

### Hepatology Highlights

Eric M. Yoshida, M.D.,\* Nahum Mendez-Sanchez, M.D. PhD\*\*

\* Division of Gastroenterology, University of British Columbia, Canada.

\*\* Liver Research Unit. Medica Sur Clinic & Foundation, Mexico City, Mexico.

#### Altered clot kinetics in patients with non-alcoholic fatty liver disease

**Ingrid J, et al.** Each and every hepatologist, is intimately familiar with the clinical challenges of both non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH). The importance of these two conditions, stages on a continuum that can terminate in end-stage cirrhosis and hepatocellular carcinoma, is such that this year, the *Annals* published a supplement devoted to NAFLD and NASH. It is well-recognized that NAFLD and NASH are associated with metabolic syndrome, a syndrome incorporating insulin-resistance, obesity, dyslipidemia etc, and are so common that it is estimated that the prevalence in the United States is approaching 30%.<sup>1</sup> Although hepatologists commonly consider the excess mortality<sup>2</sup> of these two conditions in terms of liver disease outcomes, it is important to appreciate that in the milieu of meta-

bolic syndrome, these patients are very unhealthy and are at increased risk of cardiovascular disease,<sup>3</sup> a risk that appears to be increased when the serum liver biochemistry is increased<sup>4</sup> and higher overall mortality in general.<sup>2</sup>

In this issue of the *Annals*, Hickman and colleagues from Queensland University of Australia, report their hematologic findings in NAFLD that suggests that these patients suffer from abnormal clot kinetics: stronger clot development and reduced clot lysis. Interestingly, these abnormalities in clot kinetics were associated with an increase in body mass index (BMI) in the NAFLD patients but not in the control patients without NAFLD. Likewise, no association with metabolic syndrome or diabetes mellitus was found. The implications of this hematologic study to the clinical epidemiologic studies reporting higher overall mortality and increased cardiovascular risk in the fatty liver population come across loud and clear.

#### Histological Characteristics in Late Stage Cirrhosis related to NASH

**Caldwell SH, et al.** It is also well known to all liver transplant specialists that cryptogenic cirrhosis is not an uncommon indication for transplantation, with 11% of American liver transplants occurring for this indication as reflected by the United Network for Organ Sharing (UNOS) database.<sup>5</sup> The clinical suspicion/assumption has always been that a significant proportion of patients with cryptogenic cirrhosis have "burned out" NASH. In an interesting article in this issue of the *Annals*, Caldwell and colleagues from the University of Virginia Health System, who previously reported that age and in-

flammation were associated with progressive fibrosis in NASH whereas the other factors, such as obesity and diabetes were not<sup>6</sup> continue their work in this area. The present study of Caldwell SH, et al. is a retrospective one with a small group of patients. However, it has some strengths. Firstly, the authors using an expanded NASH-Clinical Research Network (NASH-CRN) system to assess paired liver biopsies of NASH and cryptogenic cirrhosis. Although NASH-CRN use categorical data, it has been suggested that this scoring system is more relievable to assess the histologic feature of NASH. Second, they compared the NASH-cryptogenic biopsy pairs a cohort of 13 patients with cirrhosis due to hepatitis C without co-existing metabolic syndrome.

Correspondence and reprint request: Eric M. Yoshida MD, MHSc, FRCP(C), FACP, FACC

Professor of Medicine, Head, Division of Gastroenterology, University of British Columbia, Canada.

Vancouver General Hospital, Diamond Health Care Centre 5153-2775 Laurel Street, Vancouver, BC, V5Z 1M9, Canada. Telephone: 604-875-5371, Fax: 604-875-5447.

Third, the specimens were assessed blindly by an experienced pathologist. We believed that the results of the present study shed more light on the relations-

hip between cryptogenic cirrhosis/NASH and define histologic footprints of an etiology of previous NASH in those who present with cryptogenic cirrhosis.

---

**Predicting 6-week mortality  
after acute variceal bleeding:  
Role of classification  
and regression tree analysis**

**Altamirano J, et al.** Esophageal variceal hemorrhage remains a feared complication of portal hypertension, and is classically associated with a 20-30% thirty day mortality.<sup>7</sup> Although the MELD score and Child Pugh score are recognized prognosticators predicting mortality,<sup>8</sup> in this issue of the *Annals*, Altamirano and colleagues, in a collaborative effort from Barcelona Spain and Mexico City, have refined this even further. Using a Classification & Regression Tree analysis (CART), they have determined that three simple variables (ie. serum albumin, bilirubin and re-bleeding) also have prognostic clinical significance in comparison to the MELD score and Child-Pugh score. Considering its easy bed-side clinical application in a busy hospital environment, their work could be a potentially useful addition to the literature and should make for interesting reading.

**REFERENCES**

1. Bellentani S, Marino M. Epidemiology and natural history of non-alcoholic fatty liver disease (NAFLD). *Ann Hepatol* 2009; 8(Suppl.): S4-S8.
2. Increased overall mortality and liver-related mortality in non-alcoholic fatty liver disease. *J Hepatol* 2008; 49: 608-12.
3. Targher G, Arcaro G. Non-alcoholic fatty liver disease and increased risk of cardiovascular disease. *Atherosclerosis* 2007; 191: 235-40.
4. Wang CC, Lin SK, Tseng YF, Hsu CS, Tseng TC, et al. Elevation of serum aminotransferase activity increases risk of carotid atherosclerosis in patients with non-alcoholic fatty liver disease. *J Gastroenterol Hepatol* 2009; 24: 1411-6.
5. Mailey B, Buchberg B, Prendergast C, Artinyan A, Khalili J, et al. A disease-based comparison of liver transplant outcomes. *Am Surg* 2009; 75: 901-8.
6. Argo CK, Northup PG, Al-Osaimi AM, Caldwell SH. Systematic review of risk factors for fibrosis progression in non-alcoholic steatohepatitis. *J Hepatol* 2009; 51: 371-9.
7. El Serag HB, Everhart JE. Improved survival after variceal hemorrhage over an 11-year period in the Department of Veterans Affairs. *Am J Gastroenterol* 2000; 95: 3566-73.
8. Benedeto-Stojanov D, Nagorni A, Bjelakovic G, Stojanov D, Mladenovic B, Djenic N. The model for end-stage liver disease and Child-Pugh score in predicting prognosis in patients with liver cirrhosis and esophageal variceal bleeding. *Vojnosanit Pregl* 2009; 66: 724-8.