Texas Liver Institute
The Road to A Healthier Liver

TLI Quarterly

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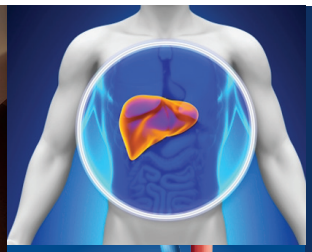

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INTRODUCING DR. JAN PETRASEK, TRANSPLANT HEPATOLOGIST

The Texas Liver Institute is thrilled to welcome Dr. Jan Petrasek to our team of providers servicing San Antonio. Dr. Petrasek earned his MD and PhD degrees from the Charles University in Prague. In 2008, he relocated to the University of Massachusetts Medical School for post-doctoral training in liver immunology. He joined the laboratory of Dr. Gyongyi Szabo, a world leader in alcoholic liver disease, to study the mechanisms of liver inflammation and fatty liver disease. His research defined several novel therapeutic targets in alcoholic liver disease and established the scientific foundation for a multicenter clinical trial investigating the role of interleukin-1 blockade in the treatment of patients with severe alcoholic hepatitis.

After completing his post-doctoral fellowship, Dr. Petrasek moved to the UT Southwestern Medical Center in Dallas where he completed his internal medicine residency, gastroenterology fellowship, and transplant hepatology fellowship. In 2021, Dr. Petrasek joined the faculty at the University of Mississippi Medical Center as an Assistant Professor and Associate Program Director for the Gastroenterology Fellowship Program.

Dr. Petrasek has authored >45 peer-reviewed manuscripts, review papers, and book chapters. An Alpha Omega Alpha inductee and recipient of numerous scholarly awards, he is an active member of the American Society of Transplantation (AST), the American Association for the Study of Liver Disease (AASLD) and the American Gastroenterology Association (AGA), among many other national and international organizations. He serves as an editorial board member for *Hepatology Communications* and is an *ad hoc* reviewer for multiple national and internationally known journals.

7th Advanced Practice Provider, Nursing and Primary Care Liver Conference

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A NEW THERAPY FOR HEPATORENAL SYNDROME-ACUTE KIDNEY INJURY (HRS-AKI)

In patients with decompensated cirrhosis with ascites, the probability of developing HRS ranges between 8%-20% per year and increases to 40% at 5 years. An estimated 35%-40% of patients with end-stage liver disease and ascites will develop HRS. In the US, hepatorenal syndrome-acute kidney injury (HRS-AKI) is associated with a high mortality rate and liver transplantation is the gold standard for treatment. Renal replacement therapy may bridge patients to liver transplant, but complete recovery of renal function after the liver transplant is rare. Prior to 2023, treatment involved volume expansion (albumin) and vasoconstriction. The vasoconstrictive component included administration of midodrine and octreotide (an alpha-adrenergic agonist combined with a selective splanchnic vasoconstrictor) or norepinephrine (an alpha-adrenergic agonist). These medications are not approved in the US for HRS-AKI but are used off-label based on results from small, non-randomized studies. Their benefits were very limited.

In late 2022, terlipressin, a vasopressin analogue that exerts vasoconstrictive activity via selective V1 and V2 receptors, was approved in the US for the treatment of HRS-AKI. It is indicated to improve kidney function in adults with hepatorenal syndrome with rapid reduction in kidney function; however, patients with a serum creatinine >5 mg/dL are unlikely to experience benefit. In the Phase 3 pivotal trial, ~85% of patients were treated on the floor avoiding ICU admission.

The American Association for the Study of Liver Diseases (AASLD) recently published an updated guidance document focusing on the diagnosis and management of HRS-AKI including how best to use terlipressin.

THE EVOLVING LANDSCAPE OF ALCOHOL-ASSOCIATED HEPATITIS

Jan Petrasek, MD, PhD

Alcohol-associated hepatitis (AH) represents the acute onset of symptomatic hepatitis, often superimposed on pre-existing cirrhosis, in patients with excessive alcohol intake. The early mortality rate for AH remains high, particularly in patients with infections, hepatic encephalopathy, and renal failure. Patients with severe AH who do not respond to medical therapy with steroids have a poor prognosis, and mortality is as high as 50-70% at six months.

Emerging translational and clinical research data have reshaped the field of AH in the past decade. As reviewed below, these advances include novel concepts of AH pathogenesis, a better understanding of the natural course of the disease and identification of predictors of spontaneous recovery, and data showing excellent outcomes of early liver transplantation (LT) in selected AH patients.

Novel understanding of AH pathogenesis

Novel mechanistic data have explained the reasons for the limited utility of steroids in AH. Although liver inflammation is crucial in the development of AH, it does not appear to be the major determinant of survival once severe AH develops. Rather, metabolic failure of the hepatocytes, lack of hepatocyte regeneration, and misguided differentiation of hepatic progenitor cells seem to explain the excessive AH mortality. Biological treatments targeting liver inflammation did not improve survival in AH in clinical trials. Future AH treatments should promote the regenerative capacity of hepatocytes, rather than target liver inflammation.

Defining a niche of AH patients who benefit from steroids

Steroids, far from being a panacea in AH, should be used sparingly. Infection, gastrointestinal bleeding or severe renal failure represent contraindications to steroids. In addition, emerging data suggest that steroids should not be used in patients with rapidly rising bilirubin (due to futility) or in patients with spontaneously decreasing bilirubin (limited utility). Steroids should be reserved for AH patients with static bilirubin trajectory and patients with peripheral neutrophil to lymphocyte ratio of 5-8 but should not be used in patients with profound synthetic dysfunction (rapidly rising bilirubin trajectory or MELD-Na exceeding 40) due to futility. Steroids should be discontinued if there is lack of improvement of synthetic function within the first week of treatment.

Predicting spontaneous recovery in AH

Emerging data from retrospective studies have demonstrated that 20-40% of patients with steroid-refractory AH spontaneously recover. This proportion is higher than previously thought. However, a minimum of these patients achieve a re-compensated state; most patients are left with complications of underlying liver disease, including ascites or hepatic encephalopathy. Lack of spontaneous recovery in steroid-refractory AH is predicted by the peak MELD-Na of >34, advanced age, presence of hepatic encephalopathy, and acute kidney injury. Complete abstinence from alcohol is a prerequisite for recovery.

Early LT in patients with AH

Early LT (i.e. before six months of abstinence) for severe, steroid-refractory AH improves survival and has excellent post-transplant outcomes. In a Franco-Belgian study, the cumulative six-month survival was significantly higher in carefully selected patients who received early LT (77% vs. 23%), and this benefit was maintained through 2 years of follow-up. The ACCELERATE-AH consortium has reported 94% post-transplant survival at 1 year and 84% survival at 3 years in patients with severe steroid-refractory AH. Approximately 15% of patients returned to sustained alcohol drinking post-transplant, and less than 5% of transplant recipients experienced allograft loss due to alcohol relapse. Predictors of return to harmful alcohol drinking post-transplant included the history of failed rehab attempts, drinking >10 units of alcohol per day, psychiatric co-morbidity, lack of social support, and history of liver disease decompensation before the admission for AH. Remarkably, the duration of sobriety before LT did not predict a return to harmful alcohol drinking post-transplant. Early LT provides substantial survival benefit when compared with mandating a period of sobriety. The criteria for the selection of AH candidates for early LT have been summarized in the meeting report from the Dallas Consensus Conference. Since 2019, there has been a reported three-fold nationwide increase in transplant listings for AH.

Summary

The new data reviewed above have already been reflected in major organization guidelines, with the AASLD and EASL recommending early transplant evaluation for selected patients with AH. Despite the significant progress over the past decade, numerous knowledge gaps remain in the field of alcohol-associated liver disease. Larger and prospective studies with longer-term follow-up will be needed to assess ways to optimally select patients who may benefit most from early LT. In addition, more work is needed to translate the novel mechanistic understanding of AH into new therapeutic avenues to treat this lethal disease.

UNIVERSITY HOSPITAL LIVER TRANSPLANT PROGRAM RECOGNIZED AS #1 PROGRAM IN US BY INTERLINK

University Hospital Transplant Institute's liver program recently received the 2023 Chairman's Award for excellence in delivering the highest quality liver transplant care. INTERLINK, a managed care company, evaluated 86 US liver transplant by considering more than 30 performance factors. The program performed 131 liver transplants in 2022 and scored well above the national average on many metrics including one-year survival rate of 97% compared to the national average of 94%.

According to Dr. Fred Poordad, Professor of Medicine, and Chief of Transplant Hepatology, "The University Hospital Transplant Institute has been focused on excellence in patient care, outcomes, and cutting-edge medicine for many decades. This takes so many dedicated people over the past 30 years, not just the healthcare providers. Being recognized for excellence means we are doing some things well. We want to continue to build on this and create a new tier of excellence in patient care, community outreach and be available for patients around the country and the world.

The Texas Liver Institute is a proud partner of the University Hospital Transplant Institute and will continue to uphold the same high standards that has made this a success story. The focus of everything we do is focused on the patient."

TEXAS LIVER TUMOR CENTER (TLTC) CELEBRATES 7 YEARS

Established in 2016, TLTC offers comprehensive, patient-centered, individualized care to patients with liver tumors in a single day visit.

The Hispanic population in South Texas has the highest rate of liver cancer in the United States and is the epicenter for liver disease and liver cancer in Texas. To address this health concern, TLTC was envisioned and with the support of University Health in partnership with UT Health San Antonio and The Texas Liver Institute, it became a unique model in healthcare.

Our highly experienced medical team evaluates patients with liver tumors and cancers in a one-day visit, eliminating the burden of scheduling multiple specialty visits and evaluations that take several weeks or months resulting in treatment delays and decreasing positive outcomes. Each visit includes a multidisciplinary tumor board review, which is a round table discussion of each patient by a team of medical experts. Upon completing the evaluation, the patient and family leave with a diagnosis, treatment recommendations and a plan of care. Procedures or additional testing are scheduled at the time of the visit.

TLTC is the only multidisciplinary clinic in South Texas to offer a single day full evaluation. For more information visit the Texas Liver Tumor Center (universityhealth.com/services/liver-health) website.

LIVER SPOT

Turmeric, the popular herbal supplement that contains a compound called curcumin, has been linked to liver injury. Ten cases in the US Drug-Induced Liver Injury Network (DILIN) were recently published (*Am J Med.* 2023 Feb; 136(2): 200-206). Liver injury was hepatocellular in nine patients and mixed in one patient and developed with a latency of one to four months. Biopsies were performed in four patients showing acute hepatitis or mixed cholestatic-hepatocellular injury with eosinophils. HLA typing demonstrated that seven patients carried the HLA-B*35:01 haplotype (two patients were homozygous) yielding an allele frequency of 0.450 (vs. frequency in population controls of less than 0.1). Chemical analysis showed additional presence of piperine (black pepper) in three out of seven tested samples. Piperine can substantially increase the systemic bioavailability of turmeric and increase the risk of hepatotoxicity.

CLINIC LOCATIONS

San Antonio – Central
607 Camden Street, Suite 101
San Antonio, Texas 78215
Phone: 210-253-3426
Fax: 210-227-6951

San Antonio – Medical Center
4751 Hamilton Wolfe Road, Suite 200
San Antonio, TX 78229
Phone: 210-253-3426
Fax: 210-227-6951

Austin
7940 Shoal Creek Blvd, Suite 205
Austin, Texas 78757
Phone: 512-454-8378
Fax: 512-454-8375

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