

The Donor Heart After Withdrawal of Life Support: Understanding and Preventing Cardiac Injury Associated with the DCD Protocol

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Background Donation after circulatory death (DCD) is a mode of organ donation that could boost the number of hearts available for transplantation. We aimed to identify signatures of myocardial injury associated with decreased transplant viability, and hypothesized that outcomes could be improved with an immune preconditioning stimulus.

Methods Rats were used for all experiments. Major endpoints were cardiac function, histochemistry, and gene expression after a period of normothermic *ex vivo* heart perfusion (EVHP). We repeated the EVHP experiments in rats that had been pre-treated with a toll-like receptor 9 (TLR-9) agonist or control.

Results With increasing warm ischemic time there were graded changes in myocardial injury signatures. Pre-treatment with a TLR-9 agonist improved myocardial function and injury signatures.

Conclusions We demonstrate a unique cardiac injury signature associated with increasing warm ischemic times in a complex milieu. We suggest that the injury signature is indicative of a viability threshold for cardiac transplantation and that immune preconditioning extends that threshold.