

RESEARCH

Open Access



Brain death and postmortem organ donation: report of a questionnaire from the CENTER-TBI study

Ernest van Veen^{1,2,3}, Mathieu van der Jagt¹, Maryse C. Clossen², Andrew I. R. Maas⁴, Inez D. de Beaufort³, David K. Menon⁵, Giuseppe Citerio^{6,7}, Nino Stocchetti^{8,9}, Wim J. R. Rietdijk¹, Jeroen T. J. M. van Dijk¹⁰, Erwin J. O. Kompanje^{1,3*} and CENTER-TBI investigators and participants

Abstract

Background: We aimed to investigate the extent of the agreement on practices around brain death and postmortem organ donation.

Methods: Investigators from 67 Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI) study centers completed several questionnaires (response rate: 99%).

Results: Regarding practices around brain death, we found agreement on the clinical evaluation (prerequisites and neurological assessment) for brain death determination (BDD) in 100% of the centers. However, ancillary tests were required for BDD in 64% of the centers. BDD for nondonor patients was deemed mandatory in 18% of the centers before withdrawing life-sustaining measures (LSM). Also, practices around postmortem organ donation varied. Organ donation after circulatory arrest was forbidden in 45% of the centers. When withdrawal of LSM was contemplated, in 67% of centers the patients with a ventricular drain in situ had this removed, either sometimes or all of the time.

Conclusions: This study showed both agreement and some regional differences regarding practices around brain death and postmortem organ donation. We hope our results help quantify and understand potential differences, and provide impetus for current dialogs toward further harmonization of practices around brain death and postmortem organ donation.

Keywords: Traumatic brain injury, Brain death, Ethics, Postmortem organ donation, Withdrawing life-sustaining measures, Ventricular drainage

Background

Before the 1950s, death was only determined using cardiovascular criteria. Due to advances in critical care medicine, especially mechanical ventilation, a new clinical state was observed in 1958 (i.e., “coma dépassé”) [1]. Although the systemic circulation was intact, the brain showed no objective evidence of function. This observation gave rise to the question of what “coma

dépassé” meant. The successful transplantation of kidneys from a “coma dépassé” patient (1965) subsequently led to the first accepted standard for the confirmation of brain death in 1968 [2]. In 1981, the Uniform Determination of Death Act made death determined by neurological and cardiovascular criteria equivalent [3]. The American Academy of Neurology (AAN) in 1995 published guidelines for brain death determination (BDD) [4], and updated these in 2010 [5]. In 2008, the Academy of Medical Royal Colleges in the United Kingdom (UK) provided broader guidance on the determination of death in a range of circumstances, including BDD [6].

Brain death and postmortem organ donation are closely linked. Also, an important, and not well investigated, issue

* Correspondence: e.j.kompanje@erasmusmc.nl

¹Department of Intensive Care, Erasmus University Medical Center, Rotterdam, the Netherlands

³Department of Medical Ethics and Philosophy of Medicine, Erasmus University Medical Center, Rotterdam, the Netherlands

Full list of author information is available at the end of the article



regarding circulatory arrest organ donation is the hands-off time after circulatory arrest. Practices around all of these mentioned topics are delicate. Thus, inconsistencies between centers can be confusing for the general public, and could expose clinicians to accusations of unethical practice. Consensus regarding practices around brain death and postmortem organ donation could prevent these inconsistencies. To facilitate this consensus, the first step is to document potential differences.

The Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI, www.center-tbi.eu) study addressed this issue. The CENTER-TBI study used questionnaires to create “provider profiles” of participating neurotrauma centers. One of these questionnaires intended to address specific practices around brain death and postmortem organ donation that currently provoke international discussion. Using this questionnaire, we aimed to quantify and understand potential differences, and provide impetus for current dialogs toward further harmonization of practices around brain death and postmortem organ donation. Regarding brain death, we investigated: criteria used for BDD; and the necessity of BDD before withdrawing life-sustaining measures (LSM). As for postmortem organ donation, we investigated: removal of the ventricular drain while continuing other LSM; the possibility for circulatory arrest organ donation; and the hands-off time after circulatory arrest.

Methods

CENTER-TBI and study sample

The CENTER-TBI study includes a prospective observational study on traumatic brain injury (TBI) [7, 8]. The investigators connected to this study collect data on patient characteristics, management, and outcomes in important centers from 20 countries across Europe and Israel. Investigators from all participating centers in the CENTER-TBI study were asked to complete several questionnaires. Centers were located in Austria ($N=2$), Belgium ($N=4$), Bosnia and Herzegovina ($N=2$), Denmark ($N=2$), Finland ($N=2$), France ($N=7$), Germany ($N=4$), Hungary ($N=2$), Israel ($N=2$), Italy ($N=8$), Latvia ($N=3$), Lithuania ($N=2$), the Netherlands ($N=7$), Norway ($N=3$), Romania ($N=1$), Serbia ($N=1$), Spain ($N=4$), Sweden ($N=2$), Switzerland ($N=1$), and the UK ($N=8$).

Questionnaire development and administration

More detailed information about the development, administration, and content of the questionnaires is available from an earlier publication by Cnossen et al. [9].

The topics covered in the current study are summarized in Table 1. A complete overview of the questionnaires for this study can be found in Additional file 1:

Questionnaire 1 (questions 1, 4, 8, and 9), 7 (questions 2 and 4), and 8 (questions 9 and 11–15). In the questionnaires, we explicitly asked for the “general policy” according to the investigators. We defined this as the local standards used in more than 75% of patients, recognizing that there might be exceptions. Most questions made use of categorical answer categories. For some questions, the investigators had the option to fill in an answer that could be different from one of the options provided. These answers were marked as “other” and consisted of free text responses. Where these free text responses from different investigators were sufficiently similar, we sought to combine them to provide additional categorical responses. We did this to facilitate summary descriptive statistics.

Analyses

We used descriptive statistics to describe our outcomes. We calculated frequencies and percentages for all variables related to the number of responses for that question. Centers at which the investigator did not respond to every question remained in our study, in order to keep groups for descriptive statistics as large as possible. The response rates per question are presented in Table 1. We grouped countries into seven regions: Baltic States (Latvia and Lithuania), Eastern Europe (Bosnia and Herzegovina, Hungary, Romania, and Serbia), Israel, Northern Europe (Denmark, Finland, Norway, and Sweden), Southern Europe (Italy and Spain), the United Kingdom, and Western Europe (Austria, Belgium, France, Germany, the Netherlands, and Switzerland). We examined potential differences between and within regions.

Results

Center characteristics

Of the 68 centers, investigators from 67 centers participated in the questionnaires (response rate: 99%) and were included in the analysis. The participating centers were mainly academic centers ($N=61$, 91%), designated as a level I or II trauma center ($N=49$, 73%). The average number of beds in the participating centers was 1187, of which on average 39 were intensive care unit (ICU) beds. The average number of annual treatments per ICU in 2013 was 1408, of which on average 130 were TBI patients.

Practices around brain death

When do you declare a patient brain dead?

We found agreement on the clinical evaluation (prerequisites and neurological assessment) for BDD in 100% of the centers. The clinical evaluation for BDD included: a Glasgow Coma Scale (GCS) of three, absence of brain stem reflexes, no respiratory efforts in response to an apnea test, and absence of confounding factors to

Table 1 Topics covered, related questions for each topic, and response rate per question

Topics covered in this study	Questions related to this topic	Response rate, N (%)
Practices around brain death		
Criteria for BDD	When do you declare a patient brain dead?	67 (99%)
Brain death and withdrawal of LSM	Must the patient, who is not suitable for organ donation, be declared brain dead before withdrawing life-sustaining measures?	67 (99%)
Practices around postmortem organ donation		
Donation after circulatory death	Would you consider organ donation after circulatory arrest in a patient in whom mechanical ventilation will be withdrawn, but who is not brain dead?	66 (97%)
Ventricular drain removal and organ donation	If the decision is made to withdraw life-sustaining measures, in a patient with high intracranial pressure, but who is not brain dead, would you remove the ventricular drain (for CSF drainage), but continue other life-sustaining measures in the hope that the patient will become brain dead and thereby becomes a suitable candidate for organ donation?	67 (99%)
Declaration of death and hands-off time in donors and nondonors	After withdrawal of mechanical ventilation and after circulatory arrest, when exactly do you declare the patient dead in case of a circulatory death organ donor?	64 (94%)
	After withdrawal of mechanical ventilation and after circulatory arrest, after how many minutes circulatory arrest do you declare the patient dead in cases not suitable as organ donor?	66 (97%)

BDD brain death determination, *CSF* cerebrospinal fluid, *LSM* life-sustaining measures

evaluate consciousness (e.g., hypothermia). However, ancillary tests were required for BDD in 43 (64%) centers (Table 2).

In three regions (43%; Israel, Southern Europe, and the UK), the same criteria for BDD were used in every center of the same region. In centers from Northern Europe and the UK, ancillary tests were rarely used for BDD ($N = 2$, 22% and $N = 0$, 0%, respectively).

Must the patient, who is not suitable for organ donation, be declared brain dead before withdrawing LSM?

The declaration of brain death in nondonor patients was mandatory before withdrawing LSM in 12 (18%) centers. In 41 (61%) centers, a poor prognosis as assessed by the treating physician(s) was considered sufficient. In 9 (13%) centers, a GCS score of three, fixed dilated pupils, and absence of confounders could motivate withdrawing LSM (Table 2).

Table 2 Practices around brain death

Answer	Region							
	Sample total (N = 67)	Baltic States (N = 5)	Eastern Europe (N = 6)	Israel (N = 2)	Northern Europe (N = 9)	Southern Europe (N = 12)	United Kingdom (N = 8)	Western Europe (N = 25)
When do you declare a patient brain dead?								
With GCS 3, fixed dilated pupils, and no confounding factors (e.g., hypothermia, barbiturates)	0	0	0	0	0	0	0	0
With GCS 3 and absent brain stem reflexes, and no confounding factors	0	0	0	0	0	0	0	0
With GCS 3, absent brain stem reflexes and apnea, and no confounding factors	31	20	17	0	78	0	88	20
With GCS 3, absent brain stem reflexes, apnea and ancillary test(s) (e.g., EEG or cerebral angiography), and absence of confounding factors	64	80	83	100	22	100	0	72
Per national protocol ^a	4	0	0	0	0	0	13	8
Must the patient, who is not suitable for organ donation, be declared brain dead before withdrawing LSM?								
No, the prospect of a very poor prognosis can be enough	61	0	17	0	78	42	100	80
No, GCS 3 and fixed dilated pupils and no confounders is enough to stop treatment	13	0	0	50	22	8	0	20
Yes, this is mandatory by law in my country	18	80	17	50	0	50	0	0
Yes, it is not mandatory by law, but I always do that to be sure	7	20	67	0	0	0	0	0

Data presented as percentage

EEG electroencephalography, GCS Glasgow Coma Scale, LSM life-sustaining measures

^aAdditional categorical responses, while free text responses were sufficiently similar. This does not mean that the other centers do not follow their national protocol

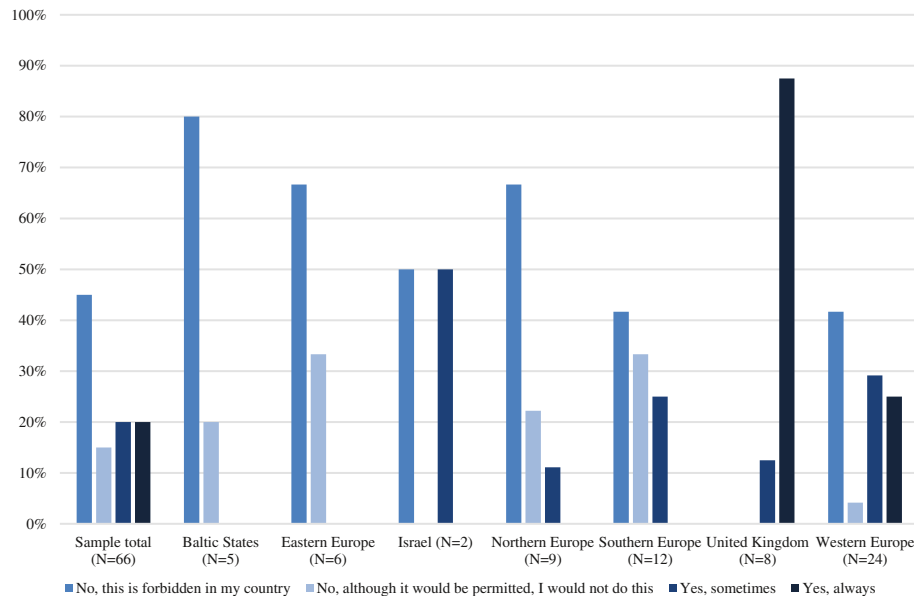


Fig. 1 Results of question 13 (Questionnaire 8): Would you consider organ donation after circulatory arrest in a patient in whom mechanical ventilation will be withdrawn, but who is not brain dead?

In all centers in the Baltic States ($N = 5$), nondonor patients were declared brain dead before withdrawing LSM. In several centers in Eastern Europe and Southern Europe ($N = 1$, 17% and $N = 6$, 50%, respectively), it was mandatory to declare a patient brain dead before withdrawing LSM in nondonor patients, whereas in other centers from the same region this was not mandatory.

Practices around postmortem organ donation
Would you consider organ donation after circulatory arrest in a patient in whom mechanical ventilation will be withdrawn, but who is not brain dead?

Organ donation after circulatory arrest was forbidden in 30 (45%) centers (Fig. 1 and Table 3).

In all centers in the UK ($N = 8$), postmortem organ donation after circulatory arrest was approved. In centers

Table 3 Practices around circulatory arrest organ donation and ventricular drain removal

Answer	Region							
	Sample total (N = 66)	Baltic States (N = 5)	Eastern Europe (N = 6)	Israel (N = 2)	Northern Europe (N = 9)	Southern Europe (N = 12)	United Kingdom (N = 8)	Western Europe (N = 24)
Would you consider organ donation after circulatory arrest in a patient in whom mechanical ventilation will be withdrawn, but who is not brain dead?								
No, this is forbidden in my country	45	80	67	50	67	42	0	42
No, although it would be permitted, I would not do this	15	20	33	0	22	33	0	4
Yes, sometimes	20	0	0	50	11	25	13	29
Yes, always	20	0	0	0	0	0	88	25
	Sample total (N = 67)	Baltic States (N = 5)	Eastern Europe (N = 6)	Israel (N = 2)	Northern Europe (N = 9)	Southern Europe (N = 12)	United Kingdom (N = 8)	Western Europe (N = 25)

If the decision is made to withdraw life-sustaining measures, in a patient with high intracranial pressure, but who is not brain dead, would you remove the ventricular drain (for CSF drainage), but continue other life-sustaining measures in the hope that the patient will become brain dead and then becomes a suitable candidate for organ donation?

No, never	33	80	33	0	0	17	88	28
Yes, sometimes	51	20	50	100	100	50	13	48
Yes, always	16	0	17	0	0	33	0	24

Data presented as percentage
 CSF cerebrospinal fluid

in the Baltic States, Eastern Europe, and Northern Europe, organ donation after circulatory arrest was often forbidden ($N = 4$, 80%; $N = 4$, 67% and $N = 6$, 67% respectively).

If the decision is made to withdraw life-sustaining measures, in a patient with high intracranial pressure, but who is not brain dead, would you remove the ventricular drain (for CSF drainage), but continue other life-sustaining measures in the hope that the patient will become brain dead and thereby becomes a suitable candidate for organ donation?

In 45 (67%) centers, the ventricular drain was sometimes or always removed. In 11 of these 45 centers (16% of the Sample total), the ventricular drain was always removed while continuing other LSM. In 22 (33%) centers, the ventricular drain was never removed while continuing other LSM (Fig. 2 and Table 3).

In 4 (80%) centers in the Baltic States and in 7 (88%) centers in the UK, the ventricular drain was never removed. In all centers from Israel ($N = 2$) and Northern Europe ($N = 9$), the ventricular drain was “sometimes” removed.

After withdrawal of mechanical ventilation and after circulatory arrest, when exactly do you declare the patient dead in case of a circulatory death organ donor, and in cases not suitable as an organ donor?

In the case of a circulatory death organ donor, it was most common ($N = 15$, 23%) to declare the patient dead after 5-min “flatliner-ECG”. In cases not suitable as an organ donor, it was most common ($N = 21$, 32%) to declare the

patient dead directly after detection of a “flatliner-ECG” on the monitor (Table 4).

In all centers in Israel, nondonor patients were declared dead directly after detection of a “flatliner-ECG” on the monitor. No other region had the same answer in every center concerning the declaration of death in donor and nondonor patients.

Discussion

We aimed to investigate specific practices that currently provoke international discussion in the area of brain death and postmortem organ donation. We aimed to quantify and understand potential differences, and provide impetus for current dialogs toward further harmonization of practices around brain death and postmortem organ donation.

Taking all results together, we found agreement on the clinical evaluation (prerequisites and neurological assessment) for brain death determination (BDD) across regions. In addition to this clinical evaluation, ancillary tests were required for BDD in 64% of the centers. BDD was deemed mandatory before withdrawal of life-sustaining measures (LSM) even outside the context of organ donation in 18% of the centers. As for practices around postmortem organ donation across regions, in 67% of the centers a ventricular drain was sometimes or always removed while other LSM were continued. Last, in 45% of the centers organ donation after circulatory arrest was forbidden.

We found important agreement and some differences regarding practices around brain death. Due to the broad

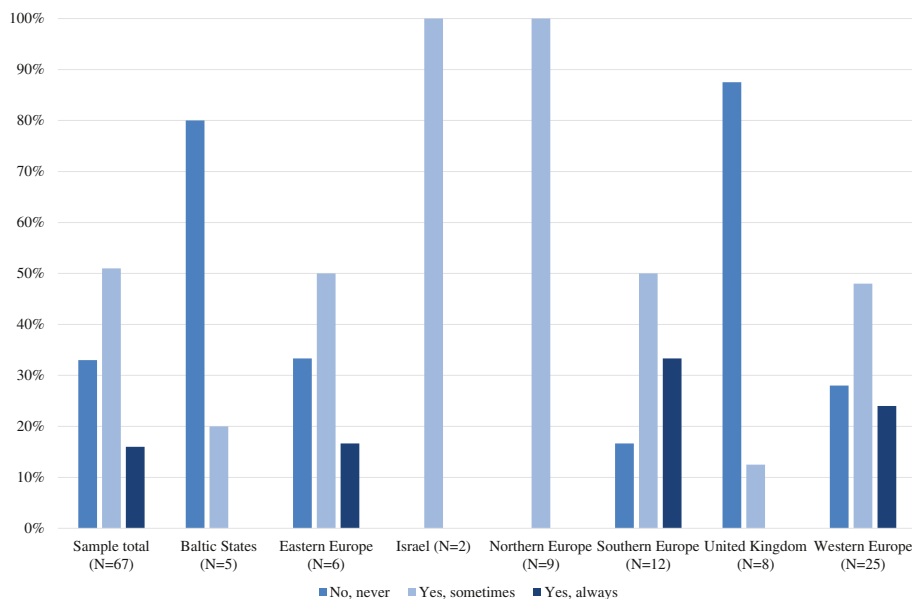


Fig. 2 Results of question 9 (Questionnaire 8): If the decision is made to withdraw life-sustaining measures, in a patient with high intracranial pressure, but who is not brain dead, would you remove the ventricular drain (for CSF drainage), but continue other life-sustaining measures in the hope that the patient will become brain dead and thereby becomes a suitable candidate for organ donation?

Table 4 Practices around the hands-off time after circulatory arrest

Answer	Region							
	Sample total (N = 64)	Baltic States (N = 5)	Eastern Europe (N = 6)	Israel (N = 2)	Northern Europe (N = 9)	Southern Europe (N = 12)	United Kingdom (N = 8)	Western Europe (N = 22)
After withdrawal of mechanical ventilation and after circulatory arrest, when exactly do you declare the patient dead in case of a circulatory death organ donor?								
Directly after circulatory arrest determined after a "flatliner-ECG" on the monitor	16	40	0	50	11	8	0	23
After 1-min "flatliner-ECG" indicating circulatory arrest	5	0	0	50	0	8	0	5
After 2-min "flatliner-ECG"	2	0	0	0	0	0	0	5
After 5-min "flatliner-ECG"	23	20	33	0	11	17	50	23
After 10-min "flatliner-ECG"	5	20	17	0	0	0	0	5
After loss of pulsatile arterial curve on the invasive arterial blood pressure tracing	6	20	17	0	0	0	0	9
After 20-min "flatliner-ECG" ^a	11	0	0	0	0	58	0	0
Not done in our hospital/country ^a	19	0	17	0	78	0	0	18
Other, please specify ^b	14	0	17	0	0	8	50	14
	Sample total (N = 66)	Baltic States (N = 5)	Eastern Europe (N = 6)	Israel (N = 2)	Northern Europe (N = 9)	Southern Europe (N = 12)	United Kingdom (N = 8)	Western Europe (N = 24)
After withdrawal of mechanical ventilation and after circulatory arrest, after how many minutes circulatory arrest do you declare the patient dead in cases not suitable as organ donor?								
Directly after circulatory arrest determined after a "flatliner-ECG" on the monitor	32	40	17	100	11	17	13	50
After 1-min "flatliner-ECG" indicating circulatory arrest	5	0	0	0	0	0	0	13
After 2-min "flatliner-ECG"	0	0	0	0	0	0	0	0
After 5-min "flatliner-ECG"	23	20	17	0	22	25	38	21
After 10-min "flatliner-ECG"	6	20	33	0	0		0	0
After loss of pulsatile arterial curve on the invasive arterial blood pressure tracing	6	20	33	0	11	0	0	0
After 20-min "flatliner-ECG" ^a	9	0	0	0	0	50	0	0
Not done in our hospital/country ^a	8	0	0	0	33	0	0	8
Other, please specify ^c	12	0	0	0	22	0	50	8

Data presented as percentage

EEG electroencephalography

^aAdditional categorical responses, while free text responses were sufficiently similar

^bSpecifications filled in under "other": "two minutes after loss of pulsatile arterial curve on the invasive arterial blood pressure tracing"; "after 3 min"; "No carotid pulses and apnoea"; "absence central pulse for 5 mins confirmed by observation for further 5 mins"; "National guidance 5 mins mechanical asystole"; "apnea test positivity"; "according to the Dutch law on organ donation"; "Protokollbogen zur Feststellung des irreversiblen Hirnfunktionsausfalls"; "at the beginning of the commission observation (6 h before)"

^cSpecifications filled in under "other": "Control 10 min later"; "After clinical death diagnosis: listen to heart sound, examination of pupils"; "At decision of the physician"; "No carotid pulses and apnoea"; "absence central pulse for 5 mins confirmed by observation for further 5 mins"; "apnea test positivity"; "according to the Dutch law on organ donation"; "Protokollbogen zur Feststellung des irreversiblen Hirnfunktionsausfalls"; "at the beginning of the commission observation (6 h before)"

categorical answer possibilities provided, the application of these findings is limited. First, agreement existed in all centers on the clinical evaluation for BDD, namely a Glasgow Coma Scale (GCS) of three, absence of brain stem reflexes, no respiratory efforts in response to an apnea test, and absence of confounding factors to evaluate consciousness. This is promising, in the light of recent calls to reach a worldwide consensus on how to determine brain death [10]. However, in addition to this clinical evaluation, ancillary tests were reported to be required for BDD in two

thirds of centers. These differences in the use of ancillary tests are in line with previous literature [11–19]. Interestingly, however, there have been calls to abandon ancillary tests for BDD [20]. In the majority of centers from Northern Europe and the United Kingdom (UK), ancillary tests were not mandatory for BDD. This is in line with the study by Wahlster et al. [11]. These discrepancies may suggest differences in ethical principles and regulatory practice between centers. In some centers it was mandatory to declare nondonor patients brain dead before

withdrawing life-sustaining measures (LSM). Withdrawal of LSM and the declaration of brain death are two different processes. The obligation of BDD before limiting treatment is debatable, since many non-brain dead patients may have a hopeless prognosis rendering further treatment futile.

We also found differences regarding practices around postmortem organ donation. First, we found differences concerning the removal of the ventricular drain. Our questionnaire did not assess in-depth the reasons why some centers opted to discontinue drainage and remove the ventricular drain as compared to maintaining the device in place, and how such continued intervention was incorporated into the care plan. Second, we found differences with regard to the possibility for organ donation after circulatory arrest. These results are in line with previous literature [21, 22]. The ventricular drain (mentioned earlier in this paragraph) seemed to be removed more often in centers where donation after circulatory arrest was not possible. If this turns out to be general practice, this might indicate the need for reevaluation of organ donation after circulatory arrest in order to prevent future burdensome care. For international figures on donation and transplantation, we refer the reader to the Newsletter Transplant 2017 produced by the Council of Europe of the European Committee [23]. There are no specific figures available for the centers involved in the Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI) study. Although the CENTER-TBI study includes important neurotrauma centers, we do not know to what extent these centers are responsible for the investigated figures of the Council of Europe. For the countries involved in our study, the number of donations after brain death in 2016 varied between 1.3 per million inhabitants (Bosnia and Herzegovina) and 33.1 per million inhabitants (Spain) [23]. Third, we found differences in hands-off times needed after circulatory arrest in order to declare a patient dead. This could indicate a lack of clear evidence on the exact time needed to be sure the brain has irreversibly lost its function.

Some of the differences appear region specific, but for other aspects we found variation between centers within a single region. Differences were even noted between regions participating in Eurotransplant, an organization that aims to optimally distribute organs by transplanting across national borders, when no matching recipient is available on the waiting list in the donor's country. Eurotransplant covers part of Europe, and includes eight countries: Austria, Belgium, Croatia, Germany, Hungary, the Netherlands, Luxembourg, and Slovenia. The differences found pertained to all topics covered in this study.

Present-day medicine is said to be affected by the cultural climate of the society in which it exists [24].

This may indicate that differences in culture could explain some of the observed variation. Other results, such as possibilities for organ donation after circulatory arrest, suggest that variations have a more legal or regulatory basis. Observed within-region differences which suggest a more legal or regulatory basis raise questions regarding the level of enforcement of pertinent laws, and may indicate a lack of knowledge, regulatory implementation, or ambiguous legislation.

This study has several limitations that should be considered when interpreting the results. First, the participating neurotrauma centers represent a select group. The data obtained may therefore not be representative for all neurotrauma centers within the geographical areas studied. Second, our sample size made it difficult to apply more advanced statistics, such as a chi-square test, cluster analysis, and multidimensional scaling. Third, the results are based on the perceptions of practices reported by specific investigators rather than on clinical data. The CENTER-TBI study will further clarify actual practices around brain death and postmortem organ donation by analyzing clinical data. Fourth, investigators may have interpreted some questions incorrectly because a questionnaire does not always permit the nuances appropriate for clinical practice. In clinical practice, potential alternative options are both more numerous and complex than can be captured by a questionnaire. Last, investigators may have presented (even unwittingly) a more favorable image or presented individual preferences instead of the general policy in a center that we asked for.

Future research should focus on extending this study to a larger group of neurotrauma centers across the world in order to examine (in more advanced statistics) whether our results also apply to other centers. Furthermore, it would be interesting to study the origin of the differences found (e.g., cultural differences and differences pertaining to legislation). The complexity of some of the drivers of reported practice makes the case for mixed methods approaches to this problem, with a potentially substantive role for qualitative research methods. These strategies are important in order to inform preferred approaches to improve harmonization in neurotrauma centers across Europe and Israel.

Most importantly, current dialogs should be continued, and we hope that our findings may provide a basis toward further harmonization of practices around brain death and postmortem organ donation.

Conclusion

This study showed both agreement and some regional differences regarding practices around brain death and postmortem organ donation. We hope our results help quantify and understand potential differences, and

provide impetus for current dialogs toward further harmonization of practices around brain death and post-mortem organ donation.

Additional file

Additional file 1: Provider profiling questionnaires used for this study (Questionnaires 1, 7, and 8). (PDF 596 kb)

Abbreviations

AAN: American Academy of Neurology; BDD: Brain death determination; CENTER-TBI: Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury; CSF: Cerebrospinal fluid; ECG: Electrocardiography; GCS: Glasgow Coma Scale; ICU: Intensive care unit; LSM: Life-sustaining measures; TBI: Traumatic brain injury; UK: United Kingdom

Acknowledgements

Cecilia Ackerslund¹, Hadie Adams², Vanni Agnoletti³, Judith Allanson⁴, Krisztina Amrein⁵, Norberto Andaluz², Nada Andelic⁷, Lasse Andreassen⁸, Azasevac Antun⁹, Audny Anke¹⁰, Anna Antoni¹¹, Hilko Ardon¹², Gérard Audibert¹³, Kaspars Auslands¹⁴, Philippe Azouvi¹⁵, Maria Luisa Azzolini¹⁶, Camelia Baciu¹⁷, Rafael Badenes¹⁸, Ronald Bartels¹⁹, Pál Barzó²⁰, Ursula Bauerfeind²¹, Romuald Beauvais²², Ronny Beer²³, Francisco Javier Belda¹⁸, Bo-Michael Bellander²⁴, Antonio Belli²⁵, Rémy Bellier²⁶, Habib Benali²⁷, Thierry Benard²⁶, Maurizio Berardino²⁸, Luigi Beretta¹⁶, Christopher Beynon²⁹, Federico Bilotta¹⁸, Harald Binder¹¹, Erta Biqiri¹⁷, Morten Blaabjerg³⁰, Hugo den Boogert¹⁹, Pierre Bouzat³¹, Peter Bragge³², Alexandra Brazinova³³, Vibeke Brinck³⁴, Joanne Brooker³⁵, Camilla Brorsson³⁶, Andras Buki³⁷, Monika Bullinger³⁸, Emiliana Calappi³⁹, Maria Rosa Calvi¹⁶, Peter Cameron⁴⁰, Guillermo Carbayo Lozano⁴¹, Marco Carbonara³⁹, Elsa Carise²⁶, K. Carpenter⁴², Ana M. Castaño-León⁴³, Francesco Causin⁴⁴, Giorgio Chevallard¹⁷, Arturo Chierogato¹⁷, Giuseppe Citerio^{45,46}, Maryse Cnossen⁴⁷, Mark Coburn⁴⁸, Jonathan Coles⁴⁹, Lizzie Coles-Kemp⁵⁰, Johnny Collett⁵⁰, Jamie D. Cooper⁵¹, Marta Correia⁵², Amra Covic⁵³, Nicola Curry⁵⁴, Endre Czeiter⁵⁵, Marek Czosnyka⁵⁶, Claire Dahyot-Fizelier²⁶, François Damas⁵⁷, Pierre Damas⁵⁸, Helen Dawes⁵⁹, Véronique De Keyser⁶⁰, Francesco Della Corte⁶¹, Bart Depreitere⁶², Godard C. W. de Ruiter⁶³, Dula Dilvesi⁹, Shenghao Ding⁶⁴, Diederik Dippel⁶⁵, Abhishek Dixit⁶⁶, Emma Donoghue⁴⁰, Jens Dreier⁶⁷, Guy-Loup Dulière⁵⁷, George Eapen⁶⁸, Heiko Engemann⁵³, Ari Ercole⁶⁶, Patrick Esse⁵⁹, Erzsébet Eze⁶⁹, Martin Fabricius⁷⁰, Valery L. Feigin⁷¹, Junfeng Feng⁶⁴, Kelly Foks⁶⁵, Francesca Fossi¹⁷, Gilles Franconi³¹, Ulderico Frea⁷², Shirin Frisvold⁷³, Alex Furmanov⁷⁴, Pablo Gagliardo⁷⁵, Damien Galanaud²⁷, Dashiell Gantner⁴⁰, Guoyi Gao⁷⁶, Karin Geleijns⁴², Pradeep George¹, Alexandre Ghuysen⁷⁷, Lelde Giga⁷⁸, Benoit Giraud²⁶, Ben Glocker⁷⁹, Jagos Golubovic⁹, Pedro A. Gomez⁴³, Francesca Grossi⁶¹, Russell L. Gruen⁸⁰, Deepak Gupta⁸¹, Juanita A. Haagsma⁴⁷, Iain Haitsma⁸², Jed A. Hartings⁸³, Raimund Helbok²³, Eirik Helseth⁸⁴, Daniel Hertle³⁰, Astrid Hoedemaekers⁸⁵, Stefan Hofer⁵³, Lindsay Horton⁸⁶, Jilske Huijben⁴⁷, Peter J. Hutchinson², Asta Kristine Håberg⁸⁷, Bram Jacobs⁸⁸, Stefan Jankowski⁶⁸, Mike Jarrett³⁴, Bojan Jelaca⁹, Ji-yao Jiang⁷⁶, Kelly Jones⁸⁹, Konstantinos Kamnitsas⁷⁹, Mladen Karan⁶, Ari Katila⁹⁰, Maija Kaukonen⁹¹, Thomas Kerforne²⁶, Riku Kivisaari⁹¹, Angelos G. Koliats², Bálint Kolombán⁹², Erwin Kompanje⁹³, Ksenija Kolundzija⁹⁴, Daniel Kondziella⁷⁰, Lars-Owe Koskinen³⁶, Noémi Kovács⁹², Alfonso Lagares⁴³, Linda Lanyon¹, Steven Laureys⁹⁵, Fiona Lecky⁹⁶, Christian Ledig⁷⁹, Rolf Lefering⁹⁷, Valerie Legrand⁹⁸, Jin Lei⁶⁴, Leon Lev⁹⁹, Roger Lightfoot¹⁰⁰, Hester Lingsma⁴⁷, Dirk Loeckx¹⁰¹, Angels Lozano¹⁸, Andrew I. R. Maas⁶⁰, Stephen MacDonald¹⁰², Marc Maegele¹⁰³, Marek Majdan³³, Sebastian Major¹⁰⁴, Alex Manara¹⁰⁵, Geoffrey Manley¹⁰⁶, Didier Martin¹⁰⁷, Leon Francisco Martin¹⁰¹, Costanza Martino³, Armando Maruenda¹⁸, Hugues Maréchal⁵⁷, Alessandro Masala³, Julia Mattern²⁹, Charles McFadyen⁶⁶, Catherine McMahon¹⁰⁸, Béla Meleg¹⁰⁹, David Menon⁶⁶, Tomas Menovsky⁶⁰, Cristina Morganti-Kossmann¹¹⁰, Davide Mulazzi³⁹, Visakh Muraleedharan¹, Lynnette Murray⁴⁰, Holger Mühlen¹¹¹, Nandesh Nair⁶⁰, Ancuta Negru¹¹², David Nelson¹, Virginia Newcombe⁶⁶, Daan Nieboer⁴⁷, Quentin Noirhomme⁹⁵, József Nyírádi⁵, Mauro Oddo¹¹³, Annemarie Oldenbeuving¹¹⁴, Matej Oresic¹¹⁵, Fabrizio Ortolano³⁹, Aarno Palotie^{116,117,118}, Paul M. Parizel¹¹⁹, Adriana Patrino¹²⁰, Jean-François Payen³¹, Natascha Perera²², Vincent Perlbarg²⁷, Paolo Persona¹²¹, Wilco Peul⁶³, Anna Piippo-Karjalainen⁹¹, Sébastien Pili Floury¹²², Matti Pirinen¹¹⁶, Horia Ples¹¹², Maria Antonia Poca¹²³, Suzanne Polinder⁴⁷, Inigo Pomposo⁴¹, Jussi Posti⁹⁰, Louis

Puybasset¹²⁴, Andreea Radoi¹²³, Arminas Ragauskas¹²⁵, Rahul Raj⁹¹, Malinka Rambadagalla¹²⁶, Ruben Real⁵³, Veronika Rehorčíková³³, Jonathan Rhodes¹²⁷, Samuli Ripatti¹¹⁶, Saulius Rocka¹²⁵, Cecilie Roe¹²⁸, Olav Roise¹²⁹, Gerwin Roks¹³⁰, Jonathan Rosand¹³¹, Jeffrey Rosenfeld¹¹⁰, Christina Rosenlund¹³², Guy Rosenthal⁷⁴, Rolf Rossaint⁴⁸, Sandra Rossi¹²¹, Daniel Rueckert⁷⁹, Martin Rusnák¹³³, Marco Sacchi¹⁷, Barbara Sahakian⁶⁶, Juan Sahuquillo¹²³, Oliver Sakowitz^{134,135}, Francesca Sala¹²⁰, Renan Sanchez-Porras¹³⁴, Janos Sandor¹³⁶, Edgar Santos²⁹, Luminita Sasu⁶¹, Davide Savo¹²⁰, Nadine Schäffer¹⁰³, Inger Schipper¹³⁷, Barbara Schlößer²¹, Silke Schmidt¹¹¹, Herbert Schoechl¹³⁸, Guus Schoonman¹³⁰, Rico Frederik Schou¹³⁹, Elisabeth Schwendenwein¹¹, Michael Schöll²⁹, Özcan Sir¹⁴⁰, Toril Skandsen¹⁴¹, Lidwien Smakman⁶³, Dirk Smeets¹⁰¹, Peter Smielewski⁵⁶, Abayomi Sorinola¹⁴², Emmanuel Stamatakis⁶⁶, Simon Stanworth⁵⁴, Nicole Steinbüchel¹⁴³, Ana Stevanovic⁴⁸, Robert Stevens¹⁴⁴, William Stewart¹⁴⁵, Ewout W. Steyerberg^{47,146}, Nino Stocchetti¹⁴⁷, Nina Sundström³⁶, Anneliese Synnot^{34,148}, Fabio Silvio Taccone¹⁸, Riikka Takala⁹⁰, Viktória Tamás¹⁴², Päivi Tanskanen⁹¹, Mark Steven Taylor³³, Braden Te Ao⁷¹, Olli Tenovuori³⁰, Ralph Telgmann⁵³, Guido Teodorani¹⁴⁹, Alice Theadom⁷¹, Matt Thomas¹⁰⁵, Dick Tibboel⁴², Christos Toliás¹⁵⁰, Jean-Flory Luaba Tshibanda¹⁵¹, Tony Trapani⁴⁰, Cristina Maria Tudora¹¹², Peter Vajkoczy⁶⁷, Shirley Vallance⁴³, Egils Valeinis⁷⁸, Gregory Van der Steen⁶⁰, Mathieu van der Jagt¹⁵², Joukje van der Naalt⁸⁸, Jeroen T. J. M. van Dijk⁶³, Thomas A. van Essen⁶³, Wim Van Hecke¹⁰¹, Caroline van Heugten⁵⁹, Dominique Van Praag⁶⁰, Thijs Vande Vyvere¹⁰¹, Julia Van Waesberghe⁴⁸, Audrey Vanhauudenhuysse^{27,95}, Alessia Vargiolu¹²⁰, Emmanuel Vega¹⁵³, Kimberley Velt⁴⁷, Jan Verheyden¹⁰¹, Paul M. Vespa¹⁵⁴, Anne Vik¹⁵⁵, Rimantas Vilcinis¹⁵⁶, Giacinta Vizzino¹⁷, Carmen Vleggeert-Lankamp⁶³, Victor Volovici⁸², Daphne Voormolen⁴⁷, Peter Vulekovic⁹, Zoltán Vámos⁵⁹, Derick Wade⁵⁹, Kevin K. W. Wang¹⁵⁷, Lei Wang⁶⁴, Lars Wessels¹⁵⁸, Eno Wildschut⁴², Guy Williams⁶⁶, Lindsay Wilson⁸⁶, Maren K. L. Winkler¹⁰⁴, Stefan Wolf¹⁵⁸, Peter Ylén¹⁵⁹, Alexander Younsi²⁹, Menashe Zaaroor⁹⁹, Yang Zhihui¹⁶⁰, Agate Ziverte⁷⁸, Fabrizio Zumbo³.

¹ Karolinska Institutet, INCF International Neuroinformatics Coordinating Facility, Stockholm, Sweden.

² Division of Neurosurgery, Department of Clinical Neurosciences, Addenbrooke's Hospital & University of Cambridge, Cambridge, UK.

³ Department of Anesthesia & Intensive Care, M. Bufalini Hospital, Cesena, Italy.

⁴ Department of Clinical Neurosciences, Addenbrooke's Hospital & University of Cambridge, Cambridge, UK.

⁵ János Szentágotai Research Centre, University of Pécs, Pécs, Hungary.

⁶ University of Cincinnati, Cincinnati, OH, USA.

⁷ Division of Surgery and Clinical Neuroscience, Department of Physical Medicine and Rehabilitation, Oslo University Hospital and University of Oslo, Oslo, Norway.

⁸ Department of Neurosurgery, University Hospital Northern Norway, Tromsø, Norway.

⁹ Department of Neurosurgery, Clinical Centre of Vojvodina, Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia.

¹⁰ Department of Physical Medicine and Rehabilitation, University Hospital Northern Norway.

¹¹ Trauma Surgery, Medical University Vienna, Vienna, Austria.

¹² Department of Neurosurgery, Elisabeth-TweeSteden Ziekenhuis, Tilburg, the Netherlands.

¹³ Department of Anesthesiology & Intensive Care, University Hospital Nancy, Nancy, France.

¹⁴ Riga Eastern Clinical University Hospital, Riga, Latvia.

¹⁵ Raymond Poincaré Hospital, Assistance Publique—Hôpitaux de Paris, Paris, France.

¹⁶ Department of Anesthesiology & Intensive Care, S Raffaele University Hospital, Milan, Italy.

¹⁷ NeuroIntensive Care, Niguarda Hospital, Milan, Italy.

¹⁸ Department Anesthesiology and Surgical-Trauma Intensive Care, Hospital Clinic Universitari de Valencia, Spain.

¹⁹ Department of Neurosurgery, Radboud University Medical Center, Nijmegen, the Netherlands.

²⁰ Department of Neurosurgery, University of Szeged, Szeged, Hungary.

²¹ Institute for Transfusion Medicine (ITM), Witten/Herdecke University, Cologne, Germany.

²² International Projects Management, ARTTIC, München, Germany.

²³ Department of Neurology, Neurological Intensive Care Unit, Medical University of Innsbruck, Innsbruck, Austria.

- ²⁴ Department of Neurosurgery & Anesthesia & Intensive Care Medicine, Karolinska University Hospital, Stockholm, Sweden.
- ²⁵ NIHR Surgical Reconstruction and Microbiology Research Centre, Birmingham, UK.
- ²⁶ Intensive Care Unit, CHU Poitiers, Poitiers, France.
- ²⁷ Anesthésie-Réanimation, Assistance Publique—Hopitaux de Paris, Paris, France.
- ²⁸ Department of Anesthesia & ICU, AOU Città della Salute e della Scienza di Torino—Orthopedic and Trauma Center, Torino, Italy.
- ²⁹ Department of Neurosurgery, University Hospital Heidelberg, Heidelberg, Germany.
- ³⁰ Department of Neurology, Odense University Hospital, Odense, Denmark.
- ³¹ Department of Anesthesiology & Intensive Care, University Hospital of Grenoble, Grenoble, France.
- ³² BehaviourWorks Australia, Monash Sustainability Institute, Monash University, VIC, Australia.
- ³³ Department of Public Health, Faculty of Health Sciences and Social Work, Trnava University, Trnava, Slovakia.
- ³⁴ Quesgen Systems Inc., Burlingame, CA, USA.
- ³⁵ Australian & New Zealand Intensive Care Research Centre, Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia.
- ³⁶ Department of Neurosurgery, Umea University Hospital, Umea, Sweden.
- ³⁷ Department of Neurosurgery, University of Pecs and MTA-PTE Clinical Neuroscience MR Research Group and Janos Szentagothai Research Centre, University of Pecs, Hungarian Brain Research Program, Pecs, Hungary.
- ³⁸ Department of Medical Psychology, Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany.
- ³⁹ Neuro ICU, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy.
- ⁴⁰ ANZIC Research Centre, Monash University, Department of Epidemiology and Preventive Medicine, Melbourne, Victoria, Australia.
- ⁴¹ Department of Neurosurgery, Hospital of Cruces, Bilbao, Spain.
- ⁴² Intensive Care and Department of Pediatric Surgery, Erasmus University Medical Center, Sophia Children's Hospital, Rotterdam, the Netherlands.
- ⁴³ Department of Neurosurgery, Hospital Universitario 12 de Octubre, Madrid, Spain.
- ⁴⁴ Department of Neuroscience, Azienda Ospedaliera Università di Padova, Padova, Italy.
- ⁴⁵ NeuroIntensive Care, ASST di Monza, Monza, Italy.
- ⁴⁶ School of Medicine and Surgery, Università Milano Bicocca, Milan, Italy.
- ⁴⁷ Department of Public Health, Erasmus University Medical Center, Rotterdam, the Netherlands.
- ⁴⁸ Department of Anaesthesiology, University Hospital of Aachen, Aachen, Germany.
- ⁴⁹ Department of Anesthesia & Neurointensive Care, Cambridge University Hospital NHS Foundation Trust, Cambridge, UK.
- ⁵⁰ Movement Science Group, Oxford Institute of Nursing, Midwifery and Allied Health Research, Oxford Brookes University, Oxford, UK.
- ⁵¹ School of Public Health & PM, Monash University and The Alfred Hospital, Melbourne, VIC, Australia.
- ⁵² Radiology/MRI Department, MRC Cognition and Brain Sciences Unit, Cambridge, UK.
- ⁵³ Institute of Medical Psychology and Medical Sociology, Universitätsmedizin Göttingen, Göttingen, Germany.
- ⁵⁴ Oxford University Hospitals NHS Trust, Oxford, UK.
- ⁵⁵ Department of Neurosurgery, University of Pecs and MTA-PTE Clinical Neuroscience MR Research Group and Janos Szentagothai Research Centre, University of Pecs, Hungarian Brain Research Program (Grant No. KTIA 13 NAP-A-II/8), Pecs, Hungary.
- ⁵⁶ Brain Physics Lab, Division of Neurosurgery, Department of Clinical Neurosciences, University of Cambridge, Addenbrooke's Hospital, Cambridge, UK.
- ⁵⁷ Intensive Care Unit, CHR Citadelle, Liège, Belgium.
- ⁵⁸ Intensive Care Unit, CHU, Liège, Belgium.
- ⁵⁹ Movement Science Group, Faculty of Health and Life Sciences, Oxford Brookes University, Oxford, UK.
- ⁶⁰ Department of Neurosurgery, Antwerp University Hospital and University of Antwerp, Edegem, Belgium.
- ⁶¹ Department of Anesthesia & Intensive Care, Maggiore Della Carità Hospital, Novara, Italy.
- ⁶² Department of Neurosurgery, University Hospitals Leuven, Leuven, Belgium.
- ⁶³ Department of Neurosurgery, Leiden University Medical Center, Leiden, the Netherlands and Department of Neurosurgery, Medical Center Haaglanden, The Hague, the Netherlands.
- ⁶⁴ Department of Neurosurgery, Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China.
- ⁶⁵ Department of Neurology, Erasmus University Medical Center, Rotterdam, the Netherlands.
- ⁶⁶ Division of Anaesthesia, University of Cambridge, Addenbrooke's Hospital, Cambridge, UK.
- ⁶⁷ Neurologie, Neurochirurgie und Psychiatrie, Charité-Universitätsmedizin Berlin, Berlin, Germany.
- ⁶⁸ Neurointensive Care, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK.
- ⁶⁹ Department of Anaesthesiology and Intensive Therapy, University of Pécs, Pécs, Hungary.
- ⁷⁰ Departments of Neurology, Clinical Neurophysiology and Neuroanesthesiology, Region Hovedstaden Rigshospitalet, Copenhagen, Denmark.
- ⁷¹ National Institute for Stroke and Applied Neurosciences, Faculty of Health and Environmental Studies, Auckland University of Technology, Auckland, New Zealand.
- ⁷² Department of Medicine, Azienda Ospedaliera Università di Padova, Padova, Italy.
- ⁷³ Department of Anesthesiology and Intensive Care, University Hospital Northern Norway, Tromsø, Norway.
- ⁷⁴ Department of Neurosurgery, Hadassah-Hebrew University Medical Center, Jerusalem, Israel.
- ⁷⁵ Fundación Instituto Valenciano de Neurorrehabilitación (FIVAN), Valencia, Spain.
- ⁷⁶ Department of Neurosurgery, Shanghai Renji Hospital, Shanghai Jiaotong University/School of Medicine, Shanghai, China.
- ⁷⁷ Emergency Department, CHU, Liège, Belgium.
- ⁷⁸ Pauls Stradins Clinical University Hospital, Riga, Latvia.
- ⁷⁹ Department of Computing, Imperial College London, London, UK.
- ⁸⁰ Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore; and Central Clinical School, Monash University, Melbourne, Victoria, Australia.
- ⁸¹ Department of Neurosurgery, Neurosciences Centre & JPN Apex Trauma Centre, All India Institute of Medical Sciences, New Delhi, India.
- ⁸² Department of Neurosurgery, Erasmus University Medical Center, Rotterdam, the Netherlands.
- ⁸³ Department of Neurosurgery, University of Cincinnati, Cincinnati, OH, USA.
- ⁸⁴ Department of Neurosurgery, Oslo University Hospital, Oslo, Norway.
- ⁸⁵ Department of Intensive Care Medicine, Radboud University Medical Center, Nijmegen, the Netherlands.
- ⁸⁶ Division of Psychology, University of Stirling, Stirling, UK.
- ⁸⁷ Department of Medical Imaging, St. Olavs Hospital and Department of Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway.
- ⁸⁸ Department of Neurology, University Medical Center Groningen, Groningen, the Netherlands.
- ⁸⁹ National Institute for Stroke & Applied Neurosciences of the AUT University, Auckland, New Zealand.
- ⁹⁰ Rehabilitation and Brain Trauma, Turku University Central Hospital and University of Turku, Turku, Finland.
- ⁹¹ Helsinki University Central Hospital, Helsinki, Finland.
- ⁹² Hungarian Brain Research Program—Grant No. KTIA 13 NAP-A-II/8, University of Pécs, Pécs, Hungary.
- ⁹³ Department of Intensive Care and Department of Ethics and Philosophy of Medicine, Erasmus University Medical Center, Rotterdam, the Netherlands.
- ⁹⁴ Department of Psychiatry, Clinical centre of Vojvodina, Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia.
- ⁹⁵ Cyclotron Research Center, University of Liège, Liège, Belgium.
- ⁹⁶ Emergency Medicine Research in Sheffield, Health Services Research Section, School of Health and Related Research (SchARR), University of Sheffield, Sheffield, UK.
- ⁹⁷ Institute of Research in Operative Medicine (IFOM), Witten/Herdecke University, Cologne, Germany.
- ⁹⁸ VP Global Project Management CNS, ICON, Paris, France.
- ⁹⁹ Department of Neurosurgery, Rambam Medical Center, Haifa, Israel.
- ¹⁰⁰ Department of Anesthesiology & Intensive Care, University Hospitals Southampton NHS Trust, Southampton, UK.
- ¹⁰¹ icoMetrix NV, Leuven, Belgium.

- ¹⁰² Cambridge University Hospitals, Cambridge, UK.
- ¹⁰³ Cologne-Merheim Medical Center (CMMC), Department of Traumatology, Orthopedic Surgery and Sportmedicine, Witten/Herdecke University, Cologne, Germany.
- ¹⁰⁴ Centrum für Schlaganfallforschung, Charité-Universitätsmedizin Berlin, Berlin, Germany.
- ¹⁰⁵ Intensive Care Unit, Southmead Hospital, Bristol, Bristol, UK.
- ¹⁰⁶ Department of Neurological Surgery, University of California, San Francisco, CA, USA.
- ¹⁰⁷ Department of Neurosurgery, CHU, Liège, Belgium.
- ¹⁰⁸ Department of Neurosurgery, The Walton Centre NHS Foundation Trust, Liverpool, UK.
- ¹⁰⁹ Department of Medical Genetics, University of Pécs, Pécs, Hungary.
- ¹¹⁰ National Trauma Research Institute, The Alfred Hospital, Monash University, Melbourne, VIC, Australia.
- ¹¹¹ Department Health and Prevention, University Greifswald, Greifswald, Germany.
- ¹¹² Department of Neurosurgery, Emergency County Hospital Timisoara, Timisoara, Romania.
- ¹¹³ Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland.
- ¹¹⁴ Department of Intensive Care, Elisabeth-TweeSteden Ziekenhuis, Tilburg, the Netherlands.
- ¹¹⁵ Department of Systems Medicine, Steno Diabetes Center, Gentofte, Denmark.
- ¹¹⁶ Institute for Molecular Medicine Finland, University of Helsinki, Helsinki, Finland.
- ¹¹⁷ Analytic and Translational Genetics Unit, Department of Medicine; Psychiatric & Neurodevelopmental Genetics Unit, Department of Psychiatry; Department of Neurology, Massachusetts General Hospital, Boston, MA, USA.
- ¹¹⁸ Program in Medical and Population Genetics; The Stanley Center for Psychiatric Research, The Broad Institute of MIT and Harvard, Cambridge, MA, USA.
- ¹¹⁹ Department of Radiology, Antwerp University Hospital and University of Antwerp, Edegem, Belgium.
- ¹²⁰ NeuroIntensive Care Unit, Department of Anesthesia & Intensive Care, ASST di Monza, Monza, Italy.
- ¹²¹ Department of Anesthesia & Intensive Care, Azienda Ospedaliera Università di Padova, Padova, Italy.
- ¹²² Intensive Care Unit, CHRU de Besançon, Besançon, France.
- ¹²³ Department of Neurosurgery, Vall d'Hebron University Hospital, Barcelona, Spain.
- ¹²⁴ Department of Anesthesiology and Critical Care, Pitié-Salpêtrière Teaching Hospital, Assistance Publique, Hôpitaux de Paris and University Pierre et Marie Curie, Paris, France.
- ¹²⁵ Department of Neurosurgery, Kaunas University of technology and Vilnius University, Vilnius, Lithuania.
- ¹²⁶ Rezekne Hospital, Rezekne, Latvia.
- ¹²⁷ Department of Anaesthesia, Critical Care & Pain Medicine NHS Lothian & University of Edinburgh, Edinburgh, UK.
- ¹²⁸ Department of Physical Medicine and Rehabilitation, Oslo University Hospital/University of Oslo, Oslo, Norway.
- ¹²⁹ Division of Surgery and Clinical Neuroscience, Oslo University Hospital, Oslo, Norway.
- ¹³⁰ Department of Neurology, Elisabeth-TweeSteden Ziekenhuis, Tilburg, the Netherlands.
- ¹³¹ Broad Institute, Cambridge, MA; Harvard Medical School, Boston, MA; and Massachusetts General Hospital, Boston, MA, USA.
- ¹³² Department of Neurosurgery, Odense University Hospital, Odense, Denmark.
- ¹³³ International Neurotrauma Research Organisation, Vienna, Austria.
- ¹³⁴ Klinik für Neurochirurgie, Klinikum Ludwigsburg, Ludwigsburg, Germany.
- ¹³⁵ University Hospital Heidelberg, Heidelberg, Germany.
- ¹³⁶ Division of Biostatistics and Epidemiology, Department of Preventive Medicine, University of Debrecen, Debrecen, Hungary.
- ¹³⁷ Department of Traumasurgery, Leiden University Medical Center, Leiden, the Netherlands.
- ¹³⁸ Department of Anaesthesiology and Intensive Care, AUA Trauma Hospital, Salzburg, Austria.
- ¹³⁹ Department of Neuroanesthesia and Neurointensive Care, Odense University Hospital, Odense, Denmark.
- ¹⁴⁰ Department of Emergency Care Medicine, Radboud University Medical Center, Nijmegen, the Netherlands.
- ¹⁴¹ Department of Physical Medicine and Rehabilitation, St. Olavs Hospital and Department of Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway.
- ¹⁴² Department of Neurosurgery, University of Pécs, Pécs, Hungary.
- ¹⁴³ Universitätsmedizin Göttingen, Göttingen, Germany.
- ¹⁴⁴ Division of Neuroscience Critical Care, John Hopkins University School of Medicine, Baltimore, MD, USA.
- ¹⁴⁵ Department of Neuropathology, Queen Elizabeth University Hospital and University of Glasgow, Glasgow, UK.
- ¹⁴⁶ Department of Biomedical Data Sciences, Leiden University Medical Center, Leiden, the Netherlands.
- ¹⁴⁷ Department of Pathophysiology and Transplantation, Milan University, and Neuroscience ICU, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy.
- ¹⁴⁸ Cochrane Consumers and Communication Review Group, Centre for Health Communication and Participation, School of Psychology and Public Health, La Trobe University, Melbourne, Australia.
- ¹⁴⁹ Department of Rehabilitation, M. Bufalini Hospital, Cesena, Italy.
- ¹⁵⁰ Department of Neurosurgery, Kings College London, London, UK.
- ¹⁵¹ Radiology/MRI Department, CHU, Liège, Belgium.
- ¹⁵² Department of Intensive Care, Erasmus University Medical Center, Rotterdam, the Netherlands.
- ¹⁵³ Department of Anesthesiology-Intensive Care, Lille University Hospital, Lille, France.
- ¹⁵⁴ Director of Neurocritical Care, University of California, Los Angeles, CA, USA.
- ¹⁵⁵ Department of Neurosurgery, St. Olavs Hospital and Department of Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway.
- ¹⁵⁶ Department of Neurosurgery, Kaunas University of Health Sciences, Kaunas, Lithuania.
- ¹⁵⁷ Department of Psychiatry, University of Florida, Gainesville, FL, USA.
- ¹⁵⁸ Interdisciplinary Neuro Intensive Care Unit, Charité-Universitätsmedizin Berlin, Berlin, Germany.
- ¹⁵⁹ VTT Technical Research Centre, Tampere, Finland.
- ¹⁶⁰ University of Florida, Gainesville, FL, USA.

Funding

Data used in preparation of this manuscript were obtained in the context of the CENTER-TBI study, a large collaborative project, supported by the Framework 7 program of the European Union (602150). The funder had no role in the design of the study, the collection, analysis, and interpretation of data, or in writing the manuscript. DKM was supported by a Senior Investigator Award from the National Institute for Health Research (UK). The funder had no role in the design of the study, the collection, analysis, and interpretation of data, or in writing the manuscript.

Availability of data and materials

There are legal constraints that prohibit us from making the data publicly available. Since there are only a limited number of centers per country included in this study (for two countries only one center), data will be identifiable. Readers may contact Dr Erwin J. O. Kompanje (e.j.o.kompanje@erasmusmc.nl) for reasonable requests for the data.

Authors' contributions

EvV analyzed the data and drafted the manuscript and the supplementary tables. All coauthors gave feedback on the manuscript. EJOK supervised the project. All coauthors were involved in the design of the survey and the distribution of the survey. All coauthors gave feedback on (and approved) the final version of the manuscript.

Ethics approval and consent to participate

Not applicable since no patients participated, and the centers have given consent by completing the questionnaire.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Author details

¹Department of Intensive Care, Erasmus University Medical Center, Rotterdam, the Netherlands. ²Center for Medical Decision Making, Department of Public Health, Erasmus University Medical Center, Rotterdam, the Netherlands. ³Department of Medical Ethics and Philosophy of Medicine, Erasmus University Medical Center, Rotterdam, the Netherlands. ⁴Department of Neurosurgery, Antwerp University Hospital and University of Antwerp, Edegem, Belgium. ⁵Department of Anaesthesia, University of Cambridge, Cambridge, UK. ⁶School of Medicine and Surgery, University of Milan-Bicocca, Milan, Italy. ⁷San Gerardo Hospital, ASST-Monza, Monza, Italy. ⁸Department of Physiopathology and Transplantation, Milan University, Milan, Italy. ⁹Neuro ICU Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico Milano, Milan, Italy. ¹⁰Department of Neurosurgery, Leiden University Medical Center, Leiden, the Netherlands.

Received: 2 May 2018 Accepted: 15 October 2018

Published online: 16 November 2018

References

- Mollaret P, Goulon M. Le coma dépassé (mémoire prélinéaire). *Rev Neurol (Paris)*. 1959;101:3–15.
- 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):337–40.
- Guidelines for the determination of death. Report of the medical consultants on the diagnosis of death to the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. *JAMA*. 1981;246(19):2184–6.
- Practice parameters for determining brain death in adults (summary statement). The Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 1995;45(5):1012–4.
- Wijdicks EF, Varelas PN, Gronseth GS, Greer DM. Evidence-based guideline update: determining brain death in adults: Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2010;74(23):1911–8.
- Academy of Medical Royal Colleges (2008) A code of practice for the diagnosis and confirmation of death. http://aomrc.org.uk/wp-content/uploads/2016/04/Code_Practice_Confirmation_Diagnosis_Death_1008-4.pdf. Accessed 5 Nov 2018.
- Maas AI, Menon DK, Steyerberg EW, Citerio G, Lecky F, Manley GT, Hill S, Legrand V, Sorgner A. Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI): a prospective longitudinal observational study. *Neurosurgery*. 2015;76(1):67–80.
- Maas AIR, Menon DK, Adelson PD, Andelic N, Bell MJ, Belli A, Bragge P, Brazinova A, Buki A, Chesnut RM, Citerio G, Coburn M, Cooper DJ, Crowder AT, Czeiter E, Czosnyka M, Diaz-Arastia R, Dreier JP, Duhaime AC, Ercole A, van Essen TA, Feigin VL, Gao G, Giacino J, Gonzalez-Lara LE, Gruen RL, Gupta D, Hartings JA, Hill S, Jiang JY, Ketharanathan N, Kompanje EJO, Lanyon L, Laureys S, Lecky F, Levin H, Lingsma HF, Maegele M, Majdan M, Manley G, Marsteller J, Mascia L, McFadyen C, Mondello S, Newcombe V, Palotie A, Parizel PM, Peul W, Piercy J, Polinder S, Puybasset L, Rasmussen TE, Rossaint R, Smielewski P, Soderberg J, Stanworth SJ, Stein MB, von Steinbuechel N, Stewart W, Steyerberg EW, Stocchetti N, Synnot A, Te Ao B, Tenovuo O, Theadom A, Tibboel D, Videtta W, Wang KKW, Williams WH, Wilson L, Yaffe K. Traumatic brain injury: integrated approaches to improve prevention, clinical care, and research. *Lancet Neurol*. 2017;16(12):987–1048.
- Cnossen MC, Polinder S, Lingsma HF, Maas AI, Menon D, Steyerberg EW. Variation in structure and process of care in traumatic brain injury: provider profiles of European neurotrauma centers participating in the CENTER-TBI Study. *PLoS One*. 2016;11(8):e0161367.
- Shemie SD, Hornby L, Baker A, Teitelbaum J, Torrance S, Young K, Capron AM, Bernat JL, Noel L. International guideline development for the determination of death. *Intensive Care Med*. 2014;40(6):788–97.
- Wahlster S, Wijdicks EF, Patel PV, Greer DM, Hemphill JCI, Carone M, Mateen FJ. Brain death declaration: practices and perceptions worldwide. *Neurology*. 2015;84(18):1870–9.
- Powner DJ, Hernandez M, Rives TE. Variability among hospital policies for determining brain death in adults. *Crit Care Med*. 2004;32(6):1284–8.
- Hornby K, Shemie SD, Teitelbaum J, Doig C. Variability in hospital-based brain death guidelines in Canada. *Can J Anaesth*. 2006;53(6):613–9.
- Greer DM, Varelas PN, Haque S, Wijdicks EF. Variability of brain death determination guidelines in leading US neurologic institutions. *Neurology*. 2008;70(4):284–9.
- Shappell CN, Frank JI, Husari K, Sanchez M, Goldenberg F, Ardeli A. Practice variability in brain death determination: a call to action. *Neurology*. 2013;81(23):2009–14.
- Greer DM, Wang HH, Robinson JD, Varelas PN, Henderson GV, Wijdicks EF. Variability of brain death policies in the United States. *JAMA Neurol*. 2016;73(2):213–8.
- Haupt WF, Rudolf J. European brain death codes: a comparison of national guidelines. *J Neurol*. 1999;246(6):432–7.
- Wijdicks EF. Brain death worldwide: accepted fact but no global consensus in diagnostic criteria. *Neurology*. 2002;58(1):20–5.
- Citerio G, Crippa IA, Bronco A, Vargiolu A, Smith M. Variability in brain death determination in Europe: looking for a solution. *Neurocrit Care*. 2014;21(3):376–82.
- Wijdicks EF. The case against confirmatory tests for determining brain death in adults. *Neurology*. 2010;75(1):77–83.
- Dominguez-Gil B, Haase-Kromwijk B, Van Leiden H, Neuberger J, Coene L, Morel P, Corinne A, Muehlbacher F, Brezovsky P, Costa AN, Rozental R, Matesanz R. Current situation of donation after circulatory death in European countries. *Transpl Int*. 2011;24(7):676–86.
- Wind J, Faut M, van Smaalen TC, van Heurn EL. Variability in protocols on donation after circulatory death in Europe. *Crit Care*. 2013;17(5):R217.
- EDQM Council of Europe. Newsletter Transplant. International figures on donation and transplantation 2016; volume 22 2017.
- Payer L. *Medicine & Culture: varieties of treatment in the United States, England, West Germany, and France*. H. Holt, New York; 1988.