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This a pre print version of the following article:

Original Citation:


This version is available http://hdl.handle.net/2318/1606920 since 2017-02-10T11:51:18Z

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The combination of Index of NASH score and liver stiffness improves the noninvasive diagnostic accuracy for severe liver fibrosis in patients with NonAlcoholic Fatty Liver Disease.

R. Ibrahim¹, C. Rosso¹, S. Petta², M. Cucco¹, M. Marietti¹, G.P. Caviglia¹, M.L. Abate¹, C. Cammà², A. Smedile¹, A. Craxi², G.M. Saracco¹, E. Bugianesi¹

¹Division of Gastroenterology and Hepatology, Department of Medical Sciences, University of Torino, Torino, Italy, ²Sezione di Gastroenterologia, DiBiMIS, University of Palermo, Palermo, Italy.

Background & Aim: The screening for NonAlcoholic Steatohepatitis (NASH) in subjects with NonAlcoholic Fatty Liver Disease (NAFLD) is hampered by uncertainties around the non-invasive tools of liver damage. This study is aimed at: 1. validating the recently developed ION (Index of NASH) and 2. assessing the diagnostic performance of single and combined noninvasive tools of liver damage in a large cohort of patients with biopsy-proven NAFLD.

Material and Methods. We analysed data from 254 Italian patients (136 from southern Italy and 118 from northern Italy) consecutively enrolled and biopsied. The following non-invasive scores of liver fibrosis were calculated according to published algorithms: ION, NFS, FIB-4. The apoptotic fragments of M30 CK-18 were measured by ELISA immunoassorbant assay and Liver Stiffness (LS) was evaluated by FibroScan. Liver histology was scored according to Kleiner. NASH was diagnosed by the local pathologist according to joined presence of steatosis, inflammation and ballooning (with or without fibrosis). Severe fibrosis was defined as fibrosis ≥ F3. Cut-off points to rule-in or rule-out F3-F4 fibrosis were calculated by the Youden index.

Results: In the whole cohort, the AUCs of ION and CK-18 for the diagnosis of NASH were 0.622 (NPV 44, PPV 81) and 0.599 (NPV 41, PPV 81), respectively, confirming the poor performance of the tests for the noninvasive diagnosis of NASH. Both tests performed better for the diagnosis of severe fibrosis: the AUCs of ION and CK-18 were 0.724 (NPV 86, PPV 41) and 0.693 (NPV 84, PPV 46). In the same population the AUCs of NFS, FIB-4 and LS for the diagnosis of severe fibrosis were 0.694 (NPV 86, PPV 45), 0.677 (NPV 82, PPV 45) and 0.816 NPV 88, PPV 57), respectively. Next we tested several combinations of all noninvasive tools in order to improve their diagnostic performance for the risk of severe fibrosis. The combination of ION plus LS, NFS plus LS and FIB-4 plus LS similarly improved the performance of each single test, providing a correct classification in 80%, 81% and 79% of cases, respectively.

Conclusions: The combination of LS with either ION, NFS or FIB-4 is better than each single noninvasive test to accurately exclude severe liver fibrosis.

Funded by: FP7/2007-2013 under grant agreement no.HEALTH-F2-2009-241762, FLIP; PRIN2009ARYX4T; Horizon2020 under grant agreement no.634413, EPoS

Keywords. NAFLD, fibrosis, noninvasive test.