changed over time, were higher in progressors, and the changes over time were greater in those with disease progression (p<0.05). In the 209 patients with a baseline Ishak fibrosis score of <5, 70 (33%) had a ≥2 point increase in Ishak fibrosis score during follow-up. A model consisting of baseline HA and platelet count was significantly associated with the risk of histological disease progression [AUROC = 0.633]. CONCLUSION: Pretreatment SFM levels are increased in CHC patients at risk of developing clinical and histological liver disease progression. A model that incorporates baseline YKL-40 levels and other markers of disease severity can stratify the risk of liver disease progression in addition, baseline HA and platelet counts are useful in identifying patients at high risk of worsening hepatic fibrosis.

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CHRONIC HEPATITIS C INFECTION IS ASSOCIATED WITH LOWER RATES OF HOSPITALIZATION FOR CORONARY HEART DISEASE

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Introduction: Chronic hepatitis C (CHC) infection has been associated with hypolipidemia. Patients with CHC have lower low density lipoprotein (LDL) and cholesterol levels than uninfected control patients. The ramifications of this hypolipidemia for the future development of coronary heart disease are unknown. We sought to analyze a large cross sectional database to evaluate the incidence of coronary heart disease hospitalizations in patients with and without CHC. Methods: The most frequent reasons for admission were collected for both groups, controlling for platelet count and histologic cirrhosis. The independence of each QLFT in predicting clinical outcomes between lowest and highest tertile is HR squared. The independence of each QLFT in predicting clinical outcomes was based on comparing the third of patients with worst function to those with medium function and medium function to high function. HR for clinical outcomes between lowest and highest tertile is HR squared. The independence of each QLFT in predicting clinical outcomes was assessed in multivariate analyses that included platelet count and histologic cirrhosis. Results: 46 of the 227 patients (20%) experienced 97 outcomes: CTP score ≥7 (N=34), death (N=30), ascites (N=18), variceal bleed (N=3), encephalopathy (N=2), and SAP (N=1). Cholate Clearance po, Methionine Breath Test, Cholate Shunt, Antipyrine Clearance, Perfused Hepatic Mass, and Spleen Volume were the most robust independent predictors of clinical outcomes. Conclusion: QLFTs, independent of histologic cirrhosis, are powerful, non-invasive predictors of subsequent hepatic decompensation in advanced chronic hepatitis C.

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HEPATIC IMPAIRMENT MEASURED BY QUANTITATIVE TESTS OF LIVER FUNCTION (QLFTs) PREDICTS CLINICAL OUTCOME IN PATIENTS WITH ADVANCED FIBROSIS: RESULTS FROM THE HEPATITIS C ANTIVIRAL LONG-TERM TREATMENT AGAINST CIRRHOSIS (HALT-C) TRIAL

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Background: Hepatic histology defines disease severity and predicts risk for clinical outcomes in patients with chronic hepatitis C. But, liver biopsy is invasive, inconvenient, risky, and prone to sampling error. QLFTs noninvasively measure hepatic impairment and correlate with biochemical and histological indices of disease severity. Aim: To prospectively evaluate the ability of QLFTs to predict clinical outcomes in compensated patients, controlling for platelet count and histologic cirrhosis. Methods: 227 patients, enrolled in the HALT-C Trial, had baseline QLFTs and were randomized to either no treatment (N=120) or peginterferon alfa-2a (PegIFN) 90 µg/week (N=107), and followed for 66 months for non-HCC, liver-related clinical outcomes. Since PegIFN did not affect outcomes (DiBisceglie 2008), these two groups were combined for analyses. QLFTs included dual (iv and po) cholate clearances and shunt, methionine breath test, antipyrine clearance, antipyrine clearance, perfused hepatic mass and liver and spleen volume from SPECT liver-spleen scan, caffeine elimination rate, MEGX concentration, and galactose elimination capacity (GEC). The hazard ratios (table) of clinical outcomes was based on comparing the third of patients with worst function to those with medium function and medium function to high function. HR for clinical outcomes between lowest and highest tertile is HR squared. The independence of each QLFT in predicting clinical outcomes was assessed in multivariate analyses that included platelet count and histologic cirrhosis. Results: 46 of the 227 patients (20%) experienced 97 outcomes: CTP score ≥7 (N=34), death (N=30), ascites (N=18), variceal bleed (N=3), encephalopathy (N=2), and SAP (N=1). Cholate Clearance po, Methionine Breath Test, Cholate Shunt, Antipyrine Clearance, Perfused Hepatic Mass, and Spleen Volume were the most robust independent predictors of clinical outcomes. Conclusion: QLFTs, independent of histologic cirrhosis, are powerful, non-invasive predictors of subsequent hepatic decompensation in advanced chronic hepatitis C.
The aim of the present study is to assess FIB4 index to predict development of HCC in chronic hepatitis C patients independent of age, gender, and response to IFN therapy. Patients with FIB4>3.25 have high risk for developing HCC and thus need intensive surveillance. Moreover, the non-invasiveness of FIB4 makes possible the real-time assessment of HCC risk over time.

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PREDICTIVE VALUE OF FIB-4 INDEX FOR HEPATOCELULAR CARCINOMA DEVELOPMENT IN CHRONIC HEPATITIS C

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Background & Aims: Advanced fibrosis has consistently shown to be a risk factor for the development of hepatocellular carcinoma (HCC). FIB4 index is a noninvasive serum marker of liver fibrosis calculated by the following formula: (age [yr] x aspartate aminotransferase [U/L])/((platelet [10^9/L] x (alanine aminotransferase [U/L])/2). The aim of the present study is to assess FIB4 index to predict development of HCC in chronic hepatitis C. Materials & Methods: A retrospective cohort of 1098 chronic hepatitis C patients who received interferon (IFN) therapy between 1994 and 2006 at a single regional hospital in Japan was studied. Inclusion criteria were positive HCV RNA before IFN therapy, absence of other causes of liver disease, follow-up for more than 1 year after IFN therapy, and absence of HCC during and within 1 year after IFN therapy. Of these patients, 361 had sustained virological response (SVR) and 737 had non-SVR to IFN. FIB-4 index at 6 months (FIB4-6M) and 3 years (FIB4-3Y) after the completion of IFN therapy was calculated. Screening for HCC was performed every six months. The average period of follow-up was 5.8 years. Results: HCC developed in 78 patients: 69 were non-SVR and 9 were SVR to IFN. Among non-SVR, the cumulative incidence of HCC at 3/5/7 years was 0%/0%/0% for FIB4-6M<1.45, 1%/3%/8% for FIB4-6M 1.45-3.25, and 4%/14%/20% for FIB4-6M>3.25. Among SVR patients, the cumulative incidence of HCC at 3/5/7 years was 0%/0%/0% for FIB4-6M<1.45, 0%/3%/6% for FIB4-6M 1.45-3.25, and 0%/7%/13% for FIB4-6M>3.25. On multivariate analysis, FIB4-6M was a risk factor for HCC independent of gender, age, and response to IFN therapy. After adjustment, the risk ratio of FIB4-6M>3.25 for developing HCC was 4.95 (95% C.I. 2.88-8.51, p<0.0001) in non-SVR and 5.55 (95% C.I. 1.34-23.01, p=0.018) in SVR. After 3 years, progression of FIB4 was more frequent in non-SVR compared to SVR (p<0.0001): FIB4-6M>3.25 progressed to FIB4-3Y>3.25 in 14% of non-SVR and 3% of SVR. In contrast, regression of FIB4 was more frequent in SVR compared to non-SVR (p<0.0001): FIB4-6M>3.25 progressed to FIB4-3Y<3.25 in 18% of non-SVR and 63% of SVR. After adjustment for age, gender, and response to IFN therapy, the risk ratio of FIB4-3Y>3.25 for developing HCC was 4.48 (95% C.I. 2.23-8.99, p<0.0001). Conclusions: FIB-4 index accurately predicted the risk for developing HCC in chronic hepatitis C patients independent of age, gender, and response to IFN therapy. Patients with FIB4>3.25 have high risk for developing HCC and thus need intensive surveillance. Moreover, the non-invasiveness of FIB4 makes possible the real-time assessment of HCC risk over time.

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PAIRED BIOPSIES ILLUSTRATE Racial DIFFERENCES IN FIBROSIS PROGRESSION IN HCV PATIENTS

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Background: African Americans (AA) with hepatitis C virus (HCV) infection were found to have slower progression of fibrosis when compared to Non-Hispanic Whites (NHW) in cross-sectional studies. To our knowledge there have been no longitudinal studies confirming racial differences in the natural history of HCV. Purpose: To compare HCV progression between AA and NHW by evaluating clinical and histological findings in patients with serial liver biopsies. Methods: A retrospective review was performed of patients with chronic HCV who underwent at least two liver biopsies without transplantation from 1997-2008 at our institution. Masked examination of liver histology was performed on a longitudinal cohort of 49 patients (25 NHW, 24 AA). Fibrosis was assessed using the four point META VIR staging system and activity was assessed using Knodell histological activity index (HAI). Change in fibrosis between paired biopsies, as well as estimated fibrosis index (fibrosis stage/estimated duration of infection per history), were compared between races. Additionally, histological activity was compared between races. Clinical features associated with fibrosis progression were compared. T test and Chi-squared tests were used to assess continuous and categorical data, respectively. Results: The mean duration of infection at first biopsy, determined by reported risk factor, was 24.7 ± 11.0 years in AA and 23.5 ± 11.8 years in NHW (p=ns). Overall fibrosis index was lower in AA ([0.08 ± 0.5] compared to NHW [0.14 ± 0.1] [p=0.05]. The HAI was lower in AA ([6.2± 2.4] than NHW ([8± 4.2] [p = 0.007]. The mean interval between biopsy samples was 4.4± 1.9 years; overall mean increase in stage was 0.4± 0.6 stages. The rate of increase in