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We are all trying to predict what we don't know!

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The current issue of Annals of Hepatology has multiple articles trying to predict different aspects of liver disease: steatohepatitis in non-alcoholic fatty liver disease (NAFLD), steatosis and fibrosis in hepatitis C virus (HCV) infected patients, presence of esophageal varices, and survival after transjugular intrahepatic portosystemic shunt (TIPS) creation.

Primary care practitioners survey of non-alcoholic fatty liver disease

In the Americas, the prevalence of NAFLD is on the rise.[1,2] The first step in attempting to control this disease is to identify it as early as possible at the primary care level. Through a survey, Said A, *et al*.[3] provide a first glimpse of primary care practitioners' knowledge and attitudes towards NAFLD. Unfortunately the results are disheartening: even in the obese and/or diabetic group with high rates of NAFLD, more than half of primary care practitioners did not screen for NAFLD at all. Only 58% of primary care practitioners recommended weight loss as the first step in management of suspected NAFLD. Majority (84%) of respondents to the survey underestimated prevalence of NAFLD in the general and obese population. This is not unique to primary care practitioners in Wisconsin, USA. Hepatologist everywhere continue to see increasing referrals of patients suspected with NAFLD for diagnosis and management. There are multiple consensus guidelines on NAFLD including one from the World Gastroenterology Organisation,[4] but these are not geared specifically for primary care practitioners. As part of their mandate regarding knowledge translation, It is necessary that hepatology associations collaborate with primary care practitioners to understand better the barriers they face for identification and management of NAFLD otherwise this condition will overwhelm the limited hepatology human resources.

Adipocytokines and cytokeratin-18 in patients with nonalcoholic fatty liver disease: introduction of CHA index

Although this is a small study involving 54 patients, Polyzos SA, *et al*.[5] approach the classification of steatohepatitis according to NAFLD Activity Score (NAS) in a systematic and comprehensive manner. Like other investigators,[6] they identified significant differences in insulin resistance specific adipocytokines, oxidative stress and apoptosis markers. But they went on performing post-hoc analysis to find out that cytokeratin-18 level, homeostatic model of assessment insulin resistance (HOMA-IR), and aspartate transaminase (AST) were all significantly higher with increasing NAS especially when combined into CHA index. Although CHA index is a non-validated preliminary instrument based on four widely available tests: cytokeratin-18, fasting glucose and insulin, plus AST. In addition CHA index appears to reflect well described pathophysiological conditions that occur with NAFLD: hepatocellular apoptosis, insulin resistance and hepatocellular injury.

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If these findings are replicated in larger population and validated, it may become an excellent and practical indicator for NAS. There is urgent need for instruments other than liver biopsy to reflect NAFLD disease activity especially in the context of clinical trials.

Non-invasive assessment of liver steatosis and fibrosis in HIV/HCV- and HCV-infected patients

The progression of HCV in human immunodeficiency virus (HIV) co-infected patients is a complex process[7] with multiple variables impacting progression of fibrosis including the interaction of the two viruses with each other and with the host immune system, in addition to potential hepatotoxicity due to highly active anti-retroviral therapy (HAART) that results in lipodystrophy and insulin resistance. This Italian research group from Palermo assessed the prevalence of steatosis in HCV mono-infected patients and HIV/HCV co-infected patients. Vecchi VL, *et al*.[8] found no difference in prevalence of steatosis in both groups (46.3 *vs*. 51.4%, respectively) but the liver stiffness was significantly higher in co-infected patients. In their multivariate analysis, hypertriglyceridemia was the only factor associated with steatosis in both groups. They found no link between steatosis identified by ultrasound and advanced fibrosis measured by transient elastography. Unfortunately, like their previous study,[9] they did not attempt to elucidate factors associated with fibrosis.

Aspartate aminotransferase-to-platelet ratio index (APRI) for the non-invasive prediction of esophageal varices

Currently screening upper endoscopy is recommended in patients with cirrhosis before initiation of primary prophylaxis in those patients with large varices. However, in the real world, identifying everyone with cirrhosis is gargantuan task; proceeding with upper endoscopy in all cirrhotic patients is an expensive and an invasive endeavour. Many groups have looked into predictors of esophageal varices or more specifically large esophageal varices.[9] De Mattos AZ, *et al*.[11] looked into the readily available APRI as possible non-invasive indicators for esophageal varices. The study included 164 patients with cirrhosis who had undergone screening upper endoscopy. In univariate analysis they confirmed that APRI, platelet count, spleen diameter, platelet count to spleen diameter ratio, model for end-stage liver disease (MELD) score, Child-Pugh classification with the presence of esophageal varices but not AST/ALT ratio. In their logistic regression, only platelet count and Child-Pugh classification were independently associated with presence of esophageal varices. It was disappointing the authors did not provide enough detail (including odds ratio) regarding this important finding (association of platelet count and Child-Pugh classification with esophageal varices) but focused on their negative findings again as they did previously.[12]

Within-patient temporal variance in MELD score and impact on survival prediction after TIPS creation

MELD score was originally created to predict the clinical outcomes after TIPS creation. MELD score is prone to variability especially in hospitalized subjects with changes in INR, creatinine and total bilirubin based on nutritional status, medications, hemorrhage and transfusions. Gaba RC, *et al*.[13] confirmed there is significant within-subject variance in MELD scores at different time points between immediate and 15-35 day MELD score ($p = 0.014$). They also confirmed that the immediate pre-procedure MELD score had statistically superior predictive capacity for 30-day mortality as compared to 7-14 day pre-procedure MELD score.

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