The Professor Merry Lecture: Endings and Beginnings

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**Abstract:** Organ transplantation has become an established and worthwhile treatment for many otherwise intractable conditions in many countries around the world. For example, over 4000 patients have benefited from heart or lung transplants (or both) since the first heart transplant in Australia or New Zealand was carried out in 1984. However, there is thought to be a worldwide shortage of donors relative to the number of organs needed. Many people, notably many of those involved with situations in which organ donation might be possible, value the opportunity to contribute organs. This has led to interest in expanding the criteria for donation. Standard criteria donation (SCD) involves the formal diagnosis of brain death, and conservative criteria for donor eligibility. Extended criteria donation allows slightly more liberal eligibility criteria, thought acceptable in light of improved results in SCD. In donation after cardiac death (DCD), an alternative approach to increasing the pool of available donors, a formal diagnosis of brain death is not required. The formal diagnosis of brain death is very reliable, but prognosis in less definitive manifestations of severe brain damage is less so, as illustrated by numerous anecdotal reports. There is a tension between providing enough time between withdrawal of treatment and declaration of death for reasonable confidence to be maintained in the process of DCD and the desirability of keeping warm ischemic time to a minimum in the interest of organ survival. In Australia and New Zealand, DCD is undertaken only in the context of planned withdrawal of support in intensive care units (Maastricht category 3). There has been a considered and carefully implemented approach to DCD, and the educational initiatives associated with its introduction may have had incidental benefit to the SCD program as well. It is, nevertheless, important that all involved are cognizant of the practical and ethical issues at stake. **Keywords:** cardiac surgery, transplantation.
The first heart-lung transplant was done in 1986, the first single lung in 1990, and the first bilateral lung in 1992. By the end of 2008, 3616 transplants had been carried out (Table 1). Typically, every year about 200 patients undergo one of these procedures in this region at one of six hospitals: St. Vincent’s in Sydney, The Alfred and The Royal Children’s Hospital in Melbourne, The Royal Perth Hospital, The Prince Charles Hospital in Brisbane, and the Green Lane Cardiothoracic Unit at Auckland City Hospital in New Zealand.

The first heart transplant in New Zealand was undertaken at Green Lane Hospital in 1987 (2). The first single lung transplant was undertaken in 1993 and the first bilateral lung transplant in 1994. By the end of 2008, 333 patients had undergone heart or lung transplant (Table 1). For the decade ending December 31, 2008, the numbers of these transplants in New Zealand were, respectively, 110, 15, and 85, giving a total of 210, or about 10 hearts and 10 lungs/year. The results of these operations are satisfactory by international standards (Table 1), and on the face of it seem to provide considerable justification for this therapy.

Waiting list activity is summarized for 2008 in Table 2. It is a bit difficult to interpret this information in relation to the question of the balance between the need for donors and their availability. Certainly a great deal of work goes into ensuring that patients receive those hearts and lungs that are donated. As part of this, a small number of Australian organs are given to New Zealand patients (3 livers in 2009, and 9 in 2008), and a similar number of New Zealand organs are given to Australian patients (5 livers and 8 lungs in 2009, and 2 livers, 2 hearts, and 2 lungs in 2008).

### OVERALL ORGAN AND TISSUE DONATION FROM DECEASED DONORS IN AUSTRALIA AND NEW ZEALAND

The overall activity related to organ donation is of course much greater than that related to hearts and lungs. For example, in 2009, in New Zealand, 43 deceased donors in 16 hospitals donated organs (and tissues, such as eyes, heart valves, and skin) (Table 3).

Overall, there are very few organs available for transplantation, and it is often very difficult to find organs in a timely way for patients who could benefit from these operations. There is a shortage of donors internationally (3,4), and this is also the case in Australia and New Zealand.

### CATEGORIES OF DONATION

In Australia and New Zealand, three categories of organ donation after death (living donors are also an important source of certain organs (5)) are now recognized: standard criteria donation (SCD), expanded criteria donation (ECD), and donation after cardiac death (DCD – formerly known as non-heart beating donation) (6). Donors in the ECD group are either 60 years or older, or between 50 and 60 years of age with at least two of the following features:

- Pre-existing hypertension (treated or untreated); and/or cerebrovascular accident as cause of death; and/or last serum creatinine before organ removal >132 mmol/L.

In the first two categories organs are removed after brain death has been diagnosed, so the circulation is intact until harvesting occurs. In DCD, organs are removed after the circulation has stopped, and blood flow to them will therefore have been reduced for a time that depends on

### Table 1. Numbers of operations undertaken by the end of 2008, and survival data, for heart and lung transplants in Australia and New Zealand (2).

<table>
<thead>
<tr>
<th>Operation and Total Number Done</th>
<th>All Heart 1990</th>
<th>Heart-Lung 169</th>
<th>Single Lung 438</th>
<th>Double Lung 1019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia (Total = 3616)</td>
<td>1781</td>
<td>169</td>
<td>411</td>
<td>922</td>
</tr>
<tr>
<td>New Zealand (Total = 333)</td>
<td>209</td>
<td>0</td>
<td>27</td>
<td>97</td>
</tr>
<tr>
<td>1-year survival</td>
<td>86.7%</td>
<td>80.8%</td>
<td>80.9%</td>
<td>86.9%</td>
</tr>
<tr>
<td>5-year survival</td>
<td>77.1%</td>
<td>51.6%</td>
<td>47.8%</td>
<td>60.4%</td>
</tr>
<tr>
<td>10-year survival</td>
<td>60.9%</td>
<td>41.0%</td>
<td>24.3%</td>
<td>41.1%</td>
</tr>
<tr>
<td>15-year survival</td>
<td>47.0%</td>
<td>30.5%</td>
<td>14.7%</td>
<td>30.9%</td>
</tr>
<tr>
<td>20-year survival</td>
<td>34.3%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 2. Waiting list activity for Australia and New Zealand, 2008 (2).

<table>
<thead>
<tr>
<th>Hearts</th>
<th>Lungs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active at January 1, 2008</td>
<td>61</td>
</tr>
<tr>
<td>New additions during 2008</td>
<td>78</td>
</tr>
<tr>
<td>Transplanted</td>
<td>90 (64.7%)</td>
</tr>
<tr>
<td>Improved and removed</td>
<td>7</td>
</tr>
<tr>
<td>Too ill, new complications, etc. and removed</td>
<td>9</td>
</tr>
<tr>
<td>Declined</td>
<td>1</td>
</tr>
<tr>
<td>Died waiting</td>
<td>8 (5.7)</td>
</tr>
<tr>
<td>Total active at year end</td>
<td>51 (plus 9 on “hold”)</td>
</tr>
</tbody>
</table>

### Table 3. Organ and tissue transplants in New Zealand, 2008 and 2009 (2).

<table>
<thead>
<tr>
<th></th>
<th>2008</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidneys</td>
<td>53</td>
<td>56</td>
</tr>
<tr>
<td>Hearts</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>Lungs</td>
<td>14</td>
<td>16</td>
</tr>
<tr>
<td>Livers</td>
<td>23</td>
<td>33</td>
</tr>
<tr>
<td>Pancreases</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Corneas</td>
<td>15</td>
<td>13</td>
</tr>
<tr>
<td>Heart valves</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Bones</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Skin</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
the criteria used and the circumstances of the case. DCD in recent times began in New Zealand in 2008, and is restricted to livers and kidneys in this country at present. Livers are more sensitive to low blood flow than kidneys, so cannot always be donated in this way.

More than one organ per donor is usual. From January 1, 1993 to December 31, 2009, 2025 organs were transplanted from 628 deceased donors, an average (SD) of 3.2 (1.3) organs per donor, with 3.4 organs per donor from the 507 SCDs, 2.3 organs per donor from 115 ECDs, and 2.0 organs per donor from the six DCDs. These numbers are comparable with overseas data but a little lower than United States benchmarks (7).

Donation after cardiac death implies donation of an organ or organs after cessation of circulation; brain death is not a requirement. Historically, this was the approach used before the criteria for brain death were established and was recognized in the law of various countries. DCD is most applicable to kidney and liver transplantation, but is also used for lung transplantation (8). Most of the experience in Australia and New Zealand over recent times has been in New South Wales. In New Zealand, implementation of DCD protocols began in 2008. The increased use of DCD is in line with trends in the United States, Canada, the United Kingdom, Holland and Japan, amongst other countries, and appears to have been at least in part a response to the desire of many relatives who wish to see donation of organs by patients who have severe brain injuries but are not brain dead.

DEFINING DEATH

In all three categories of donation, the fundamental assumption is that the patient is dead when the organs are retrieved (9). This is called the “dead donor rule”. However, there is substantial variation in what this is taken to mean the recent “Report of the Quality Standards Subcommittee of the American Academy of Neurology” (10) indicates that current criteria for brain death are not evidence based. The idea that “irreversible cessation of all functions of the entire brain” is required (11) is difficult to sustain. Neither of these points may be of any practical importance, but absence of certainty does lead to disquiet on the part of some commentators (12,13).

In SCD and ECD, brain death must have been diagnosed. The criteria for this have been well worked out and rely either on clinical evidence that the brain stem is dead, or on radiographic evidence that there is no blood flow to the brain. This approach places emphasis on the absolute requirement of brain stem function to maintain life, and the fact that there has never been a reported case of recovery after the proper diagnosis of brain death according to these criteria (6,10). Philosophically and ethically, this is a fairly straightforward situation, although some controversy may still exist over whether or not such a person could possibly be conscious (14) (in general, the likelihood of this is extremely low).

The criteria for death in DCD are much more problematic (Figure 1). They amount to saying that the circulation must have stopped for at least 2 minutes. The validity of this criterion may not seem intuitively obvious to those working in the field of cardiac surgery who are often involved in prolonged cardio-pulmonary resuscitation and have seen patients recover after more than 2 minutes of circulatory arrest. Context is relevant, however, and some understanding of the context in which DCD is considered acceptable in Australia and New Zealand is helpful when considering the problematic aspects of this approach.

THE CONTEXT OF DCD IN AUSTRALIA AND NEW ZEALAND

The first and essential requirement in this region (and most others) is that those involved with the process of deciding to withdraw treatment be strictly separated from those involved in discussions and processes related to organ donation. There is still room for different views about the ethics of withdrawing treatment (even in the absence of organ donation), and about what does or does not constitute euthanasia (see below) (9), but in modern western societies there is substantial consensus that there are circumstances in which withdrawing expensive treatments that offer no quality of life or long-term recovery is not only reasonable, but humane and highly desirable.

The Maastricht criteria were defined in 1995 to categorize potential DCD donors (6); these criteria identify four situations in which DCD might be contemplated:

Category 1: Dead on arrival at hospital—unknown warm ischemic time (WIT) – see below): “Uncontrolled.”
Category 2: Failed resuscitation (in emergency department or ICU)—known WIT: “Uncontrolled.”

ANZICS recommends that death be determined to have occurred when all of the following features are present:

- immobility;
- apnea;
- absent skin perfusion; and
- absence of circulation as evidenced by absent arterial pulsatility for a minimum of two minutes as measured by feeling the pulse or, preferably, by monitoring the intra-arterial pressure.

When all of these criteria have been met, the patient is determined to be dead and therefore organ removal may proceed.

Figure 1. Recommendations of ANZICS for determination of death in DCD (6).
Category 3: Withdrawal of treatment in ICU—known and limited WIT: “Controlled.”
Category 4: Cardiac arrest following formal determination of brain death but before planned organ procurement.

In Australia and New Zealand, only categories 3 and 4 are considered suitable for DCD. This substantially simplifies matters, if only by making possible an orderly and careful process for deciding whether the criteria apply. The fourth category in fact involves brain death, and is also uncommon, so in practice, it is only really category 3 that requires further detailed consideration.

The Australian and New Zealand Intensive Care Society (ANZICS) Statement on Death and Organ Donation gives the following examples of ventilated patients thought unlikely to recover who might be suitable for DCD: those with severe irreversible brain injury, severe cardiac or respiratory failure, or ventilator-dependent quadriplegia.

Patients with ventilator dependent quadriplegia are in a category of their own. Presumably these patients will often be fully aware, and able to participate in decisions that affect them. Their situation is perhaps one of the most challenging in the whole of healthcare ethics. One point does seem intuitively reasonable: if it is accepted that a decision to withdraw treatment could be reasonable in such a patient, there is no obvious barrier to subsequent DCD (if that is the patient’s wish). Patients with severe cardiac or respiratory failure present particular difficulties that go to the heart of the philosophy of DCD. Anyone who works regularly with such patients (for example after cardiac surgery) will know how difficult it can be to assess their prognosis reliably. It may be argued that only the most extreme and obviously hopeless situations should be considered for DCD, but in reality many of these patients declare themselves as objectively irretrievable through multi-organ failure (including bowel necrosis) before a decision to withdraw treatment could confidently be justified, and so the question of DCD does not often arise. In practice, DCD in Australia and New Zealand is most likely to arise with patients who have severe brain damage from which recovery is unlikely, but not much else wrong.

Furthermore, it is likely that the individual patients in which DCD is contemplated will have very clear cut clinical pictures in which the case for withdrawal of treatment is likely to be strong.

This view of the patients likely to be considered for DCD is quite reassuring. On the other hand, there is still an important difference between this approach and the requirement for a diagnosis of brain death. The key differentiating point is the fact that (as stated above) there has never been a reported case of recovery after the proper diagnosis of brain death, whereas partial recovery from relatively severe brain damage is seen from time to time (as illustrated in the opening anecdote of this paper). An important corollary of the former point is that criteria for brain death must be applied meticulously. Even a single failure in following these criteria properly could, if identified and publicized, jeopardize an entire transplant program.

Two minutes is a very short time for real comfort that all chance of recovery has been ruled out. WIT is also problematic. WIT is the time from treatment withdrawal (or alternatively from the moment systolic blood pressure drops below 60 mmHg) to the start of cold perfusion of the donated organs, and relates directly to graft function. A WIT over 30 minutes increases the risk of biliary stricture after liver transplantation, but 90 minutes may be acceptable for lung transplantation.

Perfusion of the organs to be retrieved (e.g., via femoral cannulae) may be one way of extending WIT (and also the time after cessation of circulation) without compromising results, but is not quite the same as simply allowing patients to die.

From a practical perspective, outcomes with DCD seem to be less reliable than with donation after brain death (15). ANZICS recommends against monitoring the electrocardiogram (6), because electrical activity may persist for some time following the cessation of circulation (14). Also, ANZICS advises that once death has been declared, measures that might restore circulation should be avoided (reintubation without ventilation to protect the lungs from aspiration is acceptable) (6). Is the possibility contemplated here that a patient may still have a functioning cortex (at least to some degree) and that modest resuscitative efforts might, at the minimum, prolong life at least for a period of time (perhaps only a few minutes)? If so, what are the implications of this possibility?

The point here is not necessarily to doubt the appropriateness of withdrawing treatment in some patients for whom intensive care appears to offer no useful benefit; rather the point is that it behoves all concerned to be clear about the practical considerations, the law, and the ethical constructs that underpin such decisions.

END-OF-LIFE DECISIONS

Death occurs every day in hospitals, notably in units that specialize in treating critically ill patients. Probably the most important element of dealing with the difficult issues around end-of-life decisions in general and DCD in particular is to place good end-of-life care firmly within the overall strategy of managing all the patients within each intensive care unit, rather than treating this fundamental aspect of medicine as secondary to saving life, and something to add in only at the last minute (3,9). Both objectives can be pursued simultaneously, with the emphasis shifting from one to the other as the patient progresses along a definable trajectory of care. It should always be
explicit that care will never be withdrawn or limited, only specific therapies, and only for explicit reasons. Attention to non-medical needs of seriously ill patients should not be deferred until there is too little time for them to be met.

QUESTIONS CONCERNING THE LIMITING AND WITHDRAWING OF TREATMENT

It is sometimes argued that withdrawal of treatment does not represent a desire for the patient’s death. The “rule of double effect” attempts to distinguish intended effects from effects that are merely foreseen.

Withdrawing treatment, it is suggested, is not intended to result in the particular patient’s death, although this outcome is foreseeable. A distinction is also often made between actively killing a terminally ill patient (i.e., euthanasia), deciding not to initiate life-supporting treatments, and withdrawing such treatments. Interestingly, some protocols for DCD have been interpreted as suggesting that opioids should not be administered to these patients because they may hasten death, even in the presence of signs (including high bispectral index numbers (14)) arguably suggesting the possibility of awareness (3). The distinction between deciding to withdraw ventilation (an allegedly acceptable decision) and giving an opioid to facilitate this process (an allegedly unacceptable action) may seem very narrow. There are well-respected moral philosophers who reject the notion that there is any morally relevant difference between these approaches, and would see the rule of double effect as disingenuous (9). People in this camp often advance the “slippery slope argument,” which holds that once doctors start actively killing patients, it may be difficult to know where they will stop. These debates are far from fully settled: there seems to be little empirical evidence to support concerns over “slippery slopes,” but lack of clear evidence may not in itself be enough to reassure those who feel reasonable concern in this regard.

To make matters worse, there is considerable variation in legislation (4), even between the different states of Australia, let alone between countries (6). Clear legal guidance is often hard to come by. This problem is discussed in the ANZICS document on this subject, with the proffered solution that the guidelines should be adopted by all within Australia and New Zealand to ensure consistency of practice (6). This seems sensible, but surely it would be more satisfying to achieve a similar consensus within the relevant legislations (4)?

The patient’s wishes, if ascertainable, are central to this debate (but perhaps not the only element that needs to be considered). Patients who are competent have the right to decline treatment, and doctors are usually expected to respect such refusals (although the psychological status of the patient may need to be considered). Requests from competent patients for assistance in dying are another matter. Doctors are not required to acquiesce with such requests, but the relevant question here is whether they may ethically elect to do so if they wish: in some jurisdictions (e.g., The Netherlands) this is legal, in defined circumstances, and in others (Australia and New Zealand included) it is not. In a slight variation of the discussion above, one might think that the moral distinction is small between giving a very high dose of morphine to a patient in pain with clearly terminal cancer with the intent of ending his or her suffering and discontinuing ventilation (or perhaps support with a ventilricular assist device) in a patient with irreversible cardiopulmonary failure. As things stand today, the former could carry substantial risk for the practitioner involved if discovered by unsympathetic authorities, whereas there is widespread tacit acceptance that the latter is essential and inevitable.

CONCLUSIONS

In one view, society may have to choose between the benefits of organ donation and the moral disquiet associated with occasionally managing the end-of-life in such a way as to allow the procurement of satisfactory organs. It is relevant, however, that the number of patients involved in DCD has been very small and that results of DCD transplantation may be less satisfactory than brain-dead donor transplantation: it is not clear that the need for this obviously much more problematic approach to transplantation warrants the increased risks associated with ethical and practical challenges that do seem to be more problematic than those associated with donation after brain death.

Within New Zealand, great care has been taken in the introduction of DCD. Intensive education has been provided to selected intensive care units before they have been included in the program. The guidelines are clear and conservative. There is uncertainty about adequate numbers of donors, particularly in the long term. If we restrict organ donation to patients with brain stem death, there will be fewer organs available for patients who need them and we can improve our supply of organs by accepting a less stringent definition of death.

Therefore the adoption of DCD is understandable. However, in going down this road it is important to ensure that the moral boundaries are not blurred, and that the position taken by those responsible is clear, explicit, and defensible—legally as well as morally (4).

REFERENCES