Abstract# 926 **Poster Board #-Session: P62-II**

Donor Preconditioning with CORM-2 Protects Against Ischemia-Reperfusion Injury in a Murine Kidney Transplant Model. Yves Caumartin,[1] Damend Lian,[1] Jian Dend,[1] Christopher Nguan,[1] Jancy Stephens,[2] Bertha Garcia,[1] Anthony Jevnikar,[1] Hao Wang,[1] Gediminas Cepinskas,[2] Patrick Luke.[1] *[1]Multi-Organ Transplant Program, London Health Sciences Centre, University of Western Ontario, London, ON, Canada; [2]Center for Critical Illness Research, Lawson Health Research Institute, London, ON, Canada.*

Background: Significant organ damage occurs as a result of ischemia-reperfusion injury (IRI) following the transplantation process. Carbon monoxide (CO) has previously been shown to reduce damage associated with IRI, but in a clinical setting, problems remain regarding safe and controlled CO delivery and carboxyhemoglobin formation. Carbon monoxide releasing molecules (CORM) permits a novel and safe delivery of CO. Herein we assess the ability of CORM-2 to prevent IRI in transplant-relevant models.

Methods: 1. Renal tubular epithelial cell (TEC) injury and endothelial cell (EC) inflammatory response were assessed in vitro after cytokine, temperature and anoxia/reoxygenation-related injury. 2. Lewis rat donors were pre-treated with CORM-2(8 mg/kg) or vehicle injected IP 18 hours before kidney retrieval. Kidneys were cold-preserved for 26 hours in UW solution. After bilateral recipient nephrectomies, kidney transplantion was performed. Post-operatively, organ function, survival and isograft histology were assessed.

Results: 1. We demonstrated the ability of CORM-2 to prevent TEC apoptosis and EC inflammatory response compared with control-treated cells. 2. All recipients that received a CORM-2-treated isograft survived to the transplant process. Their mean serum creatinine (sCr) was 59 ± 4 and 69 ± 14 µmol/L at 24h and 72h, respectively. In comparison, the animals that received the vehicle-treated allograft had a mean sCr of 566 ± 62 and 680 ± 15 µmol/L at 24h and 72h ($p<0.005$). All controls died by day 3 post-transplant. Early post-operative histology revealed that CORM-2-treated isograft suffered mild acute tubular necrosis (ATN) while vehicle-treated animals experienced severe IRI characterized by severe ATN and hemorrhage.

Conclusion: We have shown that CORM-2 can protect the renal graft from IRI through prevention of apoptosis and inflammation. This provides rationale to use CORM clinically to prevent early injury and limit interstitial fibrosis/tubular atrophy. Further studies are required to define the best administrative strategy in regards to donor and recipient treatment.

Abstract# 927 **Poster Board #-Session: P63-II**

A Calibrated Prosthetic Porto-Caval Shunt Improves Reperfusion Injury and Outcome in a Porcine Model of "Small-for-Size" Liver Transplantation. Constantino Fondevila,[1] Amelia J. Hessheimer,[1] Olga Sanchez,[1] Pilar Taura,[2] Javier Muñoz,[1] David Calatayud,[1] Nicolas de Riva,[2] Santiago Sanchez,[1] Alberto Martinez,[1] Cesar Ginesta,[1] Jose Fuster,[1] Antonio Rimola,[3] Juan C. Garcia-Valdecasas.[1] *[1]Department of Surgery, Hospital Clinic, IDIBAPS, CIBERehd, University of Barcelona, Barcelona, Spain; [2]Department of Anesthesia, Hospital Clinic, University of Barcelona, Barcelona, Spain; [3]Liver Unit, Hospital Clinic, IDIBAPS, CIBERehd, University of Barcelona, Barcelona, Spain.*

Introduction. "Small-for-size" syndrome (SFSS) may be diagnosed when prolonged cholestasis, ascites, coagulopathy, hypertransaminasemia, and/or encephalopathy arise after partial liver transplant. We previously studied SFSS in a porcine model and determined that excessive portal vein flow (PVF) triggered sinusoidal endothelial injury, a factor predictive of either graft failure or histological recovery. In this study we aimed to prophylactically decompress the portal bed with a calibrated portocaval shunt (PCS), in order to prevent the deleterious consequences of superfluous inflow.

Methods. Seventy-percent hepatectomy was performed in the donors. In two experimental groups, after cold perfusion and extraction, a 6-mm (S6) (n=6) or 12-mm (S12) (n=6) Gore-Tex® shunt was anastomosed between the portal vein and infrahepatic IVC. In the control group (CG) (n=17), no PCS was placed. The partial grafts were implanted into recipients, who were followed during five days.

Results. The average standard liver volume was 23±5% and cold ischemic time 312±36 min; neither differed among the groups. Survival was 100% in S6, 0% in S12, and 29% in CG. Shunts reduced PVF 43±9% and 79±3% in S6 and S12, respectively. Upon portal reperfusion in the recipient, the percent of the baseline PVF was 565±192% in CG, 229±62% in S6, and 89±27% in S12 ($p<0.01$ for all comparisons between groups). AST, bilirubin, and prothrombin time rose in all animals after reperfusion but normalized by the fifth day in S6. There were no differences in the rate of graft regeneration in S6, S12, and survivors in CG (65±21, 73±15, and 74±4 g/day, respectively). Effective glucose utilization was significantly lower in S12 versus S6 and CG.

Conclusions. A calibrated PCS that maintained postreperfusion PVF around twice its baseline value consistently produced a favorable outcome after SFS liver transplantation, while avoiding compromised regenerative and metabolic parameters due to excessive shunting.

Abstract# 928 **Poster Board #-Session: P64-II**

Normothermic Machine Perfusion of Livers from Donors after Cardiac Death. Constantino Fondevila,[1] Amelia J. Hessheimer,[1] Mark-Hugo J. Maathuis,[2] David Calatayud,[1] Olga Sanchez,[1] Pilar Taura,[1] Santiago Sanchez,[1] Arjan van der Plaats,[2] Jose Fuster,[1] Henri G. D. Leuvenink,[2] Antonio Rimola,[1] Gerhard Rakhorst,[2] Rutger J. Ploeg,[2] Juan C. Garcia-Valdecasas.[1] *[1]Hospital Clinic, IDIBAPS, CIBERehd, University of Barcelona, Barcelona, Spain; [2]University Medical Center Groningen, University of Groningen, Groningen, Netherlands.*

Introduction. Normothermic extracorporeal membrane oxygenation (NECMO) prior to organ recovery can partially restore cellular energy lost during the period of cardiac arrest and improve organ viability in donors after cardiac death (DCD). The objective of this study was to investigate the additional benefits over NECMO associated with the use of dual-pump normothermic machine perfusion (NMP) in the *ex vivo* phase of DCD liver preservation, as compared with traditional cold storage (CS).

Methods. Thirty-six outbred male weanling pigs weighing 30-35 kg were used (18 donor-recipient pairs). The animals were divided among three experimental groups: G1, 90 min cardiac arrest (CA) + 4 h CS + implant (n=6); G2, 90 min CA + 1 h NECMO + 4 h CS + implant (n=6); G3, 90 min CA + 1 h NECMO + 4 h NMP + implant (n=6). During both NECMO and NMP, the livers were pumped with oxygenated autologous blood, maintained at 37°C. Following graft reperfusion, the recipients were followed intensively for up to five postoperative days.

Results. The five-day mortality rate was 100%, 17%, and 0% in G1, G2, and G3, respectively. Serum AST and bilirubin rose during the first 12-24 h postreperfusion and declined subsequently in G2 and G3. AST was significantly higher G2 vs. G3 at 3, 6, and 12 h (1602±697 vs. 837±372, respectively; $p<0.05$), while bilirubin was significantly higher in G2 vs. G3 at 6 h (0.7±0.5 vs. 0.2±0.1, respectively; $p<0.05$). The prothrombin time (PT) (%) fell from baseline in the immediate hours after graft reperfusion but recovered thereafter, more rapidly in G3 than in G2. In G1, PT fell after reperfusion and never rose, staying close to 30% until death.

In samples taken 1 h postreperfusion, the gene expression of multiple pro-inflammatory molecules (TNF, IL-6, E-selectin, and MCP-1) and pro-apoptotic caspase-3 was significantly lower in G3 compared with either of the other two groups.

Conclusions. Ischemic injury and hepatocellular function were significantly improved in grafts that were preserved with NMP over those that underwent static CS. NMP offers the potential to restore the viability of hepatic grafts damaged by profound ischemia beyond what NECMO alone can offer.

Abstract# 929 **Poster Board #-Session: P65-II**

Persistent Monocyte Depletion Does Not Improve Graft Survival after Liver, Pancreas Alone and Kidney Transplants. Dionisios Vrochides,[1] Mazen Hassanain,[1] Peter Metrakos,[1] Jean Tchervenkov,[1] Jeffrey Barkun,[1] Prosanto Chaudhury,[1] Marcelo Cantarovich,[2] Steve Paraskevas.[1] *[1]Department of Surgery, Multi-Organ Transplant Program, McGill University, Montreal, QC, Canada; [2]Department of Medicine, Multi-Organ Transplant Program, McGill University, Montreal, QC, Canada.*

Purpose: To investigate whether persistent monocyte or platelet depletion is associated with decreased incidence of rejection and increased graft survival.

Methods: A total of 390 primary adult liver transplants, 29 primary adult pancreas alone transplants and 613 primary adult kideny transplants were performed between 1990 and 2006. Monocyte depletion was defined as a postoperative, 30-day average monocyte count of =< 300. Platelet depletion was defined as a postoperative, 30-day average platelet count of =< 150. Patient survival, graft survival censored for patient death and acute cellular rejection incidence were retrospectively analyzed.

Results: Persistent monodepletion was achieved in 48%, 38%, 52% of liver, pancreas alone and kidney graft recipients respectively. Persistent monodepletion does not correlate with graft survival after liver transplant (p = 0.635, 95% CI: 0.790-1.472), pancreas alone transplant (p = 0.254, 95% CI: 0.079-1.958) and kidney transplant (p = 0.995, 95% CI: 0.727-1.361). Persistent platelet depletion correlates inversely with graft survival in liver transplants (p = 0.001, 95% CI: 0.431-0.797) and kidney transplant (p = 0.001, 95% CI: 0.434-0.815). There is no correlation between monocyte count and acute rejection incidence in liver (r2 = 0.01), pancreas alone (r2 = 0.08) and kidney transplants (r2 = 0.00).

Conclusions: Persistent monodepletion does not improve graft survival after liver, pancreas alone and kidney transplants. When persistent platelet depletion is observed after orthotopic liver or kidney transplant, graft survival is significantly decreased.

Abstract# 930 **Poster Board #-Session: P66-II**

Coagulation and Inflammatory Responses in Solid Organ Transplant Recipients and Donors. Josh Levitsky,[1] Alison Freifeld,[2] Julie Stoner,[2] Elizabeth Lyden,[2] Alan Langnas,[2] R. Brian Stevens,[2] Penny Hardiman,[2] Andre C. Kalil.[2] *[1]Northwestern University Feinberg School of Medicine, Chicago, IL; [2]University of Nebraska Medical Center, Omaha, NE.*

BACKGROUND: New strategies that modify the coagulation/inflammatory cascades, e.g. activated protein C/anti-thrombin III, may be applicable to solid organ transplant (SOT) recipients in the treatment of complications. However, baseline data on the