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INCREASE IN VISCERAL ADIPOSE TISSUE POST-LIVER TRANSPLANTATION IS SIGNIFICANTLY ASSOCIATED WITH HEPATOCELLULAR CARCINOMA RECURRENCE

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Background: Hepatocellular carcinoma (HCC) is increasing as an indication for liver transplantation. Recurrence of HCC after liver transplantation is regarded as a terminal condition. Recent reports suggest that increased pre-transplantation visceral adipose tissue (VAT) is predictive of post-transplantation HCC recurrence. However, body composition is dynamic in the post-transplantation period and it remains unknown how changes in VAT affect HCC recurrence. We aimed to characterize the relationship between changes in body composition and HCC recurrence. **Methods:** We conducted a single-center retrospective cohort study of adult liver transplant recipients with HCC enrolled in the Penn State Liver Transplant Database between 2005 and 2012. Body composition analysis was completed using L3 vertebrae body slices from contrasted computed tomography (CT) scans and Aquarius Workstation Software. VAT, subcutaneous adipose tissue (SAT) and muscle mass were measured from CT scan immediately prior to transplantation and also at diagnosis of HCC recurrence or last known follow-up. Subjects with and without post-transplantation HCC recurrence were compared. Kaplan-Meier curves were constructed to model HCC recurrence. **Results:** 27 HCC recipients with mean age 58 +/- 7 years and mean MELD score 26 +/- 7 were enrolled. Overall rate of post-transplantation HCC recurrence was 19% (n=5). In general, recipients with HCC recurrence were similar to those without recurrence including pre-transplantation VAT. Recipients with HCC recurrence had inferior three- (40% vs. 86%, p=0.024) and five-year survival (0% vs. 77%, p=0.001). VAT increased in recipients with HCC recurrence (60.4cm^2, 95% CI -84.5-205.4cm^2) and decreased in recipients without recurrence (-24.0cm^2, 95% CI -53.3-66.0cm^2), p=0.035. Subjects with HCC recurrence who gained abnormal VAT (>160cm2) were more likely to develop HCC following transplantation (log-rank, p=0.005). No between group differences were seen for SAT or muscle mass. **Conclusions:** Increases in post-transplantation VAT are associated with greater HCC recurrence, especially when abnormal VAT levels are achieved. As demand for liver transplantation to cure HCC continues, an improved understanding of the relationship between VAT and HCC is vital. Further research investigating the ability of exercise and minimizing immunosuppression in recipients transplanted for HCC is paramount to lose or prevent VAT gain and lessen the risk of universally fatal HCC recurrence.

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CHRONIC KIDNEY DISEASE IS AN INDEPENDENT PREDICTOR OF THIRTY DAY READMISSIONS IN PATIENTS UNDERGOING LIVER TRANSPLANTATION: RESULTS OF NATIONWIDE DATABASE ANALYSIS

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OBJECTIVE: Liver transplantation (LT) is a major surgical procedure associated with considerable post-procedure morbidity and mortality. 30-day readmissions is a major driver of morbidity, mortality and health care utilization in our patients. We aim to look at the 30-day readmissions for patients undergoing liver transplantation and its impact on health outcomes. METHODS: We performed a retrospective study using the Nationwide Readmission Database(NRD) for the year 2016 (Data on 35.6 million discharges). We collected data on hospital readmissions of 6,911 adults who underwent liver transplantation and were discharged. All the variables used in the study were identified using ICD-10 codes. Patients with age less than 18 and admission during December month were excluded. The primary outcome was rate of all-cause readmission within 30 days of discharge. Secondary outcomes were reasons for readmission, readmission mortality rate, morbidity and resource use. Multivariate regression analysis was used to determine the independent predictors of 30-day readmission. RESULTS: Among patients admitted to US hospitals for liver transplantation, the total time at risk was 87,899 days, with the first readmission occurring at day 1 and the last readmission at day 30. The 30-day rate of readmission was 19.6%, with the most common cause of readmission being Acute Kidney Injury (8.0 %) . The mortality rate among patients in index hospital admission (4.0%), was higher than that for readmission (1.0%) (P < .01). Mean length of stay was 22.3 days for index admission and 6.3 days for readmission (p<0.01). Mean total charge for index admission was $540,029 compared to $66,447 for readmission (p<0.01). Mean total cost for index admission was $148,285 compared to $18,507 for readmission (p<0.01). A total of 8,225 hospital days were associated with readmission, and the total health care in-hospital economic burden was $24 million (in costs) and $86 million (in charges). Chronic kidney disease (CKD) was an independent predictor of readmission, (aOR 1.5, p<0.01). CONCLUSIONS: In a retrospective study of patients hospitalized for liver transplantation in 2016, 19.6% were readmitted to the hospital within 30 days of discharge. Acute Kidney Injury (AKI) was the most common reason for readmission, and patients with CKD were 1.5 times more likely to be readmitted. This is one of the first studies to show the association of CKD with readmissions in LT patients, and these patients need closer monitoring of their renal function post discharge to prevent AKI and potential readmission. Further study is necessary in the future to guide clinical practice.

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RECOMBINANT THROMBOMODULIN PREVENTED HEPATIC ISCHEMIA-REPERFUSION INJURY BY INHIBITING HIGH-MOBILITY GROUP BOX 1 IN RATS

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Background and Aims: Recombinant thrombomodulin (rTM) is a novel anticoagulant and anti-inflammatory agent that inhibits secretion of high-mobility group box 1 (HMGB1) from liver. We evaluated the protective effects of rTM on hepatic ischemia-reperfusion injury in rats. ***Methods:*** Ischemia was induced by clamping the portal vein and hepatic artery of left lateral and median lobes of the liver. At 30 min before ischemia and at 6 h after reperfusion, 0.3 ml of saline (IR group) or 0.3 ml of saline containing 6 mg/kg body weight of rTM (IR-rTM group) was injected into the liver through inferior vena cava or caudate vein. Blood flow was restored at 60 min of ischemia. Blood was collected 30 min prior to induction of ischemia and before restoration of blood flow, and at 6, 12, and 24 h after reperfusion. All the animals were euthanized at 24 h after reperfusion and the livers were harvested and subjected to biochemical and pathological evaluations. ***Results:*** Serum levels of ALT, AST, and HMGB1 were significantly lower after reperfusion in the IR-rTM group compared to IR group. Marked hepatic necrosis was present in the IR group, while necrosis was almost absent in IR-rTM group. Treatment with rTM significantly reduced the expression of TNF-α and formation of 4-hydroxynonenal in the IR-rTM group compared to IR group. ***Conclusion:*** The results of the present study indicate that rTM could be used as a potent therapeutic agent to prevent IR-induced hepatic injury and the related adverse events. *Presenting author Email: georgej@kanazawa-med.ac.jp

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TRENDS IN MORBIDITY AND MORTALITY AFTER LIVER TRANSPLANTATION IN THE UNITED STATES: ANALYSIS OF THE NATIONAL INPATIENT SAMPLE (2002 -2013).

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Background: Liver transplantation (LT) is a treatment modality of last recourse for patients with end stage liver disease. According to the United Network for Organ Sharing (UNOS), LT numbers have doubled in the last two decades. LT is however not without risk and may result in significant morbidity or mortality. The goal of this study is to evaluate temporal trends and outcomes after LT in the United States over a 12-year period (2002 – 2013). **Methods:** The National Inpatient Sample (NIS) was queried to identify patients who underwent LT from 2002 to 2013. Data on age, gender, race, comorbidities, insurance, admission type, transplant type, hospital location, region, bed size and transplant volume were extracted. We evaluated trends in postoperative morbidity and mortality as outcomes of interest. Logistic regression was used to evaluate factors associated with adverse outcomes after LT. **Results:** A weighted total of 54,131 LT procedures were identified and analyzed. Between 2002 and 2013, liver transplantation increased by over 85% in a nonlinear trend. Mean age at LT was 49.5 ± 16.5 years. Most procedures were performed in men (65%), Caucasians (66.3%) and involved dead donors (92%). Nearly all (99%) procedures were done in urban teaching centers, 75% of which were medium to high LT volume centers. Overall, postoperative mortality after LT was 5.1%. This decreased in a nonlinear trend from 6.6% in 2002 to 4.0% in 2013. On multivariate analysis, predictors of postoperative mortality include age < 18 years (OR 1.41, 95% CI 1.16, 1.72), females (OR 1.24; 95% CI 1.10, 1.38), emergent hospitalizations (OR 1.28, 95% CI 1.12, 1.47) and non-private insurance (OR 1.51; 95% CI 1.35, 1.69). Compared to low LT volume centers, mortality was higher in medium and high LT volume centers (OR 1.40; 95% CI 1.21, 1.62) and (OR 1.67; 95% CI 1.43, 1.95) respectively. Postoperative morbidity independently increased the odds of mortality after LT (OR 5.43; 95% CI 4.68, 6.30). Overall, postoperative morbidity occurred in 50% of LT procedures. It increased in a nonlinear trend from 41.8% in 2002 to 55.4% in 2010 but decreased thereafter. After adjusting for covariates, females (OR 1.10; 95% CI 1.05, 1.15), age < 18 years (OR 1.18, 95% CI 1.08, 1.28) and non-private insurance holders (OR 1.11; 95% CI 1.06, 1.16) were at higher odds of morbidity. Living donor recipients had lower odds or morbidity. **Conclusion** For patients who undergo LT, the risk of dying after the procedure has decreased significantly while morbidity rates have remained stable. Patients who experience complications after LT were at a higher risk of death regardless of prior comorbid status. While transplant type did not affect mortality, living donor recipients had lower morbidity. Higher volume LT transplant centers had more adverse outcomes after LT likely reflecting higher case complexity at these centers.

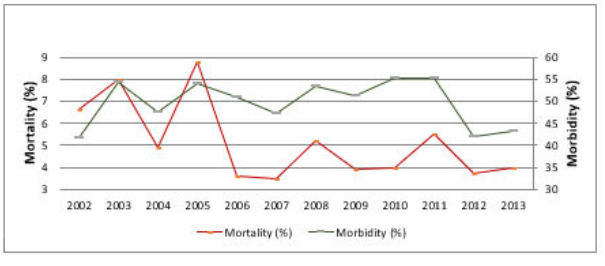

Figure 1: Trends in morbidity and mortality after liver transplantation in the United States from 2002 to 2013