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Long-Term Renoprotective Effect of Sirolimus-Based Calcineurin Inhibitor-Free Immunosuppression after Cardiac Transplantation

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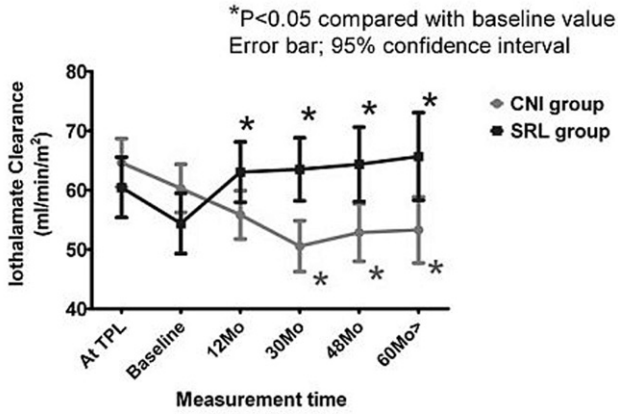
Purpose: There are few data about long-term renal effect of calcineurin inhibitor (CNI) withdrawal and substitution with sirolimus (SRL) after heart transplantation (HTPL). We evaluated long-term effect of SRL-based CNI-free immunosuppression using iothalamate clearance (Ci) test.

Methods and Materials: We evaluated 199 patients whose Ci was followed regularly after HTPL. We excluded patients with combined other organ transplantation, systemic renal disease, irregular follow-up and age <18 years. Patients were classified as SRL group (n=82) if CNI was discontinued and SRL was used >40 months and as CNI group (n=77) if CNI was not discontinued. Patients who used CNI and SRL simultaneously (n=11) or who used SRL <40 months (n=29) were excluded for Ci analysis. We checked baseline Ci before SRL was started and followed at 12, 30, 48 and >60 months later.

Results: Baseline Ci of SRL group was not significantly different between groups. In SRL group, Ci was significantly increased at 12 month (63±23 ml/min/m^2) compared to baseline (54±21 ml/min/m^2, p=0.019) and maintained thereafter. However, Ci was significantly reduced at 30 month (51±16 ml/min/m^2) compared to baseline (60±18 ml/min/m^2, p=0.001) in CNI group. Among 166 patients who tried SRL substitution for CNI, 38 (22.9%) could not tolerate SRL and



major causes were lung infiltration (5.4%) and diarrhea (5.4%) followed by malaise (4.8%) and edema (2.4%).

Conclusions: Sirolimus-based CNI-free regimen is useful for the preservation of renal function in long-term follow-up after HTPL. However, as intolerance rate of SRL is significant, careful assessment of side effect in individual patient is mandatory.

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The Virtual Crossmatch at Children's Hospital of Wisconsin – Outcomes for Predicted Positive Crossmatches

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Purpose: Heart transplant (HTx) in the setting of a pos crossmatch (XM) is associated with worse outcomes. Since 2004, we have used a virtual XM to evaluate organ offers. We risk stratify based on usual organ criteria (fxn, size, distance) along with the perceived pt specific wait risk and likelihood of a more favorable offer given the patient's strength and breadth of antibodies. We describe our experience focusing on management and outcomes.

Methods and Materials: We reviewed records of all HTx pts at our center. PRA at HTx, wait times and XM results were recorded. We reviewed peri-op care for pts with pos XM along with outcomes: rejection and death.

Results: 100 pts underwent HTx between 8/2004 and 8/2012. 43 were sensitized at HTx, 57 were not. Comparisons shown below (Table 1). When considering any DSA at HTx as VXM pos: 17 were VXM pos and 26 were neg. Of 17 with any DSA at HTx, 12 were flow XM pos and 5 neg. All VXM pos pts received pheresis in OR; post op B cell therapy and induction was based on flow XM results (Table 2).

Table 1. Comparision of sensitized vs non-sensitized patients

	Gender	Age (years)	Diagnosis	Wait Time (days) median (range)
Sensitized (43)	24M 56%	7.1	14 CM, 27 CHD, 2 ReTx	59 (2-1899)
Non sensitized (57)	33M 58%	6.6	30 CM, 26 CHD, 1 Tumor	38 (2-971)

Table 2. Virtual Crossmatch Positive (ie + DSA) managment and outcomes

	Pheresis in OR	Postop Pheresis	Thymo	Rituxan	Cell Rej Yr 1	AMR Yr 1	Survival (3 yr)
Flow XM Pos (12)	12	9	11	9	3	3: 1 hyperacute (ECMO), 2 Rx Bortezomib	100%
Flow XM Neg (5)	5	0	2	0	0	1: POD 8 (died)	60% *see below

*2 deaths, both flow XM neg, 1 with AMR POD 8, 1 with early MSOF

Conclusions: A judicious virtual XM strategy can increase the chance for sensitized pts to have a neg XM with acceptable wait times. Aggressive early B cell therapy can produce excellent outcomes for highly sensitized, critically ill pts unable to wait for a neg XM. Pts with DSA at HTx but a neg flow XM may still be at risk for early AMR. Comparison of sensitized vs. non-sensitized patients: Virtual Crossmatch Positive (ie +DSA) management and outcomes

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Dynamics of Galectin-3 Levels Following Left Ventricular Assist Device Implantation

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Purpose: Galectin-3 (gal-3) is a novel biomarker implicated in cardiac fibrosis and is shown to correlate with the severity of heart failure (HF) and to independently predict mortality in HF. We investigated if hemodynamic improvement after left ventricular assist device (LVAD) implantation affects gal-3 levels.

Methods and Materials: Plasma samples were acquired from patients at time of LVAD implantation (HMII or Heartware, n=57), at 3 (n=17) and 6 months post-LVAD (n=14), and at explantation (n=23), as well as from healthy age and gender matched controls (n=30). Gal-3 was measured using a commercially available ELISA assay (BG Medicine, Waltham, MA). Data was analyzed with Prism 5. Events rates were calculated using the Kaplan-Meier method.

Results: At time of LVAD implantation, HF patients had significantly higher gal-3 levels compared to controls (29.2±14 ng/ml vs. 13±9 ng/ml; p<0.0001). Mechanical unloading led to improvement in echocardiographic parameters (LVEDD: 6.1±1 cm vs. 6.7±1 cm pre-LVAD; p=0.04 and LA diameter: 4.4±1 cm vs. 5±1 cm pre-LVAD; p=0.002). Gal-3 levels numerically decreased at 3 (23.7±9 ng/ml; p=0.33) and 6 months (21.7±9 ng/ml; p=0.18) post LVAD.