expansion of DCD heart transplantation in the United States.

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Commentary: The future is now—heart donation after circulatory death

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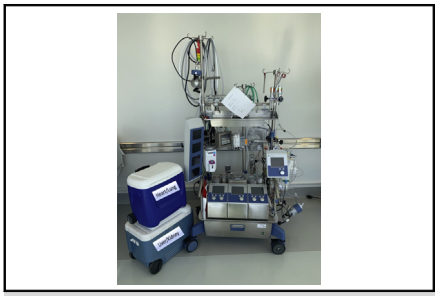

Normothermic regional perfusion has the potential to benefit all DCD organs.

CENTRAL MESSAGE

The ethical and logistical constructs should dictate the future direction of heart DCD and must include consideration for all transplant organs, not just hearts.

In this issue of the *Journal*, Rajab and co-authors[1] review the historical perspective, current techniques, and possible future directions of heart donation after circulatory death (DCD). The historical perspective is particularly relevant to this topic, as previous attempts to initiate a successful clinical program without first evaluating and defending the ethical ramifications set the field back more than a decade in the United States. In fact, as the authors point out, it previously led to homicide allegations against physicians.[2] The idea of dealing with ethical concerns in the future is unwise and must be evaluated and solved before initiation of any clinical application. To that end, our group has recently published an article thoroughly exploring this topic.[3] We believe it appropriately defended the ethical and legal permissibility of the practice before our first clinical case. Additionally, independent of true ethical concerns, national, regional, and local acceptance is paramount for the successful future of this field. All of these will need to be continuously appraised and solved as more experience with DCD heart transplantation matures. However, again, waiting until it is a problem is not the solution.

Although multiple options for DCD heart donation are possible, they are not all equal. Direct transplantation without in situ or ex situ perfusion evaluation has not been done with any meaningful frequency in the last decade, and there is no reason to think that there will be any resurgence given the other technologies. A direct comparison between normothermic regional perfusion (NRP) and ex situ perfusion approaches is important. First, as with transplantation in general, the acceptance rate of each approach can be variable. Based on the United Kingdom[4] and Australian[5] experiences, ex situ perfusion yielded a 77.7% and 69.7% use rate, respectively. In contrast, the UK experience with NRP with subsequent ex situ perfusion increased the yield to 100% of assessed

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organs. The use rate from more modern US NRP protocols has yet to be fully defined. Our initial clinical experience seems promising, and we believe NRP will significantly surpass current ex situ perfusion strategies. This may be the result of better reduction and mitigation of ischemic injury, leading to an overall better functioning organ, and allowing a true in situ assessment of cardiac function under normal physiologic conditions, leading to improved physician confidence to accept the organ. This assessment is similar to or better than a standard heart evaluation in a brain-dead donor, given the simultaneous transesophageal echocardiography and hemodynamic evaluation. NRP also uniquely allows the resolution of metabolic derangement by providing full perfusion in the setting of a functioning liver and kidneys. In comparison, ex situ perfusion only attempts to correct the ischemic insult after the additional time it takes to procure the heart and connect it to the machine with blood that cannot be cleared of metabolic waste. Direct transplantation techniques do not mitigate this at all. These significant differences have permitted the design of NRP protocols in the United States that allow up to 3 hours of expected warm ischemic time compared to less than 30 minutes for most ex situ perfusion or direct transplantation protocols, which significantly limits the number of organs able to be assessed regardless of the acceptance rate between technologies. These dissimilarities between techniques may also explain the significant rate of reported primary graft dysfunction requiring mechanical support of 39% to 57% for ex situ perfusion.[4,5] In the United Kingdom experience, the addition of NRP with ex situ perfusion more than halved this rate. However, again the rate of primary graft dysfunction requiring mechanical support using modern NRP protocols without ex situ perfusion is yet to be determined.

Moreover, the cost for the ex situ perfusion systems is considerable. Although Rajab and coauthors do reference this cost difference, they assume that this will decrease in time with additional commercial competition, citing the ex vivo lung perfusion experience. However, for lungs, the opposite is true. Most recently, with Food and Drug Administration–approved, commercially available devices, the cost per use has increased to match industry needs. It is unlikely that any such device for cardiac transplantation will be reasonably priced any time in the near future. In contrast, NRP can be as inexpensive as a standard cardiopulmonary bypass circuit, which for our center's NRP application cost less than $1000 per donor. Also, contrary to the authors assertion, ex vivo technologies unfortunately have not translated to a meaningful increase in the number of DCD lungs used in the United States, still only accounting for less than 5% of lung transplants in this country.[6] This historical perspective from another transplant organ emphasizes that new technology for organ assessment alone will not likely shift the field.

Additionally, and perhaps most importantly, hearts are not the only organ that can be procured from DCD. As cardiothoracic surgeons, we have historically exhibited a degree of tunnel vision regarding the application of new techniques and technology. The consequences or potential benefits of new approaches to DCD heart utilization are critical to its likely acceptance among the overall field of transplantation. This again seems to favor NRP over the alternative techniques. Because NRP potentially allows reperfusion of all transplantable organs, it exclusively reduces the warm ischemic injury for other organs as well. This unintended consequence can potentially improve the outcomes and utilization rates for all DCD organs. Furthermore, by the nature of the technique, NRP can significantly decrease the frenzied and at times confrontational experience of a DCD procurement to a calm and cordial event, improving patient outcomes and the physician experience at the same time.

Looking to the future, there may be some potential strengths to an ex situ perfusion approach. This would include novel therapeutics that would be best applied in isolation of the other organs while on an ex situ perfusion system. However, based on the lung transplantation *ex-vivo* perfusion experience, that promise likely remains well in the future. Moreover, for NRP specifically, further work regarding the best method for practical implementation needs to be evaluated. Options include mobilization of bypass equipment versus regionalization of DCD donation to transplant center hospitals with an active cardiac surgery program. Regardless, the article by Rajab and coauthors highlights the current excitement in heart transplantation and its promising future.

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