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Assessment of non invasive markers of fibrosis against collagen quantitation and NASH-CRN scoring in liver biopsies of NAFLD patients

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Introduction: Non-alcoholic fatty liver disease (NAFLD) is an increasing cause of chronic liver disease worldwide, with an estimated global prevalence of ~25%. Whilst liver biopsy is regarded as the reference standard for staging, it has significant limitations. Given the huge burden of NAFLD, there is much interest into the role of non-invasive assessment of fibrosis.

Aims: We compare non-invasive markers of fibrosis against semi-quantitative histology and collagen quantitation.

Material and Methods: We retrospectively assessed all consecutive patients with biopsy-proven NAFLD followed-up at the Liver Unit of St. Mary's Hospital, from January 2010 to December 2016. The AST to platelet ratio Index (APRI), BARD Score, FIB-4 and NAFLD Fibrosis Score (NFS) were calculated at the time of liver biopsyand Liver Stiffness Measurements (LSM) were obtained within 3 months from the biopsy. Liver biopsies were both scoredusing semi-quantitative scoring (NASH CRN scoring system) and automated image analysis based on machine learning for the quantitation offibrosis,expressed as Collagen Proportional Area (CPA). AUROCs were calculated to diagnose fibrosis stage and CPA.

Results: 238 patients with median age 50 ±13 years and median BMI 30.7±5.3 kg/m^2 were included. 185 NASH and 118 advanced fibrosis (F3-F4). When semi-quantitative assessment was used as reference, LSM and FIB-4 showed the best AUROCs for diagnosing ≥F3 (0.79,95%IC=0.69-0.91 and 0.75 95%IC=0.62-0.9), followed by BARD score (0.7,95%IC=0.55-0.81), NFS (0.65,95%IC=0.54-0.73) and APRI (0.6, 95%IC=0.5-0.69) (Figure 1). Using quantitative assessment as reference, LSM and NFS performed better (AUROCs 0.77,95%IC=0.63-0.89 and 0.71,95%IC=0.62-0.79) to diagnose CPA>5%, followed by BARD score (0.7,95%IC=0.61-0.78), FIB-4 (0.65,95%IC=0.49-0.69) and APRI (0.51,95%IC=0.39-0.61) (Figure1). Similarly, LSM and NFS AUROCS to diagnose CPA≥12% were 0.77 (95%IC=0.69-0.75) and 0.71 (95%IC=0.65-0.82), followed by FIB-4 and BARD (0.62,95%IC=0.51-0.62 and 0.61,95%IC=0.5-0.61) (Figure 2). PPV have been overall below 60%, while LSM and NFS showed excellent NPV: for CPA≥5% (NPV 81% and 88%) and for CPA≥12% (NPV 87% and 89%).

Conclusions: LSM remains the best surrogate marker for predicting advanced fibrosis. Quantitation of collagen in liver biopsies suggests that NFS performs better than FIB-4, with the latest performing better when NASH-CRN scoring is used. An algorithm involving both NFS and FIB-4 score should be used to stratify patients at risk of advanced fibrosis.

Disclosure of Interest: None Declared