We have shown that 2 months after renal IRI, induced by bilateral kidney clamping, there is an increased expression of several validated senescence markers, such as $p16^{Ink4a}$, Interleukin-6 and chemokine (C-C motif) ligand 2 (CCL2), whilst downregulated expression of Lamin B1 which is lost in senescent cells. The increase in senescent cell levels 2 months after IRI is accompanied by worsened kidney function, compared to SHAM operated mice.

Through SASP and by reducing regenerative capacity, we argue senescent cells are a culprit of IRI-induced long-term damage in kidneys. We aim to remove these senescent cells and improve kidney transplant outcome by the targeted eradication of senescent cells. Recent developments in the understanding of the biology of aging have led to the development of a new class of therapeutic agents aimed at eliminating senescent cells. For the first time, we have a therapeutic compound (Proxofim) to target senescence in vivo and improve kidney function in mouse models for kidney aging (Baar et al, 2017). Proxofim was shown to improve kidney function of aged mice and reduce levels of pro-inflammatory factors such as IL-6 and CCL2, as a result of the targeted elimination of senescent cells. Therefore we are using Proxofim to overcome transplantation associated injury and improve kidney function.

O18 ADDITION OF DIFFERENT OXYGEN CONCENTRATIONS DURING LONG-TERM HYPOTHERMIC MACHINE PERFUSION IN A CLINICALLY RELEVANT PORCINE DONATION AFTER CIRCULATORY DEATH MODEL

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Background: To date, hypothermic machine perfusion (HMP) has become standard care in many centres preserving deceased donor kidneys. Despite a significant reduction of metabolism at low temperatures, remaining cellular activity in the organ still requires oxygen. However, oxygen supply during HMP is not standard yet, as its role and safety has not been fully clarified yet. This study investigates the effect of administering oxygen during HMP on renal function in a clinically relevant porcine donation after circulatory death model.
Methods: After 30 min of warm ischemia, porcine slaughterhouse kidneys were preserved for 24 h by static cold storage (CS), or HMP with Belzer Machine Perfusion Solution (UW- MPS) with the addition of 0%, 21% or 100% oxygen. Next, kidneys were reperfused for 4 h in a normothermic autologous blood machine perfusion (NMP) setup. Kidneys were assessed on their renal function, oxidative stress and injury markers.
Results: HMP resulted in significantly better kidney function during NMP in terms of creatinine clearance, fractional sodium excretion and proteinuria. The addition of 100% oxygen showed the highest creatinine clearance, but did not reach statistical significance. TBARS, markers of oxidative stress, were negligibly low in all preservation modalities. Urinary TBARS at the end of NMP were highest in the CS group with a mean of 11.2 μM compared to 7.7 μM in the 100% oxygen group (NS). HMP preserved kidneys showed significantly lower injury markers compared with those preserved by CS. No such differences were found between the HMP groups with different oxygen concentrations.
Conclusion: This study demonstrated that kidney preservation with HMP is superior to CS. Although the addition of oxygen to HMP did not result in significantly improved renal function during NMP, beneficial effects were found in terms of reduced oxidative stress. Oxygen addition during HMP did not result in detrimental effects in this model.

O19 EFFECT OF PREGABALIN ON KIDNEY TISSUE IN SPINAL CORD ISCHEMIA REPERFUSION INJURY-INDUCED RATS

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Aim: The aim of this study is to investigate the protective effects of low and high doses of pregabalin administered with ischemia on renal tissue in spinal cord ischemia-reperfusion (I/R) in rats.

Method: 24 Wistar rats were randomly divided into four groups (n = 6). Control (group C), I/R (group I/R), I/R-low dose pregabalin (group I/R-LP), I/R-high dose pregabalin (group I/R-HP). All groups underwent laparotomy under anesthesia. After laparotomy in group I/R, a cross clamp was placed in the abdominal aorta for 120 min to perform spinal cord ischemia injury. Following 120 min of ischemia, reperfusion was achieved by opening the vascular clamp. 30 mg/kg (group I/R-LP) and 200 mg/kg (group I/R-HP) pregabalin was administered intraperitoneally 15 min before the ischemia. At the end of the reperfusion period, kidney tissue was taken for biochemical and histopathologic examinations.
Results: It was determined that the amount of erythrocytes leaking out of the vessel wall in the Bowman capsule in the I/R group was higher than the control group in the general tissue evaluation with Hematoxylin Eosin staining, that is, there was edema in the Bowman capsule. In the low-dose group, there was no change in this histopathological findings, but the 200 mg/kg group showed significant improvement, suggesting a similar appearance to the control group. When there were no p53 expressing cells in the control group, p53 expression was detected in the I/R group very distinctly, especially at different intensities in some Bowman capsules. Interestingly, in the low-dose group, it was found that p53 expression was markedly faded but very prominent in the 200 mg/kg group. TOS and TAS enzyme activity was significantly higher in the I/R group than in C,I/R-LP and I/R-HP groups.
Conclusion: These results indicate that different doses of pregabalin administered before ischemia in spinal cord I/R injury has partial protective effects in rats.

O20 HIGH OXYGEN PRESSURE DURING CONTINUOUS HYPOTHERMIC MACHINE PERFUSION IS ASSOCIATED WITH A BETTER *EX VIVO* RENAL BLOOD FLOW AND EARLY GRAFT FUNCTION IN A PORCINE DCD AUTO-TRANSPLANT MODEL

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Introduction: Continuous hypothermic machine perfusion (HMP) demonstrated improved early graft function compared to static cold storage (SCS) alone. The aim of this study was to evaluate the impact of different perfusate oxygen pressures during continuous hypothermic machine perfusion on physical machine perfusion parameters and early graft function in a porcine auto- transplant model.
Materials and methods: The left kidney of a ± 40 kg female Landrace pig was exposed to 30 min of warm ischemia by vascular clamping and randomized after standard procurement and *ex vivo* donor blood flush out to one of 4 studied preservation strategies: (i) 22 h SCS, (ii) 22 h (no active oxygen supply) HMP, (iii) 22 h oxygenated HMP ($HMPO_2$low) (pO_2 = 220–240 mmHg), and 4) 22 h oxygenated HMP ($HMPO_2$high) (pO_2 = 700–800 mmHg). The LifePort Kidney Transporter® (Organ Recovery Systems) was used for all machine perfusion strategies. The left kidney was auto-transplanted in a right orthotopic position.
Results: Twenty-four auto-transplants were performed with 6 pigs per study group. Renal blood flow (RBF) was significantly higher in both $HMPO_2$high and $HMPO_2$low groups compared to non oxygenated HMP. The RBF increase was faster in the $HMPO_2$high group (significant from 3 to 20 h compared to the HMP group) compared to the $HMPO_2$low group (significant from 8 to 19 h compared to HMP group). At the end of the HMP no difference was observed in RBF between the machine perfusion groups. No significant difference in RBF was observed between the $HMPO_2$low and the $HMPO_2$high group during the whole period of machine perfusion. Serum creatinine at day 1, 2, and 3 was significantly lower in the $HMPO_2$high group compared to non- oxygenated HMP ($p = 0.0126$; $p = 0.0013$ and $p = 0.0236$, respectively) and SCS ($p = 0.0001$; $p < 0.0001$; $p < 0.0001$, respectively). We observed a tendency toward better renal function during the first 3 days after transplantation in favor of the $HMPO_2$high group compared to the $HMPO_2$ low group, but the difference was not statistically significant. No difference in serum creatinine was observed between all the study groups at 7 and 13 days of follow-up.
Conclusions: The administration of high levels of perfusate oxygen concentration during HMP positively influence ex vivo renal blood flow and early graft function compared to low or no oxygen supply during HMP.