

Is donation after circulatory death necessary in Brazil? If so, when?

Valter Duro Garcia¹, José Osmar Medina de Abreu Pestana², Paulo Manuel Pêgo-Fernandes³ (1)

Donation after circulatory death (DCD), previously known as donation after cardiac death or non-heart-beating donation, refers to the retrieval of organs for the purpose of transplantation from patients whose death is diagnosed and confirmed using cardiorespiratory criteria.(1)

In this issue of the Jornal Brasileiro de Pneumologia, Reck dos Santos et al.(2) present a review and update article on DCD and lung transplantation. DCD has become an accepted practice in many countries and remains a focus of intense interest in the transplant community. However, it is not a new activity and has some ethical, legal, cultural, and economic aspects that make it difficult to use in some countries.

Since the first human kidney transplant, performed in 1933 by Yurii Y Voronoy, in Kherson, Ukraine, (3) until the late 1960s, almost all of the organs transplanted using deceased donors came from non-heart-beating donors, with unfavorable results, mainly due to renal damage caused by warm ischemia but also due to other factors such as unrefined surgical technique, inadequate preservation, insufficient immunosuppression, and inexperience in postoperative management.

At that time, only Guy Alexandre, a Belgian surgeon, based on the studies by Mollaret & Goulon(4) in Paris and Wertheimer et al. (5) in Lyon published in 1959—suggesting that the irreversible failure of brain functions can be considered as death—had not only adopted a neurological criteria for determining death but also applied those criteria in performing the first organ transplant from a brain-dead donor in 1963, a procedure that many of his colleagues considered ethically unacceptable. (6)

Only after the first heart transplant in the world, performed on December 3, 1967, by Christiaan Barnard in Cape Town, using the heart of a young woman with severe traumatic brain injury after a traffic accident and declared dead by neurological criteria, (7) the report of the Ad Hoc Committee of the Harvard Medical University School⁽⁸⁾ and the Declaration of Sydney of the 22nd World Medical Assembly⁽⁹⁾ were published, both in 1968, for the determination of death based on neurological criteria. Since then, almost all transplant centers abandoned the use of non-heart-beating donors, using organs from brain-dead donors, since warm ischemia time close to zero provided better results.

In the early 1990s, it was observed that the number of potential brain-dead donors-0.5-1.0% of deaths or 45-65 per million population (pmp)—was insufficient to meet the growing demand of patients on waiting lists for organ transplantation. In addition, for the last twenty

years, there has been a decrease in the incidence of patients with brain death in many developed countries. In Spain, for example, comparing the incidence rates of brain death through audits in ICUs between 2001 and 2010 (65 pmp and 48 pmp, respectively), there was a decrease of 26%, as well as a progressive increase in the mean age, evidencing a quantitative and qualitative exhaustion of potential donors. (10) The decrease in the incidence of death diagnosed by neurological criteria and, therefore, the potential for donation after brain death (DBD), is primarily a consequence of improved road safety and improvements in neurocritical care management and in the outcomes of acute traumatic brain injury and intracranial hemorrhage. (10,11) In some countries, such as the United Kingdom, this rate has always been low (30-35 pmp), because patients with devastating brain injury are not referred to the ICU but to palliative care.

Because of the insufficient number of brain-dead donors to meet the growing demand for transplantation, studies with circulatory death donors were summarized during the First International Congress on Non-Heart-Beating Donors, held in Maastricht in 1995, and a classification system was established: I: irreversible cardiac arrest occurs before arrival at hospital; II: irreversible cardiac arrest occurs in hospital; III: programmed cardiorespiratory arrest in the ICU; and IV: cardiorespiratory arrest before, during or after brain death is confirmed.(12)

DCD is also classified as controlled or uncontrolled. Uncontrolled DCD refers to organ retrieval after cardiac arrest that is unexpected and from which the patient cannot or should not be resuscitated (Maastricht categories I, II, and IV). Controlled DCD refers to organ retrieval after an anticipated cardiac arrest that follows the planned withdrawal of life-sustaining treatments that have been considered to be of no overall benefit to a critically ill patient (Maastricht category III).(13)

As a result of better hemodynamic maintenance, in-situ cooling, rapid en bloc organ removal, pulsatile perfusion, better preservation solutions, and, more recently, the use of regional cardiopulmonary bypass, the results were similar to those obtained with DBD donors, both for the kidney and other organs, leading to a progressive increase in the number of DCD, up to the point that, in 2020, of the 35,368 donations from dead individuals reported in the global observatory on donation and transplantation, 8,061 were DCD (22.8%).(14) The contribution of DCD to overall deceased donor numbers varies internationally. Differences in medical practices, public attitudes, legislation, and resources will all influence the practice of DCD among countries.

^{1.} Serviço de Nefrologia e Transplante Renal, Santa Casa de Misericórdia de Porto Alegre, Porto Alegre (RS), Brasil.

Serviço de Nefrologia, Hospital do Rim, Universidade Federal de São Paulo, São Paulo (SP) Brasil.

^{3.} Disciplina de Cirurgia Torácica, Instituto do Coração, Hospital das Clinicas, Faculdade de Medicina, Universidade de São Paulo, São Paulo, (SP) Brasil.



Figure 1 shows the rates of DCD, in accordance with the International Registry on Organ Donation and Transplantation,⁽¹⁵⁾ which reported that 22 countries used DCD in 2020, the rates ranging from 0.07 pmp (in Japan) to 13.1 pmp (in Spain). In some countries (the UK, the Netherlands, and the USA), emphasis was placed on controlled DCD, while in others (Spain and France),⁽¹⁶⁾ the predominant type was uncontrolled DCD.

Common sense might suggest that declaring death when the heart stops beating would be more straightforward than when the declaration of death is based on brainstem functions. However, the difficulty of introducing DCD is related to ethical and legal issues and to the technical and organizational complexity inherent to this type of donation, which makes it more complex than it might appear at first glance.

Despite the endorsement of the practice of DCD by professional and regulatory bodies in many parts of the world, concerns about ethics and lawfulness of both controlled and uncontrolled DCD persist. Such concerns are related to the lawfulness and acceptability of interventions before or after death that are necessary to facilitate DCD; timing, location, and manner of treatment withdrawal; and uncertainties regarding the time point when death can be confirmed using circulatory criteria. Organ retrieval teams have mobilized for a potential DCD "stand down" on 40% of occasions, because some potential donors do not die within the first two hours after the withdrawal of life support, causing the family distress during the wait,

which is also a burden on the already hard-pressed ICU staff. $^{\left(17\right)}$

DCD is becoming increasingly accepted and has been performed in some countries, importantly contributing to the number of organs available and providing acceptable post-transplantation outcomes. (18) However, DCD should be considered as an addition to and not as a substitute for DBD, which, in addition to having simpler logistics and lower costs, has a greater use of transplanted organs per donor. Another important aspect is that, despite the large investment in DCD, its rate is around 5-6 pmp in most countries that use this form of donation, and only 4 countries have exceeded 8 pmp (Figure 1).

The most important justification for the use of DCD is the insufficient and decreasing number of DBD to meet the demand. In each country, according to its particularities, the type of DCD is defined (controlled, uncontrolled, or both), as well as which organs will be used from these donors and how legal, ethical, logistical, cultural, and financial barriers will be addressed.

In Brazil, DCD is not used for organ transplantation, with the exception of a small number of kidney transplants, using a part of the Maastricht classification system (type IV),⁽¹²⁾ that is, in those cases in which irreversible cardiac arrest occurs after brain death has been determined and family authorization has been given before the removal of the organs, while waiting for the results of laboratory tests or the arrival of the teams to remove the organs.

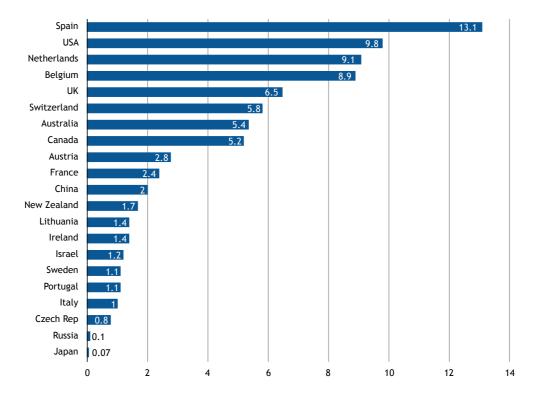


Figure 1. Rates of donation after circulatory death in various countries worldwide, as measured by donors per million population (pmp) in 2020. UK: United Kingdom.



In contrast to what is observed in developed countries, brain death rates are high and are not decreasing in Brazil. In the 1990s, it was estimated that there would be approximately 60 brain deaths pmp per year, and only a third of them (about 20 pmp) were reported as potential donors. This rate of notification of potential donors, which was 24.8 pmp in 2000, rose to 54.7 pmp in 2019, the year before the pandemic, which negatively impacted donation and transplant rates. In some Brazilian states (Paraná, Santa Catarina, and Mato Grosso do Sul), as well as in the Federal District, the annual notification rate of brain-dead cases is between 80 and 100 pmp. (19) Therefore, we currently estimate the brain death rate to be between 90 and 100 pmp in the country, which is the double that is observed in developed countries. Therefore, we can increase the notification rate of potential brain-dead donors by 50% in Brazil. In addition, the rate of effectiveness was 33% in 2019, and our goal is to reach up to 45%, which has already been the case in some states (Santa Catarina, Paraná, and Ceará). (19) On the basis of these data, we can estimate that we will reach a rate of DBD of 40 pmp (90 brain-dead individuals pmp and a 45% effectiveness rate) in 7 years.

It is necessary to improve the use of organs from brain-dead donors. Estimated rates of annual transplant demand and optimal utilization (in %) of the following organs are, respectively: kidney (70 pmp; 85%); liver (30 pmp; 80%); heart (8 pmp; 40%); and lung (8 pmp; 20%).(20) In 2019, the effective overall donor rate was 18.1 pmp—and the range of utilization was 30.1-71.0% (kidney); 10.8-55.0% (liver); 1.8-10.0% (heart); and 0.5-3.0% (lung).(20) It is believed that, in 2028, 40 donors pmp will be enough to meet the estimated need for all organs, except for the lung, if the needs remain at these levels. Therefore, although the use of DCD is an important and necessary strategy in many countries, other less complex and cheaper measures, such as DBD, will suffice in Brazil in the coming years.

AUTHOR CONTRIBUTIONS

VDG: article design, drafting, review, and approval of the final manuscript. PMPF and JM: review and approval of the final manuscript.

CONFLICT OF INTEREST

None declared.

REFERENCES

- Thuong M, Ruiz A, Evrard P, Kuiper M, Boffa C, Akhtar MZ, et al. New classification of donation after circulatory death donors definitions and terminology. Transpl Int. 2016;29(7):749-759. https:// doi.org/10.1111/tri.12776
- Reck dos Santos PA, Teixeira PJZ, Neto DMM, Cypel M. Donation after circulatory death and lung transplantation. J Bras Pneumol. 2022;48(2):e20210369. https://dx.doi.org/10.36416/1806-3756/e20210369
- Voronoy YY. Sobre el bloqueo del aparato reticuloendotelial del hombre en algunas formas de intoxicación por el sublimado y sobre la transplantación del riñón cadavérico como método de tratamiento de la anuria consecutiva a aquella intoxicación. Siglo Med. 1937,97:290-297
- MOLLARET P, GOULON M. The depassed coma (preliminary memoir) [Article in French]. Rev Neurol (Paris). 1959;101:3-15. PMID: 14423403.
- WERTHEIMER P, JOUVET M, DESCOTES J. Diagnosis of death of the nervous system in comas with respiratory arrest treated by artificial respiration [Article in French]. Presse Med. 1959;67(3):87-8. PMID: 13633814.
- Machado C. The first organ transplant from a brain-dead donor. Neurology. 2005;64(11):1938-1942. https://doi.org/10.1212/01. WNL.0000163515.09793.CB
- Hoffenberg R. Christiaan Barnard: his first transplants and their impact on concepts of death [published correction appears in BMJ 2002 Feb 23;324(7335):465]. BMJ. 2001;323(7327):1478-1480. https://doi.org/10.1136/bmj.323.7327.1478
- A definition of irreversible coma. Report of the Ad Hoc Committee of the Harvard Medical School to Examine the Definition of Brain Death. JAMA. 1968;205(6):337-340. https://doi.org/10.1001/ jama.1968.03140320031009
- Machado C, Korein J, Ferrer Y, Portela L, García Mde L, Chinchilla M, et al. The Declaration of Sydney on human death. J Med Ethics. 2007;33(12):699-703. https://doi.org/10.1136/jme.2007.020685
- Matesanz R, Domínguez-Gil B, Coll E. Uncontrolled non-heart beating donation: need, opportunity and challenge. Med Intensiva.

- 2013;37(4):221-223. https://doi.org/10.1016/j.medin.2013.01.006
- Garcia VD, Barboza AP, Dallagnese G, et al. Importância do Processo Doação - Transplante. In: Garcia CD, Pereira JD, Garcia VD, editors. Doação e Transplante de Órgãos e Tecidos. São Paulo: Segmento Pharma; 2015. p. 61-77.
- Kootstra G, Daemen JH, Oomen AP. Categories of non-heart-beating donors. Transplant Proc. 1995;27(5):2893-2894.
- D'Alessandro AM, Hoffmann RM, Knechtle SJ, Eckhoff DE, Love RB, Kalayoglu M, et al. Controlled non-heart-beating donors: a potential source of extrarenal organs. Transplant Proc. 1995;27(1):707-709.
- 14. Global Observatory on Donation and Transplantation [homepage on thee Internet]. Madrid: Organización Nacional de Trasplantes; c2016 [cited 2022 Jan 13]. Report Organ Donation and Transplantation Activities 2020. Available from: http://www.transplant-observatory. org
- International Registry on Organ Donation and Transplantation (IRODaT) [homepage on the Internet]. Barcelona: IRODaT; c2022 [cited 2022 Jan 13]. Available from: www.irodat.org
- Savoye E, Legeai C, Branchereau J, Gay S, Riou B, Gaudez F, et al. Optimal donation of kidney transplants after controlled circulatory death. Am J Transplant. 2021,21(7):2424-2436. https://doi. org/10.1111/ajt.16425 https://doi.org/10.1111/ajt.16425
- Manara AR, Murphy PG, O'Callaghan G. Donation after circulatory death. Br J Anaesth. 2012;108 Suppl 1:i108-i121. https://doi. org/10.1093/bja/aer357
- Lomero M, Gardiner D, Coll E, Haase-Kromwijk B, Procaccio F, Immer F, et al. Donation after circulatory death today: an updated overview of the European landscape. Transpl Int. 2020;33(1):76-88. https://doi.org/10.1111/tri.13506
- Associação Brasileira de Transplantes de Órgãos (ABTO) [homepage on the Internet]. São Paulo: ABTO; c2022 [cited 2022 Jan 13]. Registro Brasileiro de Transplantes. 2019; ano XXV(4). Available from: https://www.abto.org.br
- Pêgo-Fernandes PM, Pestana JOM, Garcia VD. Transplants in Brazil: where are we?. Clinics (Sao Paulo). 2019;74:e832. https://doi. org/10.6061/clinics/2019/e832