## 1107

### SIMULTANEOUS LIVER AND KIDNEY TRANSPLANTATION DOES NOT PROLONG RENAL ALLOGRAFT SURVIVAL.

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It has been suggested that a simultaneous liver and kidney transplant (SLK) may protect the renal allograft by host microchimerism induced by passenger leukocytes. However, the data available so far have been conflicting and it is not clear whether SLK confers any protection to renal allograft. Objective: To compare the graft and patient survival among those who had undergone simultaneous (SLK from a single donor)or sequential (kidney after a previous liver, KAL) transplantation with cadaveric kidney transplantation(CKT). Methods: Using UNOS database(1990-1996),patients who had SLK (n= 465), KAL (n= 134), and CKT (n = 47013)were analyzed.Results: By logistic regression, SLK was associated with poor graft survival(OR 2.58,CI 2.16 ± 3.74)despite a higher proportion of patients with normal creatitine at the time of discharge. Kaplan- Meier analysis for patient survival showed poor survival for SLK (log rank 0.0001). The 2-yr graft (62%) and patient (68%) survival of patients who had KAL(age 48.4 ± 13.9 years) were similar to those who had SLK. Conclusion: SLK does not appear to offer any protection for renal allograft and is asscociated with a poor graft and patient survival.

Comparison between Cadaveric and Simultaneous Liver KidneyTransplantation

| | Cadaveric | SLK | P value |
|---|---|---|---|
| age(years) | 43.6± 14.0 | 43.0± 16.8 | NS* |
| Sex(F/M %) | 39% / 61% | 40% / 60% | NS* |
| Race(Black/White) | 12019/17615 | 40/363 | 0.001 |
| Cold ischemic time(hrs) | 22.6 ± 9.9 | 15.5 ± 7.6 | 0.0001 |
| Donor age (years) | 32. 9 ± 16. 8 | 31.2 ± 16.3 | 0.02 |
| Normal creatinine(discharge) | 35% | 61% | 0.001 |
| Graft survival 30 days | 94 % | 85 % | 0.001 |
| Graft survival 2 years | 80 % | 59% | 0.001 |
| Re-Transplantation | 12 % | 2% | NS |
| Patient survival 2 years | 90% | 67 % | 0.0001 |

* Not significant

## 1108

### CYCLOSPORIN A PHARMACOKINETICS IN LIVER TRANSPLANT RECIPIENTS. EFFECT OF URSODEOXYCHOLIC ACID.

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Oral cyclosporin A (CsA) treatment with the microemulsion formulation Neoral® was introduced to overcome the problems related to CsA poor aqueous solubility in the intestinal lumen. Ursodeoxycholic acid (UDC), a hydrophilic bile acid which influences CsA solubilization, might also modulate CsA intestinal absorption. Patients and Methods: At entry into the study, twelve clinically stable liver transplant recipients, three of them with cholestasis, received Neoral®. They then received a cotreatment Neoral® plus *UDC* (13 mg/kg/day) for three months. The kinetic data were analyzed by a mathematical model incorporating a time dependent rate coefficient for *CsA* intestinal absorption. Serum markers of hepatic and renal injury were compared before and after *UDC* treatment. Results: Serum levels of UDC increased from 3%, before bile acid treatment, to 45% of total bile salts. The estimated model parameters indicate that *UDC* affects *CsA* intestinal absorption. In the nine non cholestatic patients, *UDC* significantly ($P<0.005$) reduced both the absorption rate and the bioavailability of *CsA*, without modifying the elimination parameters. Globally, UDC smoothed CsA blood peaks. In contrast, in the three cholestatic patients, the bioavailability tended to be higher and the absorption rate faster when *CsA* was associated with *UDC*. On the other hand, *UDC* significantly decreased elevated $\gamma$-glutamyl transferase ($P<0.01$) and creatinine ($P<0.04$) serum levels and induced clinical improvements such as disappearance of headaches. Conclusions: A three-month UDC treatment appears to modulate CsA intestinal absorption without affecting CsA elimination. In addition, UDC supplementation led to CsA improved tolerability.

## 1109

### THE EFFECT OF ORTHOTOPIC LIVER TRANSPLANTATION (OLT) ON QTC INTERVAL IN PATIENTS WITH END-STAGE LIVER DISEASE.

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In a previous study, we had shown that prolonged QTc (corrected QT interval) interval was common in patients with alcoholic and non-alcoholic liver disease, and that the prevalence of prolonged QTc interval increased with the severity of liver disease (Hepatology 1999;116:A1264). Aim of this study was to determine the effect of liver transplantation on QTc interval. Methods: 162 patients (males 58%, mean age 48± 16.9 years) with chronic liver disease (24% HCV, 14% PBC, 11% alcoholic, 10% PSC, 5% autoimmune, 31% miscellaneous) who had liver transplantation were studied. QT interval (mean) corrected for ventricular rate (QTc) was read from a 12 lead EKG with Bazetts formula before and 6 months after liver transplantation. Results: 91 patients (55.8%) had prolonged QTc (>440 ms) before liver transplantation. Mean QTc decreased significantly following liver transplantation (450.29 ± 39.21ms vs 429.20 ± 29.25ms, $p < 0.002$). 112/162 patients had normal QTc interval after liver transplantation compared to 71/162 before transplantation. Seventy six (76/91, 83.2%) patients with prolonged QTc interval had improvement in QTc interval following liver transplantation and of these 50 patients (50/91, 55%) had QTc interval returned to normal values (<440 ms); the remaining 26 (28.5%) with abnormal pre-transplant QTc interval showed a decrease in QTc interval after transplantation, but were still higher than normal values (> 440 ms). Fifteen patients with pronged QTc showed no improvement after liver transplantation. Nine (12.7%) patients with normal pre-transplant QTc had deterioration of QTc interval after transplantation to abnormal values (>440 ms), while 11 patients (12.1%) with abnormal pre-transplant QTc had further prolongation of QTc interval after liver transplantation. Conclusions:Prolonged QTc was common in patients with end stage liver disease and in about half of these patients, the QTc returned to normal values following liver transplantation. However, a significant number of patients continued to have prolonged QTc after transplantation which may suggest that prolonged QTc seen in liver disease is multifactorial in origin.

## 1110

### OUTCOME OF LIVER TRANSPLANTATION IN PATIENTS WITH IRON OVERLOAD.

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Hepatic iron overload is a relatively common, but still poorly characterized finding in patients undergoing liver transplantation (OLT), and has been associated with suboptimal survival. Aim: Evaluate the outcome following OLT in patients with iron overload in the explanted liver and determine whether Hepatic Iron Index (HII) influences graft survival. Material and Methods: Retrospective study of 50 patients with iron overload who underwent OLT between January 1990 and December 1999. The inclusion criteria included: 1) clinical diagnosis of HH prior to OLT, 2) histological findings of iron overload in the explanted liver. The degree of iron overload was assessed by Hepatic Iron Concentration (HIC), and HII. Patients were divided into 2 groups: group I, HII<1.9; and group II, HII>1.9. Patients age, sex, presenting signs and symptoms, HLA haplotype, liver tests prior to OLT, and post-OLT complications were compared between the 2 groups using Chi-square analysis. Kaplan-Meier method was used to estimate survival and the log rank test for comparing survival in both groups. Results: The median patients' age was 53 yr (range, 29-75 yr), 78% were male, and 60% Caucasian. The indication for OLT in 74% of the patients was a primary diagnosis other than HH. Thirteen patients (26%) had presumed HH pre-OLT, 3 of them had undergone therapeutic phlebotomy. Seven patients (14%) also had hepatocarcinoma at the time of OLT. Quantitative hepatic iron levels were determined in all 50 patients; HIC was 5,495 ± 3,421 mcg/g dry wt (range 77-15,817), and mean HII was 1.88 mcmol/g/yr (range 0.1-6). Twenty six patients had HII>1.9, suggesting homozygosity for HH; and 24 patients had HII<1.9. The prevalence of clinical features was similar between the 2 groups except for diabetes, which was significantly higher in group II($p=0.009$). HLA-A3 was present in 12 patients (24%) with higher incidence in group I ($p=0.053$). No significant difference was found in terms of post-OLT complications between the two groups. However, the incidence of cardiac complications was higher in group II, (35% vs 21% in group I) (p=NS). The 12 months actuarial survival in group I was 78% vs. 72% in group II (p=NS), compare with 83% overall OLT survival at our institution. Conclusions: 1) Hepatic iron overload is an important co-morbid factor in patients undergoing OLT. 2) Our data suggest that iron overload may compromise cardiac morbidity and patient survival. 3) Greater emphasis need to be placed upon the significance of iron overload in the evaluation and follow-up of patients undergoing OLT.