

Conclusions: Post transplant aspergillus infection is a rare and frequently fatal condition, occurring mostly in the first year post transplant.

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Impact of the Number of Blood Pressure Medications on the Outcome of Heart Transplant Recipients

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Purpose: Hypertension is common in heart transplant recipients due to the effects of calcineurin inhibitor immunosuppression, and often patients require multiple medications to control blood pressure (BP). The purpose of the current study was to determine if there is an association between the number of BP medications and outcomes after heart transplantation and if a particular BP medication offered significant benefit in long term outcomes.

Methods and Materials: We evaluated 558 patients transplanted between 1994 and 2008. Patients were divided into groups based on the number of BP medications taken at 6 months to 2 years post transplant (0 BP meds, N=199; 1 BP med, N=268; 2 BP meds, N=54; 3 BP meds, N=37). The following 5-year outcomes were assessed: survival, freedom from cardiac allograft vasculopathy (CAV, any stenosis > 30%), and freedom from non-fatal major adverse cardiac events (NF-MACE, myocardial infarction, heart failure, coronary intervention, defibrillator, stroke, and new peripheral vascular disease). Outcomes were compared for patients on beta blockers, calcium channel blockers, ACE Inhibitors, and angiotensin II receptor blockers.

Results: Patients on 3 BP medications exhibited a trend toward lower 5-year survival compared to patients with 0,1, or 2 BP medications (70% in 3 BP meds vs. 82%, 82%, 85% in 0, 1, 2 BP meds respectively, $p=0.06$). Subsequent freedom from CAV and NF-MACE were similar between groups. Over half of the patients were maintained on the anti-hypertensive medication for the subsequent 5-year follow up. There was no difference in outcome for the use of any particular class of BP medication. Specifically, ACE inhibitors did not reduce angiographic CAV as previously reported.

Conclusions: Patients requiring three or more BP medications demonstrate a trend towards worse survival. The number of required BP medications is likely a marker for poorly controlled BP, and emphasizes the importance of risk factor modification in heart transplant recipients.

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Long-Term Outcomes in Pediatric Heart Transplant Recipients Treated for Neoplasia: A Single-Institution Experience

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Purpose: The development of post-transplant neoplasia, typically lymphoproliferative disease (PTLD), affects approximately 12% of pediatric solid organ transplant recipients. There are few published reports of the long-term outcomes of neoplasia in the pediatric heart transplant (HT) population.

Methods and Materials: A retrospective chart review of all pediatric HT recipients followed at our institution from 1985-2010 who developed neoplasia was performed.

Results: A total of 101 pts underwent HT, 9 of whom developed neoplasia in the post-transplant period. The median age at HT was 4 yrs (0.5-17), and the median time to development of neoplasia was 93 mos (7.5-170). Primary neoplasms included monomorphic PTLD (4), non-Hodgkin's lymphoma (4), and leiomyosarcoma (1). Evidence of EBV infection was present in 6 patients. Of note, two pts were diagnosed with leiomyosarcoma, one as a primary neoplasm, the other as a secondary malignancy that was treated effectively with surgical resection, although there was recurrence 10 years later with an uncharacterized gastric tumor. One other pt developed recurrent neoplasms with monomorphic PTLD in the adenoids and plasmacytoma-like lymphoma in the terminal ileum. Three pts received reduction of immunosuppression as a primary intervention. One of the three responded completely, while the other two ultimately required chemotherapy. Six pts received chemotherapy at the time of diagnosis. Two of these required re-transplantation; one died of complicated meta-

static cancer, with hospice care involved. One pt is currently awaiting a second graft. Three pts died from neoplasia-related complications at a median of 46 days (14-120) from diagnosis.

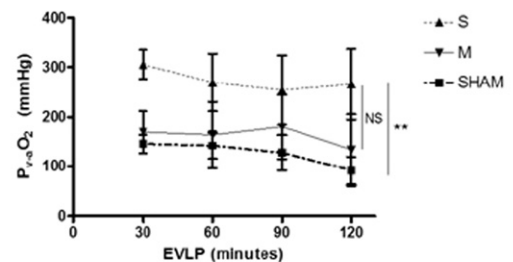
Conclusions: Neoplastic disease after HT is a known complication of immunosuppression. EBV is commonly associated with these neoplasms, as demonstrated with our pts. Withdrawal of immunosuppression alone did not appear to be effective in our population. Chemotherapy was associated with need for re-transplantation and neoplasm-related mortality.

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Preemptive Donor Treatment with Steroids Prior to Gastric Aspiration Improves Gas Exchange in a Porcine Model

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Purpose: Donor lungs are susceptible to aspiration in the period before and after brain death. We hypothesized that preemptive anti-inflammatory treatment of lung donors may result in better graft performance as evaluated during Ex Vivo Lung Perfusion (EVLP).



Veno-arterial oxygen pressure gradient ($\Delta P_{v-a}O_2$) was significantly higher in [S] compared to [SHAM] (** $p < 0.01$). No differences were seen between [S] and [M].

Methods and Materials: Eighteen pigs (25.4 ± 4.4 kg) were divided into 3 groups. Group 1 was treated with steroids (10mg/kg methylprednisolone) [S] and group 2 with 250 mg of the anti-inflammatory macrolide Clarithromycin [M]. Group 3 received saline [SHAM]. Treatment was given IV 25h, 18h, and 1h before instillation of 4mL/kg gastric juice. Two hours after the onset of acute lung injury, lungs were flushed, explanted and stored cold for 75 minutes. The left lung was cannulated and graft performance was assessed during EVLP for 2 hours. Aerodynamic parameters (compliance, airway pressure [AwP]), hemodynamic parameters (pulmonary artery pressure [PAP], left atrial pressure [LAP], flow, pulmonary vascular resistance [PVR]), and oxygenation capacity ($\Delta P_{v-a}O_2$) were recorded every 30 min. Wet to dry weight ratio [W/D] was measured in both lungs. Total and differential cells were counted in broncho-alveolar lavage fluid (BALF). Tissue samples were collected for histology.

Results: $\Delta P_{v-a}O_2$ was significantly higher in [S], but not in [M] compared to [SHAM]; $p < 0.01$ (Figure). No differences were observed in compliance, PVR, mean AwP and W/D. Total and differential cell count in BALF and histology were comparable between groups.

Conclusions: Preemptive treatment of donors with steroids, but not macrolides improves gas exchange in a porcine lung injury model independently from its anti-inflammatory activity. Further mechanistic studies are needed to clarify the beneficial effect of steroids.

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Machine Perfusion Improves Metabolic Preservation of Heart Grafts from Non Heart Beating Donors

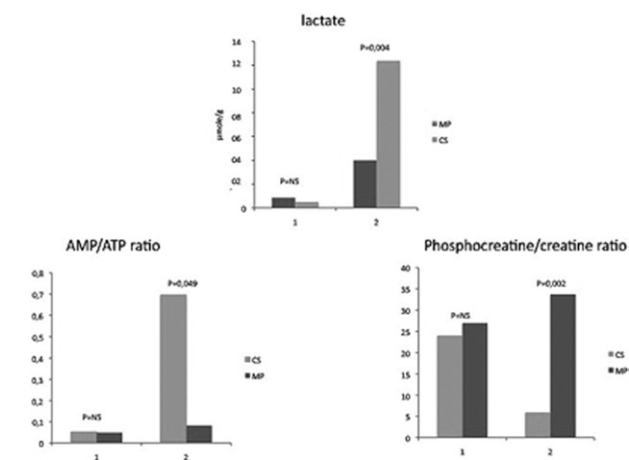
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Purpose: With respect to organ shortage, Non Heart Beating Donors (NHBD) are an alternative source of grafts for transplantation. In renal transplantation, machine perfusion has proven to be superior to cold storage (CS) in NHBD. Heart transplantation from NHBD is currently not performed because of the prolonged ischemia and risk of primary non-functioning. We investigated in a pig model whether machine perfusion could improve heart preservation and allow cardiac transplantation using NHBD.

Methods and Materials: 16 pigs were prospectively randomised in 2 groups of NHBD. After anoxia induced cardiac arrest, hearts were harvested and preserved for 4 hours. In the first group, organs were preserved in a classical CS solution. In the second group, hearts were preserved by hypothermic machine perfusion (MP) on a modified Heartport system (Organ Recovery System; Des Plaines; IL). After preservation, the hearts were reperfused on a Langendorff system during 1 hour. Myocardial energy states (intracellular lactate, nucleotides and phosphocreatine/creatinine ratio) were evaluated in myocardial biopsies taken respectively before cardiac arrest (normoxia) (1) and after 4 hours preservation (2).

Results: Hearts from the MP group showed significant less lactate accumulation (4 vs 12.4 μ mole/g; $p=0.004$), lower AMP/ATP ratio (0.083 vs 0.69; $p=0.049$) and higher phosphocreatine/creatinine ratio (33 vs 6; $p=0.002$) after 4 hours preservation compared to CS.



Conclusions: Compared to cold storage, Machine perfusion allows better preservation of the energy states of heart grafts in an in vitro model of pig NHBD.

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Evaluation of Load-Independent Biventricular Contractility during Machine Perfusion of the Donor Heart

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Purpose: Donor hearts are commonly rejected for transplantation on the basis of apparent poor function. Ex-vivo machine perfusion may provide an opportunity to objectively evaluate donor heart function outside the detrimental milieu of the brain dead donor. This may also be useful for assessment of hearts from DCD donors. We describe a method that enables assessment of right and left ventricular contractility during ex-vivo cardiac perfusion.

Methods and Materials: Following cardiectomy in pigs (n=5), hearts were machine perfused. Initial resuscitation was achieved via perfusion of the aortic root and coronary circulation. After recovery of cardiac function and rhythm the left and right atrium were perfused to establish biventricular working mode. Conductance catheters were inserted into the ventricles for acquisition of pressure and volume data. Pressure-volume loops were used to measure load-independent ventricular contractility: end-systolic pressure-volume rela-

tionship (ESPVR) and pre-load recruitable stroke work (PRSW). A dobutamine infusion was administered to assess contractile reserve.

Results: During working mode the LV ESPVR was 23.1 ± 11.1 and the LV PRSW was 67.8 ± 7.2 . Both measures increased significantly after infusion of dobutamine (LV ESPVR: 45.1 ± 12.2 , $p=0.01$; LV PRSW 102.5 ± 18.2 , $p=0.03$). The RV ESPVR (pre 4.1 ± 2.3 vs. post 11.9 ± 4.1) and RV PRSW (pre: 6.7 ± 2.4 vs post. 8.7 ± 4.6) were also measured in 2 animals and increased followed dobutamine. Hearts were perfused for 219 ± 64 minutes with no apparent deterioration of cardiac function. Although cardiac weight increased from 282 ± 33 grams to 332 ± 63 gram this was statistically not significant, $p=0.16$.

Conclusions: Load-independent biventricular contractility and contractile reserve can be evaluated during machine perfusion. Such methods may allow for a more discerning examination of the human donor heart, including organs from borderline and extended criteria donors. Techniques to prevent or minimize myocardial edema during machine perfusion may be necessary.

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Retrograde Coronary Sinus Perfusion: An Alternate Approach for Machine Perfusion Preservation of Donor Hearts for Transplantation

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Purpose: We previously demonstrated that antegrade machine perfusion preservation resulted in reduced myocardial injury and apoptosis compared to conventional static storage. Aortic valve incompetence and nonnutrient flow are potential limitations of this technique. Retrograde perfusion through the coronary sinus avoids this issue. The purpose of this study was to evaluate retrograde machine perfusion preservation in a large animal model of heart transplantation.

Methods and Materials: Canine hearts were stored for 4 hours in Celsior organ preservation solution by one of 3 techniques: 1) Hypothermic static storage (n=6) 2) Antegrade perfusion (n=6) 3) Retrograde perfusion (n=5). Myocardial oxygen consumption (MVO_2) and machine perfusion parameters were measured continuously in perfused hearts. At end preservation, hearts were implanted into recipient animals. After 1 hour reperfusion, animals were separated from cardiopulmonary bypass and pre-load recruitable stroke work (PRSW) as a load independent measure of myocardial function was obtained hourly for 6 hours. Groups were compared by ANOVA. A p-value less than .05 was considered significant.

Results: MVO_2 and perfusion pressures were similar in both perfusion groups. Donor ischemic times, ionotropic support, and myocardial water content were not different between groups. PRSW 1 hour after reperfusion was highest in the Antegrade group. By 6 hours of reperfusion, PRSW was highest in the Retrograde group. See Table.

Table Transplantation Data

Group	Ischemic Time (min)	Water Content (%)	PRSW (1 hour)	PRSW (6 hour)
Retrograde	321 ± 6	$80.1 \pm .8$	67.6 ± 14	$72.2 \pm 10^*$
Antegrade	320 ± 4	$78.8 \pm .3$	$129 \pm 21^*$	38.6 ± 6
Static	318 ± 5	$78.3 \pm .2$	78.3 ± 11	39.6 ± 11

Data are Mean $\pm$ SEM;

*- $p < .05$ versus all other groups

Conclusions: Retrograde machine perfusion preservation is an effective strategy for protecting donor hearts. It is at least equivalent to conventional static storage or antegrade machine perfusion preservation. Further experiments under more severe ischemic conditions are warranted.

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Improved Lung Preservation by Increasing Flush Temperature in Rats

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