A COMPOSITE SCORE INCLUDING BMI, LIVER STIFFNESS AND rs738409 PNPLA3 GENOTYPE MIGHT SPARE LIVER BIOPSIES TO MOST NAFLD PATIENTS MAINTAINING 95% DIAGNOSTIC ACCURACY

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Background and aim. To perform a liver biopsy on every patient with suspected fatty liver (NAFLD) would be impractical and costly; therefore, non-invasive methods such as hepatic elastography and the Mayo score (Hepatology 2007;45:846) have been proposed in conjunction with/in alternative to liver biopsy. Recently, it has been shown that carriers of the minor G allele in the patatin-like phospholipase domain-containing protein 3 (PNPLA3) gene polymorphism rs738409 have increased liver fat and inflammation, but how to translate this information into a clinical decision tool is unclear. In the present paper, we aimed to evaluate if the addition of rs738409 genotyping might help to spare the use of liver biopsy in NAFLD patients.

Methods. Sixty patients (37 males; median age 56 years, 95%CI 53-59) had a valid to liver stiffness measurement (LSM) by hepatic elastometry according to manufacturer's criteria and were categorized according to the Mayo score as at low, intermediate or high risk of fibrosis. All underwent percutaneous liver biopsy and were genotyped for rs738409 by restriction-fragment length polymorphism. Scoring of hepatic necroinflammmation and fibrosis was performed using the criteria devised by Brunt et al. (Am J Gastroenterol. 1999;94:246).

Results. Fibrosis stages were F0=23, F1=10, F2=10, F3=10, and F4=7. At univariate analysis, patients with F3 or more had higher median body mass index (BMI; 27.6 kg/m^2, 95%CI 26.4-28.3, vs. 28.6, 95%CI 27.0-38.3, p=0.03) and LSM (6.1 kPa, 95%CI 5.3-7.1 vs. 11.4, 95%CI 8.7-16.4, p=0.0001), but similar Mayo score, age and sex distribution. The proportion of patients with stage F3 or higher increased from 5/28 (18%) in C/C rs738409 homozygotes, to 4/19 (21%) in heterozygotes and 8/13 (62%) (p=0.008). At multivariate logistic regression, obesity (WHO definition) (p=0.003), LSM >7.9 kPa (p=0.005) and rs738409 G/G genotype (p=0.006) were all independent predictors of histologic stage F3 or higher. A simple composite score comprising BMI categories (<30 kg/m^2=0, 30-34.9=1, >35=2), rs738409 genotypes (C/C=0, G/C=1, G/G=2) and LSM (≤7.9 kPa=0, >7.9 kPa=1) had an AUC=0.894, 95%CI 0.787-0.959 vs. an AUC=0.823, 95%CI 0.703-0.909 observed with LSM alone. Limiting liver biopsies to patients with composite score=1 (vs. 0 or 2+) would have spared 42/60 (70%) biopsies with final (composite score + biopsy) 95% accuracy, whereas using LSM >7.9 kPa as single decision point would have spared 36/60 (60%) biopsies with final (LSM + biopsy) 85% accuracy vs. liver biopsy alone.

Conclusions. Adding PNPLA3 genotype and BMI categorization to LSM might allow better selection of NAFLD patients to propose for a liver biopsy.

(405 words, 2690 characters)