Delayed withdrawal of life support in candidate organ donors through a DNR 4 protocol: preliminary impact on deceased donation rates

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Abstract

Background: **Deceased organ donation plays a critical component in addressing donor organ shortages, but it often faces challenges in timing and consent processes. At our center, a "delayed donation" protocol was developed that would facilitate a natural progression towards brain death by temporarily delaying the withdrawal of life-sustaining therapy in intensive care unit (ICU) patients where brain death is anticipated but not immediate. This protocol relies on a clearly outlined "Do-Not-Resuscitate (DNR) Code 4" practice, which ensures ethical and informed management of potential donors and their families.**

Methods: **A retrospective, single-center analysis of our experience with delayed donation through a DNR 4 protocol at AZ Delta Roeselare, Belgium. We retrospectively analyzed all potential deceased donors evaluated at our ICU between January 1, 2009 and December 31, 2022.**

Results: **Among 415 potential donors, 84 patients were managed through the delayed donation pathway, of whom 40 progressed to brain death and were classified as delayed DBD (dDBD) donors. The use of DNR 4 allowed for an ethical extension of care, resulting in additional DBD donations without compromising family consent or patient comfort. The number of effective dDBD donations accounted for 10% of all potential donors and 19% of effective donations during the study period, contributing to stable DBD numbers in our center.**

Conclusion: **The DNR 4 protocol within the delayed donation framework holds potential to increase DBD opportunities and addressing donor shortages in an ethical manner. It ensures clear communication with families and maintains respect for donor autonomy while facilitating optimal donor organ recovery.**

Keywords: **Organ Donation, Brain Death, Transplantation.**

Introduction

Organ transplantation is a life-saving treatment for patients with end-stage organ failure, but the gap between organ demand and supply continues to grow. This shortage persists despite advances in donor management and the expansion of donor acceptance criteria[1]. Addressing this shortfall requires innovative strategies.

Deceased organ donation begins with the identification of a potential donor, marking a clear delineation between curative patient care and the management of a potential donor. Although this transition is a critical step in the donation process, structured protocols to guide healthcare professionals in providing optimal donor care while maintaining transparency and ethical integrity are not well described.

Deceased organ donation typically occurs through one of two pathways: donation after brain death (DBD) or donation after circulatory death (DCD)[2]. DBD involves organ donation following determination of death by neurological criteria, i.e. the complete and permanent cessation of all cerebral and brainstem function. DCD occurs when death is determined by cardio-circulatory criteria, i.e. after irreversible circulatory arrest has occurred. Most DCD donations follow the withdrawal of life-sustaining therapy in critically ill patients for whom continued treatment offers no reasonable hope of improvement and is therefore considered 'futile' (controlled DCD or Maastricht category 3). DBD is the preferred pathway due to its superior organ yield and better graft outcomes.

However, the development of brain death is not an instantaneous process, and it often requires time to establish following devastating brain injuries. Premature decisions to withdraw life-sustaining therapy in patients may exclude them from organ donation or inadvertently redirect potential DBD donors to the DCD pathway. Therefore, it is essential for physicians to recognize that the natural progression towards brain death may take time and, when appropriate, it is advisable to provide stabilizing care to allow this process to occur must be provided.

To ensure a transparent, medically and ethically sound transition from patient care to donor management, a Do-Not-Resuscitate (DNR) Code 4 was introduced in our center in the mid-1990s which formed a distinct category from other well-known DNR codes in Belgium (Table I). This protocol applies to all potential donors, independent of whether DBD or DCD is anticipated. DNR Code 4 formally marks the shift in care goals from curative treatment to the stabilization of the donor, setting a clear boundary between the two phases.

Here, we describe the implementation of the DNR 4 protocol as an integral part of our end-of-life care strategy for potential organ donors and share preliminary results of its impact across the organ donation pathways (standard DBD, delayed DBD, and DCD), and total numbers of organ transplants.

Methods

This is a retrospective, single-center analysis of our experience with delayed donation at AZ Delta Roeselare, Belgium, a 1,358-bed hospital with 54 intensive care unit (ICU) beds that refers potential deceased donors to the transplant coordinating center at University Hospitals Leuven, Belgium. Between January 1, 2009, and December 31, 2022, every potential organ donor in our ICU was identified and the following data were collected: patient characteristics, reason of ICU admission, clinical course, decision on futility of care, declaration of brain death and number of organs procured. This study was approved by the Research Ethics Committee KU Leuven (protocol MP021166).

Institutional definition of Do-Not-Resuscitate code 4 (DNR 4) for potential organ donors

Once futility of care has been determined in a potential organ donor in the ICU, a 'Do-Not-Resuscitate (DNR) Code 4' is signed, clearly delineating the management transition from curative treatment to donor optimization. This DNR 4 protocol provides clear guidance for both the patient's family and the ICU team, ensuring alignment and transparency during this transition. If the patient is expected to progress towards brain death, the delayed donation strategy is discussed with the patient's next of kin. It is proposed that if, within 24-36 hours, brain death has not occurred, further stabilizing care will be provided for an additional 72 hours or longer, to await potential spontaneous evolution towards brain death.

Delayed Donation Pathway

The donation program at our center consists of two distinct time phases and two main donation pathways, as illustrated in Figure 1. Phase 1 begins with the determination of futility of care, which is marked by the establishment of DNR Code 4, and ends with the assignment of the type of donation. This phase captures the critical period during which potential donors are evaluated for their likelihood to progress to brain death or other outcomes. Phase 2 encompasses the time from the assignment of the type of donation to the actual procurement of organs.

The program distinguishes between the standard donation pathway and the delayed donation pathway. The standard donation pathway includes three subgroups. The first subgroup, standard DBD (sDBD), consists of patients in whom brain death occurs within 24 hours of declaring futility of care (Phase 1 < 24 hours). The second subgroup, standard DCD (sDCD), includes patients for whom spontaneous progression to brain death is clinically considered unlikely. These individuals are redirected to controlled DCD donation, typically Maastricht category III. The third subgroup is

Table I. — Definitions of Do-Not-Resuscitate codes.

DNR Code 0	Maximum care with resuscitation
DNR Code 1	No reanimation, possible restrictions: do not initiate dialysis; intubation; increase vasopressors; antibiotics; blood/blood products; antiarrhythmics; ICU admission; non-invasive ventilation; artificial nutrition; chemotherapy; artificial ventilation.
DNR Code 2	No resuscitation, continue prescribed therapy, do not initiate new therapy.
DNR Code 3	Stop curative therapy, start comfort therapy.
DNR Code 4	The patient is temporally placed on stabilizing care within the context of an organ donation procedure or the expected arrival of family/relatives.

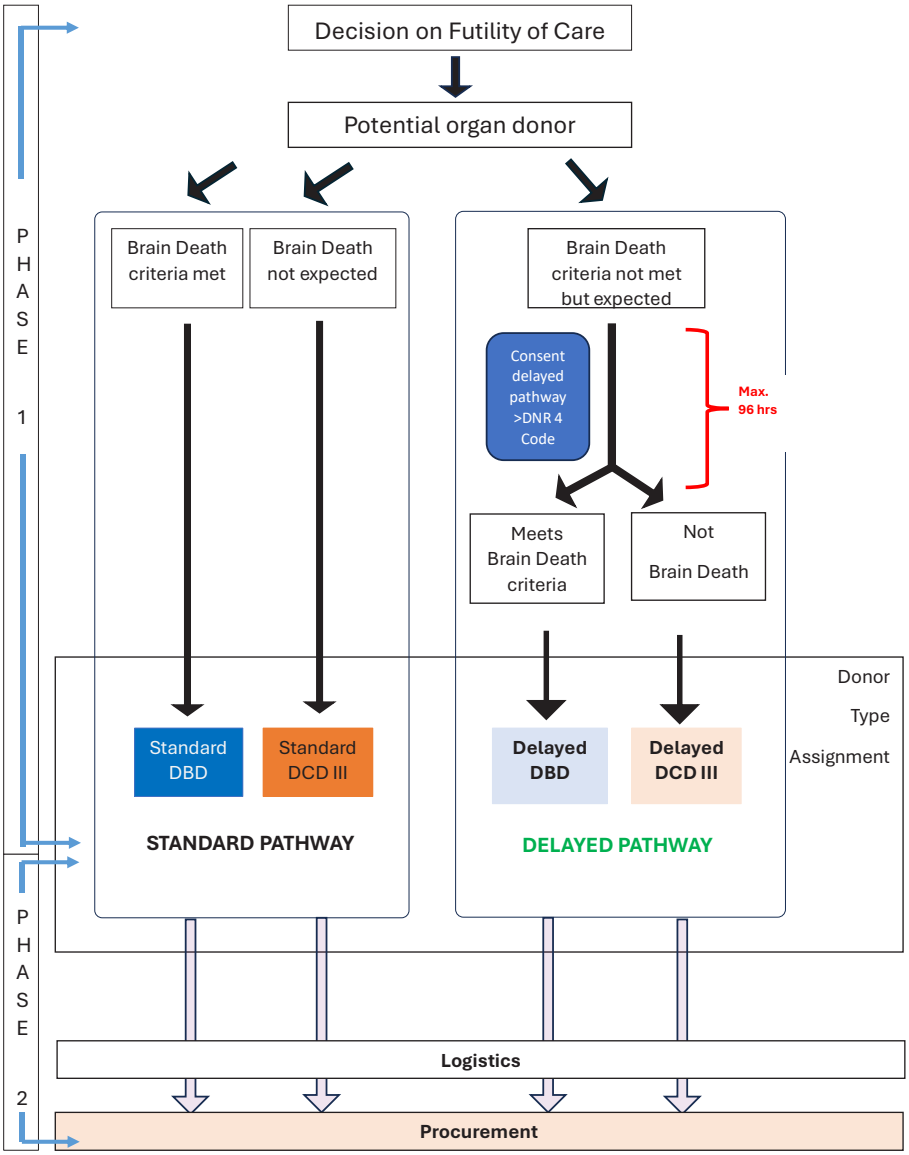

Fig. 1 — The delayed donation pathway.

the no-donation group, comprising patients who do not proceed to organ donation due to medical contraindications, logistical challenges, or lack of consent from the family or patient's representatives.

The delayed donation pathway is designed for patients who do not progress to brain death within 24 hours of declaring futility of care but are clinically predicted to do so within a slightly longer timeframe. Predictions of brain death progression are made by experienced ICU clinicians based on neurological assessments and radiological findings. The delayed donation pathway encompasses three subtypes of donation. The first subtype is delayed DBD (dDBD), involving patients who progress to brain death within 72 hours and are managed as DBD donors. The second subtype is delayed DCD (dDCD), which includes patients who do not develop brain herniation within 72 hours and are subsequently assigned to the DCD pathway. The final subtype is the no-donation group, which includes patients who do not meet criteria for donation due to medical contraindications, lack of consent, or other limiting factors.

Results

Impact of DNR 4 on Donation Pathway

Between January 1, 2009, and December 31, 2022, a total of 415 ICU patients were assessed for deceased organ donation. Of these, 331 (80%) followed the standard pathway, while 84 (20%) were managed through the delayed donation pathway. Within the standard pathway, 86 (21%) patients became sDBD donors, 72 (17%) became sDCD donors, and 173 (42%) did not proceed to donation. In the delayed pathway, 40 (10%) patients effectively became dDBD donors, 16 (4%) did not progress to brain death and became dDCD donors. The remaining 28 (8%) were declined. Main reasons for decline in both groups were related to medical

contraindications such as personal history, findings on thoracoabdominal computed tomography (TA-CT) screening or findings during procurement, opposition by next of kin and logistical reasons. Screening with TA-CT was introduced at our center in 2019 for candidate donors with selected risk factors (>60 years of age, cardiovascular comorbidity, BMI >30, history of malignancy, significant smoking or alcohol consumption). By 2021, it became standard for all potential donors 20213.

Thus, 40 potential donors, who in the standard pathway were expected to be considered for DCD donation, were redirected and became effective DBD donors. Of the total 214 accepted donors, 88 (41%) were DCD donors (72 (82%) sDCD and 16 (18%) dDCD donors), and 126 (59%) DBD donors (86 (68%) sDBD and 40 (32%) dDBD donors), as shown in Figure 2.

Characteristics of standard DBD, delayed DBD and DCD donors

Hemorrhagic stroke as the predominant cause for ICU admission in both standard and delayed DBD, whilst post-anoxemic brain damage was the main reason for DCD donors. Table II provides a detailed breakdown of the number and type of organs procured per donation pathway. Over the 15-year period, a total of 533 organs were procured: 225 organs from 86 sDBD donors (averaging 2.62 organs/donor), 105 from 40 dDBD donors (2.63 organs/donor) and 203 from 88 DCD donors (2.31 organs/donor).

The dDBD pathway facilitated an additional 9 hearts and 3 pancreas transplants that were previously regarded unfeasible in DCD cases. This is attributed to the absence of established protocols for DCD heart and pancreas transplantation prior to 2023, as well as the increased risk perception of pancreas transplantation from DCD donors at our center.

Notably, 14 patients over 75 years of age for whom further care was considered futile transitioned to the dDBD pathway. This resulted in the procurement of 53 organs: 26 organs from 24 sDBD donors (1.1 organs/donor; 1 kidney, 24 livers and 1 lung), 23 from 14 dDBD donors (1.64 organs/donor, 7 kidneys, 14 livers and 2 lungs) and 4 from 4 DCD donors (1 organs/donor, 3 livers and 1 lung).

Discussion

This paper describes a clinical practice that emerged from direct experience and continual learning, designed to address key challenges in organ donation. The DNR 4 guided delayed donation pathway is presented as a framework developed over 15 years to align practical donor management strategies with ethical principles. Preliminary data indicate that this approach is not only valuable in optimizing organ recovery but also maintains a clear ethical foundation. It aligns with principles of non-maleficence, ensuring patient comfort while respecting family consent. The protocol avoids premature transitions to less favorable donation pathways and addresses ethical concerns by clearly distinguishing donor management from curative efforts.

The strategy of delayed DBD resulted in more effective organ donors as well as more organs procured per donor. Moreover, our strategy resulted in 14 extra DBD donors (and 23 extra organs) older than 75 years who would otherwise probably have been refused as DCD donors because of age. Between 2009 and 2022, 9 additional hearts were procured from delayed DBD donors. In the context of heart transplantation, the standard procedure has been DBD until recently. There has been increasing interest in DCD donors for heart transplantation to expand the pool of potential donors. Accumulated clinical experience shows that heart transplantation

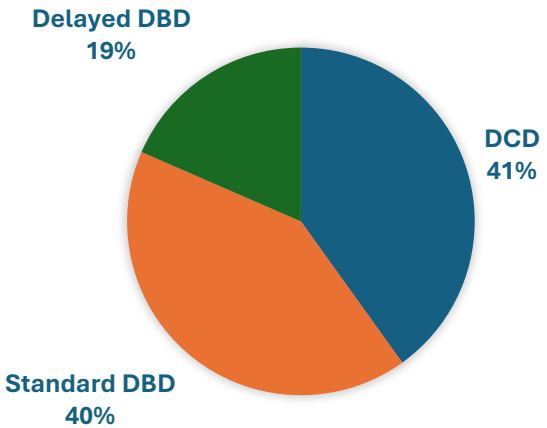

Fig. 2 — Types of organ donation in our center between 2009 and 2022.

Table II. — Number and type of organs procured per donation pathway.

	Standard DBD (n = 86)	Delayed DBD (n=40)	DCD (n=88)
Total number of organs procured and transplanted, n	225	105	203
Type of organ procured, n			
- Kidneys	90	43	111
- Liver	77	36	64
- Lungs	28	14	28
- Heart	26	9	0
- Pancreas	4	3	0
number of organs/donor			
- mean (n)	2.62	2.63	2.31
- median (n)	3	3	2
- range	1-6	1-6	1-4

from selected DCD donors is feasible and safe with outcomes comparable to the outcomes of DBD heart transplant recipients4. However, there is extensive experience with heart donation after DBD and it is much easier to arrange logistically.

Our program is based on some pivotal principles. First and foremost, our hospital emphasizes early donor detection across emergency, intensive care, and anesthesia departments, and fosters collaboration across these disciplines[5,6]. Training and education of the staff on donor detection and referral are considered priorities[7,8], including the systematic screening using imminent brain death criteria in patients with devastating brain injuries and the integration of organ donation in end-of-life care discussions. We ensure timely and unbiased referral of all potential deceased donors and defer the final decision on donor suitability to the coordinating transplant center.

The strategy of delayed DBD may raise considerable ethical concerns. The initial decision that the situation of the patient has become hopeless and that further curative treatment is futile must be taken without any conflict of interest and totally independent of organ donation regardless future planning[9]. Offering the opportunity of postmortem organ donation is considered as an integral part of end-of-life care and is both an ethical and professional obligation for any physician[10]. As organ donation may provide consolation to a grieving family coping with the loss of a loved one, the clinician plays an important role in informing the family about organ donation and the possibility to save other lives[11]. Once the decision on futility of care is made and a DNR code 4 is agreed, withdrawal of life sustaining therapy (WLST) is postponed allowing spontaneous evolution towards brain death in a selected group of patients that could be initially labelled as DCD III. This practice challenges several ethical principles. Firstly, postponing WLST may be perceived as an infringement on the non-maleficence principle as the patient is subject to a prolongation of a non-beneficent therapy. However, in normal life the actual act to WLST rarely follows immediately in time after the decision on futility. Commonly WLST is postponed for the relatives to accommodate with the new situation and to create time to say goodbye as long as the comfort of the dying patient can be warranted. Secondly, this practice may not collide with the principle of autonomy of the patient. According to Belgian law, patients can either refuse organ donation, passively rely on the opt-in legislation (presumed consent) or actively register as an organ donor. Refusal will always be respected, and active donor registration will be honored as much as medically possible. After active registration one may argue that the donor implicitly wants to donate as much organs as possible in the best conditions, by avoiding the harmful warm ischemia period of a classical DCD procedure. Patients who passively consented presumably remain the most difficult group as the vast majority lacks decision making capacity when WLST has been decided. One must rely on shared decision making with the legal representative. Physicians should provide support and guidance for relatives facing difficult decisions for their loved one who has sustained devastating brain injury. Communication should be clear, concise, and supportive and include simple terminology that relatives can understand. Only after obtaining full informed consent by the legal representative the procedure of delayed DBD can be started, warranting a dignified dying process. Thirdly, the use of ICU resources for this specifical goal, possibly jeopardizing chances of other patients raises questions on distributive justice. The unique instrumental value of scarce donor organs and the goal to serve as much receptors as possible are in

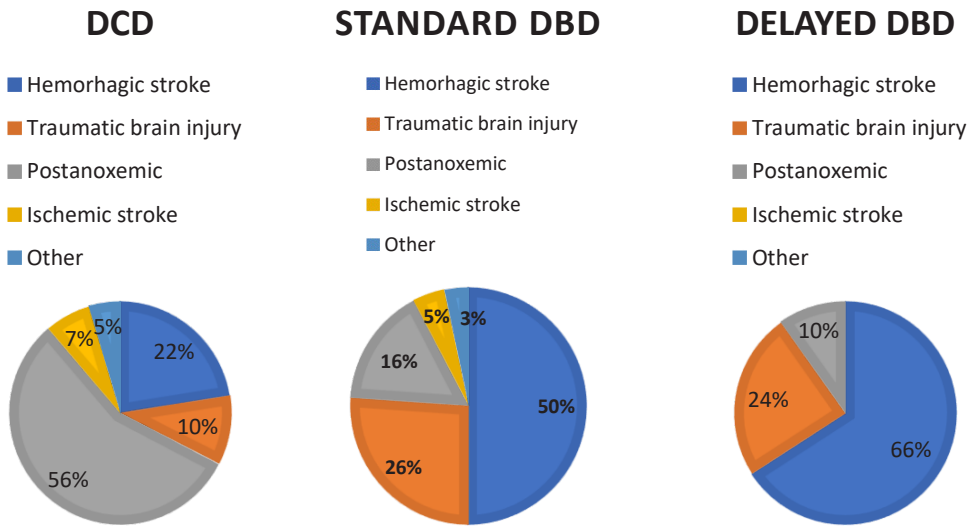

Fig. 3 — Reasons for ICU admission per type of organ donation.

keeping with the principle of utilitarianism. It has been estimated that a multi-organ donation of six organs provides 55.8 years of life to the various recipients[12]. Another method to mitigate agonal post ischemic damage in DCD donors are either in vivo or ex vivo perfusion entailing inextricable financial costs and use of critical resources. Finally, the entire ICU team should be fully and transparently informed about the goals and limits of the procedure. For this purpose, our center uses a DNR code 4 practice which serves as a clear directive for all healthcare professionals and the relatives.

As a first step towards introducing the concept of delayed donation beyond our center, we conducted an electronic survey amongst all local donor coordinators from 47 Dutch-speaking donor centers in Belgium. With a response rate of 38%, preliminary findings showed that 70% of respondents supported the delayed DBD concept, 22% were neutral, and 8% were opposed, and revealed that informing the donor's next of kin as the principal challenge. Although the survey indicates regional support for the new concept, the low response rate raises concerns about potential bias due to non-response.

Although the current results highlight the potential of DNR 4 in facilitating DBD, further studies are needed. At present, prediction of evolution towards brain death relies mainly on clinical judgement and robust predictive models could assist us in unnecessarily prolonging WLST. Future research should be directed towards the development of robust prediction models enabling precise labeling of potential delayed DBD donors. Also, further studies should investigate graft function and graft survival of organs transplanted from delayed DBD donors. In addition, one could argue that the delayed DBD pathway imposes a higher burden on the patient's family. Therefore, further research on the donor family's perspective on this delay, by comparing the number of family refusals per donor group, is needed. The financial and personnel burden of extending the total stay on the ICU should also be investigated, as well as the need for hemodynamic support in these brain-dead donors who are less hemodynamically stable compared to DCD donors.

Conclusion

The adoption of DNR 4 within a structured delayed donation framework has demonstrated its ability to enhance DBD rates ethically. This protocol preserves the integrity of donor management, respects family decisions, and ensures optimal organ recovery, contributing significantly to the organ donor pool at our center. The delayed donation pathway may reduce the need for expensive and logistically challenging DCD preservation methods such as ex situ and in situ dynamic preservation. Further research is needed to define criteria for postponing withdrawal of life-sustaining therapy, to analyze potential problems encountered during a delayed pathway such as hemodynamic instability or family opposition to donation, and to investigate the short- and long-term outcome of delayed DBD transplants.

Disclosure: The authors declare no conflict of interest.

Data availability statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Statement on ethical approval and compliance with relevant laws and institutional guidelines: All procedures were performed in compliance with relevant laws and institutional guidelines and have been approved

by the Research Ethics Committee KU Leuven, Leuven, Belgium, (jan 2023, reference MP021166). Informed consent has been obtained by relatives of the organ donors, and data have been collected and analyzed anonymously.

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References

1. Citerio G, Cypel M, Dobb GJ, Dominguez-Gil B, Frontera JA, Greer DM, et al. 2016. Organ donation in adults: a critical care perspective. Intensive Care Med. 42:305–315.
2. Domínguez-Gil B, Delmonico FL, Shaheen FAM, Matesanz R, O'Connor K, Minina M, et al. 2011. The critical pathway for deceased donation: reportable uniformity in the approach to deceased donation. Transplant International. 24:373–378.
3. Lormans P, Monbaliu D, Ferdinande P. 2020. Balancing Cost and Efficiency in Screening Potential Organ Donors With Whole Body CT. Transplant Direct. 6.
4. Scheuer SE, Jansz PC, Macdonald PS. 2021. Heart transplantation following donation after circulatory death: Expanding the donor pool. The Journal of Heart and Lung Transplantation. 40:882–889.
5. Domínguez-Gil B, Coll E, Elizalde J, Herrero JE, Pont T, Quindós B, et al. 2017. Expanding the Donor Pool Through Intensive Care to Facilitate Organ Donation: Results of a Spanish Multicenter Study. Transplantation. 101: 265–272.
6. Matesanz R, Domínguez-Gil B, Coll E, Mahíllo B, Marazuela R. 2017. How Spain Reached 40 Deceased Organ Donors per Million Population. American Journal of Transplantation. 17:1447–1454.
7. Saidi RF, Kenari SKH, Saidi RF. 2014. Challenges of Organ Shortage for Transplantation: Solutions and Opportunities. Int J Organ Transplant Med. 5:87–96.
8. De Groot YJ, Bakker J, Wijdicks EFM, Kompanje EJO. 2011. Imminent brain death and brain death are not the same: Reply to Verheijde and Rady. Intensive Care Med. 37:174.
9. Vincent A, Logan L. 2012. Consent for organ donation. Br J Anaesth. 108:80–87.
10. Domínguez-Gil B, Murphy P, Procaccio F. 2016. Ten changes that could improve organ donation in the intensive care unit. Intensive Care Med. 42:264–267.
11. Merchant SJ, Yoshida EM, Lee TK, Richardson P, Karlsbjerg KM, Cheung E. 2008. Exploring the psychological effects of deceased organ donation on the families of the organ donors. Clin Transplant. 22: 341–347.
12. Schnitzler MA, Whiting JF, Brennan DC, Lentine KL, Desai NM, Chapman W, et al. 2005. The life-years saved by a deceased organ donor. American Journal of Transplantation 5: 2289–2296.

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