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Liver Digest

A weekly update of PLRC happenings

March 28, 2019

PITTSBURGH LIVER RESEARCH CENTER

A partnership of University of Pittsburgh & UPMC

www.livercenter.pitt.edu

Featured Faculty - Dr. Lawrence Vernetti

In this issue

Next Week's Seminar

PLRC Seminar Series

Tue, 04/01/2019

12:00 noon - 1:00 p.m.

1103 Scaife

Saul Karpen, MD, PhD

Professor of Pediatrics

Raymond F. Schinazi Distinguished Biomedical Chair

Emory University School of Medicine

"Bile acid based approaches to treating cholestatic diseases"

This activity has been approved for AMA PRA Category 1 Credit. #6242 Liver Center Seminars.

Pizza will be provided.

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Registration URL: https://attendee.gotowebinar.com/register/6607572696840938499

For those viewing thru the webinar, please follow the directions below:

- Please Register for the live Webinar ASAP
- After registering, you will receive the confirmation email
- You will be prompt to download the CitrixOnline application and install on your PC or Laptop
- Please contact your local PC Support if you need help installing the application
- Feel free to email Ishtiaque Ahmed (**ahmedi@upmc.edu**) if you have any questions

NOTE Webinar attendees -- use Telephone/Speakerphone and dial-in instead of using desktop/laptop speakers for better audio quality.

Telephone/Speakerphone Audio option is shown right at the Click to Join Webinar prompt.

For a complete list of upcoming PLRC seminars, please visit our website: **http://www.livercenter.pitt.edu/events**

Liver-Themed Gut Club - May 2

Dr. Fasiha Kanwal, the division chief at Baylor, will speak at the May 2, 2019

Pittsburgh Gut Club accredited dinner/lecture series on "The Changing Epidemiology of Liver Cancer."

Liver-related clinical and research trainees are invited to attend the lecture with fee-waived registration. All faculty are invited to attend as well but are required to pay to attend. But, they welcome your trainees as fee-waived participants.

To register for this event, please complete the registration form found in the brochure available on the here (trainees mark "fee waived" in the payment section), and scan (joj2@pitt.edu) or fax (412-578-9537) it to Joy Merusi by April 15th.

Faculty Highlights

Original Article:

Patrick D. Wilkinson, Evan R. Delgado, Frances Alencastro, Madeleine P. Leek, Nairita Roy, Matthew P. Weirich, Elizabeth C. Stahl, P. Anthony Otero, Maelee I. Chen, Whitney K. Brown, **Andrew W. Duncan**. The Polyploid State Restricts Hepatocyte Proliferation and Liver Regeneration in Mice. Hepatology 69(3): 1242-1258, March 2019.

ABSTRACT

The liver contains a mixture of hepatocytes with diploid or polyploid (tetraploid, octaploid, etc.) nuclear content. Polyploid hepatocytes are commonly found in adult mammals, representing ~90% of the entire hepatic pool in rodents. The cellular and molecular mechanisms that regulate polyploidization have been well characterized; however, it is unclear whether diploid and polyploid hepatocytes function similarly in multiple contexts. Answering this question has been challenging because proliferating hepatocytes can increase or decrease ploidy, and animal models with healthy diploid-only livers have not been available. Mice lacking E2f7 and E2f8 in the liver (liver-specific E2f7/E2f8 knockout; LKO) were recently reported to have a polyploidization defect, but were otherwise healthy. Herein, livers from LKO mice were rigorously characterized, demonstrating a 20-fold increase in diploid hepatocytes and maintenance of the diploid state even after extensive proliferation. Livers from LKO mice maintained normal function, but became highly tumorigenic when challenged with tumor-promoting stimuli, suggesting that tumors in LKO mice were driven, at least in part, by diploid hepatocytes capable of rapid proliferation. Indeed, hepatocytes from LKO mice proliferate faster and out-compete control hepatocytes, especially in competitive repopulation studies. In addition, diploid or polyploid hepatocytes from wild-type (WT) mice were examined to eliminate potentially confounding effects associated with E2f7/E2f8 deficiency. WT diploid cells also showed a proliferative advantage, entering and progressing through the cell cycle faster than polyploid cells, both in vitro and during liver regeneration (LR). Diploid and polyploid hepatocytes responded similarly to hepatic mitogens, indicating that proliferation kinetics are unrelated to differential response to growth

stimuli. Conclusion: Diploid hepatocytes proliferate faster than polyploids, suggesting that the polyploid state functions as a growth suppressor to restrict proliferation by the majority of hepatocytes.

For full text, please **click here**.

Original Article:

Squires JE, Rudnick DA, Hardison RM, Horslen S, Ng VL, Alonso EM, Belle SH, **Squires RH**. Liver Transplant Listing in Pediatric Acute Liver Failure: Practices and Participant Characteristics. Hepatology. 2018 Dec;68(6):2338-2347. doi: 10.1002/hep.30116. Epub 2018 Nov 1. PubMed PMID: 30070372; PubMed Central PMCID: PMC6275095.

ABSTRACT

Liver transplant (LT) decisions in pediatric acute liver failure (PALF) are complex. Three phases of the PALF registry, containing data on 1,144 participants over 15 years, were interrogated to characterize clinical features associated with listing status. A decrease in the cumulative incidence of listing ($P < 0.005$) and receiving ($P < 0.05$) LT occurred without an increase in the cumulative incidence of death ($P = 0.67$). Time to listing was constant and early (1 day; quartiles 1-3 = 0-2; $P = 0.88$). The most frequent reasons for not listing were "not sick enough" and "medically unsuitable." Participants listed for LT were more likely male, with coma grade scores >0; had higher international normalized ratio, bilirubin, lactate, and venous ammonia; and had lower peripheral lymphocytes and transaminase levels compared to those deemed "not sick enough." Participants listed versus those deemed "medically unsuitable" were older; had higher serum aminotransferase levels, bilirubin, platelets, and albumin; and had lower lactate, venous ammonia, and lymphocyte count. An indeterminate diagnosis was more prevalent in listed participants. Ventilator (23.8%) and vasopressor (9.2%) support occurred in a significant portion of listed participants but less frequently than in those who were not "medically suitable." Removal from the LT list was a rare event. Conclusion: The cumulative incidence of listing for and receiving LT decreased throughout the PALF study without an increase in the cumulative incidence of death. While all participants fulfilled entry criteria for PALF, significant differences were noted between participants listed for LT and those deemed "not sick enough" as well as those who were "medically unsuitable." Having an indeterminate diagnosis and a requirement for cardiopulmonary support appeared to influence decisions toward listing; optimizing listing decisions in PALF may reduce the frequency of LT without increasing the frequency of death.

For full text, please **click here**.

Original Article:

Cannella R, Fowler KJ, **Borhani AA**, Minervini MI, Heller M, **Furlan A**. Common pitfalls when using the Liver Imaging Reporting and Data System (LI-RADS): lessons learned from a

multi-year experience. Abdom Radiol (NY). 2019 Jan;44(1):43-53. doi: 10.1007/s00261-018-1720-z. Review. PubMed PMID: 30073400.

ABSTRACT
The goal of the Liver Imaging Reporting and Data System (LI-RADS) is to standardize the interpretation and reporting of liver observations on contrast-enhanced CT and MR imaging of patients at risk for hepatocellular carcinoma. Although LI-RADS represents a significant achievement in standardization of the diagnosis and management of cirrhotic patients, complexity and caveats to the algorithm may challenge correct application in clinical practice. The purpose of this paper is to discuss common pitfalls and potential solutions when applying LI-RADS in practice. Knowledge of the most common pitfalls may improve the diagnostic confidence and performance when using the LI-RADS system for the interpretation of CT and MR imaging of the liver.

For full text, please **click here**.

Review Article:
Lemon K, Al-Khafaji A, **Humar A.** Critical Care Management of Living Donor Liver Transplants. Crit Care Clin. 2019 Jan;35(1):107-116. doi: 10.1016/j.ccc.2018.08.001. Epub 2018 Oct 25. Review. PubMed PMID: 30447773.

ABSTRACT
This article represents a review of the postoperative management of donors and recipients after living donor liver transplant, including monitoring, liberation from mechanical ventilation, nutritional support, and pain control. Vascular complications, such as biliary and sepsis, and bleeding are also discussed. Finally, commonly used immunosuppression and antimicrobial prophylaxes are reviewed.

For full text, please **click here**.

Funding Opportunities

Cystic Fibrosis Research and Translation Centers (P30 Clinical Trial Optional)
(RFA-DK-19-003)
National Institute of Diabetes and Digestive and Kidney Diseases

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