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Lung Transplant From an Uncontrolled Donation After Circulatory Determination of Death Donor: Moving to Other Countries

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Lung transplant is an effective therapy for end-stage lung disease. However, it is limited by too few suitable lungs from donors after brain death and controlled donation after circulatory determination of death donors. Another potential source of lungs is individuals who die unexpectedly outside or inside hospitals: uncontrolled donation after circulatory determination of death donors (uDCDDs). In this issue, Valenza and colleagues reported the first successful lung transplant in Italy from a uDCDD donor (1). The authors began a program in their emergency room to recover lungs from uDCDD donors (formerly Maastricht category 2 non-heart-beating donors), with assessment by *ex vivo* lung perfusion (EVLP). Over 7 mo, the authors considered 10 potential uDCDD donors. Only one (the first) had lungs recovered, assessed with EVLP, and transplanted.

As the authors pointed out, lungs have been recovered from uDCDD donors and transplanted in other European countries (France, the Netherlands, and Spain) since Steen's landmark case in Sweden, reported in 2001. Our group is also recovering lungs from uDCDD donors and assessing them with EVLP for transplant (ClinicalTrials.gov identifier NCT0161 5484) (2).

The most extraordinary aspect of the case described by Valenza et al was the duration of warm ischemic time. The authors reported 4 h 48 min (2 h 40 min nonventilated, 2 h 8 min ventilated) of ischemia (no blood flow) after declaration of death and before Perfadex (XVIVO Perfusion AB, Göteborg, Sweden) flush cooled the lungs. However, because death was due to aortic dissection, flow into the lungs was likely minimal or absent during cardiopulmonary resuscitation (CPR) because of tamponade. Consequently, the total lung ischemic time was more likely closer to 5.5 h. Nevertheless, the lungs and the recipient made a full recovery, with excellent forced expiratory volume at 1 s (FEV-1) at 6 mo after transplant. This is truly remarkable.

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Disclosure

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After consent, the authors ventilated potential donors with a low rate (four breaths per minute) and a very low tidal volume (6 mL/kg). In their EVLP circuit, lungs were perfused with Steen solution and packed red blood cells (RBCs) to a hematocrit level of 3–5%. The need for RBCs is controversial, but higher hematocrit (10–15%) is commonly used. The authors' EVLP method does not deoxygenate the perfusate because the membrane oxygenator is ventilated with room air and CO₂. Even during the “evaluation phase,” perfusate partial pressure of oxygen (pO₂) going into the pulmonary artery was 75 mmHg, so inflow perfusate was well above 90% saturated.

The safe duration of human lung ischemia is unknown. In animal models, ventilation provides better function after transplant than unventilated ischemia. *In situ* lung cooling may be superior to ventilation (3), but this is practical only for in-hospital uDCDD donors. The extent of necessary ventilation is also unknown.

The exclusion criteria used by Valenza et al may be more strict than necessary. Unwitnessed arrests should be excluded. We have observed pulmonary edema during EVLP in lungs from unwitnessed arrests. The interval from witnessed arrest to initiation of CPR (no-flow period) probably relates more to the likelihood of meaningful recovery, but for lungs, it is simply an added interval of warm ischemia. Limiting this to 15 min is conservative. CPR delivers some blood flow to lungs, regardless of duration. Valenza et al limited this “low-flow period” to 60 min. In survivors of CPR, even if prolonged, pulmonary ischemic injury has not been described. Some causes of death make CPR ineffective, such as aortic dissection with tamponade (this case), ruptured aortic aneurysm or death from hemorrhage. However, effective CPR provides lungs with blood flow. Lung ischemia resumes when CPR is halted.

The poor utilization rate of lungs from uDCDD donors, unfortunately, mirrors our experience (unpublished data). We have not yet transplanted lungs recovered from a uDCDD donor. The case described by Valenza et al and all lung transplants performed in Europe from uDCDD donors had CPR cessation and death declarations in hospitals where lungs could be recovered. We are not performing CPR in uDCDD donors because of concerns in the United States about restoring circulation after declaration of death (4).

The authors obtained consent from next of kin before ventilation and recovery. Our organ procurement organization (OPO) also requires next-of-kin consent, even though state law stipulates that first-person authorization (FPA) for organ donation (50% of North Carolina residents) does not allow next of kin to revoke consent and allows OPOs to recover organs from FPA decedents even before next of kin are aware of the death (5). Next of kin are understandably bereft after a sudden death; OPO personnel are not accustomed to interacting with next of kin in this situation. Lung recovery from uDCDD donors is more feasible in countries where consent is presumed or indicated premortem.

Better use of organs from uDCDD donors would alleviate the organ donor shortage. Establishing and implementing protocols to recover lungs from uDCDD donors is very challenging but could definitely contribute to the inadequate donor pool. The authors should be congratulated for their efforts. The next challenge is to consider liberalizing their protocol and extending it to other hospitals in Milan and throughout Italy, as in Spain. This is a life-

saving opportunity for potential lung transplant recipients but also an opportunity to honor the wishes of individuals who expressed the intent to be organ donors.

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