American Journal of Transplantation 2017; 17: 1922–1927
Wiley Periodicals Inc.

doi: 10.1111/ajt.14286

Brief Communication

The Influence of End-of-Life Care on Organ Donor Potential

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Many patients with acute devastating brain injury die outside intensive care units and could go unrecognized as potential organ donors. We conducted a prospective observational study in seven hospitals in the Netherlands to define the number of unrecognized potential organ donors outside intensive care units, and to identify the effect that end-of-life care has on organ donor potential. Records of all patients who died between January 2013 and March 2014 were reviewed. Patients were included if they died within 72 h after hospital admission outside the intensive care unit due to devastating brain injury, and fulfilled the criteria for organ donation. Physicians of included patients were interviewed using a standardized questionnaire regarding logistics and medical decisions related to end-of-life care. Of the 5170 patients screened, we found 72 additional potential organ donors outside intensive care units. Initiation of end-of-life care in acute settings and lack of knowledge and experience in organ donation practices outside intensive care units can result in under-recognition of potential donors equivalent to 11–34% of the total pool of organ donors. Collaboration with the intensive care unit and adjusting the end-of-life path in these patients is required to increase the likelihood of organ donation.

Abbreviation: DBI, devastating brain injury; ICU, intensive care unit

Received 14 November 2016, revised 16 March 2017 and accepted for publication 18 March 2017

Introduction

The large gap between donor organ availability and organ demand is, despite many initiatives, a major healthcare issue worldwide. Between countries there is a wide variety of deceased donor rates, from nonexistent to rates over 30 deceased donors per million population (pmp) (1). In 2015, the Netherlands had 15.8 deceased organ donors pmp while at the end of 2014, there were still 984 (63.5 pmp) patients on the waiting list and many patients who died while waiting for an organ (2).

Postmortem organ donors are mostly patients with acute devastating brain injury (DBI) who die in intensive care units (ICU). However, similar patients with DBI also die outside ICUs and could be under-recognized as potential organ donors. Organ donation awareness is high in the ICUs. In the Netherlands almost 100% of the potential organ donors in the ICU are recognized as such (2). However, awareness outside the ICU is lower and this could result in the loss of potential organ donors, especially when patients die outside the ICU (3,4). We aimed to analyze the effect of initiating end-of-life care outside the ICU on organ donor potential in patients admitted to the emergency department with DBI.

Methods

A prospective observational study was performed in seven hospitals (two hospitals with neurosurgical facilities, including one University hospital, and five general hospitals) between January 2013 and April 2014. Patients were included if they were 18–85 years old, were admitted to the hospital due to acute DBI (e.g. ischemic or hemorrhagic strokes; traumatic brain injury), were not admitted to the ICU during their hospital stay, and died within 72 h after hospital admission. The age criterion of 85 years was selected based on the oldest-known Dutch postmortem organ donor. Patients with medical contraindications for organ donation, who had registered an objection to donation in the Dutch Donor Registry, or cases in

Table 1: Age criteria for organ donation according to the Dutch Transplant Foundation

	Age criteria donation after brain death
Kidneys	No age limit
Liver	No age limit
Lungs	Until ±75 years
Heart	Until ±65 years
Pancreas	Until ±60 years
Islets of Langerhans	Until ±75 years
Small intestine	1 to ±50 years
	Age criteria donation after circulatory death
Kidneys	5 to ±75 years
Lungs	5 to ±75 years
Liver	1 month to ±60 years
Pancreas	5 to ±50 years
Islets of Langerhans	Until ±75 years

which organ donation was requested (i.e. patients were recognized as potential organ donors), were excluded. General contraindications for organ donation are as follows: unknown cause of death; untreated sepsis; malignancies (with the exception of nonmetastatic brain tumors and curatively treated malignancy); active viral infection with rabies, herpes zoster, rubella, or human immunodeficiency virus, and active tuberculosis. The age criteria for organ donation, according to the Dutch Transplant Foundation, are shown in Table 1.

Screening occurred in two phases. First, the in-house transplantation coordinators screened the records of all deceased patients. If the inclusion criteria were met, medical files were subsequently analyzed by an intensivist who specialized in organ donation. Second, the intensivist interviewed the physicians who had treated the patient and made the decision to start end-of-life care. This standardized interview focused on the medical decisions about initiating end-of-life care. In addition, national data on the number of potential organ donors in the study period were collected from the database of the Dutch Transplant Foundation. The Medical Ethical Committee of Radboud university medical center waived the need for informed consent.

Descriptive statistics were used to describe the population and to identify factors within end-of-life care that affect the potential donor pool.

Results

Out of 5170 deaths (Figure 1), we found 72 patients with DBI who fulfilled the inclusion criteria. In 68 cases, we were able to perform a structured interview with the treating physicians. Demographic characteristics are shown in Table 2. Fifty percent of the patients died within 16 h after hospital admission and 75% within 44 h (Figure 2).

In 51% of the patients, the decision to start end-of-life care was made in the emergency department (Table 3). These patients died within a median time of 12.0 (Q1–Q3, 5.3–26.8) h after hospital admission, and had a median Glasgow Coma Scale (GCS) of 4.0 (Q1–Q3, 3.0–7.0). In the other 49% of the patients, the decision to start end-of-life care was made after admission to a non-ICU ward after a median time of 21.3 (Q1–Q3, 4.4–33.8) hours, based on deterioration of their clinical state. These patients died within a median time of 24.0 (Q1–Q3, 10.0–50.0) h after hospital admission, and had a median GCS of 5.0 (Q1–Q3, 3.0–7.0). Patients in whom end-of-life care was started at the emergency department were significantly younger than patients in whom end-of-life care was started after admission to a non-ICU ward (median 76.0 vs. 81.0 years; $p = 0.016$). The main reason to initiate end-of-life care was because of ethical or medical objections to active treatment, which was thought not to be beneficial to these patients.

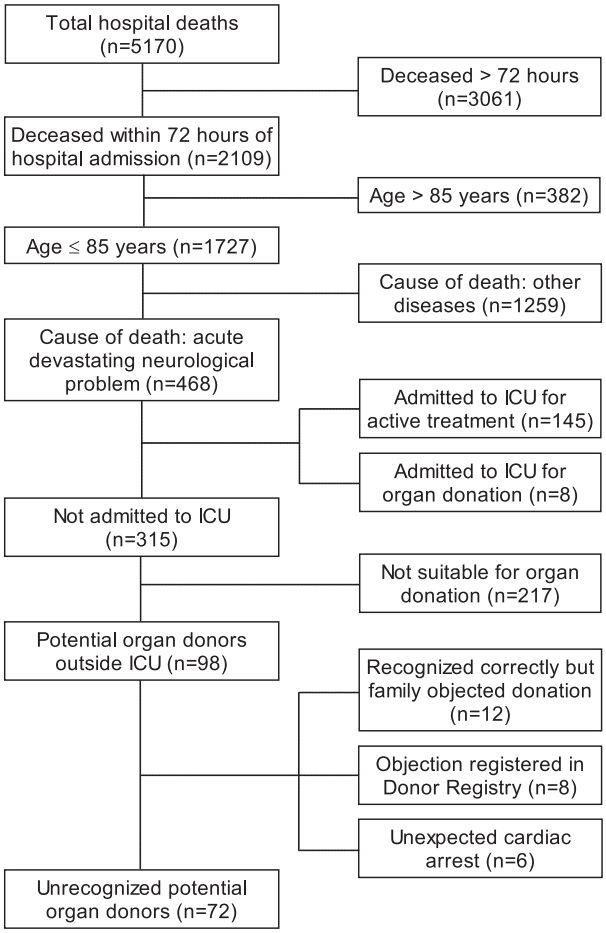

Figure 1: Flow diagram showing the inclusion of deceased patients outside the intensive care unit (ICU).

In 7% of the patients, brain stem reflexes were already absent at hospital admission. In another 44% of the patients who still had brain stem reflexes, progression to brain death could likely have occurred within 48 h, according to the treating physician.

Table 2: Demographic characteristics of the potential organ donors outside the intensive care unit

	Median (Q1–Q3)
Age (n = 72)	78.0 (72.3–83.0)
Glasgow Coma Score (n = 66)	4.0 (3.0–7.0)
	No. (%)
Gender (n = 72)	
Male	40 (56)
Female	31 (43)
Missing	1 (1)
Diagnosis (n = 72)	
(Intra)cerebral/brain stem hemorrhage	45 (63)
Subarachnoid hemorrhage	5 (7)
Subdural hemorrhage	4 (6)
Cerebral infarction	18 (25)

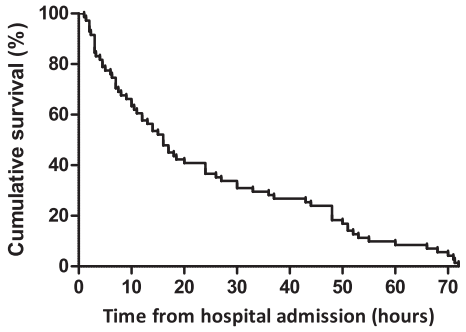

Figure 2: Kaplan–Meier curve: time from hospital admission until death.

The main reasons for not discussing organ donation (Table 2) were that the treating physician forgot or did not consider discussion of organ donation (n = 23) and the incorrect assumption that the patient was too old (n = 11) or not suitable as a donor (n = 7). Five patients were considered unsuitable as donor because the patients were not brain dead and were not expected to die within 2 h. This specific timeframe is mentioned because in the Netherlands patients should die within 2 h after extubation in case of donation after circulatory death.

A total of 10 801 patients died in Dutch ICUs between January 2013 and March 2014, of which 1123 patients (10.4%) were registered as official potential organ donors, including 213 from the seven participating hospitals (2). Corrected for the official donor potential in the seven participating hospitals, we extrapolated the effect of these 72 additional potential donors to a national level. Using the age criterion of 18–85 years, this would result in 379 additional potential organ donors in the Netherlands in our study period. Using the more stringent age criterion for donation after circulatory death, which is up to 75 years in the Netherlands, the additional potential donor pool would be 24 in the seven hospitals. Extrapolation would lead to 126 additional potential organ donors. In total, this would amount to an additional 11–34% in organ donor potential nationally. Table 4 shows the increase in potential organ donors using different age limits.

Discussion

We found that within a large cohort of patients who are hospitalized with acute DBI and die outside the ICU, there are many potential organ donors equivalent to 11–34% of the known organ donor pool. Organ donation expertise tends to be focused within the ICU. The consequential knowledge gap in organ donation practices in non-ICU physicians leads to a loss of potential organ donors (3,4). A continuing professional education and collaborative approach to patients with DBI is required to reduce this knowledge gap and eventually to reduce the transplantation waiting list.

Earlier studies have shown that organ donors in the United States and other European countries are missed in the emergency department (3,5). However, besides formal organ criteria, a planned timing of withdrawal of life-sustaining therapies is also a requisite for controlled organ donation. In our study, we show that the patients who fulfilled the organ donation criteria died because of the medical decision to withdraw or withhold life-sustaining treatments in the acute phase. This means that timing of withdrawal of life-sustaining therapies can, to a large extent, indeed be planned in these patients.

In comparison to the United States, European countries use older donors due to shorter travel distances between hospitals. In addition, in the Netherlands all kidneys (donation after cardiac death and donation after brain death) are being transported on a pump. In our article, we showed the increase in potential organ donors using different age limits.

Our study has some limitations. We interviewed the physicians who treated the patients, which inherently means that answers could be influenced by subjectivity. In addition, interviewing subjects means that recall bias could have influenced the answers. We tried to limit this bias by interviewing the physicians in the days or weeks following the inclusion. Another point of discussion is that not all patients in the potential donor group will be effectuated as organ donors. Most of our patients would fall within the donation after circulatory death group, and only a minority in donation after brain death. In the Netherlands, donation after circulatory death is only possible if the potential organ donor dies within 2 h after withdrawal of life-sustaining treatment and extubation. It

Table 3: End-of-life care conditions of the potential organ donors outside the intensive care unit (ICU)

	No. (%)
Unit/ward where death was confirmed (n = 72)	
Emergency department	9 (13)
Neurology/stroke unit	54 (75)
Neurosurgery	3 (4)
Ward[1]	6 (8)
Scenario that describes the care of patient during final illness (n = 72)	
Admission for palliative care on grounds of futility of active treatment	37 (51)
Admission to ward, but subsequent withdrawal of active treatment due to deteriorating neurological state	35 (49)
Active treatment until unexpected cardiac arrest for which the patient could not be resuscitated	0 (0)
Decision to admit on ICU, which was not possible due to unavailability of critical care bed	0 (0)
Decision to admit on ICU, which was not effectuated due to clinical decision of ICU physician because of futility of active treatment	0 (0)
Did the patient had absent brainstem reflexes (corneal, pupil, spontaneous breathing and cough; excluding apnea and caloric testing) at the time treatment was withdrawn? (n = 72)	
Yes	5 (7)
No	66 (92)
Missing	1 (1)
For patients without brainstem reflexes, did the treating physician think the patient could become brain dead within 48 h? (n = 66[2])	
Yes	29 (44)
No	6 (9)
No statement/Missing	37 (56)
If brain death was expected, why was active treatment not continued? (n = 29)	
Ethical/medical objections to active treatment nonbeneficial to patient	24 (83)
Family objected further treatment	1 (3)
Other[3]	1 (3)
Missing	3 (10)
Was the patient intubated at time of death or decision to withdraw treatment? (n = 72)	
Yes	10 (14)
No	61 (85)
Missing	1 (1)
Reasons for not discussing organ donation (n = 44[4])	
Treating physician forgot/did not consider to discuss organ donation	23 (52)
Unable to contact family	1 (2)
Incorrectly considered that the patient was not suitable as organ donor[5]	7 (16)
Incorrectly considered that the patient was too old for organ donation	11 (25)
Other[6]	3 (7)

[1]Acute admission ward (n = 1), coronary care unit (n = 2), internal medicine (n = 2), medium care (n = 1).
[2]Excluding patients who met preconditions for brain stem death (n = 5) or if this was unknown (n = 1).
[3]Deteriorating hemodynamic situation (n = 1).
[4]In the other cases a reason for not discussing tissue donation was given (n = 20) or no reason was given (n = 8). More than one answer could be given to this question.
[5]Not brain dead, or not expected to die in 2 h in case of donation after circulatory death (n = 5), medical history (n = 1), patient was not intubated (n = 1).
[6]No ICU admission policy (n = 2), not admitted to ICU (n = 1).

Table 4: Increase in potential organ donors using different age limits

Age criteria	Increase potential organ donors
60 years	1.4%
65 years	2.8%
70 years	6.6%
75 years	11.3%
80 years	21.6%
85 years	33.8%

is plausible that patients within this group could not become a donor, as they would not die within the 2-h timeframe. In addition, it might not always be possible to admit patients to the ICU due to a shortage of ICU beds. However, in none of the cases of included patients was this given as the reason why patients were not admitted to the ICU. As the number of potential organ donors from the emergency department is rather low compared to the ICU beds capacity, we believe that these patients will have little impact on ICU beds availability or finances.

Although not all potential donors will be effectuated as organ donors, we think that organ donation, and a possible ICU admission, should at least be considered in these patients.

Over the last decade, we have witnessed a transition in which end-of-life care has become an increasingly essential part of care for the critically ill (6,7). At the same time, there is an ongoing debate on the role and resources that ICU admissions should have at the end of life (8). Incorporating organ donation in end-of-life care in patients who die in the ICU is recommended to increase the number of donors and to comply with the wishes of patients and family (9,10). Can we justify the use of valuable ICU resources in many more patients with DBI and a presumed futile prognosis? First, personalized end-of-life care and family-centered care, including sufficient time to understand the prognosis, is important to prevent prolonged grief (11,12). Given the tasks of the emergency department, sufficient time for end-of-life care is practically impossible. Second, different rules for prognostication exist for patients with DBI. However, there are no accepted guidelines on how or when to use them in daily clinical practice. In 2015, the Neurocritical Care Society recommended delaying decisions regarding end-of-life care within the first 72 h in patients with DBI in order not to miss the small potential for good medical outcomes (13). Different attitudes toward end-of-life care practices exist worldwide (14). Likewise, a universal approach to patients with DBI with a presumed futile prognosis is unlikely, due to different social, religious, legal, economic, and ethical differences (15–17).

In conclusion, we found that initiation of end-of-life care in acute settings and lack of knowledge and experience in organ donation practices outside ICUs results in underrecognition of patients who could potentially donate. Therefore, we argue that the decision to initiate end-of-life care in patients hospitalized with acute DBI should be a multidisciplinary approach even when futility of the prognosis seems evident. Ideally, medical personnel trained in organ donation practices would be part of such a multidisciplinary team, or at least a consultation with such trained personnel should occur. Irrespective of the decision to withdraw or withhold life-sustaining treatments, or to delay such a decision in the acute phase, a nontherapeutic ICU admission in such patients could improve the recognition of potential organ donors and create better conditions to discuss organ donation with relatives. Although our data show the possibility of increasing the pool of potential organ donors, the actual increase in effectuated organ donors could be smaller as there could be different reasons why such patients will not convert to organ donors. Further studies and efforts are needed to conclude whether a change in approach in these patients would lead to more effectuated organ donors.

Acknowledgments

This study was, in part, funded by the Dutch Ministry of Health. Dr. W.F. Abdo is supported by a research grant from the Netherlands Organization for Health Research and Development (ZonMw Clinical Fellowship Grant 90715610). Funding agencies had no role in design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclosure

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation.*

References

1. Newsletter Transplant 2016 of Organización Nacional de Trasplantes. [cited 2016 May 10]. Available from: http://www.ont.es/publicaciones/Documents/NEWSLETTER%202016%202.pdf.
2. Annual report 2015 of the Dutch Transplant Foundation. [cited 2016 May 5]. Available from: http://www.transplantatiestichting.nl/sites/default/files/product/downloads/nts_jaarverslag_2015.pdf.
3. Le Conte P, Riochet D, Labastire L, et al. Identification of potential organ donors of advanced age in EDs. Am J Emerg Med 2012; 30: 170–173.
4. Traino HM, Alolod GP, Shafer T, Siminoff LA. Interim results of a national test of the rapid assessment of hospital procurement barriers in donation (RAPiD). Am J Transplant 2012; 12: 3094–3103.
5. Riker RR, White BW. Organ and tissue donation from the emergency department. J Emerg Med 1991; 9: 405–410.
6. Curtis JR, Vincent JL. Ethics and end-of-life care for adults in the intensive care unit. Lancet 2010; 376: 1347–1353.
7. Angus DC, Barnato AE, Linde-Zwirble WT, et al. Use of intensive care at the end of life in the United States: An epidemiologic study. Crit Care Med 2004; 32: 638–643.
8. Angus DC, Truog RD. Toward better ICU use at the end of life. JAMA 2016; 315: 255–256.
9. Dominguez-Gil B, Murphy P, Procaccio F. Ten changes that could improve organ donation in the intensive care unit. Intensive Care Med 2016; 42: 264–267.
10. Citerio G, Cypel M, Dobb GJ, et al. Organ donation in adults: A critical care perspective. Intensive Care Med 2016; 42: 305–315.
11. Ingles J, Spinks C, Yeates L, McGeechan K, Kasparian N, Semsarian C. Posttraumatic stress and prolonged grief after the sudden cardiac death of a young relative. JAMA Intern Med 2016; 176: 402–405.
12. Murthy SB, Moradiya Y, Hanley DF, Ziai WC. Palliative care utilization in nontraumatic intracerebral hemorrhage in the United States. Crit Care Med 2016; 44: 575–582.
13. Souter MJ, Blissitt PA, Blosser S, et al. Recommendations for the critical care management of devastating brain injury: Prognostication, psychosocial, and ethical management: A position statement for healthcare professionals from the neurocritical care society. Neurocrit Care 2015; 23: 4–13.

14. Koh M, Hwee PC. End-of-life care in the intensive care unit: How Asia differs from the West. JAMA Intern Med 2015; 175: 371–372.
15. Myburgh J, Abillama F, Chiumello D, et al. End-of-life care in the intensive care unit: Report from the task force of world federation of societies of intensive and critical care medicine. J Crit Care 2016; 34: 125–130.
16. Parker M, Shemie SD. Pro/con ethics debate: Should mechanical ventilation be continued to allow for progression to brain death so that organs can be donated? Crit Care 2002; 6: 399–402.
17. Price D. End-of-life treatment of potential organ donors: Paradigm shifts in intensive and emergency care. Med Law Rev 2011; 19: 86–116.