The diagnostic value of transient elastography compared to clinical acumen, laboratory tests and ultrasound? Is there added value?

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1G E Dolman, 2A Ferguson, 3S Harris, 4A M Zaitoun, 5M James, 2S D Ryder, 2G P Aithal, 1N Guha. 1Nottingham Digestive Diseases Centre/Biomedical Research Unit, 2Nottingham Digestive Diseases Centre/Biomedical Research Unit, University of Nottingham, Nottingham, UK; 2Public Health Sciences and Medical Statistics, University of Southampton, UK; 4Department of Histopathology, Nottingham University Hospitals NHS Trust

Introduction
The diagnostic performance of transient elastography (TE), and other non-invasive biomarkers of fibrosis, is assessed by direct comparison with liver biopsy. However clinical acumen, laboratory tests and ultrasonography are utilised for the assessment of fibrosis in clinical practice.

Aim
The aim of this study was to assess the incremental value of elastography compared to routine diagnostic tools.

Method
We included consecutive patients with both fibroscan and biopsy data. Patients with decompensated cirrhosis or suboptimal fibroscan readings were excluded (success rate <60% or IQR/median >0.21). Four consultant/attending hepatologists (who were blinded to TE and biopsy results) were asked to assess the severity of fibrosis on the basis of anonymised clinical data. Simple laboratory tests (eg, full blood count, liver function tests and clotting) and ultrasonography for each case were then given to the clinicians to assess the incremental increase in diagnostic performance. One independent pathologist formally assessed the degree of fibrosis on biopsy, which was the reference standard. Receiver Operating Characteristics (ROC) curves were calculated for (1) clinical acumen (2) clinical acumen + laboratory tests + ultrasonography and (3) TE, for the prediction of significant fibrosis (greater or equal to F2) and cirrhosis.

Results
130 patients were enrolled in the study with paired data and a biopsy deemed adequate for staging. The cohort (65% male; mean age 46 years) was of mixed aetiology (15% ALD, 48% chronic viral hepatitis, 24% NALFD, 24% other). The average biopsy length was 25 mm with 16 portal tracts. The median TE reading was 6.5 (median IQR 0.8 and 100% success rate).

Conclusion
There appears to be little additional benefit in AUC performance of transient elastography to diagnose cirrhosis compared to clinical acumen and routinely available tests. There is however incremental diagnostic benefit for the assessment of significant fibrosis. The baseline performance of simple diagnostic tools, which will vary depending on the stage of fibrosis, needs to be accounted for when assessing liver biomarker performance.

Abstract P03 Table 1

<table>
<thead>
<tr>
<th>Clinician</th>
<th>Clinical acumen AUC</th>
<th>Clinical acumen/lab tests/radiology AUC</th>
<th>TE alone AUC</th>
<th>p Value for AUC of TE vs clinical/lab/ radiology*</th>
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<td>Detection of cirrhosis</td>
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<tr>
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Method 44 children with AIH (33 AIH-1 and 11 AIH-2, median age 13.5 yrs, 23 females), 65 FDR from 54 families (25 fathers, 47 yrs (32–53); 28 mothers, 44 yrs (24–53) and 14 siblings, 7 females, 13 yrs (5–24)) and 42 healthy subjects [HS, 56 yrs (22–54), 37 females] were studied. Tregs were purified from PBMCs using immunomagnetic beads and their phenotype and frequency was assessed by Flowcytometry. CD25^{hi} cells were used as responders in co-culture with Tregs and their proliferation was measured by 3H-thymidine incorporation. HLA genotyping was performed by PCR using gene specific primers.

Results The frequency of the disease predisposing gene HLA DR3 was significantly higher in patients (71%) and their FDR (56%) than in HS (25%, p<0.0001 and p<0.005). The frequency of homozygous DR3 was higher in patients (29%) than in FDR (9%, p=0.015) and HS (0%, p=0.001). In patients the frequency of HLA A1-B8-DR3 haplotype (42%) was higher than in FDR (27%, p=0.15) and HS (16%, p=0.02). The frequency of conventional CD4^{+}CD25^{hi} Tregs was lower in patients (6.0%±0.5) than in FDR (9.3%±0.7, p=0.0016) and HS (9.7%±0.8, p=0.001). Though the frequency of CD4^{+}CD25^{hi}CD127^{lo}‘True’ Tregs was similar among patients, FDR and HS (6.0%±0.6, 6.5%±0.4 and 6.2%±0.5), their suppressive function was lower in patients (13.6% reduction of CD25^{neg} cell proliferation) than in FDR (25.9%, p=0.007) and HS (36.9%, p<0.0001). Among subjects positive for HLA DR3, the frequency of conventional Tregs was lower in patients (5.6%±0.5) than in FDR (8.4%±0.97, p=0.01) and in HS (9.1%±1.4, p=0.006). Among subjects positive for HLA A1-B8-DR3 haplotype, the frequency of Tregs was lower in patients (6.0%±0.7) than in FDR (9.1%±1.5, p=0.045) and HS (9.8%±1.8, p=0.02).

Conclusion A numerical and functional impairment of Tregs in AIH patients is associated with possession of HLA disease predisposing genes, and in particular HLA DR3 homozygosity. Possession of DR3 was not associated to a similar immune regulatory impairment in FDR and HS, suggesting that a gene dose effect contributes to the impairment of immunoregulation and to the development of AIH.

P06 ROLE OF SERUM HYALURONIC ACID IN PREDICTING MORTALITY IN PATIENTS WITH CHRONIC LIVER DISEASE
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N Plevis, N C Mcavoy, P C Hayes. 1University of Edinburgh, UK; 2Department of Hepatology, Royal Infirmary of Edinburgh, UK

Introduction Currently liver biopsies are used to assess extent of liver fibrosis and provide prognostic information in liver disease. Hyaluronic acid (HA) is a non-invasive serum marker that has been shown to correlate well with different degrees of hepatic fibrosis. Despite this the prognostic abilities of HA still remain to be established.

Aim In this study we aim to establish the relationship between levels of serum HA and survival, as well as determine the sensitivity and specificity of HA for predicting death in patients with chronic liver disease of varying aetiology.

Method Patients seen at the department of hepatology, Royal Infirmary of Edinburgh between 1995 and 2010 who had serum HA levels measured were followed up for death from the date of HA measurement until the 1 November 2010 by examination of clinical records on TRAK (NHS Lothian). The cumulative probability for survival from liver related death and overall deaths at 1-, 3- and 5-year follow-up was determined. Receiver operating characteristic (ROC) curves were generated to assess the sensitivity and specificity of HA levels at predicting liver-related death at 1, 3 and 5 years.

Results HA levels were available for 632 patients. The median follow-up time (from HA measurement to death or ‘last known alive’) was 2.7 years (range 0.0–8.0; IQR 0.9–4.4). Survival analysis showed that HA levels >400 μg/l are associated with a significantly lower probability of survival from liver related death compared to patients with values of <100 μg/l and 100–400 μg/l at 1 year (88%, p<0.01), 5 years (68%, p<0.001) and 8 years (49%, p<0.05). In addition, the probability of survival from liver related death at 8 years was also significantly less in patients with HA value of 100–400 μg/l compared to patients with HA <100 μg/l (83%, p<0.05). Similar results were observed when assessing probability of survival from overall deaths. The unadjusted area under the ROC curve for predicting liver related mortality for HA at 1-, 3- and 5 years was 0.88 (CI 0.85 to 0.91), 0.85 (CI 0.81 to 0.88) and 0.79 (CI 0.73 to 0.85) respectively. Optimum cut-off value for 1-, 3- and 5-year predicting liver death was 256 μg/l (83% sensitivity/90% specificity), 267 μg/l (74% sensitivity/79% specificity) and 205 μg/l (71% sensitivity/72% specificity) respectively.

Conclusion In this study we have shown that patients with high levels of serum HA have an increased liver and all cause mortality. In addition, HA levels are both sensitive as well as specific at determining liver related mortality. This highlights the potential use of