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Hepatology Highlights

Gonzalo Crespo, Andres Cardenas

Hospital Clinic, Barcelona, Spain.

Validation and comparison of simple noninvasive models for the prediction of liver fibrosis in chronic hepatitis C.

Fenili Amorim, *et al*. Evaluation of liver fibrosis is of key importance in the management of patients with hepatitis C virus (HCV) as it helps guide therapy and serves as a prognostic marker of the disease. International guidelines recommend prompt initiation of antiviral therapy in patients with HCV and advanced fibrosis (METAVIR F3-F4) and recommend that treatment should be strongly considered in patients with METAVIR F2.[1] Liver biopsy has been classically considered the gold-standard to evaluate liver fibrosis. However, biopsy presents several limitations such as sampling error, intra- and inter-observer variability, and the possibility of infrequent but potentially life-threatening complications. These limitations have led in recent years to the development of noninvasive methods to assess liver fibrosis.[2] Among these, indirect serologic markers are routine, easy-to-perform and inexpensive serum tests that allow, alone or in combination, to identify patients with advanced stages of liver fibrosis.

Fenili Amorim, *et al*., studied the performance of three indirect serologic algorithms (AST/ALT ratio, FIB-4 and APRI) in the assessment of liver fibrosis in a cohort of patients with chronic hepatitis C. Among the 217 HCV-infected patients who underwent liver biopsy at their institution between 2001 and 2010, 119 patients with clinical, histological and laboratory data were retrospectively selected. Three algorithms (AST/ALT ratio, APRI, and FIB 4) were calculated according to published data and biopsies were classified following the METAVIR scoring system. Thirty-one percent had stage F2-F3 fibrosis and only 3% of the cohort had stage 4 fibrosis (cirrhosis).

Not surprisingly, patients with significant fibrosis ($F \geq 2$) had higher AST, ALT and GGT levels and lower prothrombin time than patients with F0/F1. The values of the 3 evaluated algorithms were also significantly higher in patients with $F \geq 2$. For the diagnosis of significant fibrosis, AUROCs of AST/ALT, FIB-4 and APRI were, respectively, 0.66, 0.81 and 0.79. The AUROC of FIB-4 was significantly higher than that of AST/ALT, while there were no other differences in AUROC comparisons. Using published thresholds of the methods, APRI could have avoided 58% of biopsies and 47% would have been correctly classified, while figures for FIB-4 were 77% and 63%, respectively.

The study by **Fenili Amorim, *et al*.**, seems to support the use of these simple, routine serological markers to identify or discard the presence of fibrosis. Despite the limitations of the study, which include a low number of patients and a low proportion of patients with significant fibrosis (F4); the results are encouraging, and would suggest, as previous reports also do, that the use of FIB-4 could help avoid of biopsies in the assessment of liver fibrosis.

Correspondence and reprint request: Andrés Cárdenas, MD, MMSc, AGAF
Faculty Member. Institute of Digestive Diseases and Metabolism.
University of Barcelona. Hospital Clinic - Villarroel 170, Esc 3-2. 08036
Barcelona, Spain
Tel: (+34) 93 227 5513. Fax: (+34) 93 227 9850
E-mail: acardena@clinic.ub.es

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Steatotic livers. Can we use them in OLTX? Outcome from a prospective baseline liver biopsy study

Gabrielli, *et al.* The increasing gap between liver donation and patients in the waiting list for a transplant, with its consequent impact on list mortality, has led to the use of the so-called extended criteria donors. These organs, which were previously though to be associated with an unacceptable rate of primary dysfunction, may on the other hand expand the donor pool and improve survival. Among extended criteria grafts; steatotic livers are probably the most frequently assessed given the high prevalence of NAFLD in Western countries. While there is general agreement that <30% steatosis does not significantly impact outcomes, the use of grafts with moderate (30-60%) steatosis is still controversial.[3] In this regard, the use of protocol-bench biopsies of the graft to assess the presence of steatosis may be useful for a better selection of organs.

Gabrielli, *et al.* designed a prospective study to investigate the usefulness of protocol-bench biopsies in the assessment of graft steatosis. The authors analyzed 59 donors evaluated between 2004 and 2009, one of the grafts was not implanted and thus the study finally included 58 grafts. The degree of steatosis was assessed as none (<6%), mild (6-33%), moderate (34-66%) and severe (>66%), the type of steatosis (macro/micro) was also evaluated. Other data from the donor (age, vasoactive drug requirement, cold ischemia time, BMI) and the recipient outcome were similarly registered.

Among the 58 included donor grafts, 29 (50%) presented steatosis. The degree of steatosis was mild in 13, moderate in 7 and severe in 9 grafts. Macrosteatosis was present in 15 donors, predominantly in those with severe steatosis. Steatotic donors (>6%) were significantly older and presented a higher BMI than non-steatotic donors. Only 2 patients suffered primary non function of the graft and both recipients had received a severely steatotic liver. Authors found a significant difference in 3-year survival between normal livers and patients with severe steatosis. Similarly, macrosteatotic grafts had a significantly lower 3-year survival than non steatotic or microsteatotic donors. In addition, the outcome of patients that received grafts with mild/moderate steatosis seemed similar to that of recipients of non-steatotic grafts.

In this study, the authors highlight the increasing prevalence of liver steatosis among Chilean donors, a situation that is not expected to improve in the near future. In this regard, as stated by the authors, several donor characteristics such as old age, high BMI or the presence of cardiovascular risk factors, may indicate the need to perform a protocol-bench biopsy to assess the presence of severe steatosis. While the number of patients in the study does not allow definite conclusions, it definitely seems that severe steatosis is associated with poorer outcomes.

Prognostic factors associated with in-hospital mortality in patients with spontaneous bacterial peritonitis

Musskopf, *et al.* Spontaneous bacterial peritonitis (SBP) is a dreaded complication of cirrhosis with morbidity and high short-term mortality.[3,4] In this regard, the early identification of those patients at higher risk of worse outcomes may be useful for decision making, which may eventually improve prognosis.

Musskopf, *et al.*, evaluated the factors associated with early (in-hospital) mortality in a cohort of 40 patients admitted for SBP at their institution. Patients were treated with antibiotics according to international guidelines, and albumin was used at the discretion of the attending physician. Authors registered demographic, laboratory and other clinical data, and calculated the Child-Pugh, MELD and iMELD (which adds age and serum sodium to MELD) scores at admission. In-hospital mortality was 40% (16/40).

At univariate analysis, bilirubin, creatinine, MELD, and iMELD were significantly associated with in-hospital mortality, while there were no significant differences between survivors and deceased patients regarding other variables such as INR, Child-Pugh score or serum sodium. The AUROC of iMELD and MELD to predict in-hospital mortality were 0.8 and 0.77, respectively, and there seemed to be a lower rate of inconclusive results in the prediction of outcomes using the iMELD score.

The study from Musskopf et al highlights the importance of renal and hepatic reserve in the prognosis of SBP. Both MELD and iMELD seem to accurately identify patients with high probabilities

of early mortality, although the numbers of patients in this study was insufficient in order to extract differences between them. While further studies should also evaluate these scores in the prediction of outcomes in SBP, the identification of high-risk patients should clearly indicate the use of albumin.

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