FORUM

Is Organ Donation From Brain Dead Donors Reaching an Inescapable and Desirable Nadir?

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The brain dead patient is the ideal multiorgan donor. Conversely, brain death (BD) is an undesirable outcome of critical care medicine. Conditions that can lead to the state of BD are limited. An analysis showed that a (aneurysmal) subarachnoid hemorrhage, traumatic brain injury, or intracerebral hemorrhage in 83% precede the state of BD. Because of better prevention and treatment options, we should anticipate on an inescapable and desirable decline of BD. In this article, we offer arguments for this statement and discuss alternatives to maintain a necessary level of donor organs for transplantation.

Keywords: Transplantation, Brain death, Organ donation.

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The brain dead patient is the ideal multiorgan donor for organ transplantation. Conversely, brain death (BD) is an undesirable outcome of critical care medicine and an artifact of nature that results from the ability of medical technology to prolong and distort the process of dying. Conditions that can lead to the state of BD are limited. An analysis of 71 published series of brain dead patients (n=6317) showed that a (aneurysmal) subarachnoid hemorrhage (SAH), traumatic brain injury (TBI), or spontaneous intracerebral hemorrhage (ICH) in 83% precede the state of BD; SAH is the most common BD-associated condition (*1*). These findings concur with earlier reports regarding the causes of BD (*2–5*). BD is a rare outcome of critical care medicine. Among 4248 patients who died in 1999 to 2000 in European intensive care units, only 330 (7.8%, regional differences between 3.2% [Northern Europe] and 12.4% [Southern Europe]) deaths have been diagnosed as brain dead (*6*). BD can be observed exclusively in intensive care units that have policies and facilities to admit and treat patients with SAH, TBI, and ICH. BD is susceptible to changes and differences in its causes and in the location and time of its occurrence. Progress in the prevention and treatment of these conditions that lead to BD can result in a decline in the actual number of brain dead patients in the coming few decades in almost all industrialized countries in the Western world. In The Netherlands, the number of donation after brain death (DBD) declined from 915 patients in the period 1995 to 1999 to 637 patients in period 2005 to 2009 (30%; Table 1) according to the annual reports of the Dutch Transplant Foundation (available at http://transplantatiestichting.nl/cms/index.php?page=jaarverslagen). However, the number of donation after cardiac death (DCD) increased from 118 patients in first period to 453 patients in the period of 2005 to 2009 (282%). This is in line with the study of Saidi et al. (*7*).

The result of this ongoing process can be a further widening gap between the number of donors and the number of recipients. Furthermore, the diminishing role of DBD will have great ramifications for transplantation medicine as a whole. In this article, we will place this in a future perspective. We also mention some possible opportunities, within acceptable legal and ethical frameworks, to maintain a necessary level of organ donors.

SAH is the most common condition that precedes BD. An SAH accounts for approximately 1% to 7% of all cerebral strokes. The incidence is approximately 6 to 7 per 100,000 person-years (*8*). Women are at a 1.6 times higher risk of SAH than men (*9*). When untreated, an SAH is a life-threatening condition. The case fatality in population-based studies is approximately 50% but have tended to show declining trends in the incidence and case fatality after SAH during the past 3 decades (*10*, *11*). A recent population-based study from the United Kingdom showed that mortality because of SAH decreased by approximately 50% during the past 2 decades; this reduction is mainly due to improved outcome in cases that surviving until arrival at hospital. This improvement was consistent with a significant decrease in case fatality during the past 25 years in a pooled analysis of 31 population-based studies, which reflects the improvements in the management of SAH (*12*). Endovascular coiling for the treatment of intracranial aneurysms was introduced in 1990. Hospital use of coiling has increased during recent years. The International

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TABLE 1. Comparing effectuated DCD and DBD in different eras in The Netherlands over the past 15 yr

	Era 1 (1995–1999)	Era 2 (2000–2004)	Era 3 (2005–2009)	P^a
No. of donors	1033	1042	1090	0.695
DBD (% of total number of donors)	915 (88.6)	697 (66.9)	637 (58.4)	0.008
DCD (% of total number of donors)	118 (11.4)	345 (33.1)	453 (41.6)	<0.0001

[a] *P* value from one-way analysis of variance with post hoc Tukey for comparison of multiple groups. $P<0.05$ was considered significant.

DBD, donation after brain death; DCD, donation after cardiac death.

Subarachnoid Aneurysm Trial demonstrated that coiling was associated with a reduction in the risk of death and dependency at 1 year after SAH (*13*). Elective coiling of unruptured intracranial aneurysms and calcium-channel blocker greatly improved outcome (*14–16*).

SAH and ICH have two common risk factors: cigarette smoking and untreated hypertension (*17*, *18*). Cigarette smoking is an independent risk factor not only for SAH but also for aneurysm formation (*19*, *20*). In population-based or cohort studies, 70% to 75% of patients with SAH have a history of smoking, and 50% to 60% are current smokers (*21*). Regarding the prevention of SAH and ICH, recent studies that examined the impact of antismoking legislation showed that crude rates of admission to hospital because of cardiovascular conditions, including stroke, decreased almost 40% during the ban period that affected restaurant settings; this reinforces the value of smoking bans to public health (*22*). Smoking plays a critical role in aneurysm development, especially in younger patients, but physiological mechanisms exist for the repair of the damage that is induced by this toxic insult if cessation is possible (*19*).

The pharmacologic treatment of high blood pressure reduces the risk of stroke, including SAH and ICH, which has been confirmed in a large number of randomized controlled trials. Effective delivery of hypertension care in the community requires a rigorous approach in terms of identification, follow-up, and treatment, which could lead to a notable reduction in the incidence of SAH and ICH. Countries with effective delivery of hypertension care show a lower incidence of SAH than other countries (*23*). Therefore, cessation of smoking and treatment of hypertension are the most effective prevention measures for SAH and ICH.

Road traffic accidents (RTAs) causing TBI, the second major cause of BD, account for more than 60% of the patients, who become brain dead after TBI (*3*). Much societal and political effort is aimed at RTA prevention (*24*). Although the total number of road traffic deaths will increase in the coming decade worldwide, it is declining in most European industrialized countries and in the United States, which reflects effective prevention measures (*25*, *26*). In the United States, in 2009, RTA fatalities were the lowest on record since 1954 (*25*). In 16 European countries, fatalities of vehicle occupant have declined between 1970 and 1999 by 19% to 62%. Pedestrian deaths show an even more significant decline of up to 95% (*26*). Belgium is often mentioned as being successful in providing a high number of organ donors; however, BD as a result of TBI declined from 69% to 39% between the period 1991 to 1992 and 2006 to 2007 in 26 hospitals in Belgium (*27*). In 2009, the absolute number of organ donors was the lowest since 1996, which was linked to the decline in RTAs by the Belgium lay press. RTA-associated deaths have declined in Belgium by 36% in the past decade. In addition to Belgium, Spain is commonly cited as an example of good practice as demonstrated by having the world's highest rate of organ donation. However, this successful Spanish model is likely to be challenged as the number of RTAs has decreased in the past decade. Spain also adopted one of the strictest smoking bans of Europe, which became effective January 2011, which could challenge DBD in Spain and could therefore be reaching a nadir (*28*). The decline of RTAs is also observed in many other European countries. In 2006, the United Kingdom reported one of the lowest numbers of RTA deaths in the European Union: 5.4 of 100,000. In 1967, there were 199 casualties per 100 million vehicle kilometers. By 2007, this declined to 48 per 100 million vehicle kilometers.

The ongoing efforts in the prevention of SAH and ICH that result from effective smoking bans and effective delivery of hypertension control and progress in the endovascular treatment of cerebral aneurysms and improvements in road traffic safety in Western industrialized countries can eventually lead to an inescapable and desirable decline in BD as an outcome of neurocritical care. This can have a dramatic effect on the availability of organs, especially hearts, for transplantation. It is clear that no physician or policymakers wants to intervene in this process of prevention and treatment of these causes with the sole reason to increase the number of brain dead organ donors. For this reason, we should anticipate the further decline in the availability of brain dead donor donors and investigate other possible sources as living kidney/liver donors and cardiac death donors, and we may have to consider possible alternatives beyond the more accepted sources.

Currently, donation of hearts is only possible, respecting the "dead donor rule," from brain dead donors. Boucek et al. reported donation of hearts obtained from hopelessly ill infants who were pronounced death according to cardiopulmonary criteria after withdrawal of mechanical ventilation. They transplanted the hearts of two infants after an observation period of less than 2 min after they were declared death (*29*). A review confirmed heart transplantation in a pediatric setting after DCD in several hospitals in the United States (*30*). Although this form of donation may be a new source of hearts, there are serious ethical and conceptual questions surrounding this practice (*31–35*). Extreme solutions as neuro-euthanasia and euthanasia by surgical heart removal as suggested by Wilkinson and Savulescu (*36*) face many ethical, practical, and societal concerns. In addition to the actual decline of potential organ donors, we are also confronted with a high family refusal rate. Improvement in communication skills proved to be beneficial in raising the consent rate (*37*).

The lungs and lung lobes can be obtained from DCD donors, DBD donors, and living donors (*38*). However, living lung lobe transplantation raised many practical and ethical concerns and is therefore not widely accepted. In recent report from the University of Wisconsin concerning the long-term outcomes for all lung transplant recipients who received lungs from DCD donors showed that graft survival rates were equivalent of those who received lungs from DBD donors (*39*). Some new lung protective strategies are proposed in brain dead patients to prevent deterioration during the time between the declaration of BD and transplantation suitability. A recently published study showed an increase in the number of eligible and harvested lungs compared with conventional ventilation strategies (*40*). Optimal identification and management of controlled DCD could increase the number of donors with 10% (*41*). A combination of improved care of the potential organ donors and further improvement of the supply of DCD donors could limit the gap between the numbers of donors and recipients.

The kidneys and livers could be obtained from DCD donors, DBD donors, and living-related or -unrelated organ donation. With the possible decline of BD as a outcome of critical care medicine, we need to further investigate DCD and more importantly living organ donation, which can be seen as the cornerstone of kidney transplantation worldwide. Many incentives have been proposed to remove the barriers for living donors. Because of the concerns of possible exploitation of uninformed and poor donors, the World Health Organization reaffirmed recently their statement "to the principles of human dignity and solidarity which condemn buying of human body parts for transplantation and exploitation of the poorest and most vulnerable populations and the human trafficking that result from such practices" (*42*). Davis (*43*) proposes the removal of hurdles such as the lack of funding to cover the lost of wage, travel, and living expenses for potential living organ donors.

The means proposed in this article to improve living kidney and liver donation in addition to the aforementioned are community-specific campaigns, expanding research on the long-term risk of living organ donation and teach patients to tell their stories to the community. DCD, the other major source of kidneys and livers, remains a topic of investigation. Recent studies concerning the long-term graft survival of kidney and liver transplants showed and equivalent survival compared with organs obtained from DBD donors (*44*, *45*).

The transplant community should anticipate on a possible decline of brain dead patients because of better prevention and treatment of the causes leading to BD. This decline is desirable and inescapable. Concerning the decline of hearts eligible for transplantation, there is no alternative source without violating the dead donor rule. For obtaining the lungs, kidneys, and livers, there is still potential for further improvement. Better and timely identification and care of the potential organ donor (*46*) and removal of the hurdles of living organ donation will offer us some time to further investigate more challenging alternative sources that may force us to shift our moral and ethical boundaries (*32*, *36*).

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