organ that is most sensitive to ischemia, so until recently, heart transplantation from euthanized persons was not possible. To override this problem, some have suggested abandoning dead donor rule and performing heart procurement while the euthanasia candidate is still alive (with other organs procured

while heart still beating) [12,13,14]. However, respecting the dead donor rule is crucial to preserving trust in transplantation medicine and physicians. This makes the procurement of a heart from euthanized patients using NRP, which was recently reported in Belgium [3] a preferable alternative. In the recent report on 10-year experience transplanting organs from donors euthanized from psychiatric disorders in the Netherlands, two hearts were donated, without details on procurement technique reported [11].

All these procedures make it difficult for patients (and their families) to understand the burden they will be carrying when donating their organs. These problems are already apparent with the "change of setting where death takes place" referenced above. Euthanasia patients typically want to die at home which complicates organ donation. For this reason, this preference is not commonly satisfied. Since a certain vision of death experience, including the setting, is one of the main motivators for euthanasia, efforts have been made to combine the two. This has been accomplished by having patients (to-be-donors) deeply sedated at home surrounded by their loved ones for a farewell, and then driven to the hospital accompanied by an anaesthesiologist, where termination of patient's life still takes place [15]. This is a convoluted series of steps with a potential for being misunderstood and the possibility of the need for donor to be resuscitated on their way to the hospital. Finally, although procedural guidelines make sure that euthanasia patients are faced with organ donation decisions only after they have decided to pursue euthanasia, increasing number of patients may already be familiar with the possibility of organ donation combined with euthanasia and may request both. However, they are likely to be making this request without fully realizing the specifics of the burden of donation, possibly including NRP. Only when they are well on their way to donation are they likely to fully understand what that entails, making potential reversal of their decisions difficult, as lives of others are now dependent on them [9]. It has already been published that some patients who requested euthanasia admitted to their physicians that they still wanted to live, however, they were now afraid to confess this to their families [15]. In directed organ donation (to a specific person) after (or even before) euthanasia the risk of coercion may be difficult to avoid [16].

Increasingly complex transplant procedures and convoluted definitions of death may pose risk of invalid informed consent

NRP (which includes blocking of arteries perfusing brain despite death is already declared) is a complex procedure which is not easy to understand. A regular person is unlikely to be familiar with the finer details of regular transplant protocols, much less with NRP. Yet,

full understanding of "what one has signed-up for" is not only a prerequisite for the patient's exercise of autonomy but also for legal procedures involving informed consent.

Large numbers of people are prone to "routinize" consent, i.e. sign consent forms without reading them [17]. Yet, informed consent hinges on the patient's capacity and willingness to understand what he is consenting to. More complex the procedures necessitate longer explanations, increasing the risk that patients are signing them without reading them. It has already been argued that, despite opt-out system of organ donation, citizens of the UK should fill out a separate form to spell-out their wishes in respect to increasingly complex procedures (such as NRP), that are involved in the actual process of organ donation [4].

Finally, already convoluted definitions of death are further strained by NRP. A common-sense understanding of death implies irreversibility and permanence. However, the mechanics of NRP-the fact that blood flow to the brain needs to be blocked although the person is already declared to be dead (by circulatory criteria)-implies that irreversibility and permanency of the initial circulatory death was not complete. In the US, Uniform Determination of Death Act laws demand that, to be considered dead, either circulation or all functions of the entire brain function must have ceased irreversibly; NRP violates this condition [18]. It is therefore not surprising that American College of Physicians urged a pause in use of NRP to allow further study before wide adoption [19].

Discussion

The slippery slope in organ donation after euthanasia is a reality. Euthanasia was primarily introduced to end suffering of "the sickest of the sick". This was, and still is, the basis for its public support. However, at this point the practice has shown that, once introduced, euthanasia laws tend to expand, to include individuals experiencing mental pain, to children, and to organ procurement. Patients euthanized for neuromuscular disease, and those for euthanized for psychiatric disorders and mental suffering are the main candidates for organ donation. Abandoning the dead donor rule as a way to enable heart transplantation from euthanasia candidates acting as living donors is explored (and endorsed) in top scientific journals [12,13,15].

However, more attention needs to be paid to the often invisible costs carried by donors and their families. Euthanasia patients interested in organ donation will only learn about the details of the compromises they will have to undertake to optimize quality of organs for recipients when they are already deeply involved in the process, making it difficult to reverse their decision because they feel that "I'd better do this because people are waiting for my organs". Initial cause to

request euthanasia for suffering may be overshadowed by the need to save lives. Vulnerable individuals prone to entertaining such thoughts should not face additional donation burdens. These suggestions may be all the more relevant for heart donation after euthanasia requiring NRP.

Transplantation medicine is one of the major achievements of the 20th century. Together with artificial organs, it was involved in the birth of modern bioethics. Transplantation medicine is deeply involved in our understanding and definition of death. However, alongside predominant triumphalist reports in scientific journals [20], ethical concerns about organ donation related practices should continuously be explored. As suggested by anesthesiologist Claire Middleton, euthanasia combined with organ donation »must surely give everyone in the transplant community (including organ recipients) a pause for thought« [21].

Acknowledgement: The positions presented in this paper are from the authors and do not necessarily represent the positions of the committees or institutions affiliated with.

Funding: The authors acknowledge the financial support from the Slovenian Research Agency (research core funding No. P3-0323) ^(1,2), R&R grant from the University Medical Centre Ljubljana, Slovenia (Grant No 20220008)¹ and the support of the 2023 Research Program of the Institute of Social Sciences with the support of the Ministry of Science, Technological Development and Innovation of the Republic of Serbia.

Conflict of interest statement. None declared.

References

1. Alamouti-Fard E, Garg P, Wadiwala IJ, *et al.* Normothermic regional perfusion is an emerging cost-effective alternative in donation after circulatory death (DCD) in heart transplantation 2022. *Cureus* 2022; 14(6): e26437.
2. Lee C, Tsal C, Adler E, Pretorius V. Emerging frontier in heart transplantation: Donation after circulatory death. Expert analysis. Published November 1, 2022. Available: <https://www.acc.org/latest-in-cardiology/articles/2022/11/21/13/31/emerging-frontier-in-heart-transplantation> (Accessed 19 February 2023).
3. Tchana-Sato V, Hans G, Brouckaert J, *et al.* Successful heart transplantation from donation after euthanasia with distant procurement using normothermic regional perfusion and cold storage. *Am J Transplant* 2022; 22(12): 3146-3149.
4. Moorlock G, Draper H. Proposal to support making decisions about the organ donation process. *J Med Ethics* 2023; 49(6): 434-438.
5. Cooper J, Harvey D, Gardiner D. Examining consent for interventional research in potential deceased organ donors: a narrative review. *Anaesthesia* 2020; 75(9): 1229-1235.

6. Niemann CU, Feiner J, Swain S, *et al.* Therapeutic hypothermia in deceased organ donors and kidney-graft function. *N Engl J Med* 2015; 373: 405-414.
7. Mulder J, Sonneveld H, Van Raemdonck D, *et al.* Practice and challenges for organ donation after medical assistance in dying: A scoping review including the results of the first international roundtable in 2021. *Am J Transplant* (2022); 22(12): 2759-2780.
8. Buturovic Z. Procedural safeguards cannot disentangle MAiD from organ donation decisions. *J Med Ethics* 2021; 47: 706-708.
9. Buturovic Z. Euthanasia and organ donation still firmly connected: reply to Bollen *et al.* *J Med Ethics* 2022; 48: 488-489.
10. Tuffrey-Wijne I, Curfs L, Finlay I, Hollins S. Euthanasia and assisted suicide for people with an intellectual disability and/or autism spectrum disorder: an examination of nine relevant euthanasia cases in the Netherlands (2012-2016). *BMC Medical Ethics* (2018): 19: 17.
11. Van Dijk J, Starcke P, de Jongh V, *et al.* Organ donation after euthanasia in patients suffering from psychiatric disorders: 10-years of preliminary experience in the Netherlands. *Transplant Int* 2023; 36: 10934.
12. Ball IM, Sibbald R, Truog RD. Voluntary euthanasia: implications for organ donation. *N Engl J Med* 2018; 379: 909-911.
13. Bollen JAM, Shaw D, de Wert G, *et al.* Euthanasia through living organ donation: ethical, legal and medical challenges. *J Heart Lung Transplant* 2019; 38: 111-113.
14. Rosenbaum L. Altruism *in extremis* -The evolving ethics of organ donation. *N Engl J Med* 2020; 382(6): 493-496.
15. Mulder J, Sonneveld JPC. Organ donation after medical assistance in dying at home. *Can Med Assoc J* 2018; 190(44): E1305-E1306.
16. Middleton C. Directed organ donation after medical assistance in dying: little to gain and much to lose. *Can J Anesthes* 2020; 67: 13101311.
17. Ploug T, Holm S. Informed consent and routinization. *J Med Ethics* 2013; 39: 214-218.
18. Glazier AK, Capron AM. Normothermic regional perfusion and US legal standards for determining death are not aligned. *Am J Transplant* 2022; 22: 1289-1290.
19. American College of Physicians Statement of Concern. Ethics, determination of death, and organ transplantation in normothermic regional perfusion (NRP) with controlled donation after circulatory determination of death (cDCD), 2021. Available at: https://www.acponline.org/sites/default/files/documents/clinical_information/resources/end_of_life_care/ethics_determination_of_death_and_organ_transplantation_in_nrp_2021.pdf (Accessed January 13, 2023).
20. Durand C, Duplantie A, Chabot Y, *et al.* How is organ transplantation depicted in internal medicine and transplantation journals. *BMC Medical Ethics* 2013; 14: 39.
21. Middleton C. Organ donation after MAiD: it's not so simple. *Can Med Assoc J* 2019; 191: E1062.