Diagnosis of different liver fibrosis characteristics by blood tests in non-alcoholic fatty liver disease

Paul Calès¹,², Jérôme Boursier¹,², Julien Caigneau³, Fabrice Laine³,⁴, Jeremy Sandrin³, Sophie Michalak⁵, Isabelle Hubert¹,², Nina Dib¹,², Frédéric Oberti¹,², Sandrine Bertrais⁶, Gilles Hunault⁵, Christine Cavaro-Ménard⁶, Yves Galois⁷, Yves Deugnier³,⁴ and Marie C. Rousselet⁵,⁶

¹ Service d’Hépatologie-Gastroentérologie, CHU Angers, France
² Laboratoire HPH, Université d’ Angers, PRÉS UNAM, Angers, France
³ CCIC, Inserm U1293, Hopital Pontchaillou, CHU, Rennes, France
⁴ Service des Maladies du Foie, Hopital Pontchaillou, CHU, Rennes, France
⁵ Département de Pathologie Cellulaire et Tissulaire, CHU, Angers, France
⁶ Laboratoire d’Ingénierie des Systèmes Automatisés, Université d’ Angers, PRÉS UNAM, Angers, France
⁷ Laboratoire de Biochimie et Biologie Moléculaire, CHU, Angers, France

Abstract

Aim: Our aim was to develop an accurate, non-invasive, blood-test-based method for identifying the main characteristics of liver fibrosis in non-alcoholic fatty liver disease (NAFLD). Methods: Fibrosis was staged according to NASH-CRN and Metavir systems in 226 patients with NAFLD. A fully automated algorithm measured the fractal dimension (FD) and the area of fibrosis (AOF). Independent predictors of diagnostic targets were determined using bootstrap methods. Results: (i) Development. Significant fibrosis defined by NASH-CRN F≥2 was diagnosed by weight, glycemia, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and prothrombin index (API) under the receiver operating characteristic (AUROC) of 0.867; significant fibrosis defined by Metavir F≥2 was diagnosed by weight, age, glycemia, AST, ALT, ferritin, and platelets (FibroMeter AUROC = 0.941, P < 0.005). AOF was estimated by the combination of hyaluronic acid, glycemia, AST, ALT, platelets and prothrombin index (β² = 0.530), while FD was estimated by hyaluronic acid, glycemia, AST/ALT, weight and platelets (β² = 0.529). (ii) Evaluation. Although NASH-CRN was a better system for fibrosis staging, Metavir staging was a better reference for blood test. Thus, the patient rate with predictive values ≥90% by tests was 97.3% with Metavir reference vs. 66.5% with NASH-CRN reference (P < 10⁻⁶). FibroMeter showed a significantly higher AUROC than the NAFLD fibrosis score for significant fibrosis, but not for severe fibrosis or cirrhosis, with both staging systems. Relationships between fibrosis lesions were well reflected by blood tests, e.g., the correlation between histological area and FD of fibrosis (r = 0.971, P < 10⁻²) was well reflected by the relationship between respective blood tests (r = 0.852, P < 10⁻²). Conclusions: Different characteristics of fibrosis in NAFLD can be diagnosed and quantified by blood tests with excellent accuracy.

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Non-alcoholic fatty liver disease (NAFLD) has become the most common form of chronic liver disease in both children and adults (1). The primary lesion is fatty liver – or steatosis – in the putative benign form of NAFLD, which is called non-alcoholic fatty liver. Ballooning and necro-inflammatory lesions characterize the progressive form, called non-alcoholic steatohepatitis (NASH), which is thought to be the main cause of liver fibrosis in NAFLD (2).

It is valuable to stage these lesions. For example, significant fibrosis is associated with the development of liver complications in NAFLD (3). As the burden of NAFLD on public health is high, it is important to dispose of non-invasive diagnostic tools as a complement to liver biopsy. The NAFLD fibrosis score (NFS) was developed for this purpose (4). Recently, we also developed a NAFLD-specific blood test for liver