



Observational Study

# Haemodynamic management in brain death donors: Influence of aetiology of brain death

Chiara Lazzeri, Manuela Bonizzoli, Stefano Batacchi, Cristiana Guetti, Walter Vessella, Alessandra Valletta, Alessandra Ottaviano, Adriano Peris

**Specialty type:** Critical care medicine

**Provenance and peer review:** Invited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review report's scientific quality classification**

Grade A (Excellent): 0  
Grade B (Very good): 0  
Grade C (Good): C, C, C  
Grade D (Fair): D, D  
Grade E (Poor): 0

**P-Reviewer:** Luo W, China; Sef D, United Kingdom; Verran DJ, Australia

**Received:** December 20, 2022

**Peer-review started:** December 20, 2022

**First decision:** February 20, 2023

**Revised:** February 28, 2023

**Accepted:** April 21, 2023

**Article in press:** April 21, 2023

**Published online:** June 18, 2023



Chiara Lazzeri, Manuela Bonizzoli, Stefano Batacchi, Cristiana Guetti, Walter Vessella, Alessandra Valletta, Alessandra Ottaviano, Adriano Peris, Department of Emergency, Intensive Care Unit and Extracorporeal Membrane Oxygenation Center, Florence 50134, Italy

**Corresponding author:** Chiara Lazzeri, MD, Chief Physician, Senior Researcher, Department of Emergency, Intensive Care Unit and Extracorporeal Membrane Oxygenation Center, Largo Brambilla 3, Florence 50134, Italy. [lazzeri.ch@gmail.com](mailto:lazzeri.ch@gmail.com)

## Abstract

### BACKGROUND

In brain death donors (BDDs), donor management is the key in the complex donation process. Donor management goals, which are standards of care or clinical parameters, have been considered an acceptable barometer of successful donor management.

### AIM

To test the hypothesis that aetiology of brain death could influence haemodynamic management in BDDs.

### METHODS

Haemodynamic data (blood pressure, heart rate, central venous pressure, lactate, urine output, and vasoactive drugs) of BDDs were recorded on intensive care unit (ICU) admission and during the 6-h observation period (Time 1 at the beginning; Time 2 at the end).

### RESULTS

The study population was divided into three groups according to the aetiology of brain death: Stroke ( $n = 71$ ), traumatic brain injury ( $n = 48$ ), and postanoxic encephalopathy ( $n = 19$ ). On ICU admission, BDDs with postanoxic encephalopathy showed the lowest values of systolic and diastolic blood pressure associated with higher values of heart rate and lactate and a higher need of norepinephrine and other vasoactive drugs. At the beginning of the 6-h period (Time 1), BDDs with postanoxic encephalopathy showed higher values of heart rate, lactate, and central venous pressure together with a higher need of other vasoactive drugs.

### CONCLUSION

According to our data, haemodynamic management of BDDs is affected by the aetiology of brain death. BDDs with postanoxic encephalopathy have higher requirements for norepinephrine and other vasoactive drugs.

**Key Words:** Brain death donor; Postanoxic encephalopathy; Stroke; Acute traumatic injury; Haemodynamic management; Utilization rate

©The Author(s) 2023. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core Tip:** In our single centre observational study including 138 brain death donors (BDDs), haemodynamic management is affected by the aetiology of brain death. BDDs with postanoxic encephalopathy had higher requirements for norepinephrine and other vasoactive drugs.

**Citation:** Lazzeri C, Bonizzoli M, Batacchi S, Guetti C, Vessella W, Valletta A, Ottaviano A, Peris A. Haemodynamic management in brain death donors: Influence of aetiology of brain death. *World J Transplant* 2023; 13(4): 183-189

**URL:** <https://www.wjgnet.com/2220-3230/full/v13/i4/183.htm>

**DOI:** <https://dx.doi.org/10.5500/wjt.v13.i4.183>

## INTRODUCTION

Management of potential organ donors is the key in the complex donation process, considering that haemodynamic instability may be responsible for the loss of organs of brain death donors (BDDs)[1-8]. Changes in epidemiologic characteristics of BDDs, becoming older and with more comorbidities[9], do make haemodynamic management more challenging[10].

Donor management goals, which are standards of care or clinical parameters, have been considered an acceptable barometer of successful donor management[9,10]. Meeting donor management goals has been associated with an increased number of retrieved organs per donor[1,11-13] and, more recently, a reduced incidence of delayed graft function[14,15].

We hypothesized that aetiology of brain death could influence haemodynamic management in BDDs. In the present study, we tested this hypothesis in 138 BDDs consecutively admitted to our intensive care unit (ICU).

## MATERIALS AND METHODS

In the present single centre observational study, we enrolled 138 BDDs consecutively admitted to our ICU from January 1, 2018 to October 31, 2022. The study was approved by the Institutional Review Board of Regional Authority for Transplantation and performed in accordance with the Helsinki Declaration of 1975.

### Study population

Diagnosis of death was confirmed by strict adherence to standardized clinical, neurologic, and electroencephalogram criteria in accordance with the Italian law and related guidelines. According to the Italian law, death by neurologic criteria is certificated after a 6-h observation period. Time 1 refers to the beginning of this period, and time 2 to the end of this period.

Clinical data included age, risk factors (hypertension, diabetes mellitus, and known previous coronary artery disease). Data were prospectively recorded and retrospectively analysed. The study population was divided into three groups according to the aetiology of brain death: Stroke ( $n = 71$ ), traumatic brain injury ( $n = 48$ ), and postanoxic encephalopathy ( $n = 19$ ).

### Donor management

All potential donors were managed as previously described[8,10]. Management goals were as follows: Mean arterial pressure  $> 70$  mmHg, central venous pressure of 6 to 10 mmHg, urine output of 1.2 mL/kg/h, and haemoglobin levels to  $\geq 10$  g/dL. Ventilatory management was aimed to reach the target partial pressure of oxygen  $\geq 90$  mmHg[6,8,13]. Haemodynamic management also included replacement therapy with cortisone and thyroid hormone (T3). Antidiuretic hormone and intravenous insulin (target glucose values  $< 180$  mg/dL) were considered on a case-by-case basis.

The following parameters were recorded on ICU admission and during the 6-h observation period (Time 1 at the beginning; Time 2 at the end): Systolic (SBP) and diastolic (DBP) blood pressure (mmHg), heart rate (bpm), central venous pressure (CVP) (cmH<sub>2</sub>O), lactate (mg/dL), and urine output (mL/h).

### Statistical analysis

Data were analysed with the use of SPSS 20 statistical software (SPSS Inc, Chicago, IL, United States). A two-tailed *P* value < 0.05 was considered statistically significant. Categorical variables are reported as frequencies and percentages, and continuous variables are reported as the mean ± SD or median [and 25<sup>th</sup>-75<sup>th</sup> interquartile range (IQR)]. For continuous variables, between-group comparisons were made using analysis of variance (followed by Bonferroni posttests if the overall *P* value was significant) or by means of Kruskal-Wallis *H* test. Categorical variables were compared by chi-square tests.

## RESULTS

The study population included 138 consecutive BDDs. Stroke was the most frequent aetiology (51%). **Table 1** shows the comparisons between the three subgroups. BDDs with postanoxic encephalopathy were the youngest (aged 59 ± 19 yr). No differences were detectable among the three subgroups in risk factors and refusal rates. In BDDs with postanoxic encephalopathy, the utilization rate showed a trend towards lower values, which did not reach statistical significance.

Haemodynamic data are depicted in **Table 2**, recorded at ICU admission and Time 1 and Time 2, respectively.

On ICU admission, BDDs with postanoxic encephalopathy showed the lowest values of SBP and DBP (98 ± 33 and 77 ± 22 mmHg, respectively) associated with higher values of heart rate and lactate and a higher need of norepinephrine and other vasoactive drugs. Urine output and CVP were comparable among the three subgroups.

At the beginning of the 6-h period (Time 1), SBP and DBP were comparable among the three subgroups, as well as urine output and norepinephrine use. BDDs with postanoxic encephalopathy showed higher values of heart rate, lactate, and CVP together with a higher need of other vasoactive drugs.

At the end of the 6-h period (Time 2), no significant differences in haemodynamic data were detectable among the three groups except higher value of CVP in BDDs with postanoxic encephalopathy.

Other vasoactive drugs were vasopressin in all cases except dobutamine used in one BDD.

## DISCUSSION

Our investigation, performed in 138 consecutive BDDs managed with the same donor management protocol, documented that haemodynamic management in BDDs is affected by the aetiology of brain death. BDDs with postanoxic encephalopathy require an aggressive treatment, that is, a higher need of norepinephrine and other vasoactive drugs. Utilization rates did not differ among the BDDs with different aetiologies of brain death, probably due to a strict haemodynamic monitoring and donor haemodynamic management.

Brain death has been reported to occur in about one-sixth of patients after successfully resuscitated cardiac arrest [16], thus creating opportunities for organ donation. In a recent review by Sandroni *et al* [17], kidneys, livers, hearts, and intestines retrieved from BDDs with postanoxic encephalopathy showed survival rates comparable to organs transplanted from BDDs from other aetiologies. No data are so far available on haemodynamic management in these donors.

In our investigation, we specifically addressed haemodynamic management in BDDs from postanoxic encephalopathy upon ICU admission and after brain death developed. Haemodynamic management in these donors is more challenging since norepinephrine administration is more frequently needed to reach and maintain donor management goals and, in about one third of cases, another vasoactive drug is required. This phenomenon may be attributed to post-cardiac resuscitation syndrome. Higher values of heart rate can be related to reduced cardiac function (as a compensatory mechanism), as indicated by higher values of CVP. Despite the achievement of donor management goals, lactate values were the highest in BDDs from postanoxic encephalopathy but urine output (an indirect index of systemic perfusion) was maintained.

The utilization rate in BDDs with postanoxic encephalopathy did not differ from that of BDDs with stroke and traumatic brain injury. This may be related to the strict haemodynamic monitoring and haemodynamic donor management, performed at our centre.

Our data underscore the utility of the relevant data on potential organ donors being reported to a national registry and how this can be used to drive practice improvement and eventually to develop consensus statements.

**Table 1 Study population, n (%)**

	Stroke	Traumatic brain injury	Postanoxic encephalopathy	
Number	71	48	19	
Age (yr, mean $\pm$ SD)	79 $\pm$ 14	68 $\pm$ 20	59 $\pm$ 19	0.0007 <sup>a</sup>
Males	34 (48)	31 (65)	10 (53)	0.197 <sup>b</sup>
Risk factors				0.673 <sup>b</sup>
Hypertension	51	10	24	
Diabetes	24	9	16	
Heart disease	6	2	5	
Refusals to donation	13	10	2	0.613 <sup>b</sup>
Utilized donors (n)	54	35	15	0.808 <sup>b</sup>
Utilization rate (%)	93	92	89	

<sup>a</sup>One way analysis of variance.<sup>b</sup> $\chi^2$ .**Table 2 Haemodynamic data, n (%)**

	Stroke	Traumatic brain injury	Postanoxic encephalopathy	
Number	71 (51)	48 (35)	19 (14)	
<i>ICU admission</i>				
SBP (mmHg), mean $\pm$ SD	112 $\pm$ 44	123 $\pm$ 34	98 $\pm$ 33	0.002 <sup>a</sup>
DBP (mmHg), mean $\pm$ SD	74 $\pm$ 21	74 $\pm$ 18	77 $\pm$ 22	0.001 <sup>a</sup>
HR (bpm), mean $\pm$ SD	75 $\pm$ 22	77 $\pm$ 34	82 $\pm$ 35	0.015 <sup>a</sup>
CVP (cmH <sub>2</sub> O), mean $\pm$ SD	10 $\pm$ 3	11 $\pm$ 4	10 $\pm$ 3	0.819 <sup>a</sup>
Norepinephrine	31 (44)	29 (60)	14 (74)	0.03 <sup>b</sup>
Other vasoactive drugs	5 (7)	9 (18)	6 (32)	0.015 <sup>b</sup>
Urine output, median (IQR)	200 (125-393)	261 (124-408)	287 (186-440)	0.279 <sup>a</sup>
Lactate (mg/dL), median (IQR)	1.5 (1-2.6)	2.1 (1.3-3.1)	1.8 (0.8-4.6)	0.033 <sup>a</sup>
<i>Time 1</i>				
SBP (mmHg), mean $\pm$ SD	123 $\pm$ 19	125 $\pm$ 23	122 $\pm$ 21	0.818 <sup>a</sup>
DBP (mmHg), mean $\pm$ SD	63 $\pm$ 13	65 $\pm$ 14	68 $\pm$ 17	0.497 <sup>a</sup>
HR (bpm), mean $\pm$ SD	86 $\pm$ 16	92 $\pm$ 17	94 $\pm$ 22	0.037 <sup>a</sup>
Norepinephrine	56 (78)	43 (89)	18 (95)	0.120 <sup>b</sup>
CVP (cmH <sub>2</sub> O), mean $\pm$ SD	10 $\pm$ 3	11 $\pm$ 5	12 $\pm$ 7	0.001 <sup>a</sup>
Other vasoactive drugs	7 (9.8)	10 (20)	5 (26)	0.113 <sup>b</sup>
Urine output, median (IQR)	113 (57-210)	115 (85-285)	110 (65-220)	0.374 <sup>a</sup>
Lactate (mg/dL), median (IQR)	1.2 (0.9-1.7)	1.4 (1-3.1)	1.7 (1.3-3.1)	0.006 <sup>a</sup>
<i>Time 2</i>				
SBP (mmHg), mean $\pm$ SD	133 $\pm$ 25	131 $\pm$ 22	126 $\pm$ 27	0.510 <sup>a</sup>
DBP (mmHg), mean $\pm$ SD	66 $\pm$ 14	65 $\pm$ 12	70 $\pm$ 17	0.784 <sup>a</sup>
HR (bpm), mean $\pm$ SD	94 $\pm$ 19	95 $\pm$ 15	99 $\pm$ 25	0.760 <sup>a</sup>
Norepinephrine	57	43	18	0.172 <sup>b</sup>
Other vasoactive drugs	8 (11)	6 (12)	5 (26)	0.227 <sup>b</sup>

CVP (cmH <sub>2</sub> O), mean $\pm$ SD	10 $\pm$ 4	12 $\pm$ 4 (12)	13 $\pm$ 4	0.040 <sup>a</sup>
Urine output, median (IQR)	143 (79-240)	160 (95-250)	200 (92-250)	0.785 <sup>a</sup>

<sup>a</sup>One-way analysis of variance.

<sup>b</sup> $\chi^2$ .

IQR: Interquartile range; ICU: Intensive care unit; CVP: Central venous pressure; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; HR: Heart rate.

This study has several limitations. It is a single-centre study, and the number of enrolled BDDs is quite small. However, they were managed with the same donor management protocol.

## CONCLUSION

According to our data, haemodynamic management in BDDs is affected by the aetiology of brain death. BDDs with postanoxic encephalopathy have higher requirements for norepinephrine and other vasoactive drugs.

## ARTICLE HIGHLIGHTS

### Research background

In brain death donors (BDDs), donor management is the key in the complex donation process. Donor management goals, which are standards of care or clinical parameters, have been considered an acceptable barometer of successful donor management.

### Research motivation

Meeting donor management goals has been associated with an increased number of retrieved organs per donor and, more recently, a reduced incidence of delayed graft function.

### Research objectives

To test the hypothesis that aetiology of brain death could influence haemodynamic management in BDDs.

### Research methods

Haemodynamic data (blood pressure, heart rate, central venous pressure, lactate, urine output, and vasoactive drugs) were recorded on intensive care unit (ICU) admission and during the 6-h observation period (Time 1 at the beginning; Time 2 at the end).

### Research results

The study population was divided three groups according to aetiology of brain death: Stroke ( $n = 71$ ), traumatic brain injury ( $n = 48$ ), and postanoxic encephalopathy ( $n = 19$ ). On ICU admission, BDDs with postanoxic encephalopathy showed the lowest values of SBP and DBP associated with higher values of heart rate and lactate and a higher need of norepinephrine and other vasoactive drugs. At the beginning of the 6-h period (Time 1), BDDs with postanoxic encephalopathy showed higher values of heart rate, lactate, and central venous pressure together with a higher need of other vasoactive drugs.

### Research conclusions

According to our data, haemodynamic donor management is affected by the aetiology of brain death. BDDs with postanoxic encephalopathy have higher requirements for norepinephrine and other vasoactive drugs.

### Research perspectives

Our data underscore the utility of the relevant data on potential organ donors being reported to a national registry and how this can be used to drive practice improvement and eventually to develop consensus statements.

## FOOTNOTES

**Author contributions:** Lazzeri C, Bonizzoli M, and Peris A designed the research study; Guetti C, Batacchi S, and Ottaviano A performed the research; Valletta A and Vessella W analyzed the data and wrote the manuscript; all authors have read and approved the final manuscript.

**Institutional review board statement:** The study protocol was approved by our Internal Editorial Board.

**Informed consent statement:** Patients were not required to give informed consent to the study because the analysis used anonymous clinical data.

**Conflict-of-interest statement:** All the authors declare that they have no conflict of interest to disclose.

**Data sharing statement:** No additional data are available.

**STROBE statement:** The authors have read the STROBE Statement—checklist of items, and the manuscript was prepared and revised according to the STROBE Statement—checklist of items.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

**Country/Territory of origin:** Italy

**ORCID number:** Chiara Lazzeri 0000-0003-0131-4450; Manuela Bonizzoli 0000-0002-6435-5754; Stefano Batacchi 0000-0002-6682-047X; Adriano Peris 0000-0002-9729-2331.

**S-Editor:** Liu JH

**L-Editor:** Wang TQ

**P-Editor:** Ju JL

## REFERENCES

1. Patel MS, De La Cruz S, Sally MB, Groat T, Malinoski DJ. Active Donor Management During the Hospital Phase of Care Is Associated with More Organs Transplanted per Donor. *J Am Coll Surg* 2017; **225**: 525-531 [PMID: 28739153 DOI: 10.1016/j.jamcollsurg.2017.06.014]
2. Greer DM, Shemie SD, Lewis A et al Determination of brain death/death by neurologic criteria. The World Brain Death Project. *JAMA* 2020; **324**(11): 1078-1097 [DOI: 10.3410/f.738423716.793581021]
3. Thet MS, Verzelloni Sef A, Sef D. Can adequate hemodynamic management of brain-dead donors improve donor organ procurement? *World J Transplant* 2022; **12**: 79-82 [PMID: 35633852 DOI: 10.5500/wjt.v12.i4.79]
4. McKeown DW, Bonser RS, Kellum JA. Management of the heartbeating brain-dead organ donor. *Br J Anaesth* 2012; **108** Suppl 1: i96-107 [PMID: 22194439 DOI: 10.1093/bja/aer351]
5. Frenette AJ, Williamson D, Weiss MJ, Rochweg B, Ball I, Brindamour D, Serri K, D'Aragon F, Meade MO, Charbonney E. Worldwide management of donors after neurological death: a systematic review and narrative synthesis of guidelines. *Can J Anaesth* 2020; **67**: 1839-1857 [PMID: 32949008 DOI: 10.1007/s12630-020-01815-0]
6. Meyfroidt G, Gunst J, Martin-Loeches I, Smith M, Robba C, Taccone FS, Citerio G. Management of the brain-dead donor in the ICU: general and specific therapy to improve transplantable organ quality. *Intensive Care Med* 2019; **45**: 343-353 [PMID: 30741327 DOI: 10.1007/s00134-019-05551-y]
7. Patel MS, Zatarain J, De La Cruz S, Sally MB, Ewing T, Crutchfield M, Enestvedt CK, Malinoski DJ. The impact of meeting donor management goals on the number of organs transplanted per expanded criteria donor: a prospective study from the UNOS Region 5 Donor Management Goals Workgroup. *JAMA Surg* 2014; **149**: 969-975 [PMID: 25054379 DOI: 10.1001/jamasurg.2014.967]
8. Lazzeri C, Bonizzoli M, Guetti C, Fulceri GE, Peris A. Hemodynamic management in brain dead donors. *World J Transplant* 2021; **11**: 410-420 [PMID: 34722170 DOI: 10.5500/wjt.v11.i10.410]
9. Nozary Heshmati B, Ahmadi F, Azimi P, Tirgar N, Barzi F, Gattmiri SM. Hemodynamic factors affecting the suitability of the donated heart and kidney for transplantation. *Int J Organ Transplant Med* 2013; **4**: 150-154 [PMID: 25013668]
10. Peris A, Lazzeri C, D'Antonio L, Bombardi M, Bonizzoli M, Guetti C, Maccherini M, Migliaccio ML. Epidemiological changes in potential heart donors after brain death: a retrospective 15 year cohort study. *Intern Emerg Med* 2019; **14**: 371-375 [PMID: 29943077 DOI: 10.1007/s11739-018-1897-8]
11. McKeown DW, Ball J. Treating the donor. *Curr Opin Organ Transplant* 2014; **19**: 85-91 [PMID: 24553498 DOI: 10.1097/MOT.0000000000000059]
12. Franklin GA, Santos AP, Smith JW, Galbraith S, Harbrecht BG, Garrison RN. Optimization of donor management goals yields increased organ use. *Am Surg* 2010; **76**: 587-594 [PMID: 20583513 DOI: 10.1177/000313481007600621]
13. Bera KD, Shah A, English MR, Harvey D, Ploeg RJ. Optimisation of the organ donor and effects on transplanted organs: a narrative review on current practice and future directions. *Anaesthesia* 2020; **75**: 1191-1204 [PMID: 32430910 DOI: 10.1097/00000539-202007000-00010]

- 10.1111/anae.15037]
- 14 **Kothari R**, Tolles J, Adelmann D, Lewis RJ, Malinoski DJ, Niemann CU. Organ donor management goals and delayed graft function in adult kidney transplant recipients. *Clin Transplant* 2022; **36**: e14528 [PMID: 34739731 DOI: 10.1111/ctr.14528]
  - 15 **Malinoski DJ**, Patel MS, Ahmed O, Daly MC, Mooney S, Graybill CO, Foster CE, Salim A; United Network for Organ Sharing (UNOS) Region 5 Donor Management Goals (DMG) Workgroup. The impact of meeting donor management goals on the development of delayed graft function in kidney transplant recipients. *Am J Transplant* 2013; **13**: 993-1000 [PMID: 23406284 DOI: 10.1111/ajt.12090]
  - 16 **Adrie C**, Haouache H, Saleh M, Memain N, Laurent I, Thuong M, Darques L, Guerrini P, Monchi M. An underrecognized source of organ donors: patients with brain death after successfully resuscitated cardiac arrest. *Intensive Care Med* 2008; **34**: 132-137 [PMID: 17932649 DOI: 10.1007/s00134-007-0885-7]
  - 17 **Sandroni C**, Adrie C, Cavallaro F, Marano C, Monchi M, Sanna T, Antonelli M. Are patients brain-dead after successful resuscitation from cardiac arrest suitable as organ donors? A systematic review. *Resuscitation* 2010; **81**: 1609-1614 [PMID: 20932627 DOI: 10.1016/j.resuscitation.2010.08.037]





Published by **Baishideng Publishing Group Inc**  
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

**Telephone:** +1-925-3991568

**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)

**Help Desk:** <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

