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Extracorporeal Support: Improves Donor Renal Graft Function After Cardiac Death

A. Rojas-Pena[a,b,*], J. L. Reoma[b], E. Krause[b], E. L. Boothman[b], N. P. Padiyar[b], K. E. Cook[b], R. H. Bartlett[b] and J. D. Punch[a]

[a] *General Surgery Department, Division of Transplantation, University of Michigan Health System, Ann Arbor, MI and* [b] *General Surgery Department, Extracorporeal Life Support (ECS) Laboratory, University of Michigan Health System, Ann Arbor, MI*
** Corresponding author: Alvaro Rojas-Pena, alvaror@umich.edu*
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Donors after cardiac death (DCD) could increase the organ pool. Data supports good long-term renal graft survival. However, DCDs are <10% of deceased donors in the United States, due to delayed graft function, and primary nonfunction. These complications are minimized by extracorporeal support after cardiac death (ECS-DCD). This study assesses immediate and acute renal function from different donor types. DCDs kidneys were recovered by conventional rapid recovery or by ECS, and transplanted into nephrectomized healthy swine. Warm ischemia of 10 and 30 min were evaluated. Swine living donors were controls (LVD). ECS-DCDs were treated with 90 min of perfusion until organ recovery. After procurement, kidneys were cold storage 4–6 h. Renal vascular resistance (RVR), urine output (UO), urine protein concentration (UrPr) and creatinine clearance (CrCl), were collected during 4 h posttransplantation. All grafts functioned with adequate renal blood flow for 4 h. RVR at 4 h post-transplant returned to baseline only in the LVD group (0.36 mmHg/mL/min ± 0.03). RVR was higher in all DCDs (0.66 mmHg/mL/min ± 0.13), without differences between them. UO was >50 mL/h in all DCDs, except in DCD-30 (6.8 mL/h ± 1.7). DCD-30 had lower CrCl (0.9 mL/min ± 0.2) and higher UrPr >200 mg/dL, compared to other DCDs >10 mL/min and <160 mg/dL, respectively. Normothermic ECS can resuscitate kidneys to transplantable status after 30 min of cardiac arrest/WI.

Key words: Donor pool, donor preconditioning, early graft function, experimental models, extracorporeal membrane oxygenation, graft function, injury and preservation, ischemia time, kidney graft function, kidney, large animal model, nonbeating heart donor, normothermic recirculation, organ and tissue procurement, organ storage

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End-stage renal disease is treated successfully with kidney transplantation; however, this therapeutic option is limited due the shortage of organs available for transplantation. The waiting list for kidney transplants in the United States reached more than 82 500 patients in 2008, despite a 30% increase in the number of renal transplants performed in 2007 (16 628) compared to 10 years ago (11 703). In 2007, a vast majority of transplanted renal grafts were from donors after neurologic determination of death (DND), or brain dead donors, with a significant portion (6041) from living donors (1).

The use of organs recovered from donors following circulatory determination of death (DCD)—previously known as non-heart beating donors—has the potential to increase the donor pool; but currently accounts for less than 8% of all organ transplants (2). The reason is that organs taken by 'rapid recovery' from DCD donors do not function as well as organs from DND, especially initially. Poor immediate graft function can be tolerated for renal transplants because of renal replacement therapies like dialysis, so almost all organs from DCD are kidneys. The incidence of delayed graft function and primary graft nonfunction for kidneys from DCD is significantly higher than kidneys from DND, in some series more than double (3,4). This is presumed to be due to the warm ischemic and hypoxic injury that inevitably occurs following withdrawal of life support until the organs are cold perfused.

The use of normothermic venoarterial extracorporeal membrane oxygenation support (hereafter called ECS) after cardiac arrest restores circulation of warm oxygenated blood to the abdominal organs. It can be initiated immediately following declaration of death. Experimental data from our lab has shown that kidney and liver function returns and is maintained while on ECS (5). In animals, perfusing with warm oxygenated blood has been shown experimentally to increase the energy charge (ADP) and antioxidant levels in the recovered organs (6,7). By restarting circulation after cardiac arrest, the agonal, hypoxic and ischemic events

surrounding death and subsequent reperfusion can be turned into an ischemic preconditioning phenomenon (8).

In our clinical experience the donor pool was expanded by 33% by establishing normothermic, oxygenated blood perfusion of abdominal organs using ECS shortly after circulatory determination of death. Moreover it allowed for controlled, unhurried organ procurement; delayed graft function was developed in only two grafts (8%) (9).

The use of DCD grafts is encouraged in all the US transplant programs, but there is hesitation among clinical personnel due to uncertainty about the immediate and long-term outcomes of these grafts, especially when the organs come from DCD donors that also fit criteria for expanded criteria donors (ECD). These donors are over 60 years of age or over 50 years of age with a history of hypertension, poor renal function at the time of recovery, or death due to cerebrovascular accident. While ECS–DCD offers potentially improved results, it is also perceived as costly. However, if ECS–DCD can improve initial graft function, the cost of ECS is offset by the reduced hospital stay and need for dialysis if the kidneys function immediately. We developed an animal study to assess the immediate renal graft function from DCD donors under various warm ischemia times. This study was designed to evaluate ECS compared to rapid recovery in a swine model of renal transplantation after DCD.

Material and Methods

This study was approved by the University of Michigan University Committee on Use and Care of Animals (UCUCA). All pigs received humane in compliance with the Guide for the Care and Use of Laboratory Animals.

Experimental design

Using a standard swine model of cardiac death and warm ischemia, kidneys were removed by conventional rapid recovery or ECS, stored for 4–5 h cold ischemia, transplanted into nephrectomized swine recipients. Warm ischemia times of 10 and 30 min were compared. Kidneys transplanted from living donors (LVD) served as a control group. Five groups of 5 animals each were compared as shown in Table 1.

Animal model

The following model was used in all experiments. Female swine (weighing 25–30 kg), were sedated with an intramuscular (i.m) mix of 5 mg/kg Tiletamine HCl and Zolepam HCl (Telazol, Wyeth Holdings Corporation; Carolina, Puerto Rico) and 3 mg/kg Xylazine (TranquiVed Vedco, St. Joseph, MO). Swine were intubated and mechanically ventilated (MV) with 100% O_2 and 1–3% Isofluorane (Hospira, Lake Forest, IL). Initial MV settings were adjusted to maintain pCO_2 between 35–45 mmHg, and peak inspiratory pressures <25 cmH_2O. The right carotid artery and right internal jugular vein were catheterized to monitor arterial blood pressure and heart rate and to collect blood samples. A CCOmbo-CCO/SvO_2/VIP pulmonary artery catheter (Edwards Lifesciences, Irvine, CA) was placed via the internal jugular vein for administration of fluids and monitoring of cardiac output and central venous pressure. At the end of surgical instrumentation and prior to baseline data collection, a 20 min acclimation period was allowed for all animals.

Donor models

1. *LVD model:* 100 U/kg Heparin Sodium (APP Pharmaceuticals; Schaumburg, IL) was administered 5 min before proximal ligation of the renal artery. The kidneys were subsequently resected, flushed with 300–500 mL of Custodiol (Methapharm Inc, Brantford, ON, Canada), and stored cold for 4–5 h before transplantation.
2. *DCD model:* Anesthetized pigs were paralyzed using Pancuronium Bromide (Hospira) and cardiac death was achieved by apnea. The agonal period was 17 $\pm$ 1.8 min, simulating at some extent the clinical reality. Circulatory death was defined as: asystole or pulse-less arrhythmia with a pulse pressure less than 15 mmHg. After death, warm ischemia (WI)/asystole times of 10 and 30 min were examined. These times are two and six times longer than the 5 min period that is frequently used in the United States as a 'no touch' period. To achieve anticoagulation, heparin (100 U/kg) was administered 1min after withdrawal of respiratory support. Kidneys were then recovered in one of the following ways.

    a. *Rapid recovery/Conventional:* After death, a midline laparotomy was performed to obtain access to the kidneys. The vessels were identified and surrounding soft tissue was dissected. After a period of 10 or 30 min of warm ischemia, the pig was cooled via ice in the abdominal cavity, followed by rapid removal of the renal grafts. Grafts were managed as in the LVD protocol with immediate cold perfusion and storage.
    b. *ECS procurement:* After death, both external jugular veins were cannulated with two 20–23 Fr venous cannulae (to obtain access to the RA), and a 14–16 Fr arterial cannula was advanced into the abdominal aorta via right iliac or femoral artery. The V-A ECS circuit animal model is represented in Figure 1, include: a roller pump (Cobe Cardiovascular, Lakewood, CO), an external heat-exchanger (Seabrook Medical System, Cincinnati, OH), and a membrane oxygenator (Affinity· NT, Medtronic; Minneapolis, MN; Rochester, NY) and then stepped up to 3/8" tubing to connect them to the oxygenator outlet. Pump flows were continuously monitored using a T208 monitor (Transonic System, Ithaca, NY). The membrane oxygenator was primed with saline and 50 mEq of HCO_3 and maintained at 38°C. After 10 or 30 min of WI venoarterial perfusion was begun and maintained at 50 cc/kg/min for 90–100 min, aiming to maintain a CVP between 7–16 cmH_2O during

Table 1: Donor type and characteristics

Donor type	Group name	Warm ischemia	Procurement technique	Cold ischemia	(n)
Living donor	LVD	<1 min	Standard	4–5 h	5
DCD	DCD l0 min	10 min	Rapid raceway	4–5 h	5
	DCD30 min	30 min	Rapid leeway	4–5 h	5
ECS-DCD	ECS-DCD l0 min	10 min	90 min ECS	4–5 h	5
	ECS-DCD 30 min	30 min	90 min ECS	4–5 h	5

LVD = living donors; DCD = donors after cardiac death; ECMO = extracorporeal membrane oxygenation.

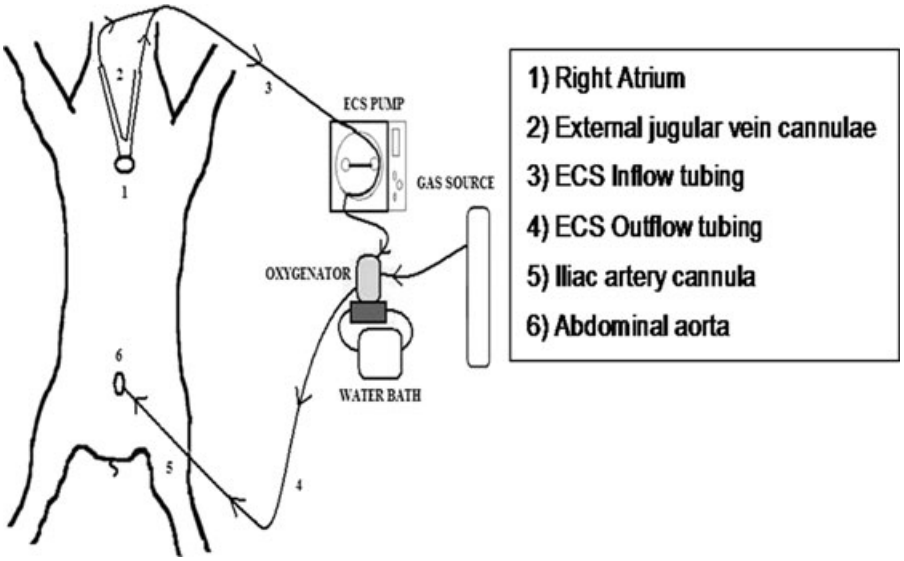


Figure 1: ECS-DCD laboratory model.

ECS, avoiding cavitation or hemodilution (targeting hematocrit value >23%). The kidneys were removed while warm perfusion continued, and managed as in the LVD protocol with immediate cold perfusion and similar storage time.

Recipient model

Healthy swine underwent surgical instrumentation as described above plus bilateral nephrectomies. After removal of one kidney, a perivascular renal (Transonic System, Ithaca, NY) flow probe was placed to obtain measurement of normal renal blood flow to the contralateral kidney for baseline. A blood sample was collected, and urine output was quantified and collected for determination of creatinine and protein concentration. The donor kidney was implanted and the remaining kidney was removed. The inferior vena cava and infrarenal abdominal aorta were prepared for side-to-end vascular anastomosis of the experimental renal graft. Heparin (100 U/kg) and 125 mg of methylprednisolone (Solumedrol, Pharmacia & Upjohn, New York, NY) were administered 5 min before surgical anastomosis. A catheter was advanced in the ureter for urine output collection. The pig remained under anesthesia for the entire experiment. For all recipients, maintenance i.v fluid was 120–150 mL/h, plus 1:1 replacement of urine output with NSS, maintaining CVP between 12 ± 3 cmH_2O.

Data acquisition

Data collected during the experiment are summarized in Table 2. Baseline (BL) data were collected on the single recipient kidney after surgical instrumentation but before implantation of renal grafts.

Data analysis

Renal vascular resistance (RVR) was calculated using the following equation: RVR = (MAP-CVP)/RAF. Creatinine clearance (mL/min) was calculated using the following equation: CrCl = ([U] × (UO/60))/[P], in which [U] = urine concentration of creatinine, [P] = plasma concentration of creatinine, and UO = urine output in mL/h. Urine was collected continuously from the ureter, during the total length of the study (4 h). This measurement is not affected by serum concentration of creatinine because it did not change significantly during the collection period. A mixed model analysis was performed within SPSS 17.0 (Chicago, IL) to examine the effect of procurement technique on all acquired data. The pig/experiment number is the repeated measure variable, and the independent variables were the experimental group, and the experimental time. The dependant variables were recipient hemodynamics (MAP, CVP), renal hemodynamics (flows, resistance), UO, CrCl and urine protein concentration. Last, *post hoc* analysis using a Bonferroni-corrected confidence interval was used to determine

Table 2: Data acquisition

Variable Type	Frequency	Description
Renal Hemodynamics	Recorded every 30 min after transplantation	MAP: mean arterial pressure; CVP: central venous pressure; RAF: renal artery flow; RVR: renal vascular resistance
Renal function	Baseline and every 1h after transplantation	Urine output (UQ); urine protein concentration (UrPr)
Venous & arterial Blood gases	Baseline, end of CA, every 1h after transplantation	Blood pH; pCO_2 pO_2; hemoglobin; hematocrit; oxyhemoglobin saturation; electrolytes (Na, K, Ca, Cl and HCO_3)**
Chemistry panel	Baseline; immediately after reperfusion, and 4 h after trainsplantation.	Plasma creatinine; BUN and ADL; urine creatinine; BUN and protein. ***

*BIOPAC Systems, Goleta, CA; **Radiometer A/S, Copenhagen NV Denmark; ***Animal Diagonostic Lab of the University of Michigan.

Table 3: Graft cold ischemia time and DCD-ECS run characteristic

Average graft cold ischemia time per donor group in minutes					
LVD	DCD l0 min	DCD 30 min	ECS-DCD 10 min		ECS-DCD 30 min
288.7 ± 11.8	266.0 ± 18.9	262.6 ± 11.9	263.0 ± 11.9		265.8 ± 10.7
DCD-ESC run characteristics (n = 3)					
	ECS-DCD group	Baseline	30 min ECS	60 min ECS	90 min ECS
MAP (mmHg)	10 min	67.3 ± 5.7	48.3 ± 6.2	70.3 ± 13.6	76.3 ± 9.9
	30 min	76.3 ± 5.0	41.6 ± 8.4	46.0 ± 7.5	51.0 ± 10.6
ECS flows (L/min)	10 min	N/A	1.6 ± 0.5	1.6 ± 0.5	1.7 ± 0.4
	30 min	N/A	1.6 ± 0.1	1.75 ± 0.01	1.7 ± 0.2
CVP (cmH_2O)	10 min	13.0 ± 1.8	12.7 ± 2.8	9.2 ± 3.6	9.1 ± 3.3
	30 min	10.4 ± 0.5	10.1 ± +4.4	11.1 ± 3.2	8.3 ± 2.0
Hematocrit %	10 min	31.6 ± 1.5	28.4 ± 2.0	32.4 ± 1.8	34.8 ± 3.3
	30 min	33.8 ± 0.6	30.1 ± 0.6	24.6 ± 1.5	28.4 ± 2.2

differences between experimental groups. Values of $p < 0.05$ were considered statistically significant. Results are expressed as mean values with errors bars representing standard error. At the end of the study, the entire kidney was removed for histopathology; two, 2 cm × 2 cm tissue samples were placed in formalin. The histoslides were processed by the University of Michigan Unit for Laboratory Animal Medicine, and read by a blinded pathologist.

Results

All grafts were successfully transplanted into each healthy but nephrectomized swine recipient. Average cold storage times per group and ECS-DCD perfusion characteristics are summarized in Table 3.

Recipients systemic hemodynamics

In all experimental groups, mean arterial pressure (MAP) was kept between 60–90 mmHg as shown in Figure 2; and CVP was maintained between 12 ± 3 cmH_2O during the whole experimental time in all groups. In most cases, MAP was maintained at baseline levels. However, MAP decreased significantly ($p < 0.05$) immediately after reperfusion in the DCD 30 min group. This decrease in MAP resolved after approximately 5 min of reperfusion and returned to baseline values by the 30 min data point. After this point there were not significant differences between groups.

Renal hemodynamics and function

Renal artery flow (RAF) following transplantation was higher at the end of the experiment in the group that received grafts from LVD ($p < 0.05$) compared to all DCD groups (Figure 3). RAF was lower only in the DCD-10 min group through all the experimental time, compared to other DCD groups.

As expected renal vascular resistance (RVR) Figure 4, correlated with RAF. It increased significantly immediately after reperfusion in all groups due to cold preservation, and returned to normal only in the LVD group ($p < 0.05$). In the other four groups, RVR was slightly higher than normal, baseline values during the whole experiment, without significant differences between them.

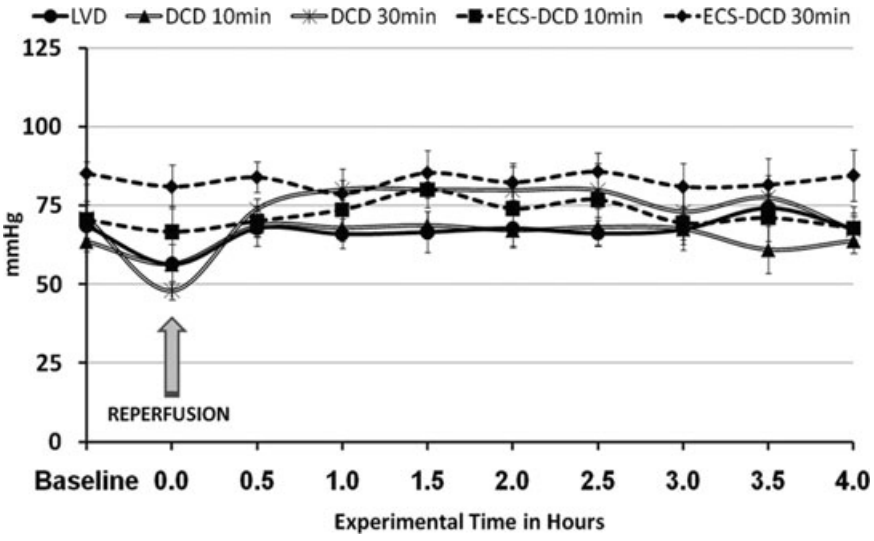


Figure 2: Recipients mean artial pressure (MAP). Error Bars = SEM/ (n = 5).

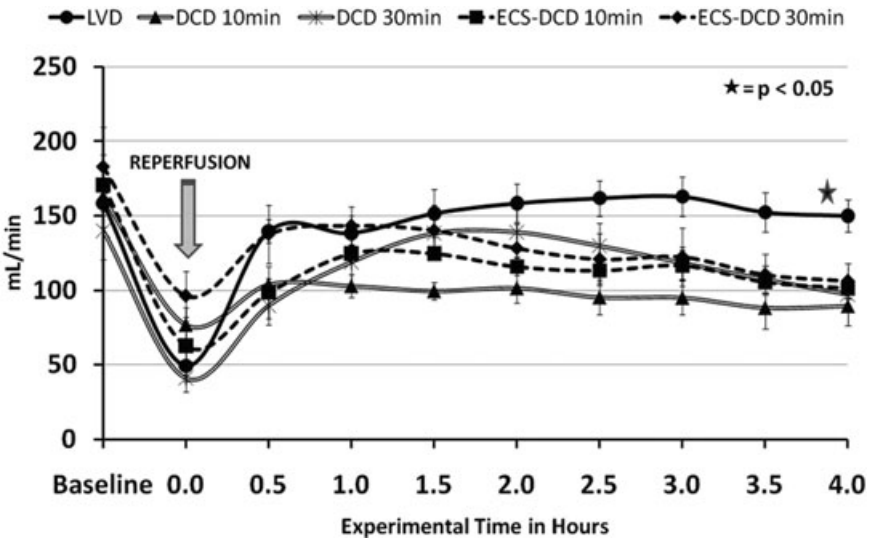


Figure 3: Recipients renal artery blood flow (RAF). Error Bars = SEM/(n = 5).

Urine Output is represented in Figure 5. Although all groups had some urine output, the amount produced in the DCD-30 min group was minimal (6.8 ± 1.7 mL/h), and significantly less than in the other groups that all had urine output of more than 50 mL/h by the fourth hour.

Creatinine Clearance (CrCl) is represented in Figure 6: CrCl was significantly lower ($p < 0.05$) in the DCD-30 group 0.9 ± 0.2 mL/min, compared to the other groups after 1-h posttransplant. Only grafts from the LVD group returned back to normal values (~25 mL/min) after 4 h of reperfusion. The DCD-30 min group had significantly lower CrCl at 1 and 4-h posttransplantation, compared to all the groups. In particular, when ECS support was used, after 30 min of warm ischemia (ECS-DCD 30 min), the CrCl was similar to those DCD that sustained only 10 min of warm ischemia.

Urine protein concentration (UrPr) at 1 and 4 h following reperfusion is represented in Figure 7. UrPr was significant higher ($p < 0.05$) in the DCD 30-min group compared to all other groups where normal values for healthy swine of this size were evident at the end of the experimental time.

Renal pathology

A summary of the pathologic findings from renal tissue collected at the end of the experiment can be found in Table 4. Grafts from DCD 30 min shown some signs of reversible acute tubular necrosis. No infarcts were seen.

Discussion

The increasing gap between organ demand and organ sources has led the medical community to go back to the

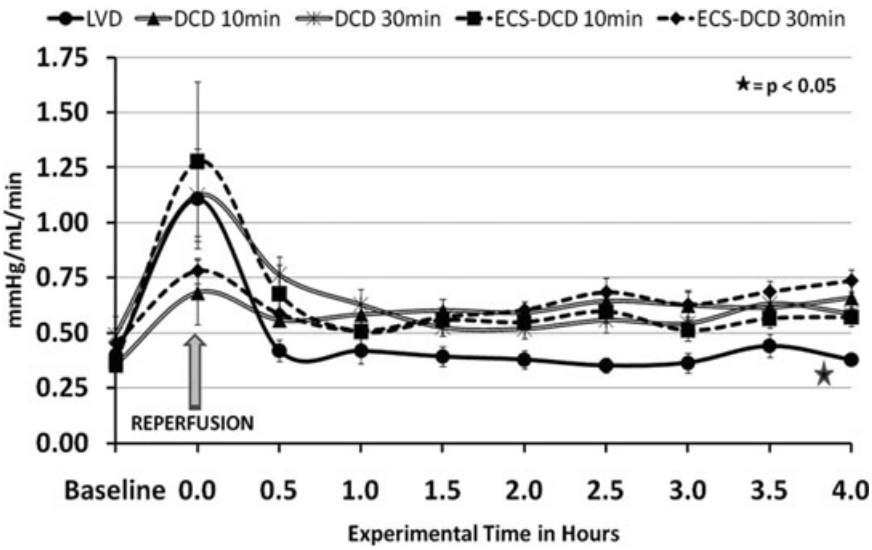


Figure 4: Calculated renal vascular resistance (RVR). Error Bars = SEM/(n = 5).

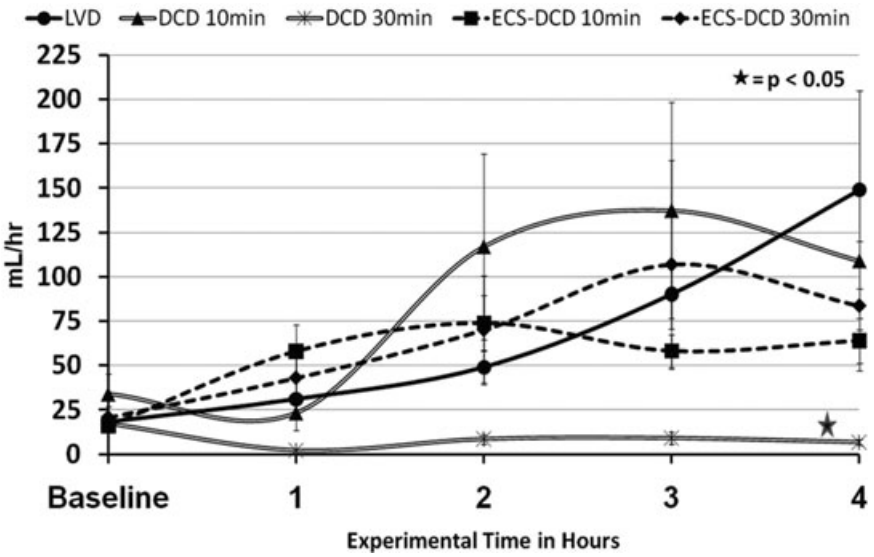


Figure 5: Recipients urine output (UO). Error Bars = SEM/(n = 5).

way that grafts were procured in the early days of transplantation through the use of grafts from DCD. However renal grafts from DCD are associated with higher rates of delayed-graft function, primary graft-non-function and, in some series, long-term graft survival (10–12).

After procurement with conventional techniques (rapid recovery) renal grafts had different outcomes directly related to the extent of warm ischemia time. In 1995, Chang et al. (13), reported 26% of PGNF (excluding rejection) when organs from nonheart beating donors (NHBD) were used. More recently the rates of PGNF in renal grafts are: LVD 2%, brain dead/heart beating donors 3%, and NHBD 7%. The rate of DGF after rapid recovery is 40–50%. The rates of DGF in kidneys from heart-beating donors is 25–30%, significant lower compared to DCD organs. (4,11,14,15) Despite higher rates of DGF reported when kidneys from DCD are used the long-term survival rates some reports show graft survival that is similar to heart-beating donors at 2, 4 and 6 years (16–24).

Due to the poor outcomes when DCD grafts were used, *ex-vivo* perfusion with a cold acellular solution is often used to measure renal vascular resistance in the donor kidney. This method allows transplant centers to identify grafts with elevated resistance and these kidneys were simply discarded. When implemented, the rates of PGNF were reduced to as little as 5% (25). The use of this technique became standard in many DCD programs (26–28).

Hypothermic extracorporeal support has been used in association with rapid recovery. Koyoma et al. used cardiopulmonary bypass at 18°C and reported high rate of DGF in kidneys subjected to long periods of warm ischemia (29

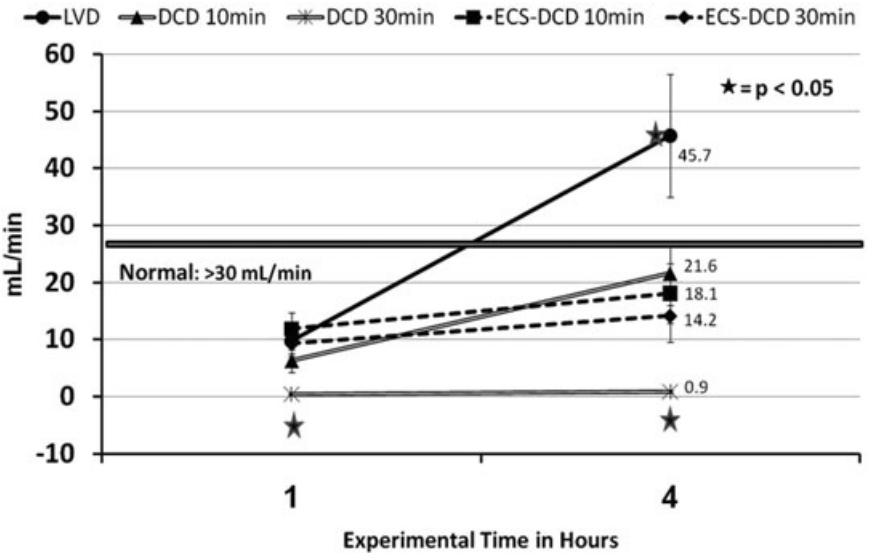


Figure 6: Recipients measurement of CrCl. Error Bars = SEM/(n = 5).

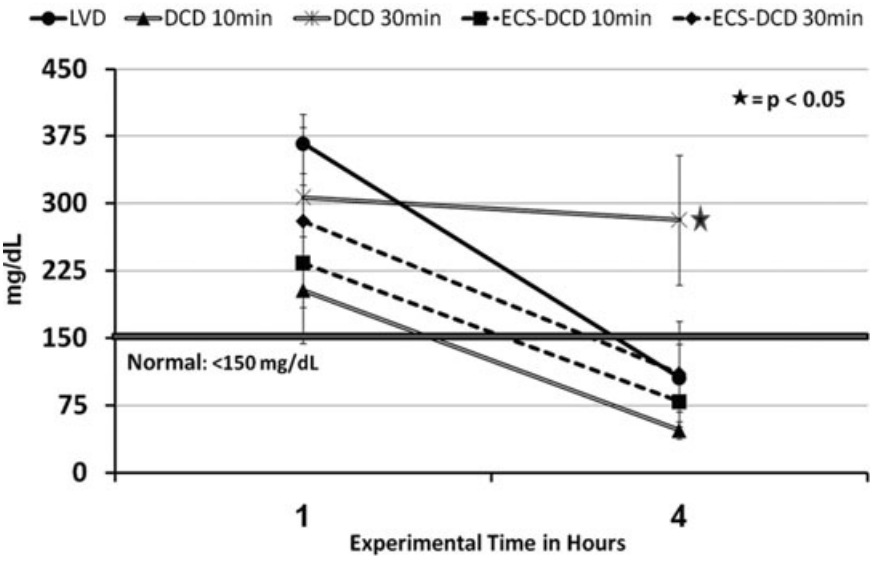


Figure 7: Recipients urineprotein concentration (UrPr). Error Bars = SEM/(n = 5).

out of 32 kidneys) but similar long-term survival rates compared to other type of donors (29). The transplant group from The National Taiwan University Hospital, used VA perfusion with oxygenation (ECS) at 4°C. They reported 66% of immediate graft function, and 33% incidence of DGF that resolved with short-term (1–2 weeks) hemodialysis therapy (30–32). A group from Japan used rapid cooling techniques to procure organs from DCD obtaining similar results (12,20,32,33).

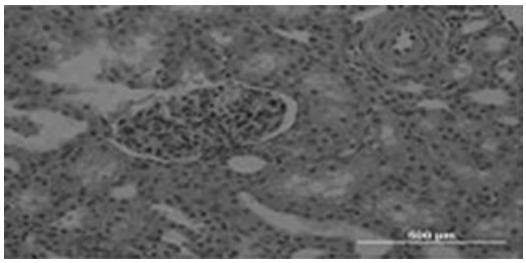
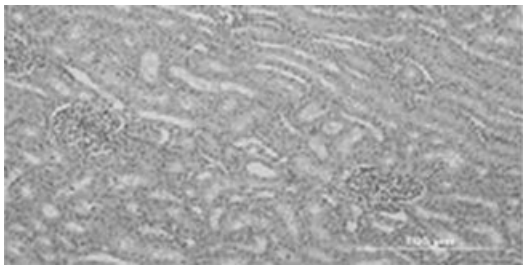
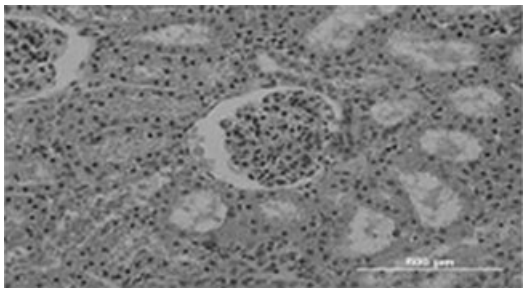
A transplant group in Spain has reported using normothermic ECMO perfusion to support the potential donor until organ procurement (34). In 2000, Valero et al. reported significantly lower rates of DGF (13%) and no PGNF in kidneys from DCD when ECMO was used during organ donation in DCD (21). Our group at the University of Michigan Hospital, uses normothermic ECMO in DCD Maastricht type II and IV donors and reported low rates of DGF (8%), no PGNF, and an increment of the organ pool at our institution by 33% (9,21,35).

Almost all the studies on DCD kidneys are based on 5 min of warm ischemia after cardiac arrest. This study evaluated the effectiveness of ECS during organ procurement after longer periods of cardiac arrest/warm ischemia time. The results indicate that implementation of ECS in the donor during organ procurement can resuscitate kidneys to transplantable state with immediate graft function after 30 min of warm ischemia. The use of standard rapid recovery technique that is the most common method to procured DCD organs effectively resuscitated renal grafts after 10 min of warm ischemia, but not after 30 mins. ECS may be useful in situations where prolonged ischemia is probable including Maastricht type 1 and 2 donors ('uncontrolled') and situations where local practice involves withdrawal of support in a setting other than in the operating suite. We used 37°C (normothermic) perfusion in these experiments because the best clinical results were achieved at normothermia.

In this study, 90–100 min of ECS was used to perfuse the donors because it represents our standard clinical and laboratory practice (5,9). Current studies in our laboratory assess the effects of longer ECS runs during the procurement of abdominal organs. Despite the difference of warm ischemia (10 min and 30 min) in the two groups in which ECS was implemented for organ recovery there were no significant differences between ECS perfusion flows between them. Postreperfusion renal arterial flow was achieved in all transplanted kidneys, indicating no complications during vascular anastomosis, but normal values were only achieved in the LVD group. Renal flow and function, as measured by urine output, urine protein and creatinine clearance, was adequate during the first 4 h posttransplant after 10 min of warn ischemia with or without ECS, indicating kidneys could probably be recovered from clinical DCD donors after 10 min of warm ischemic arrest. However, in the groups that sustained longer cardiac arrest times (30 min), kidney function was established only when ECS was used during organ procurement. ECS helps in the correction of the acidosis before cold ischemia, restores ATP levels, regulates calcium homeostasis, and removes locally (renal) formed free radicals, in the donor and before cold storage. It is possible that ECS plays an important role in the preconditioning of organs before cold storage; this may explains why ECS resuscitated kidneys after 30 min of arrest/ischemia (36). This observation, suggests that ECS has a protective role following a moderately severe ischemic insult, and may allow organs to recover from prolonged warm ischemia injury during donor reperfusion prior to cold preservation/storage.

Limitations of this study are: (1) the swine model of cardiac arrest does not exactly mimic the clinical situation. The

Table 4: Histopathology of renal grafts

Group	Histoslide	Characteristics
LVD		Normal capsule, glomeruli, tubules and blood vessels.
DCD 10 min ECS-DCD 10 min ECS-DCD 30 min		Mild mesengial cellularity was observed with focal protein casts in the tubules, no signs of ATN were observed.
DCD 30 min		Moderate mesangial cellularity in the glomeruli was seen. High protein casts and signs of mild patchy ATN were found. Intravascular microthrombi were seen without infarcts.

model is both an asset and a limitation of this study. Cardiac arrest by apnea in the swine is a very reproducible model that permits evaluation of the variables in a standardized fashion. However, many potential uncontrolled DCD subjects will have a prolonged period of attempted resuscitation by CPR and ventilation including many resuscitative drugs. We acknowledge this limitation, but we argue that the details of ECS must be characterized in the apneic arrest model before adding the variables of CPR and donor treatment; (2) The ECS cannulae used for blood inflow into the circuit were placed into the EJV, due to the limited size of the femoral vein in these size pigs; but we believe that the insertion site of the cannulae did not affect the results. Also, an intrathoracic balloon was not used in these studies, but it will be implemented in our DCD model for further studies with the goal of isolating the brain from the circulation; (3) Grafts function were not evaluated beyond 4 h. The swine model simulates the agonal period in 'controlled' DCD, but is certainly less variable than observed in clinical practice. We did not evaluate graft function beyond 4 h to avoid the problems of animal recovery and graft rejection. Kidneys that did not function immediately might recover with longer time (as in DGF). Conversely, kidneys that function immediately after transplant will function indefinitely depending on prevention of rejection; (4) CrCl was measured using a 4-h timed collection, not the clinical standard based on a 24-h urine sample collection, but Bloor et al., proposed that when healthy subjects with normal renal function preoperative (such as the scenario of our study) are used a 4-h CrCl prediction method correlates with CrCl measurement (37).

In a different model, we have reported that room temperature perfusion is equivalent to perfusion at 37°. We have also reported that heparin given 5 min after arrest (with CPR) is as effective as heparin before arrest (38). We also evaluated if pulmonary congestion occurs during ECS with the heart arrested and we described an *in vivo* method to assess if lungs are suitable for transplantation from DCD donors following ECS resuscitation. ECS does not cause pulmonary congestion, and lungs retain adequate function for transplantation, and compliance correlated with lung function (39). Our results indicated that ECS resuscitation of DCD kidneys is feasible and allows for assessment of function prior to procurement by quantification of UO and urine components in the donor. Future studies include the

identification of the maximal cardiac arrest/warm ischemia time in which organs from DCD can be successfully resuscitated with ECS, as well as the optimization of the ECS perfusion (temperature, diuretics, n-acetylcysteine, thrombolytic agents, etc.) with the goal to minimize the ischemic reperfusion injury of DCD abdominal grafts, and/or the addition of leukocyte depletion filters to the ECS circuit. Finally, this model also creates the opportunity to improve DCD–ECS organ recovery runs with the goal to increase the ratio of functional organs per donor, including liver, lung and pancreas donation in DCD.

Conclusions

(1) Kidneys may be successfully recovered from DCD donors after 10 min of arrest/warm ischemia (but not after 30 min); (2) The use of normothermic venoarterial perfusion of oxygenated blood (ECS) can resuscitate kidneys to transplantable status after 30 min of warm ischemia in a large animal model of DCD organ donation; (3) This study adds supporting physiologic data from a large animal model to the clinical data in human DCD donors that ECS improves posttransplant outcomes.

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