SAT278

The liver outcomes and equity (LOEq) index: neighborhood social determinants independently predict outcomes in liver transplantation

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Background and aims: The impact of social determinants of health (SDOH) at the neighborhood-level on patient outcomes in adult liver transplantation (LT) is unknown. We constructed the novel Liver Outcomes and Equity (LOEq) index to characterize area-based SDOH specific to the population with liver disease in the United States (US) and examined association with LT outcomes.
Method: The LOEq index was derived from 16, 713 unique ZIP codes (42% of all US ZIP codes) of adult waitlisted patients in the Scientific Registry of Transplant Recipients database between 6/18/2013–5/18/2018. We selected 38 ZIP code-level variables across five SDOH domains from the 2014–2018 American Community Survey as a comprehensive measure of neighborhood SDOH. Principal component analysis conducted with a structured and iterative process identified the most influential 13 variables to be included in the final index. Primary predictor was the LOEq index categorized into quintiles (Q1 = lowest to Q5 = highest SDOH). Outcomes were 1) waitlist (WL) mortality (= delisting for too sick/death) and 2) post-LT patient survival, examined with competing risk and Cox regression, respectively. Models were adjusted for transplant region and relevant demographic/clinical factors, with insurance tested as an effect modifier.
Results: Adult LT patients disproportionately resided in neighborhoods with higher SDOH, with 14.0% vs 30.3% of waitlisted patients (n = 59, 298) and 13.9% vs 30.2% of transplanted patients (n = 37, 598) in Q1 vs Q5, respectively. Lower LOEq quintiles had higher proportion minorities, public insurance, hepatitis C etiology, diabetes, and obesity. 47% in Q1 vs 17% in Q5 lived in transplant regions with a short wait time to LT; 5.6% in Q5 vs 2.4% in Q1 underwent living donor LT. The 3-year cumulative incidence of WL mortality was higher in Q1 (22.9%) vs Q5 (20.6%), while 3-year post-LT survival was lower in Q1 (85.8%) vs Q5 (87.4%). In the multivariable model of waitlisted patients, LOEq Q1–4 were associated with increased WL mortality compared to Q5 (all p < 0.01), with Q1 patients incurring 23% excess deaths compared to Q5 (HR 1.23, 95% CI 1.16–1.31). Among transplanted, risk of post-LT death was also elevated for LOEq Q1 (HR 1.14, 1.04–1.24) and Q3 (HR 1.12, 1.03–1.21) compared to Q5. There was a non-significant interaction between LOEq and insurance type: higher WL mortality for Q1 vs Q5 (HR 1.28 for private vs 1.15 for public; p = 0.08) and lower post-LT deaths for Q1 vs Q5 (HR 1.01 for private vs 1.17 for public; p = 0.09).
Conclusion: More LT patients living in higher LOEq quintiles highlights a neighborhood-level disparity in access to LT. Lower neighborhood SDOH predicted worse outcomes in LT independent of patient demographics and clinical characteristics. The liver disease-specific LOEq index might be leveraged to identify the most vulnerable patients for interventions in clinical settings to increase LT equity.

SAT279

Prevalence, prognosis, clinical, biological and histological features of incidentally found hepatocellular carcinoma after liver transplantation

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Background and aims: An incidentally found hepatocellular carcinoma (iHCC) is an HCC diagnosed postoperatively after the analysis of the liver explant from patients who underwent liver transplantation (LT) for non-oncological indication. Data about the prevalence and prognosis of iHCC are scarce. The aim of this study is to evaluate the prevalence of iHCC in our LT patients and to compare the mortality, the risk of recurrence and the clinical, biological, and histological features between patients who underwent LT for preoperatively known HCC (pkHCC) and patients with a postoperative diagnosis of iHCC.

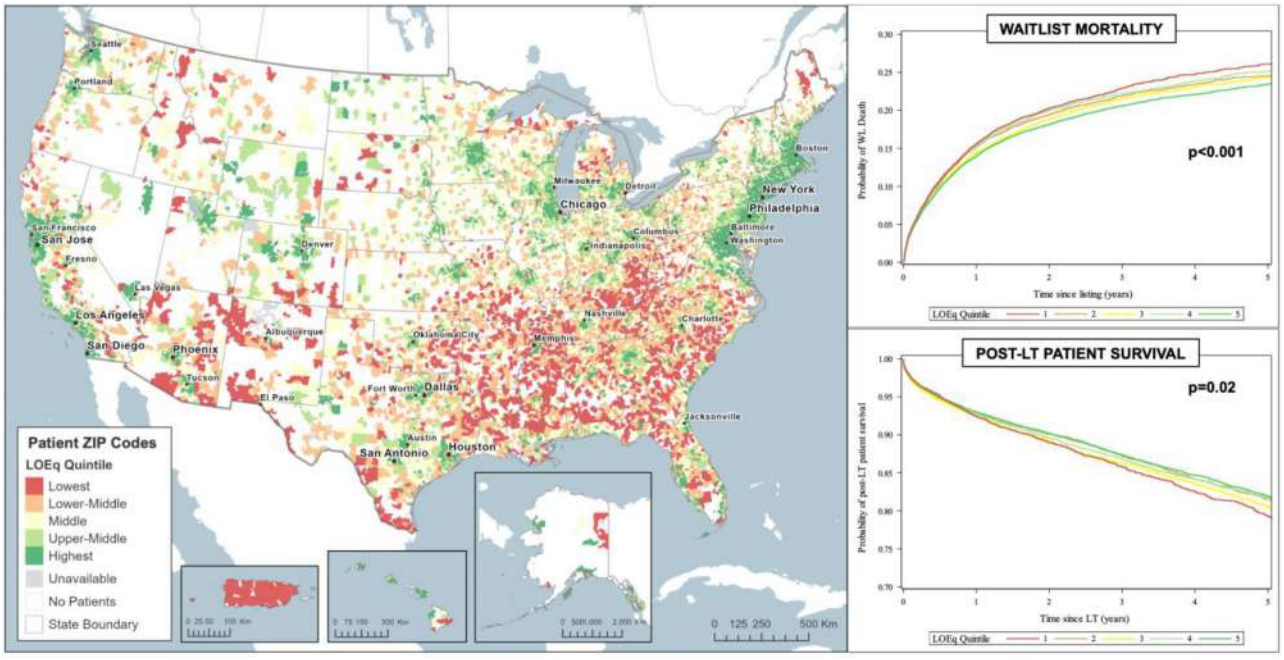

Figure: (abstract: SAT278)

Method: We retrospectively reviewed 268 adult patients who underwent LT at the Cliniques Universitaires Saint-Luc, Brussels, Belgium, from January 2010 to January 2020. Results were compared using Fisher's exact test or Mann-Whitney U test as appropriate. The Kaplan-Meier method was used to analyze the rate of death and graft loss. Log-rank tests were run to compare the survival curves. The significance of statistical tests was taken at a P value of <0.05. Analyses were run with SPSS Statistics.
Results: Among the 268 adult patients who underwent LT, 98 cirrhotic patients were transplanted for a pkHCC. Prevalence rate of iHCC was 12%. Alcoholic cirrhosis was predominant in the iHCC cohort (88.9% vs 48%, $p = 0.032$). As expected, the patients of the iHCC cohort had a higher MELD score (19.0 (17.0–20.0) vs 10.0 (8.0–13.0); p <0.001) both, at the registration on the waiting list and at LT. Value of Child-Pugh score was also higher for the iHCC cohort compared to pkHCC patients (10.0 (9.0–11.0) vs 5.0 (5.0–6.0); p <0.001). None of the iHCC patients got Child-Pugh A score vs 76, 3% of the patients with pkHCC (p <0.001). Child-Pugh class C cirrhosis at LT was mainly found in the iHCC cohort (55.6% vs 6.2%; p <0.001). No statistical difference was observed between the 2 cohorts for the level of alfa-fetoprotein, neither at time of registration nor at LT. However, des-carboxy-prothrombin level was significantly higher at time of LT in the iHCC cohort (273.8 (228.9–551.1) vs 42.0 (22.5–96.0); p = 0.022). The interval between the last imaging and LT was longer in iHCC cohort than pkHCC (2.7 months (1.9–3.7) vs 1.0 (0.5–1.7); p <0.004). Based on histological analysis, Edmondson grade II lesions were more frequently found in the iHCC cohort. However, there was no difference regarding the microvascular invasion rate. None of the 9 iHCC patients got recurrence of HCC post-LT. Cumulated recurrence at 1, 3 and 5 years post-LT for pkHCC patients were respectively 3%, 7% and 11%). No significant difference was observed for 1, 3 and 5-year survivals rates for iHCC patients compared to pkHCC patients (respectively 100%, 88% and 53% vs 90%, 87% and 65%; p = 0.565).
Conclusion: While the prevalence of iHCC is not negligible (12% in our patients), it impacts neither the neoplastic recurrence rate nor the survival rate compared to pkHCC patients.

SAT280

Survival benefit from liver transplantation for patients with and without hepatocellular carcinoma

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Background and aims: In the US, inequal liver transplantation (LT) access exists between patients with and without hepatocellular carcinoma (HCC). Survival benefit considers survival without and with LT and could equalize LT access. We calculated and compared LT survival benefit scores for patients with (out) HCC, based on longitudinal data in a recent US cohort.
Method: Adult LT candidates with (out) HCC between 2010 and 2019 were included. Waitlist survival over time was contrasted to posttransplant survival, to estimate 5-year survival benefit from the moment of LT. Waitlist survival was modeled with bias-corrected time-dependent Cox regression and posttransplant survival was estimated through Cox proportional hazards regression.
Results: Mean HCC survival without LT was always lower than non-HCC waitlist survival. Below MELD (-Na) 30, HCC patients gained more life-years from LT than non-HCC patients at the same MELD (-Na) score. Only non-HCC patients below MELD (-Na) 9 had negative benefit. Most HCC patients were transplanted below MELD (-Na) 14 and most non-HCC patients above MELD (-Na) 26. Liver function. (MELD (-Na), albumin) was the main predictor of 5-year benefit. Therefore, during five years, most HCC patients gained 0.12 to 1.96 years from LT, whereas most non-HCC patients gained 2.48 to 3.45 years.
Conclusion: On an individual level, transplanting patients with HCC resulted in survival benefit. However, on a population level, benefit was indirectly wasted, as non-HCC patients were likely to gain more survival due to decreased liver function. Based on these data, we now provide an online calculator to estimate 5-year survival benefit given specific patient characteristics. Survival benefit scores could serve to equalize LT access.

SAT281

Long-term outcomes of liver transplantation (LT) using grafts from donors with active and chronic hepatitis B virus (HBV) infection: multi-center cohort study

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Background and aims: We report the long-term outcome of liver transplantation (LT) using grafts from donors with active and chronic hepatitis B virus infection using Hepatitis B immunoglobulin (HBIG) and Nucleos (t)ide analogues (NA).
Method: Among 2260 LTs performed in Seoul National University Hospital, SNU Bundang Hospital, and SNU Boramae Hospital between January 2000 and April 2019, 26 (1.2%) grafts from donors with HBsAg (+), HBeAb (+) or HBV DNA (+) were referred as active and chronic HBV hepatitis grafts and reviewed retrospectively. Demographics and transplantation outcome were analyzed. HBV reactivation redefined as the increase of viral DNA for HBsAg (+) grafts and HBsAg positive seroconversion for chronic hepatitis grafts. Also, we adopted the stage of chronic HBV infection to evaluate and manage of recipients transplanted HBV infected grafts.
Results: Sixteen deceased donor LT were performed with active HBsAg (+) grafts. Ten living donor LT were performed with inactive HBV infected grafts; 8 patients in inactive hepatitis status; HBsAg (−), HBcAb (+) and HBV DNA (+), and 2 patients in chronic HBV hepatitis with seroconversion; HBsAg (−), HBsAb (+) and HBeAg (+). Average follow-up period was 82.6 ± 60.1 months. NA and HBIG were administered during perioperative period depending on donor and recipient's serology. Deaths (n = 8) were occurred 2.0–47.3 months after transplantation. Comparing LT using non-hepatitis virus-infected grafts, there was no difference in patient survival (30.8% vs. 18.6%, p = 0.247). Most common causes of death were infection (n = 4) and HCC recurrence (n = 3). HBV reactivation was identified in 1 patient but resolved spontaneously without additional management. All 10 LDLT recipients survived and were in good condition during follow-up. Survivors were in inactive or resolved status for HBV infection under the HBIG and NA. No graft failure was observed. Fourteen patients followed-up more than 5 years were stable and no increase in HCC recurrence rate was observed 5 years after transplantation.
Conclusion: Considering their long-term outcome, liver grafts with active and chronic HBV infection can be safely used in HBV endemic area.