



Prediction of potential for organ donation after cardiac death in patients in neurocritical state: a prospective observational study

Alejandro A Rabinstein, Alan H Yee, Jay Mandrekar, Jennifer E Fugate, Yorick J de Groot, Erwin J O Kompanje, Lori A Shutter, W David Freeman, Michael A Rubin, Eelco F M Wijdicks

Summary

Background Successful donation of organs after cardiac death (DCD) requires identification of patients who will die within 60 min of withdrawal of life-sustaining treatment (WLST). We aimed to validate a straightforward model to predict the likelihood of death within 60 min of WLST in patients with irreversible brain injury.

Methods In this multicentre, observational study, we prospectively enrolled consecutive comatose patients with irreversible brain injury undergoing WLST at six medical centres in the USA and the Netherlands. We assessed four clinical characteristics (corneal reflex, cough reflex, best motor response, and oxygenation index) as predictor variables, which were selected on the basis of previous findings. We excluded patients who had brain death or were not intubated. The primary endpoint was death within 60 min of WLST. We used univariate and multivariable logistic regression analyses to assess associations with predictor variables. Points attributed to each variable were summed to create a predictive score for cardiac death in patients in neurocritical state (the DCD-N score). We assessed performance of the score using area under the curve analysis.

Findings We included 178 patients, 82 (46%) of whom died within 60 min of WLST. Absent corneal reflexes (odds ratio [OR] 2.67, 95% CI 1.19–6.01; $p=0.0173$; 1 point), absent cough reflex (4.16, 1.79–9.70; $p=0.0009$; 2 points), extensor or absent motor responses (2.99, 1.22–7.34; $p=0.0168$; 1 point), and an oxygenation index score of more than 3.0 (2.31, 1.10–4.88; $p=0.0276$; 1 point) were predictive of death within 60 min of WLST. 59 of 82 patients who died within 60 min of WLST had DCD-N scores of 3 or more (72% sensitivity), and 75 of 96 of those who did not die within this interval had scores of 0–2 (78% specificity); taking into account the prevalence of death within 60 min in this population, a score of 3 or more was translated into a 74% chance of death within 60 min (positive predictive value) and a score of 0–2 translated into a 77% chance of survival beyond 60 min (negative predictive value).

Interpretation The DCD-N score can be used to predict potential candidates for DCD in patients with non-survivable brain injury. However, this score needs to be tested specifically in a cohort of potential donors participating in DCD protocols.

Funding None.

Introduction

Donation after cardiac death (DCD) protocols allow families of patients who are dying but not brain dead to donate organs. Such protocols have been implemented in many countries and might reduce the shortage of available organs for transplantation.¹ After withdrawal of life-sustaining treatment (WLST), DCD allows organ procurement in an operating room after irreversible cessation of respiration and circulation has been declared.² Although such donation contributes an increasing proportion of viable organs for transplantation, identification of appropriate candidates is a restricting factor.

Patients with catastrophic, irreversible brain injury who do not meet criteria for brain death are the most frequent candidates for DCD,^{3–5} but about half of these patients continue to breathe and maintain circulation for more than 60 min after WLST.⁶ The success of DCD relies on identification of patients who are most likely to die within

60 min of WLST. Prolongation of the withdrawal phase of warm ischaemia time (ie, the time between WLST and end of cardiopulmonary function) beyond 60 min can compromise organ function.^{2,7} Thus, most DCD protocols do not continue with organ retrieval if the patient is still alive 60 min after WLST.⁸ However, good outcomes have been reported with organ transplants (particularly kidneys) retrieved after up to 4 h of warm ischaemia.^{9,10}

Available scores used by organ-procurement organisations to estimate the time to death after WLST, such as the Wisconsin criteria³ or the United Network for Organ Sharing (UNOS) criteria,⁴ include little information about the neurological status of the patient before WLST. Calculation of these scores requires temporary disconnection of the patient from the mechanical ventilator and the scores are tailored to assess the degree of pulmonary and circulatory support. These variables might be of less prognostic value in patients with catastrophic neurological injury who have not progressed

Published Online

April 10, 2012

DOI:10.1016/S1474-4422(12)70060-1

See Online/Comment

DOI:10.1016/S1474-4422(12)70068-6

Department of Neurology (Prof A A Rabinstein MD, J E Fugate DO, E F M Wijdicks MD) and Department of Biomedical Statistics and Informatics (J Mandrekar PhD), Mayo Clinic, Rochester, MN, USA; Department of Neurology, University of California, San Francisco, CA, USA (A H Yee DO); Department of Intensive Care, Erasmus MC University Medical Center, Rotterdam, Netherlands (Y J de Groot MD, E J O Kompanje PhD); Departments of Neurosurgery and Neurology, University of Cincinnati, OH, USA (L A Shutter MD); Department of Neurology, Mayo Clinic, Jacksonville, FL, USA (W D Freeman MD); and Department of Neurology, Washington University School of Medicine, St Louis, MO, USA (M A Rubin MD)

Correspondence to:

Prof Alejandro A Rabinstein, 200 First Street SW, Mayo W8B, Rochester, MN 55905, USA
rabinstein.alejandro@mayo.edu

to brain death than in patients with major non-neurological injury. This notion was reinforced by our previous analysis⁶ in which several respiratory and haemodynamic parameters were associated with death within 60 min of WLST on univariate analyses, but not on the multivariable analysis that included elements of a neurological examination. This single-centre study⁶ of 149 patients who were in coma with irreversible brain injury suggested that, after WLST, four clinical variables were associated with death within 60 min of extubation: absent corneal reflex, absent cough reflex, extensor or absent motor response, and higher oxygenation index. These associations were confirmed subsequently in a smaller, independent cohort.¹¹

To further validate this approach, we undertook a prospective study to produce a new model to predict death within 60 min of WLST in patients with catastrophic cerebral damage, which was based on the previously described clinical variables. We aimed to develop a practical score for assessment of potential candidates for DCD.

Methods

Study design and participants

In this multicentre, observational study, we prospectively obtained data from consecutive adult, comatose patients with irreversible brain damage who underwent WLST at the intensive care units of six participating centres in the USA and the Netherlands. We enrolled patients in the study if anticipated death was attributable directly to severe brain injury (eg, massive head trauma, intracranial haemorrhage, ischaemic stroke with malignant oedema, or anoxic damage after cardiorespiratory arrest). We excluded patients without tracheal intubation or who fulfilled criteria for brain death. The study protocol was

approved by the institutional review board of each centre and consent for data collection was obtained from the next of kin when requested by the individual board.

We selected variables for data collection on the basis of findings from our previous comprehensive analysis.⁶ Data obtained for this study included age, sex, corneal reflex (present or absent), cough reflex (present or absent), motor response to pain (absent or extensor response or better response), oxygenation index, and time to death after WLST. We calculated oxygenation index with the following formula: $100 \times (\text{FiO}_2 \times \text{mean airway pressure in cm H}_2\text{O}) / \text{PaO}_2$ in torr), where mean airway pressure is half the combination of peak airway pressure in cm H₂O and peak end expiratory pressure in torr.

We assessed these variables at the last examination before WLST, which occurred after discontinuation of sedation and opiate analgesia. The endpoint for the analysis was death within 60 min of WLST.

Statistical analysis

We used univariate and multivariable logistic regression analyses with death within 60 min as a binary outcome variable to assess the associations with predictor variables identified in our previous study.⁶ The area under the receiver operating characteristic (ROC) curve was estimated as a measure of the ability of the model to discriminate between individuals who died within 60 min of WLST versus those who died after 60 min. An area under the ROC estimate of 0.7–0.8 was regarded as acceptable, 0.8–0.9 was regarded as excellent, and more than 0.9 was regarded as outstanding.¹² We did sample size calculations with the assumption that oxygenation index would be the dichotomised variable that would need the maximum sample size.⁶ Assuming a rate of death within 60 min of 50% and a total sample size of 150 patients (ie, 75 per group), we would have 80% power to detect a difference of 45% versus 23% for the presence of higher oxygenation index level between patients who died within 60 min and those who died after 60 min, at a 5% level of significance with the χ^2 test. We used NQuery advisor (version 6) for sample size and power calculations. To account for the possibility of missing or unusable data we aimed to recruit at least 15% more patients, meaning that our target enrolment was 175–180 patients. We used ROC curve analysis to identify the cutoff to dichotomise continuous variables of interest, such as oxygenation index, or the estimated score that increased the sum of sensitivity and specificity to the highest amount. We also applied parameter estimates from the multivariable logistic regression model (fitted to prospective data) to the previous retrospective data to calculate the predicted probabilities of health for every patient. We then used these predictive probabilities to estimate the area under the ROC. We did all analyses apart from the sample size calculation with SAS version 9.2.

	Patients (n=178)
Age, years	63.4 (17.1, 17–94)
Sex, female	84 (47%)
Primary diagnosis	
Intracerebral haemorrhage	60 (34%)
Ischaemic stroke	33 (19%)
Subarachnoid haemorrhage	30 (17%)
Head trauma*	26 (15%)
Others	26 (15%)
Active cancer	11 (6%)
Renal failure†	16 (9%)
Liver failure‡	6 (3%)
Sepsis§	5 (3%)

Data are mean (SD, range) or n (%). *Includes subdural haematoma. †Creatinine >221 µmol/L, creatinine clearance <0.5 mL/s, or renal replacement therapy. ‡Documented cirrhosis or acute hepatitis with altered protein synthesis (ie, increased international normalised ratio >1.5 without alternative explanation). §Sepsis syndrome with documented bacteraemia.

Table 1: Baseline characteristics

Role of the funding source

There was no funding source for this study. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Between March 30, 2010, and April 1, 2011, we assessed 178 patients. Table 1 summarises baseline characteristics of our study population. We enrolled 70 patients at the Mayo Clinic in Rochester (MN, USA), 39 at the Erasmus MC University Medical Center in Rotterdam (Netherlands), 30 at the University of Cincinnati (OH, USA), 17 at the Mayo Clinic in Jacksonville (FL, USA), 12 at Washington University in St Louis (MO, USA), and ten at the University of California, San Francisco (CA, USA).

82 patients (46%) died within 60 min of WLST, 97 (54%) died within 2 h, and 109 (61%) died within 4 h. Absent corneal reflex ($p=0.0334$), absent cough reflex ($p=0.0002$), extensor or absent motor response to pain ($p=0.0331$), and higher oxygenation index ($p=0.0183$) were associated with death within 60 min of WLST in a multivariable logistic regression model including oxygenation index as a continuous variable.

Construction of a straightforward scoring system that allows quick estimation of probabilities of death within 60 min required all variables to be categorical or dichotomised. Thus, we explored the distribution of oxygenation index in the entire cohort and, using ROC analysis, we established that an oxygenation index of 3.0 had the best combination of sensitivity and specificity to discriminate between patients who died within 60 min and those who died more than 60 min after WLST. Table 2 shows the distribution of the variables of interest in the two groups of patients and the strength of the associations.

We created a score to predict the chance of death within 60 min of WLST (ie, the DCD-N score) on the basis of odds ratios for every variable, assigning 2 points for absent cough reflex and 1 point each for absent corneal reflexes, absent or extensor motor response to pain, and oxygenation index of more than 3.0. The probability of death within 60 min of WLST increased as the score increased (table 3). The area under the curve for the score was 0.81 (95% CI 0.75–0.87) for prediction of death within 60 min (figure), 0.77 (0.70–0.84) for death within 2 h, and 0.76 (0.69–0.83) for death within 4 h. Compared with a score of 0–2, a score of 3–5 had a sensitivity of 72%, a specificity of 78%, a positive predictive value of 74%, and a negative predictive value of 77% to predict death within 60 min of WLST. In other words, 59 of 82 (72%) patients who died within 60 min had a score of 3 or more (sensitivity) and 75 of 96 (78%) of patients who did not die within this interval had a score of 0–2 (specificity). Taking into account the prevalence of death within 60 min in this population, a score of 3 or more translates into a 74%

	Death within 60 min (n=82)	Death after 60 min (n=96)	Odds ratio (95% CI)	p value
Absent corneal reflex	64 (74%)	31 (33%)	2.67 (1.19–6.01)	0.0173
Absent cough reflex	45 (55%)	12 (13%)	4.16 (1.79–9.70)	0.0009
Extensor or absent motor response	72 (88%)	52 (54%)	2.99 (1.22–7.34)	0.0168
Oxygenation index >3.0	60 (73%)	50 (52%)	2.31 (1.10–4.88)	0.0276

Data are n (%) unless otherwise stated. Oxygenation index presented as a categorical variable (>3.0 vs ≤3.0).

Table 2: Distribution of variables of interest according to time to death after withdrawal of life-sustaining measures

	Deaths within 60 min	Deaths after 60 min
0	1 (5%)	18 (95%)
1	11 (27%)	30 (73%)
2	11 (29%)	27 (71%)
3	15 (52%)	14 (48%)
4	12 (80%)	3 (20%)
5	32 (89%)	4 (11%)
Overall	82 (46%)	96 (54%)

Table 3: Frequency of death after withdrawal of life-sustaining measures according to donation after cardiac death in patients in a neurocritical state (DCD-N) score

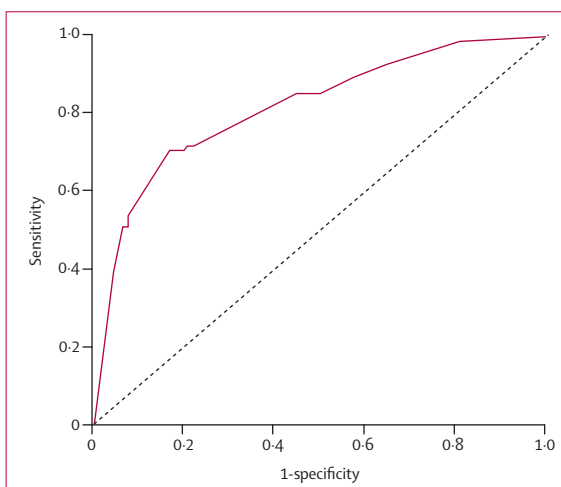


Figure: Receiver operating characteristic curve based on a multivariable model for prediction of death within 60 min

Dashed line shows equivalent sensitivity and 1-specificity.

probability of death within 60 min (positive predictive value) whereas a score of 0–2 translates into a 77% probability of survival beyond 60 min (negative predictive value). Table 4 shows the probabilities of death within 60 min according to specific combinations of variables. We validated the performance of the score in our previously reported retrospective cohort of 149 patients (table 5). In this retrospective cohort,⁸ a cutoff score of 3 (scores 3–5 vs 1–2) had a sensitivity of 81%, a specificity of 73%, a positive predictive value of 75%, and a negative predictive value of 79% to predict death within 60 min of WLST.

Absent corneal reflex	Absent cough reflex	Extensor or absent motor response	Oxygenation index >3.0	Score	Probability
No	No	No	No	0	0.08
No	No	No	Yes	1	0.16
Yes	No	No	No	1	0.18
No	No	Yes	No	1	0.20
No	Yes	No	No	2	0.26
Yes	No	No	Yes	2	0.34
No	No	Yes	Yes	2	0.37
Yes	No	Yes	No	2	0.40
No	Yes	No	Yes	3	0.45
Yes	Yes	No	No	3	0.48
No	Yes	Yes	No	3	0.51
Yes	No	Yes	Yes	3	0.61
Yes	Yes	No	Yes	4	0.68
No	Yes	Yes	Yes	4	0.71
Yes	Yes	Yes	No	4	0.74
Yes	Yes	Yes	Yes	5	0.87

1 point was assigned for each of absent corneal reflex, absent or extensor motor response to pain, and oxygenation index of more than 3.0. 2 points were assigned for an absent cough reflex.

Table 4: Probabilities of death within 60 min according to the combinations of predictive variables

	Death within 60 min	Death after 60 min
0	0	14 (100%)
1	6 (12%)	21 (78%)
2	8 (30%)	19 (70%)
3	18 (62%)	11 (38%)
4	15 (71%)	6 (29%)
5	28 (90%)	3 (10%)
Overall	75 (50%)	74 (50%)

Table 5: Frequency of death after withdrawal of life-sustaining measures according to donation after cardiac death in patients in a neurocritical state (DCD-N) score in the retrospective cohort of 149 patients⁶

We also tested a previously described linear predictor, model with oxygenation index as a continuous variable.¹¹ We adjusted the weight of the variables on the basis of the strength of the associations identified in this prospective cohort, which was much larger than the one used to develop the linear predictor model. The resulting model used the following formula:

$$\text{Logit} = -2.49 + (0.90 \times \text{absent corneal reflex}) + (1.65 \times \text{absent cough reflex}) + (0.98 \times \text{extensor or absent motor response}) + (0.12 \times \text{oxygenation index})$$

The equation $\text{Exp}(\text{logit}) / 1 + \text{Exp}(\text{logit})$ can then be used to calculate the probability of death within 60 min of WLST for individual patients. Thus, for a patient with absent corneal reflex, present cough reflex, absent motor response to pain, and an oxygenation index of 6 (whose

DCD-N score would be 3) the logit would be 0.11 and the predicted probability of death within 60 min of WLST would be 53%.

Discussion

When the decision to proceed with WLST is reached, medical teams in many countries contact local organ-procurement organisations to address the possibility of organ donation. In these situations, reliable identification of appropriate DCD candidates is essential for all concerned. Because catastrophic brain injury is the most common cause of death in patients who might be suitable for DCD, such methods should be especially applicable to patients in neurocritical state. In this study, we validated the predictive value of a small set of variables that can be used to identify such patients confidently (panel). Furthermore, we present a method—the DCD-N score—that can be used at the bedside to quantify the likelihood of death within the time required in most DCD protocols.

The variables included in the present study were identified after a comprehensive analysis of various neurological and non-neurological parameters in a retrospective cohort of patients in neurocritical state.⁶ In that analysis, several other variables were associated with death within 60 min of WLST, including several haemodynamic and additional respiratory function measures. However, on multivariable analysis only three neurological variables (absent cough, absent corneal reflexes, and absent or extensor motor response to pain) and pulmonary function (oxygenation index) were independently associated with death within 60 min of extubation.

Prediction of time to death after WLST on the basis of clinical impression has proven inaccurate. In a recent prospective, multicentre, observational study of potential DCD donors, the clinical judgment of the treating intensive-care doctor had a fairly high sensitivity (73%) but a low specificity (56%) to predict death within 60 min.¹³ Because of this restricted ability to predict the time of death reliably, the authors of that study suggested that the DCD procedure should be used for every potential donor to avoid loss of viable organs. However, this approach is troublesome for grieving families, labour-intensive for transplantation teams, and very expensive for hospitals. Instead, improvement of our ability to identify good candidates for donation should remain the objective.

Other scores to estimate early death after WLST are in use (eg, UNOS and the University of Wisconsin criteria) but have disadvantages.³⁴ These scores incorporate neurological information only at the level of consciousness, which is not a reliable predictor of early death after terminal extubation in patients in neurocritical state.¹⁴ Moreover, their calculations require disconnection from mechanical ventilation for 10 min. Our scoring system has been specifically designed to be used in neurological

Panel: Research in context**Systematic review**

We searched Medline and Embase databases up to Feb 29, 2012, for articles published in any language with the search terms "donation after cardiac death", "donation after circulatory death", and "prediction of time to death". We also reviewed the reference lists of the papers identified by this search. We assessed these articles for data for predictors of early death after withdrawal of life-sustaining treatment in patients with severe brain injury.

Interpretation

The findings from our prospective, multicentre observational study suggest that the donation after cardiac death in patients in a neurocritical state (DCD-N) score predicts which patients with severe brain injury undergoing withdrawal of life-sustaining treatment will die within 60 min of extubation. This measure relies mainly on findings from neurological examination and can be applied at the bedside without the need for transient disconnection from mechanical ventilation, unlike presently used predictive criteria (such as the United Network for Organ Sharing or Wisconsin criteria), which are more complex and might have reduced predictive value in patients with severe brain injury.^{3,4} Currently, donation after cardiac death protocols are sometimes underused because of concern that the potential donor will not die within the period of time compatible with an acceptable duration of warm ischaemia.¹⁰ The DCD-N score might be useful to identify the best candidates for donation among patients in a neurocritical state, thus reducing the chances of unsuccessful activation of retrieval teams and improved allocation of resources.

patients with severe, irreversible brain injury and it can be fully assessed while the potential donor remains supported by mechanical ventilation. Furthermore, the information used to calculate the DCD-N score is usually available as part of the routine medical care of these patients.

To develop the DCD-N score, we transformed oxygenation index into a categorical variable. However, its predictive value is best when it is analysed as a continuous variable.¹¹ The linear predictor model that incorporates the actual oxygenation index measurement is a valid alternative to the DCD-N score. Thus, the two approaches provide different ways of assessing the chance of death within 60 min: the DCD-N score offers cutoffs (eg, a DCD-N score of >2 suggests that 74% of patients will die within this time interval) and the linear predictor model expresses the likelihood of this outcome as a percentage. One model has the advantage of simplicity, the other delivers greater precision.

Our study has limitations. We prospectively collected data for only those variables that we had identified previously as predictive of death within 60 min of WLST in a retrospective cohort.⁶ We regarded this approach as sufficient because the previous study consisted of a

comprehensive exploratory analysis of many neurological and systemic variables, including those listed in presently used criteria. Furthermore, the validity of the predictive value of the variables we had identified had been subsequently confirmed in a different cohort of patients with severe, irreversible brain injury.¹¹ Nevertheless, other variables not included in our predictive technique might also influence the likelihood of early death after extubation^{5,13,15} and the DCD-N score has not been compared against other predictive criteria. Although sedatives and opiates were stopped before assessment, a residual effect from medication might have had a confounding role. Moreover, our study was not restricted to patients deemed potential candidates for DCD and consequently some patients with advanced age, cancer, and severe infections were entered in the analysis. However, because our models rely mostly on neurological criteria, we would not expect their predictive performance to change substantially when used to screen patients in neurocritical state who are under consideration for DCD. Finally, the score we propose should be used only for patients dying from irreversible acute brain disease and should not be extrapolated to other candidates for DCD.

DCD protocols are used increasingly in the USA, UK, and Europe, although there are notable exceptions such as Germany.¹⁶ However, in some centres these protocols are underused because of concerns that the potential donor might not die within the accepted maximum time of warm ischaemia. We believe that the DCD-N score has good potential to advance the practice of DCD by improving the identification of appropriate candidates. Its discriminative power is supported by the area under the curve noted in our ROC analysis. Nevertheless, the score does not identify all patients who die within 60 min of WLST or at later times up to 4 h. Thus, future studies might help refine the score to reduce this under-recognition of potential donors. Such studies could explore combination of the DCD-N score with the Wisconsin or the UNOS criteria or incorporation of haemodynamic or additional respiratory variables. More importantly, the DCD-N score needs to be tested specifically in a prospective cohort of patients participating in DCD protocols as potential donors.

The DCD-N score provides a readily accessible estimate of the likelihood of death within 60 min of WLST in patients with critical brain injury who are dependent on artificial life support. The score needs to be tested in patients for whom consent of DCD has been obtained. If the reliability of its performance is confirmed, this scoring technique could help guide resource allocation without compromising the availability of viable DCD donors.

Contributors

AAR, AHY, and EFMW designed the study with statistical assistance from JM, JEF, AHY, YJdG, EJOK, LAS, WDF, and MAR collected the data from their respective centres. AAR, AHY and EFMW supervised the

study. JM did the statistical analysis. AAR, JM, AHY, and EFMW interpreted the results of the analysis with subsequent substantial contributions from all co-authors. AAR wrote the report. All authors contributed with revisions and gave approval to the final version of the manuscript.

Conflicts of interest

We declare that we have no conflicts of interest.

Acknowledgments

We thank Maggie Brenner and Carolyn Koenig for their assistance with enrolment of patients and data collection.

References

- 1 Tuttle-Newhall JE, Krishnan SM, Levy MF, McBride V, Orlowski JP, Sung RS. Organ donation and utilization in the United States: 1998–2007. *Am J Transplant* 2009; **9**: 879–93.
- 2 Bernat JL, D'Alessandro AM, Port FK, et al. Report of a national conference on donation after cardiac death. *Am J Transplant* 2006; **6**: 281–91.
- 3 Lewis J, Peltier J, Nelson H, et al. Development of the University of Wisconsin donation after cardiac death evaluation tool. *Prog Transplant* 2003; **13**: 265–73.
- 4 De Vita MA, Mori Brooks M, Zawistowski C, Rudich S, Daly B, Chaitin E. Donors after cardiac death: validation of identification criteria (DVIC) study for predictors of rapid death. *Am J Transplant* 2008; **8**: 432–41.
- 5 Suntharalingam C, Sharples L, Dudley C, Bradley JA, Watson JE. Time to cardiac death after withdrawal of life-sustaining treatment in potential organ donors. *Am J Transplant* 2009; **9**: 2157–65.
- 6 Yee AH, Rabinstein AA, Thapa P, Mandrekar J, Wijdicks EFM. Factors influencing time to death after withdrawal of life support in neurocritical patients. *Neurology* 2010; **74**: 1380–85.
- 7 D'Alessandro AM, Fernandez LA, Chin LT, et al. Donation after cardiac death: the University of Wisconsin experience. *Ann Transplant* 2004; **9**: 68–71.
- 8 Fugate JE, Stadler M, Rabinstein AA, Wijdicks EFM. Variability in donation after cardiac death protocols: a national survey. *Transplantation* 2011; **91**: 386–89.
- 9 Reid Awn, Harper S, Jackson CH, et al. Expansion of the kidney donor pool by using cardiac death donors with prolonged time to cardiorespiratory arrest. *Am J Transplant* 2011; **11**: 995–1005.
- 10 Manara AR, Murphy PG, O'Callaghan G. Donation after circulatory death. *Br J Anaesth* 2012; **108** (suppl 1): i108–21.
- 11 de Groot YJ, Lingsma HF, Bakker J, Gommers DA, Steyerberg E, Kompanje EJ. External validation of a prognostic model predicting time of death after withdrawal of life support in neurocritical patients. *Crit Care Med* 2012; **40**: 233–38.
- 12 Hosmer DW, Lemeshow S. Applied logistic regression, 2nd edn. Hoboken, NJ, USA: John Wiley and Sons, 2000.
- 13 Wind T, Snoeijs MG, Brugman CA, et al. Prediction of time of death after withdrawal of life-sustaining treatment in potential donors after cardiac death. *Crit Care Med* 2012; **40**: 766–69.
- 14 Mayer SA, Kossoff SB. Withdrawal of life support in the neurological intensive care unit. *Neurology* 1999; **12**: 1602–09.
- 15 Cooke CR, Hotchkiss DL, Engelberg RA, Rubinson L, Curtis JR. Predictors of time to death after terminal withdrawal of mechanical ventilation in the ICU. *Chest* 2010; **138**: 289–97.
- 16 Dominguez-Gil B, Haase-Kromwijk B, Van Leiden H, et al. Current situation of donation after circulatory death in European countries. *Transpl Int* 2011; **24**: 676–86.

Donation after cardiac death: enter the neurologist



Donation after cardiac death (DCD) is the process through which donation of solid organs takes place after the heart stops (usually within 5 min of cardiac arrest). Because the permanent cessation of heartbeat satisfies the dead donor rule, which states that donor transplantation should not kill the patient but rather that the patient be already dead, DCD procedures have been approved in many countries.¹ During the past decade, the disparity between the number of patients waiting for a transplant and the number of organs available has increased. As such, transplantation programmes in many countries have revisited the use of organs from donors after cardiac death. Previously, most programmes relied solely on organs from donors who were brain dead. As a result, DCD has greatly boosted organ donation beyond that which occurred after the declaration of brain death or neurological determination of death.²

In a study reported in this issue of *The Lancet Neurology*,³ Rabinstein and colleagues have tested a neurologically-based scoring system that should increase the accuracy of donor selection. Successful DCD requires selection of patients whose hearts are likely to stop within 1–2 h after withdrawal of life-sustaining treatment (WLST), to reduce anoxic injury that occurs during the withdrawal process and thus allow the organs to remain viable for transplantation. However, the DCD process needs substantial resources and therefore the ability to predict with reasonable certainty which patients will die within 1–2 h is key. The Wisconsin guidelines⁴ were developed by non-neurological intensive-care specialists to provide a measure of the probability of cardiac arrest within 1 h of WLST. The factors used in these guidelines include presence of spontaneous respiration after 10 min off the ventilator, body-mass index, use of vasopressors, age of the patient, use of tracheostomy versus use of endotracheal tube, and oxygen saturation after 10 min. Each of these variables was assigned a value and the aggregate score was used to predict cardiac death within 1 h of WLST. However, subsequent attempts to define risk factors for early death more accurately have suggested that a reliable technique for prediction of time of death after WLST is not available.⁵

Most patients who become DCD donors have severe CNS damage but are not brain dead. Although neurologists are at least one step removed from the DCD process, such professionals might be better qualified than other specialists to establish the neurological factors that

predict cardiac arrest after WLST in patients who have brain damage. Since the withdrawal process includes the removal of the endotracheal tube in the operating room (and hence most patients die of asphyxic cardiac arrest), the presumption is that patients who are closer to brain death and are either not able to breathe adequately or protect the airway have a higher chance of prompt cardiac arrest. Whether or not health-care providers have qualms or philosophical concerns about DCD, when it is adopted as an accepted practice, as it currently is in many countries, the improvement of the process becomes a priority.⁶

Rabinstein and colleagues report a prospective observational study³ that aimed to validate the use of a neurological scoring system to assess likelihood of death within 60 min after WLST. The scoring system was built on a previous retrospective study⁷ by the investigators of patients who had brain injury and underwent WLST for compassionate reasons.⁶ Rabinstein and colleagues' study³ included 178 patients with heterogeneous disorders, but more than 85% of them had structural brain damage (intracranial haemorrhage, ischaemic stroke, or head injury). Borrowing from the FOUR score tabulation⁸ of neurological assessment of patients in coma, four factors were statistically associated with death within 1 h of WLST: absent corneal reflexes, absent cough reflex, no better than extensor (decerebrate) posturing, and oxygen index. Each of these factors was assigned a score (1 point each for absent corneal reflex, extensor or absent motor response, and oxygenation index of >3.0 , and 2 points for absent

Published Online

April 10, 2012

DOI:10.1016/S1474-4422(12)70068-6

See Online/Articles

DOI:10.1016/S1474-4422(12)70060-1



cough reflex) and the aggregate score was related directly to the likelihood of death within 1 h of WLST. For patients who had the highest score (5 points), the probability of cardiac arrest within 1 h of WLST was 0.87. However, in patients with scores of less than 5 points, the probability of death within 1 h of WLST varied with the combination of variables (eg, from 0.45 to 0.61 in patients with an aggregate score of 3 points). Thus, for aggregate scores of less than 5 points, specific factors need to be taken into consideration and not just the aggregate score.

Although the population in Rabinstein and colleagues' study³ was small and heterogenous and their scoring system was not compared with the established Wisconsin criteria,⁴ their analysis provides an encouraging step in refining the prediction of cardiac arrest within 1–2 h of WLST and thus selection of patients for DCD. Further refinements and validation studies are needed. In the meantime, reliance on the Wisconsin scoring system⁴ or that developed by Rabinstein and colleagues³ would be imprudent. Selection of the best potential DCD donors will need good clinical judgment and incorporation and analysis of both scoring systems.

G Bryan Young, Michael D Sharpe

Division of Critical Care, Western University, Room B10–106, University Hospital, 339 Windermere Road, London, Ontario, Canada N6A5A5

bryan.young@lhsc.on.ca

We declare that we have no conflicts of interest.

- 1 Bernat JL. Contemporary controversies in the definition of death. *Prog Brain Res* 2009; **177**: 21–31.
- 2 Hernandez-Alejandro R, Wall W, Jevnikar A, et al. Organ donation after cardiac death: donor and recipient outcomes after the first three years of the Ontario experience. *Can J Anaesth* 2011; **58**: 599–605.
- 3 Rabinstein AA, Yee AH, Mandrekar J, et al. Prediction of potential for organ donation after cardiac death in patients in neurocritical state: a prospective observational study. *Lancet Neurol* 2012; published online April 5. DOI:10.1016/S1474-4422(12)70060-1.
- 4 Lewis J, Peltier J, Nelson H, et al. Development of the University of Wisconsin donation after cardiac death evaluation tool. *Prog Transplant* 2003; **13**: 265–73.
- 5 Wind J, Snoeijs MGJ, Brugman CA et al. Prediction of time of death after withdrawal of life-sustaining treatment in potential donors after cardiac death. *Crit Care Med* 2012; **40**: 766–79.
- 6 Dharamsi S, Ho A, Spadafora SM, et al. The physician as health advocate: translating the quest for social responsibility into medical education and practice. *Acad Med* 2011; **86**: 1108–13.
- 7 Yee AH, Rabinstein AA, Thapa P, Mandrekar J, Wijdicks EFM. Factors influencing time to death after withdrawal of life support in neurocritical patients. *Neurology* 2010; **74**: 1380–85.
- 8 Wijdicks EF, Bamlet WR, Maramattom BV, et al. Validation of a new coma scale: the FOUR score. *Ann Neurol* 2005; **58**: 585–93.