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Survival outcomes after combined heart-kidney transplantation compared to kidney transplantation alone

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Introduction: The first successful combined heart-kidney transplantation (HKTx) underwent in 1986 and since then the prevalence of this procedure has increased dramatically. Survival outcomes in HKTx seem to be similar to those for kidney transplantations alone (KTx).

Aim: Aim of this study is to examine whether combined HKTx have the same survival outcomes or not, compared with those of kidney transplantation in the first two years.

Methods: Temple University Hospital Database was queried from 1990-2015 for patients with heart and renal failure, who underwent HKTx and we found 20 cases. Data were extracted with reference to age (at transplantation), gender, race, weight (BMI), diabetes mellitus status, coronary artery disease status, hypertension status and date of transplantation. A control group of solitary KTx recipients was selected from the same database that underwent transplantation during the same time period. The control group was matched with HKTx for age at transplantation (±2 years), gender and race. Kaplan-Meier method was used to identify the first two years survival outcomes in these two cohorts.

Results: Out of 20 patients who underwent HKTx, seven died during the first year after transplantation and from the cohort of solitary KTx only one patient died, particularly during the second year. Mortality in the HKTx group was higher in comparison with the mortality in solitary KTx cohort, particularly with statistically significant difference (.012).

Conclusions: Combined heart-kidney transplantations have higher incidence of mortality during the first year after transplantation. Additional studies are needed to determine the long-term mortality and which patients are suitable for HKTx.

Stimulation of islet revascularization modulating HIF-1α expression using siPHD3

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Deleterious events for islet engraftment are related to insufficient islets revascularisation inducing β cells death. HIF-1α is involved in various survival molecular pathways like cell proliferation and angiogenesis whereas for a chronic stabilization, it induces apoptosis. Prolyl-hydroxylase 3 (PHD3) mediates the degradation of HIF1α under normal oxygen conditions. It could be interesting to find the best level of HIF-1α expression in islets inhibiting PHD3 to induce angiogenesis while limiting apoptosis. The aim of this work was to realize a proof of concept of a new strategy of angiogenesis stimulation inhibiting PHD3 expression using siRNA on β-cell lines. RINm5F β-cells were lipofected (Lipofectamine RNAiMax) or not with 50 µM of siPHD3. Apoptosis was determined using Apo-ONE® Homogeneous Caspase-3/7 Assay, PHD3 expression by western blotting and VEGF secretion using Elisa kit 48 and 72 hours after lipofection. Caspase 3/7 activity is reduced with siPHD3, 48h (Control: 450±18 RFU; siPHD3: 155±12 RFU, $p<0.001$) and 72h post lipofection (Control: 689±10 RFU; siPHD3: 213±21 RFU, $p<0.001$). A significant decrease of PHD3 protein expression was observed using siPHD3 validating the efficiency of our approach (Control 48h: 0.48±0.15 and siPHD3: 0.14±0.03 PHD3 protein expression/β-actin; $p<0.01$). Finally, siPHD3 shown a significant pro-angiogenic effect increasing VEGF secretion 72h post lipofection (Control: 9837±470 and siPHD3: 17306±2118 pg/mg of protein; $p<0.05$). Inhibition of PHD3 using siRNA, decreases apoptosis and increases VEGF secretion in RINm5F cells. Thus, modulation of HIF-1α expression using lipofection of siRNA could increase islet vascularization and could be a realistic approach to improve graft survival.

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