MAYO CLINIC

MAYO CLINIC PROCEEDINGS: INNOVATIONS, QUALITY & OUTCOMES

COMMENTARY

Donation After Circulatory Death Donor Prognostication: An Emerging Challenge in Heart Transplantation

Stephen W. English, MD, MBA; Alejandro A. Rabinstein, MD; and Melissa A. Lyle, MD

From the Department of Neurology (S.W.E.) and Division of Heart Failure and Transplant, Department of Transplantation (M.A.L.), Mayo Clinic College of Medicine and Science, Jacksonville, FL; and Departments of Neurology and Critical Care Medicine, Mayo Clinic College of Medicine and Science, Rochester, MN (A.A.R.).

Neuroprognostication is a core responsibility of neurologists, neurointensivists, and neurosurgeons after devastating neurologic insults. After traumatic brain injury, stroke, or cardiac arrest, these clinicians use their examination and ancillary tests to provide realistic expectations for neurological recovery and have dedicated immense research and educational effort to provide training, evidence, and guidelines to support neuroprognostication. This comes in sharp juxtaposition to heart transplant physicians, who have little neurologic training, limited evidence, and no guidelines to support their assessment of potential donation after circulatory death (DCD) organ donors. These donors undergo withdrawal from life-sustaining treatments (WLST) and die naturally before organ retrieval commences, and it is critical to limit organ ischemic times after WLST because longer ischemic times may impair heart function after transplantation. With recent increase of DCD heart donation to address critical organ shortages, transplant physicians must predict early death after WLST in potential DCD organ donors, often with essentially no information about the donor's neurologic status. Therefore, we sought to highlight the current state of DCD heart transplantation and provide potential solutions to improve the ability of transplant physicians to field these challenging DCD donor offers.

CURRENT STATE

Recent advances in ex vivo perfusion technology have facilitated more widespread adoption of DCD heart transplantation, increasing the donor pool and broadening regional sharing of organs. In 2023, a large United States based randomized control trial found that DCD cardiac transplantation using ex vivo perfusion was noninferior to donation after brain death transplantation at 6 months.[1] Although this has the potential to increase the cardiac donor pool by 30% in the United States,[2] new challenges arise. Organ retrieval and transplantation is a costly, time-sensitive, and resource-intense process, and current DCD donation protocols limit functional warm ischemic time—the time from inadequate organ perfusion or oxygenation to reperfusion—to less than 30 minutes to reduce the risk to the recipient. Accepted hearts from DCD donors who experience prolonged death after WLST may lead to futile mobilization of organ retrieval teams, wasted operating room time, and potentially excess trauma for the intended recipient and donor family.

Given the societal impact of a larger donor pool afforded through DCD donation, there is an urgent need to improve this process. In the United States, Organ Procurement Organizations (OPOs) assess DCD donor potential by collecting and conveying clinical information for transplant physicians. Unfortunately, the available neurologic information is often incomplete, inaccurate, or outdated in practice, often only including details such as "breathing over the vent" or "pupils reactive."[3] Transplant physicians may request additional information regarding the donor's neurologic status, but there are no standardized guidelines for OPOs to follow.

DCD heart transplantation is likely to grow as centers become more comfortable with this shift in practice. To assist in organ selection, several selection tools have been developed including the University of Wisconsin DCD evaluation tool, the United Network of Organ Sharing scoring system, and the DCD-N score.[4-6] Notably, the DCD-N score—a simple

5-point score that assigns 2 points for absent cough reflex and 1 point each to absent corneal reflex, absent or extensor motor response, and oxygenation index greater than 4—has shown the most promise in determining likelihood of early death after WLST. One study found a score of 0-2 translated into a 77% chance of survival beyond 60 minutes, whereas 72% of patients with a score of 3 or greater died within 60 minutes.[6] Unfortunately, these tools have limited applicability because they require either the temporary disconnection of ventilatory support or essential variables, often not provided by OPOs, to compute these scores.

Opportunities for Improvement

Training and Certification. Neuroprognostication discussions frequently follow in the setting of drug overdose, cardiac arrest, or traumatic brain injury, and neurologists, neurointensivists, and neurosurgeons receive dedicated training to elicit and interpret brainstem reflexes and motor response and interpret ancillary tests including neuroimaging and electroencephalography. There are well-researched consensus guidelines in performing brain death examinations and how various aspects of the evaluation impact a patient's prognosis.[7,8] Although these prognostication discussions may lead to a decision to WLST, DCD donor prognostication focuses on how quickly a donor passes away after WLST. Despite this critical difference, there are clear lessons to learn given the overlapping mechanisms of injury (eg, trauma, anoxic brain injury). Currently, there are essentially no dedicated training opportunities for transplant physicians to enhance their interpretation of the neurologic examination and its role in prognostication and no certification requirements for providers performing these assessments. Therefore, we propose the development of resources (eg, online certifications, educational videos, practice guidelines, and simulations) to supplement their training. The target audience should include intensivists, transplantation specialists, and OPO coordinators. These training opportunities can improve consistency and accuracy of the neurologic examination in potential organ donors and emphasize its value as part of a comprehensive donor assessment.

Validation and Incorporation of Standardized Scoring Systems. As discussed, there are several tools to assist in DCD organ selection, but the DCD-N score has shown the most promise. This scoring system stemmed from efforts to identify clinical factors associated with earlier time of death after WLST in patients with catastrophic neurologic injury. They analyzed 149 comatose patients, of whom 75 died within 60 minutes of WLST. Although this population was substantially older than typical DCD donors, they identified variables independently associated with death within 60 minutes including absent corneal and cough reflexes, extensor or absent motor response, and an oxygenation index greater than 4.2.[9] These findings prompted a prospective study of 178 comatose patients to assess these 4 characteristics as predictive variables of death within 60 minutes of WLST, which ultimately led to the DCD-N score. Again, this patient population was older (mean age, 63.4 years), potentially limiting the generalizability of their findings. Subsequent efforts to validate the DCD-N score have yielded mixed results, and other groups have created their own scoring systems leveraging alternative variables including pupillary asymmetry, cerebral edema, brain herniation, intraventricular hemorrhage, and use of intravenous opioids and benzodiazepeines.[10,11] There is a clear need for more research in this area. We believe one path forward should include retrospective studies incorporating the Organ Procurement and Transplant Network data registries. Although these data sets are subject to selection bias given the information will be limited to donors who had organs placed, we are hopeful they will serve as a catalyst to develop and prospectively validate better scoring systems for prognosis that can be more readily applied to clinical practice.

Teleneurology Consultations. Neurologists helped pioneer telemedicine via telestroke for acute stroke management, which is now leveraged in almost 30% of US hospitals. Neurologists have established infrastructure for real-time video evaluations that incorporate acute neuroimaging review and have developed systems to reach patients broadly. In the United States, the care model for organ retrieval mirrors that of stroke care, where tertiary hospitals receive calls from numerous

 Mayo Clin Proc Inn Qual Out ■ October 2024;8(5):431-434 ■ https://doi.org/10.1016/j.mayocpiqo.2024.07.006
www.mcpiqojournal.org

smaller facilities regarding potential organ donors and transplant physicians perform remote evaluations to make time-sensitive organ retrieval decisions. This is a multidisciplinary effort involving surgeons (both procurement and receiving teams), transplant physicians, critical care physicians, organ care teams, and procurement coordinators. The addition of a teleneurologist may be a reasonable solution to support these acute decisions. We propose a new role for the teleneurologist to partner with transplant centers and OPOs to enhance the organ selection process. Involvement can range from remote asynchronous review of the documentation and neuroimaging to real-time assessment via audiovisual connections to perform an independent neurologic examination, especially when there are incomplete, confusing, or outdated assessments. At the onset, much of this burden will likely require support transplant centers to engage neurologists at their institutions, but as the practice becomes increasingly adopted, centralized dedicated service lines can be deployed to handle requests for independent, remote neurologic consultations (Figure).

Artificial Intelligence. In 2022, more than 42,800 organ transplantation were performed in the United States, including a 39% increase in DCD donation over the past 5 years. There are a vast number of data points being actively collected by the Organ Procurement and Transplant Network, creating a ripe environment for deep-learning artificial intelligence models. Already, machine learning models are being developed for transplantation by predicting mortality and graft failure, enhancing donor-recipient matching, and performing clinical imaging analysis to improve outcomes.[12] Artificial intelligence models may yield an algorithmic response that outperforms any neurologist or transplant specialist and may include variables not previously considered. The authors feel this represents an excellent application given the access to such rich datasets and computational power and may serve as powerful tools in future practice to ensure that we are maximizing organ retrieval from DCD donors.

Conclusion

Recent improvements in survival after DCD heart transplantation will continue to bolster this practice, and with this, heart transplant physicians will face the issue of DCD donor prognostication more routinely. In this study, we outlined the urgent need to develop tools and solutions to address this issue and provide

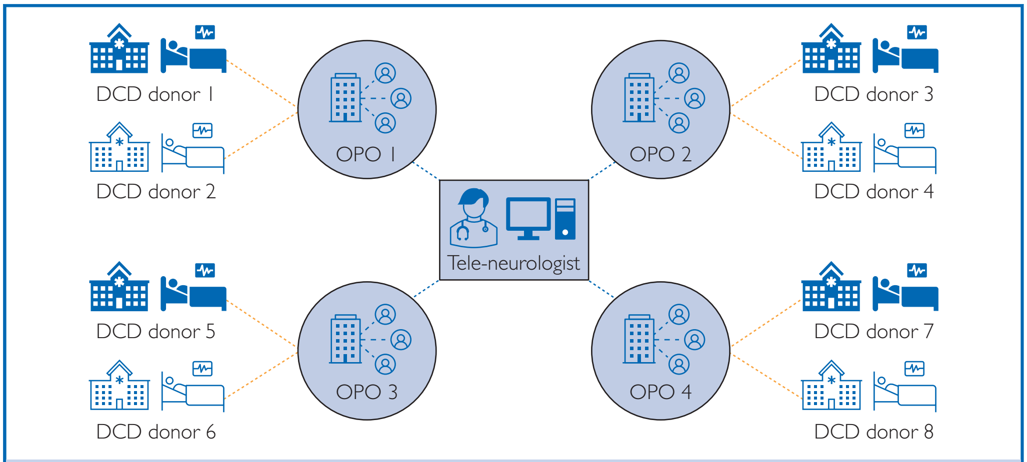

FIGURE. Schematic representation of a proposed transplant teleneurology service depicting a central teleneurologist interfacing directly with several OPOs, each presenting their own DCD donor offers to transplant centers. Transplant centers could then request their OPO for a teleneurology consultation if there were concerns about the donor's neurologic status, which could occur either asynchronously via a detailed donor chart review or real-time video assessment of the potential DCD donor if/when video is available at donor hospital. DCD, donation after circulatory death; OPO, organ procurement organization.

4 strategies to consider, including the development of dedicated training and certification courses, validation of standardized scoring systems, expansion of teleneurology, and creation of predictive artificial intelligence algorithms.

POTENTIAL COMPETING INTERESTS

Dr Rabinstein is a member of Clinical Ethics Committee committee of Boston Scientific; medical safety monitor for National Institutes of Health; and is a member of advisory boards of Chiesi and Shionogi. The other authors report no competing interests.

Abbreviations and Acronyms: **DCD**, donation after circulatory death; **OPO**, organ procurement organization; **WLST**, withdrawal from life-sustaining treatments

Publication dates: Received for publication June 28, 2024; accepted for publication July 11, 2024.

Correspondence: Address to Stephen W. English, MD, MBA, Department of Neurology, Mayo Clinic College of Medicine and Science, 4500 San Pablo Rd, Jacksonville, FL 32224 (english.stephen@mayo.edu; Twitter: @SWEnglishMD).

ORCID

Stephen W. English: https://orcid.org/0000-0002-8460-2193

REFERENCES

1. Schroder JN, Patel CB, DeVore AD, et al. Transplantation outcomes with donor hearts after circulatory death. *N Engl J Med*. 2023;388(23):2121-2131. https://doi.org/10.1056/NEJMoa2212438.
2. Truby LK, Casalinova S, Patel CB, et al. Donation after circulatory death in heart transplantation: history, outcomes, clinical challenges, and opportunities to expand the donor pool. *J Card Fail*. 2022;28(9):1456-1463. https://doi.org/10.1016/j.cardfail.2022.03.353.
3. Lyle MA, English SW, Goswami RM, et al. Donation after circulatory death: A transplant cardiologist's take on neuroprognostication. *J Heart Lung Transplant*. 2023;42(10):1481-1483. https://doi.org/10.1016/j.healun.2023.05.015.
4. DeVita MA, Brooks MM, 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(2):432-441. https://doi.org/10.1111/j.1600-6143.2007.02087.x.
5. Lewis J, Peltier J, Nelson H, et al. Development of the University of Wisconsin donation after cardiac death evaluation tool. *Prog Transplant*. 2003;13(4):265-273. https://doi.org/10.1177/152692480301300405.
6. 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;11(5):414-419. https://doi.org/10.1016/S1474-4422(12)70060-1.
7. Greer DM, Kirschen MP, Lewis A, et al. Pediatric and adult brain death/death by neurologic criteria consensus guideline. *Neurology*. 2023;101(24):1112-1132. https://doi.org/10.1212/WNL.0000000000207740.
8. Rajajee V, Muehlschlegel S, Wartenberg KE, et al. Guidelines for neuroprognostication in comatose adult survivors of cardiac arrest. *Neurocrit Care*. 2023;38(3):533-563. https://doi.org/10.1007/s12028-023-01688-3.
9. Yee AH, Rabinstein AA, Thapa P, Mandrekar J, Wijdicks EF. Factors influencing time to death after withdrawal of life support in neurocritical patients. *Neurology*. 2010;74(17):1380-1385. https://doi.org/10.1212/WNL.0b013e3181dad5f0.
10. Xu G, Guo Z, Liang W, et al. Prediction of potential for organ donation after circulatory death in neurocritical patients. *J Heart Lung Transplant*. 2018;37(3):358-364. https://doi.org/10.1016/j.healun.2017.09.015.
11. Kotsopoulos AMM, Böing-Messing F, Jansen NE, Vos P, Abdo WF. External validation of prediction models for time to death in potential donors after circulatory death. *Am J Transplant*. 2018;18(4):890-896. https://doi.org/10.1111/ajt.14529.
12. Connor KL, O'Sullivan ED, Marson LP, Wigmore SJ, Harrison EM. The future role of machine learning in clinical transplantation. *Transplantation*. 2021;105(4):723-735. https://doi.org/10.1097/TP.0000000000003424.