



## ORIGINAL

# End-of-life practices in patients with devastating brain injury in Spain: Implications for organ donation <sup>☆</sup>



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Brain death;  
Critical care;  
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Organ transplantation;  
Tissue and organ procurement;  
Ventilation

### Abstract

**Objective:** To describe end-of-life care practices relevant to organ donation in patients with devastating brain injury in Spain.

**Design:** A multicenter prospective study of a retrospective cohort. Period: 1 November 2014 to 30 April 2015.

**Setting:** Sixty-eight hospitals authorized for organ procurement.

**Patients:** Patients dying from devastating brain injury (possible donors). Age: 1 month-85 years.

**Primary endpoints:** Type of care, donation after brain death, donation after circulatory death, intubation/ventilation, referral to the donor coordinator.

**Results:** A total of 1970 possible donors were identified, of which half received active treatment in an Intensive Care Unit (ICU) until brain death (27%), cardiac arrest (5%) or the withdrawal of life-sustaining therapy (19%). Of the rest, 10% were admitted to the ICU to facilitate organ donation, while 39% were not admitted to the ICU.

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<sup>◇</sup> Further information on the components of the Consorcio ACCORD-España is available in an annex.

Of those patients who evolved to a brain death condition (n = 695), most transitioned to actual donation (n = 446; 64%). Of those who died following the withdrawal of life-sustaining therapy (n = 537), 45 (8%) were converted into actual donation after circulatory death donors. The lack of a dedicated donation after circulatory death program was the main reason for non-donation.

Thirty-seven percent of the possible donors were not intubated/ventilated at death, mainly because the professional in charge did not consider donation after discarding therapeutic intubation.

Thirty-six percent of the possible donors were never referred to the donor coordinator.

**Conclusions:** Although deceased donation is optimized in Spain, there are still opportunities for improvement in the identification of possible donors outside the ICU and in the consideration of donation after circulatory death in patients who die following the withdrawal of life-sustaining therapy.

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## PALABRAS CLAVE

Daño cerebral  
catastrófico;  
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urgencias;  
Muerte encefálica;  
Trasplante de  
órganos;  
Unidades de Cuidados  
Intensivos;  
Ventilación

## Prácticas clínicas al final de la vida en pacientes con daño cerebral catastrófico en España: implicaciones para la donación de órganos

### Resumen

**Objetivo:** Describir las prácticas clínicas al final de la vida relevantes para la donación de órganos en pacientes con daño cerebral catastrófico en España.

**Diseño:** Estudio multicéntrico prospectivo de una cohorte retrospectiva. Periodo: 1 de noviembre de 2014 al 30 de abril de 2015.

**Ámbito:** Sesenta y ocho hospitales autorizados para donación.

**Pacientes:** Pacientes fallecidos por daño cerebral catastrófico (posibles donantes). Edad: 1 mes-85 años.

**Variables de interés principales:** Cuidado recibido, donación en muerte encefálica, donación en asistolia controlada, intubación/ventilación, notificación al coordinador de trasplantes.

**Resultados:** Se identificaron 1.970 posibles donantes. La mitad recibió tratamiento activo en una Unidad de Críticos (UC) hasta evolucionar a muerte encefálica (27%), sufrir una parada cardiorrespiratoria (5%), o hasta la limitación de tratamiento de soporte vital (19%). Del resto, un 10% ingresó en una UC para facilitar la donación y el 39% nunca ingresó en una UC.

De los pacientes que evolucionaron a muerte encefálica (n = 695), la mayoría derivaron en una donación eficaz (n = 446; 64%). De los pacientes fallecidos tras limitación de tratamiento de soporte vital (n = 537), 45 (8%) se convirtieron en donantes en asistolia eficaces. La ausencia de un programa de donación en asistolia controlada fue el motivo más frecuente de no donación.

El 37% de los posibles donantes falleció sin intubar/ventilar, fundamentalmente porque el profesional responsable no consideró la donación tras descartar intubación terapéutica.

El 36% de los posibles donantes no fue notificado al coordinador de trasplantes.

**Conclusiones:** Aunque el proceso de donación está optimizado en España, existen oportunidades para la mejora en la detección de posibles donantes fuera de UC y en la consideración de la donación en asistolia controlada en pacientes fallecidos tras limitación de tratamiento de soporte vital.

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## Introduction

Organ donation has reached extraordinary levels in Spain, with sustained rates of 32–36 donors per million inhabitants in recent years.<sup>1</sup> These results are the consequence of a highly effective system capable of identifying donation opportunities and of transforming possible donors into effective donors. The system is centered on the transplant coordinator (TC) and on close cooperation between the TC and the professionals in the Intensive Care Unit (ICU).<sup>2</sup>

However, the need to continue progressing with the aim of achieving self-sufficiency in transplantation<sup>3,4</sup> is confronted by a gradual decrease in the incidence of brain death (BD) in this country.<sup>5</sup> On the other hand, we are witnessing substantial changes in end-of-life care, including the consideration of limitation or withdrawal of life-sustaining treatment (WLST) once a situation of therapeutic futility has been reached.<sup>6</sup>

The development of new strategies capable of increasing organ availability requires very precise knowledge of the

donation process. Such knowledge must also refer to the initial phases, including clinical decision making by the professionals attending patients with devastating brain injury in the end-of-life stage, since such decisions serve to either maintain or discard the donation options. This information is essential in order to identify possibilities for improvement from a dual perspective: that of the transplant coordination system, which must adapt its activity to the new circumstances; and that of the critical care professionals, who must integrate donation options with end-of-life care in variable clinical scenarios.<sup>3</sup>

*ACCORD-España*,<sup>7</sup> an extension of the ACCORD joint initiative,<sup>8</sup> is a project led by the Spanish National Organization of Transplants (NOT) with the support of the Transplants Commission of the Inter-territorial Health Council. The project aims to determine the relevant end-of-life clinical practices referred to organ donation in patients with devastating brain injury in Spain, and to offer hospitals tools for change. The present article focuses on the description of these practices and on the opportunities for improvement in the donation process identified at national level.

## Patients and methods

A prospective multicenter study of a retrospective cohort was carried out.

The hospitals authorized for organ harvesting in Spain through their corresponding Autonomous and Hospital Coordination of Transplant Systems were invited to participate in the study. The hospitals that were interested reported their participation to the National Organization of Transplants and assigned a professional belonging to Hospital Coordination of Transplants as the person in charge of the study. Specific approval was obtained from the management board of each center, with a positive opinion from the Clinical Research Ethics Committee or Reference Committee.

## Terminology

- *Possible donor*: a patient who has died as a consequence of devastating brain injury.
- *Potential brain dead donor*: a patient who has died in a clinical situation consistent with BD, in the absence of medical contraindications to organ donation.
- *Potential non-heart beating donor*: a patient who has died following WLST, in the absence of medical contraindications to organ donation and aged under 70 years – this usually being taken as the age limit for controlled non-heart beating donation (CNHBD).<sup>9</sup>
- *Effective donor*: a patient who has died and has been subjected to surgical incision with the purpose of harvesting organs for transplantation.
- *Non-therapeutic elective ventilation (VENT)*: the start of mechanical ventilation with the purpose of facilitating organ donation.

## Inclusion criteria for possible donors

We included all possible donors aged between one month and 85 years (both included) that died in any Unit of the

hospital during the period between 1 November 2014 and 30 April 2015.

The identification of possible donors was based on a review at least twice a week of the diagnoses of those patients that died in the hospital. The list of diagnoses according to the International Classification of Diseases—Tenth Edition (ICD-10) most frequently related to serious brain damage allowed the retrospective assessment of thoroughness in the exclusion of cases.<sup>7,10</sup> After identification of the possible donors on the basis of these diagnoses, the professional in charge of the study in each center reviewed the patient case history to discard alternative causes of death that would lead to exclusion of the case and to collect the necessary information for the study. Where required, the information available in the case history was contrasted with the team in charge of patient management.

## Variables and data collection

An ad hoc questionnaire was designed to compile information referred to the clinical and demographic characteristics of the possible donors and the clinical decisions made during end-of-life care, particularly:

- The scenario that best described the care received: A: active treatment in an ICU until the patient evolved to BD, independently of whether this diagnosis was subsequently confirmed or not; B: active treatment in an ICU until the patient suffered unexpected cardiac arrest (CA) without recovery; C: admission to an ICU with the purpose of incorporation the option of donation to end-of-life care; D: active treatment in an ICU until WLST was decided, with ulterior CA; E: no admission to an ICU.
- Whether the patient was intubated and subjected to mechanical ventilation at the time of death or when WLST was decided.
- Whether the situation evolved toward a clinical condition consistent with BD.
- Whether a diagnosis of BD was made and confirmed.
- Whether CNHBD was considered in the event WLST was decided.
- Whether the possible donor was reported to the TC.
- Whether the possibility of donation was commented with the family.
- Whether surgical incision was made with the purpose of harvesting organs for transplantation (effective donation).

Information was collected on the main reason for each decision discarding the option of donation and on the professionals that participated in the decisions in each phase of the process.

## Statistical analysis

A descriptive analysis (absolute numbers and percentages) was made. A study was made of the relationship between different factors and the intubation/ventilation of possible donors, the reporting of such possible donors to the TC, and the obtainment of consent for donation. The chi-squared

**Table 1** Demographic and clinical characteristics of the possible donors.

n = 1970	n	%
<b>Age</b>		
<18 years	28	1.4
18–59 years	472	23.9
60–69 years	371	18.8
70–79 years	618	31.4
≥80 years	481	24.4
<b>Sex</b>		
Male	1112	56.4
<b>Main cause of death (ICD-10)</b>		
Stroke	1257	63.8
Trauma	290	14.7
Other brain damage	299	15.2
Central nervous system infection	42	2.1
Brain tumor	78	4.0
Other	4	0.2
<b>Time of devastating brain injury</b>		
Before hospital admission	1634	83.0
During hospital stay	336	17.0
<b>Time from devastating brain injury to death</b>		
0 days	326	16.5
1 day	460	23.4
2 days	268	13.6
3 days	181	9.2
4 to 9 days	496	25.1
≥10 days	241	12.2
Absolute or relative medical contraindications to donation	640	32.5

test (with Fisher test correction where required) was used. A binary logistic regression model was developed to analyze the independent relationship between each of the variables and the outcomes referred to intubation/ventilation, reporting to the TC, and consent, respectively. Those

variables found to exhibit a statistically significant relationship ( $p < 0.05$ ) in the univariate analysis were entered in each of the constructed models. The SPSS version 15.0 statistical package was used throughout.

## Results

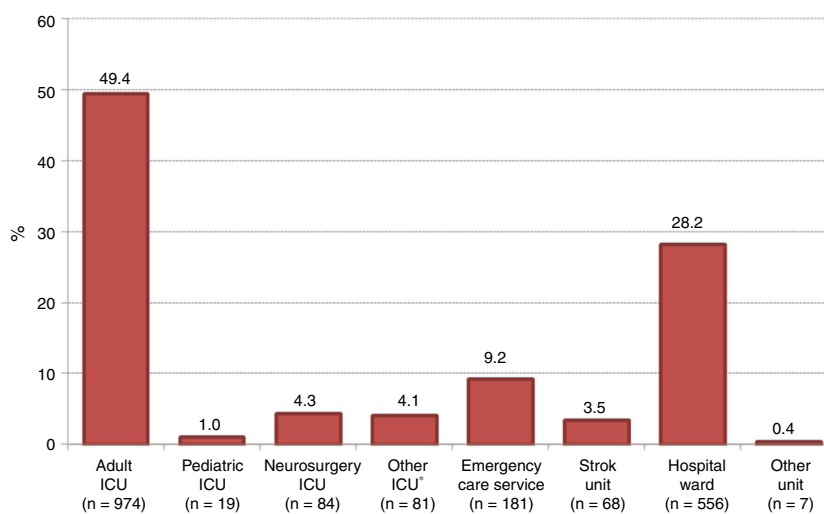
A total of 68 of the 189 hospitals authorized for organ harvesting (36%) participated in the study. These centers contributed 66% of the effective donors in Spain during the year 2013. Of the participating hospitals (all public centers), 38 (56%) had a Department of Neurosurgery, and 25 (37%) performed some type of organ transplantation. This hospital distribution is similar to that recorded for the global hospitals authorized for organ harvesting in Spain.

### Demographic and clinical data of the possible donors

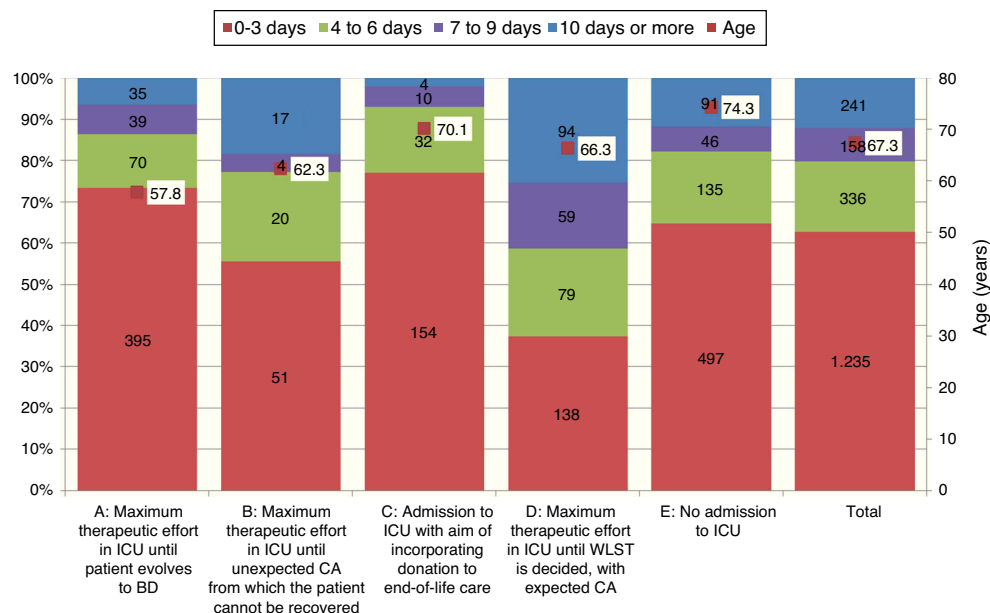
During the study period, we identified 1970 possible donors that met the specified inclusion criteria. Their characteristics are shown in Table 1. In relation to the cause of death, intracranial hemorrhage (161), stroke (163), postanoxic encephalopathy (G931) and diffuse brain injury (S062) accounted for the death of 70% of the possible donors.

Although devastating brain injury was the reason for admission to hospital in most cases, 17% of the patients developed devastating brain injury during admission to hospital. The time elapsed from brain damage to death was  $\leq 3$  days in 63% of the patients. In one-third of the cases, it was considered that there were absolute or relative medical contraindications to donation—the most frequent being current or past antecedents of malignant disease (49%), vascular disease and multi-disease processes (21%) and sepsis or active infectious diseases (11%).

Fig. 1 shows the Units in which the possible donors died. A total of 41% were seen to have died outside an ICU—fundamentally in a hospital ward.



**Figure 1** Units where death of the possible donors took place. ICU: Intensive Care Unit. \*Resuscitation unit and coronary unit.



**Figure 2** Age (mean) and distribution (n and percentage) of days from devastating brain injury to death; overall and according to scenario. BD: brain death; WLST: withdrawal of life-sustaining treatment; CA: cardiac arrest; ICU: Intensive Care Unit.

### Scenario best describing end-of-life care

The distribution of possible donors according to the scenario is detailed below:

- A (active treatment in ICU until BD): 539 (27%)
- B (active treatment in ICU until unexpected CA): 92 (5%)
- C (admission to ICU for donation): 200 (10%)
- D (active treatment in ICU until WLST decision): 370 (19%)
- E (no admission to ICU): 769 (39%)

The characteristics of the possible donors varied according to the scenario involved. Fig. 2 shows these variations for age and time from brain damage to death.

### Dead brain donation process

Fig. 3 shows the distribution of the patients that evolved to BD. Of the 695 patients that reached this clinical situation, 569 (29% of the possible donors and 82% of the patients in BD) had no medical contraindications to organ donation, and thus represented the potential sample for dead brain donation.

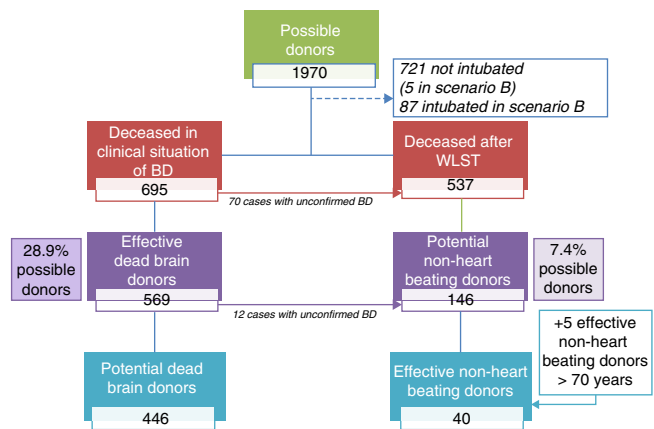
The reasons why dead brain patients did not progress to effective donation were medical contraindication (41%) followed by family refusal (36%), the impossibility of confirming the diagnosis of BD (9%), CA or hemodynamic instability (6%) and other reasons (8%).

A total of 446 possible donors resulted in effective donation under conditions of BD (23% of the total possible donors and 64% of the cases in BD).

### Controlled non-heart beating donation process

As can be seen in Fig. 3, 537 patients died after WLST, which included terminal extubation in 58% of the cases. Of these

possible donors, only 146 had no medical contraindications and were under 70 years of age—representing the potential sample for CNHBD (7% of the possible donors and 27% of those who died after WLST).



**Figure 3** Graphic representation of the transition from possible donors to potential and effective donors, under conditions of brain death and controlled asystole. Possible donor: death secondary to devastating brain injury. Potential brain dead donor: death in clinical situation consistent with BD and without absolute or relative medical contraindications to organ donation. Potential non-heart beating donor: death following WLST, without absolute or relative medical contraindications to organ donation, and aged under 70 years. Effective donor: death with surgical incision made for organ harvesting for transplantation. Scenario B: includes possible donors actively treated in an Intensive Care Unit until unexpected cardiac arrest occurs from which the patient cannot be recovered. WLST: withdrawal of life-sustaining treatment; BD: brain death.



The possibility of CNHBD was not considered in 79% of the patients who died after WLST—the main reason being the lack of a program of this kind in the corresponding hospital.

Of the 115 cases in which CNHBD was indeed considered after WLST, the main reasons for non-progression to effective donation were medical contraindication (60%), family refusal (13%) and other reasons (27%). None of these cases involved death occurring beyond the time considered compatible with CNHBD once the procedure had been activated.

Lastly, 45 possible donors resulted in effective CNHBD (2% of the possible donors and 8% of those who died after WLST).

### Intubation and ventilation

Of the 1970 possible donors, 721 (37%) were not intubated/ventilated at the time of death or when the decision of WLST was made. In over one-half of the cases, the reason for non-intubation/ventilation was that the professional in charge of the patient did not consider the possibility of non-therapeutic elective ventilation (VENT) after making the decision to not intubate/ventilate with curative intent. In contrast, of those patients who were indeed intubated/ventilated at the time of death, the purpose of intubation/ventilation was considered to be the facilitation of organ donation (VENT) in 14% of the cases.

Several factors corresponding to the hospital and possible donor were identified referred to the intubation/ventilation of possible donors (Table 2). Of the potentially modifiable factors, the availability of WLST protocols in the hospital was independently correlated to a greater probability of mechanical ventilation (OR 1.78 [1.31–2.43];  $p < 0.001$ ). On the other hand, the probability of intubation/ventilation was greater when the decision depended on the intensivists or out-hospital care professionals, compared with professionals of other areas or specialties.

### Reporting of possible donors to the transplant coordinator

Thirty-six percent of the possible donors were not reported to the TC at any time during their evolutive course. In over one-half of the cases the reason for not notifying the TC was failure by the supervising physician to identify the patient as a possible organ donor, followed in order of frequency by the existence of medical contraindications to donation.

The study of the factors related to notification of possible donors to the TC (Table 3) showed the existence of written notification criteria in the hospital to significantly increase the probability of notification (OR 1.46 [1.07–1.99];  $p = 0.017$ ). The probability of notifying the TC also increased significantly when the notification of a possible donor depended upon Intensive Care Medicine, Anesthesia or Cardiology versus other specialties or disciplines.

### Interviewing of the family for donation

No interviewing of the family to explain about organ donation was carried out in 61% of the total possible donors. The

main reason for not interviewing the family was the existence of medical contraindications to donation, though in 21% of the cases the reason was failure by the supervising physician to identify the patient as a possible organ donor.

Consent to organ donation was obtained in 76% of the 765 family interviews carried out. Participation of the TC in the family interview significantly increased the probability of obtaining consent (OR 1.86 [1.37–2.52];  $p < 0.001$ ) (Table 4). The probability was also seen to be greater when the interview took place after notifying the patient to the TC. Although statistical significance was not reached in the multivariate model, differences were observed in the obtainment of consent according to the timing of the family interview. In this sense, consent was greater when the interview took place with the patient in BD, or when BD was expected to occur within the ICU, compared with the rest of the clinical situations.

### Admission to an Intensive Care Unit for donation intent

Two hundred patients were admitted to intensive care for intended organ donation (scenario C). Of these patients, 150 (75%) evolved toward BD and 113 became effective dead brain donors. The main reasons why the remaining 37 patients did not progress to effective donation were medical contraindication (46%) followed by family refusal (35%), non-confirmation of the diagnosis of BD (5%), and other reasons (14%).

Of the 55 patients admitted to intensive care for intended organ donation and which did not evolve toward BD or in which the diagnosis of BD was not confirmed, 11 (20) were considered for CNHBD, and 7 (64%) became effective non-heart beating donors.

Admission to the ICU for donation (either BD or CNHBD) contributed 24% of the effective donations during the study period (120 of the 491 effective donations).

The possibilities for improving donation via admission to intensive care were illustrated by the analysis of the possible donors not admitted to the ICU (scenario E). In over one-half of the 769 patients, the possibility of admission to intensive care for incorporating organ donation to end-of-life care was not considered. Specifically, 342 patients without medical contraindications for donation were never reported to the TC. Most of these patients were not intubated/ventilated at the time of death.

### Discussion

To our knowledge, this is the first study to offer a detailed evaluation of the decision-making process in end-of-life care from the organ donation perspective in Spain.

In concordance with the profile of the effective brain dead donors in this country, a high percentage of possible donors are very elderly ( $\geq 80$  years). This reflects the increasingly imperative need to use organs from elderly donors—a practice that has already been implanted in Spain, with adequate post-transplantation outcomes.<sup>11–14</sup>

The study shows that the donation process in cases of BD is optimized in this country from the moment in which the patient suffers BD, and thus in the different phases of the

**Table 2** Univariate and multivariate analysis of the factors related to intubation/ventilation of possible donors.

	n	% intubated/ventilated possible donors	Univariate analysis	Multivariate analysis	
			p	OR [CI]	p
<i>Number of beds in adult ICU</i>					
<30	803	55.4%	<0.001	Ref.	0.562
≥30	1167	68.9%		1.12 [0.76–1.66]	
<i>Neurosurgery</i>					
Yes	1470	68.9%	<0.001	1.47 [1.01–2.3]	0.043
No	500	47.2%		Ref.	
<i>Transplant</i>					
Yes	1249	72.3%	<0.001	2.00 [1.41–2.82]	<0.001
No	988	54.6%		Ref.	
<i>WLST protocols</i>					
Yes	1318	67.1%	<0.001	1.78 [1.31–2.43]	<0.001
No/not known	652	55.8%		Ref.	
<i>Age of possible donor</i>					
<60 years	500	85.4%	<0.001	3.37 [2.21–5.15]	<0.001
≥60 years	1470	55.9%		Ref.	
<i>Cause of death of possible donor</i>					
Stroke	1.257	56.2%	<0.001	Ref.	<0.001
Trauma	290	72.4%		1.58 [1.03–2.41]	<0.001
Other brain damage	303	87.8%		5.07 [2.97–8.64]	<0.001
CNS infection	42	81%		9.59 [3.30–27.99]	0.795
Brain tumor	78	42.3%		1.11 [0.49–2.51]	
<i>Contraindications to donation</i>					
Yes	640	51.4%	<0.001	0.35 [0.26–0.47]	<0.001
No	1330	69.2%		Ref.	
<i>Patient referred to neurosurgery</i>					
Yes	925	70.9%	<0.001	1.76 [1.28–2.41]	<0.001
No/not known	1045	56.7%		Ref.	
<i>Specialty/working area of the main professional in intubation/ventilation decision</i>					
Critical care medicine <sup>a</sup>	878	82%	<0.001	Ref.	<0.001
Out-hospital medicine	263	98.9%		17.91 [5.58–57.57]	<0.001
Emergency care medicine	319	55.8%		0.29 [0.21–0.40]	<0.001
Neurology/Neurosurgery	275	5.5%		0.01 [0.05–0.02]	<0.001
Other specialty	132	11.4%		0.03 [0.02–0.07]	

WLST: withdrawal of life-sustaining treatment; Ref.: reference; CNS: central nervous system; ICU: Intensive Care Unit.

<sup>a</sup> Includes Anesthesia, Cardiology and Intensive Care Medicine.

process that take place in an ICU. These Units are the great strength of our system.<sup>2,15</sup>

Despite the above, the study has identified opportunities for improvement that are evidenced in the description of the end-of-life care scenarios: 40% of the possible donors never enter the ICU (scenario E)—often without admission for possible organ donation having been considered. On the other hand, almost 20% of the possible donors die following WLST (scenario D). Only recently has donation under these circumstances of death become possible in our country.

The possibilities for donation among patients who currently die outside an ICU require some consideration

referred to the notification of possible donors to the TC, admission to intensive care for donation and VENT, derived from this study.

Routine and early notification (before death occurs) of possible donors to the TC is considered good practice at international level.<sup>16–18</sup> However, 36% of the possible donors in Spain are not notified to the TC at any time during their evolution—mainly because the professionals in charge do not identify the patient as a possible donor, or because they consider that there are contraindications—without having discussed them with the TC. In Spain, it is recommended that the professionals attending neurocritical

**Table 3** Univariate and multivariate analysis of factors related to the notification of possible donors to the transplant coordinator.

	n	% possible donors notified to the TC	Univariate analysis <i>p</i>	Multivariate analysis	
				OR [CI]	<i>p</i>
<i>Neurosurgery</i>					
Yes	1.470	66.8%	<0.001	0.70 [0.48–0.1.01]	0.056
No	500	52.6%		Ref.	
<i>Transplantation</i>					
Yes	982	70.8%	<0.001	1.86 [1.35–2.56]	<0.001
No	988	55.7%		Ref.	
<i>WLST protocols</i>					
Yes	1.318	67.4%	<0.001	1.30 [0.96–1.75]	0.091
No/not known	652	54.8%		Ref.	
<i>Written criteria for notification to TC</i>					
Yes	1.408	65.6%	<0.001	1.46 [1.07–1.99]	0.017
No/not known	562	57.1%		Ref.	
<i>Age of the possible donor</i>					
<60 years	500	82.2%	<0.001	2.36 [1.63–3.43]	
≥60 years	1.470	56.7%		Ref.	<0.001
<i>Cause of death of the possible donor</i>					
Stroke	1.257	61.3%	<0.001	Ref.	<0.001
Trauma	290	64.8%		0.49 [0.33–0.73]	<0.001
Other brain damage	303	75.6%		0.82 [0.53–1.27]	0.374
CNS infection	42	69%		0.89 [0.37–2.16]	0.126
Brain tumor	78	35.9%		0.22 [0.11–0.52]	<0.001
<i>Contraindications to donation</i>					
Yes	640	53.8%	<0.001	0.58 [0.45–0.79]	<0.001
No	1.330	67.7%		Ref.	
<i>Patient referred to Neurosurgery</i>					
Yes	1.249	85.8%	<0.001	1.86 [1.37–2.52]	<0.001
No/not known	721	24.0%		Ref.	
<i>Specialty/working area of the main professional deciding notification to TC</i>					
Critical care medicine <sup>a</sup>	1.091	86.7%	<0.001	Ref.	<0.001
Emergency care medicine	201	46.3%		0.15 [0.10–0.21]	<0.001
Neurology/neurosurgery	275	22.5%		0.04 [0.03–0.06]	<0.001
Other specialty	127	9.4%		0.02 [0.01–0.05]	<0.001

TC: transplant coordinator; WLST: withdrawal of life-sustaining treatment; Ref.: reference; CNS: central nervous system.

<sup>a</sup> Includes Anesthesia, Cardiology and Intensive Care Medicine.

patients should systematically consider the option of donation when brain damage is devastating and any ulterior treatment is regarded as futile.<sup>19</sup> This consideration requires a training effort targeted particularly to the professionals of Units outside the intensive care setting, since these are professionals who, according to the results of our study, generated fewer notifications to the TC. On the other hand, we also observed that the existence of written notification criteria increased the probability of notification by 46%. In establishing these criteria, it is essential to emphasize the need to discuss apparent contraindications with the TC, since the absolute contraindications to organ donation are currently very limited. In fact, external audits of Spanish

hospitals have found that the existence of contraindications was established inadequately in over 10% of the potential donors not notified due to medical reasons.<sup>5</sup>

If the notification of possible donors were to be systematically implemented from Units outside the intensive care setting, it would be necessary to consider a policy of admission to the ICU for donation and VENT. Our study shows that this strategy could very significantly increase the opportunities for donation. Non-therapeutic elective ventilation (VENT) is warranted by our ethical-legal and deontological guidelines.<sup>20</sup> At international level, it is also increasingly accepted that health professionals must work in the best interest of the patient—such interest



**Table 4** Univariate and multivariate analysis of factors related to the obtainment of consent to donation.

	n	% family interviews with consent	Univariate analysis	Multivariate analysis	
			p	OR [CI]	p
<b>Number of adult ICU beds</b>					
<30	262	180 (68.7%)	<0.001	1.78 [1.23–2.57]	0.002
≥30	491	394 (80.2%)		Ref.	
<b>Neurosurgery</b>					
Yes	593	465 (78.4%)	0.007	0.86 [0.50–1.49]	0.595
No	160	109 (68.1%)		Ref.	
<b>Transplantation</b>					
Yes	444	356 (80.2%)	0.002	1.17 [0.73–1.89]	0.511
No	309	218 (70.6%)		Ref.	
<b>Cause of death of the possible donor</b>					
			0.015	–	0.286
Stroke	497	361 (72.6%)			
Trauma	115	96 (83.5%)			
Other brain damage	118	96 (81.4%)			
CNS infection	11	11 (100%)			
Brain tumor	12	10 (83.3%)			
<b>Protocolized training of professionals participating in the interview<sup>a</sup></b>					
Yes	719	554 (77.1%)	<0.001	–	–
No/not known	13	3 (23.1%)			
<b>Time of interview</b>					
			<0.001		<0.001
After notifying TC	611	475 (77.7%)		Ref.	0.001
Before notifying TC	94	54 (57.4%)		0.42 [0.24–0.70]	0.024
The family asked	42	41 (97.6%)		10.18 [1.36–76.41]	
<b>Time of interview</b>					
			0.001		0.062
On deciding WLST	93	58 (62.4%)		Ref.	
Before intubation/ventilation	79	55 (69.6%)		1.74 [0.88–3.45]	0.116
Intubated before BD-outside ICU	56	39 (69.6%)		1.43 [0.66–3.13]	0.366
Intubated but before BD-within ICU	93	75 (80.6%)		2.23 [1.08–4.58]	0.029
BD but prior to confirmation	108	92 (85.2%)		2.95 [1.45–5.98]	0.003
After confirmation of BD	317	250 (78.9%)		1.77 [1.04–3.03]	0.037
<b>Participation of the TC in the interview</b>					
Yes	511	180 (68.7%)	<0.001	1.86 [1.37–2.52]	<0.001
No	219	394 (80.2%)		Ref.	

TC: transplant coordinator; WLST: withdrawal of life-sustaining treatment; Ref.: reference; CNS: central nervous system. Includes refusal expressed by family or by patient while alive.

<sup>a</sup> Multivariate analysis not included, due to few non-trained professionals participating in the interview.

being understood not only from the clinical perspective but also as a holistic concept including the beliefs and moral values of the person.<sup>21–23</sup> If the patient wished to serve as a donor, raising the option of donation and facilitating it should be viewed as an ethical imperative and a standard of professional practice. In this context, and without breaching the principle of nonmaleficence, the current international literature is mostly favorable to VENT,<sup>24–29</sup> and several countries now describe this practice.<sup>8</sup>

Our experience shows that admission to intensive care for donation and VENT has become a reality in Spain<sup>30,31</sup> and makes a key contribution to donation activity—making it possible to underscore the challenges that face this practice:

- Although the time to death is under three days in most of the possible donors admitted to the ICU for donation (scenario C), one out of every four patients does not evolve toward BD. It is therefore crucial to ensure strict selection of those cases with a high probability of evolution to BD and to introduce WLST protocols—this being a factor independently correlated to the intubation/ventilation of possible donors. In some cases, and following patient admission to the ICU, contraindications to donation are established that were not previously detected. It is important to inform the family about this possibility.
- Communication with the family to consider admission to the ICU for donation and VENT is complex, with a lesser probability of obtaining consent than when the interview is made with the patient already admitted to intensive

care. The participation of the TC in these interviews is therefore particularly important, and has been identified as an independent predictor of increased probability of consent.

- Lastly, and despite the policy of maximum transparency, it is not always possible to conduct an interview prior to admission because of the emotional situation of the family, the absence of relatives with decision making capacity or the clinical severity of the patient at risk of immediate respiratory arrest.

In consideration of all the above, admission to the ICU for donation and VENT requires institutional support, training of the professionals attending neurocritical patients and of the TCs, as well as protocols for intervention and for informing the families.

Lastly, our study corroborates the existence of sup-optimized CNHBD in Spain<sup>32</sup>: in effect, CNHBD is not considered in 79% of the patients that die following WLST (most with terminal extubation), mainly due to the lack of the required program in the hospital involved. Although CNHBD has increased exponentially in recent years,<sup>33</sup> the introduction of new programs seems to be necessary. It is also essential for this type of donation not to have a negative impact upon dead brain donation—an issue that remains a source of concern at international level.<sup>34,35</sup> The fact that in our series the time elapsed from brain damage to death was longer in the WLST setting (scenario D) than in other scenarios probably reflects the current practice of waiting some time due to the possibility of evolution toward BD before suspending life support measures that have already become futile. On the other hand, as experience is progressively gained with CNHBD in Spain, it will become necessary to reconsider the maximum age of the potential donors—currently defined in most centers as 65–70 years.<sup>36</sup>

The present study has several limitations. Those in charge of data collection belonged to Hospital Coordination of Transplants, and in many aspects conducted a review of their own activities—a fact that may have exerted some influence upon data recruitment. On the other hand, we did not collect information on non-deceased patients with devastating brain injury—a fact that limits some aspects of understanding of the donation process. Lastly, although data collection was conducted on a prospective basis, it was inevitably fundamented upon a retrospective cohort, which required interpretation by the study supervisor of the information contained in the case history—though due contrasting and completion was attempted with the team in charge of the patient.

In conclusion, dead brain donation has been optimized in our system once the patients have evolved to BD. Admission to the ICU for donation and VENT is an established practice contributing 24% of all the effective donations. The opportunities for improvement are represented by the introduction of a systematic policy of possible donor notification to the TC, together with an expanded practice of admission to the ICU in order to facilitate organ donation. Lastly, CNHBD is confirmed to be a great opportunity for ensuring that donation forms an integral part of end-of-life care, independently of the circumstances of death of our patients.

## Authorship/collaborators

BDG, EC, TP, ML, EM and RM conceived of and designed the study, and participated in the interpretation of the data. BDG and EC performed the data analysis. All the authors participated in the preparation of the article, its critical review and in definitive approval of the manuscript version submitted for publication. The authors of the hospital centers represented in the study participated in the identification of possible donors and facilitated acquisition of the data required for the study.

## Conflicts of interest

The authors declare that they have no conflicts of interest.

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## Annex. Supplementary data

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