Results: The HD incidence in the DAA cohort was 7.07 (4.56–10.96) per 100-person-years (PYs), significantly higher than in the active HCV cohort, 19.75 (13.81–28.25) per 100 PYs. DAA therapy was an independent protective factor for HD development (hazard ratio [HR], 0.177; 95% Interval-of-confidence [IC], 0.081–0.390). SSM≥54 kPa was independently associated with HD despite SVR achievement (HR, 4.678; 95% IC 1.307–16.744). SSM and its changes after therapy predicted HD development better than LSM.
Conclusions: The risk of HD is markedly reduced after DAA therapy. SSM is confirmed as an accurate surrogate of portal hypertension, able to stratify for the risk of HD development after DAA therapy more accurately than LSM.

P.04.3

SPLEEN AND LIVER ELASTOGRAPHY AS A NON-INVASIVE TOOL FOR DETECTION OF ESOPHAGEAL VARICES IN PATIENTS WITH LIVER CIRRHOSIS

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Background and aim: Recently, Baveno VI guidelines have suggested that screening for varices with upper endoscopy (EGD) can be avoided in patients with advanced liver disease, based on platelet count (PLT) and liver stiffness (LS). Our aim is to analyze spleen stiffness (SS) as noninvasive method of diagnosis for clinically significant portal hypertension in order to avoid EGD in low-risk patients for esophageal varices. We also want to compare the SS to other non-invasive techniques and analyze their reproducibility and inter-observer concordance
Material and methods: In this prospective study, we detected the SS and LS in 205 patients diagnosed with liver cirrhosis. In addition, we enrolled 70 healthy control individuals. We compares the discriminatory capacity for the presence of varices of the SS with other noninvasive procedures (LS, splenic diameter and surface, PLT, and other scores). Optimal SS cut-offs were sought to exclude the presence of varices. We searched for correlations of the SS with ultrasound parameters of portal hypertension and PLT. Finally, we studied in a double-blind fashion interoperator concordance with 50 measurements for LS, and 25 for SS
Results: SS values were higher in cirrhotic patients with varices (n=83) compared to patients without esophageal varices (n=122), $p<0.001$. SS showed an AUROC of 0.94, statistically different from the other predictors, $p<0.001$. The cut-off, chosen according to Youden's Index, was 38.69 kPa and showed sensitivity of 89%, specificity of 90%, NPV of 92%, and PPV of 86%. The cut-off of 27.85 kPa has sensitivity and NPV of 100%. The cut-off of 69.73 kPa has specificity and PPV of 100%. The SS had weak linear correlation with the splenic dimensions. Moreover, it has a linear correlation with the platelet count, greater than that present with LS (r =0.5 vs r =0.32). There was excellent intraclass correlation coefficient, 0.96 for SS and 0.97 for LS
Conclusions: LS has proven to be useful, but not excellent predictor of varices (AUROC 0.77), whereas PSR and LSPS showed a slightly better performance (AUROC 0.81 and 0.83). SS showed higher performance than other variables (AUROC 0.94), proving to be the best noninvasive test. There is a correlation between spleen stiffness and splenic dimensions, and PLT better correlates with SS than to LS. The results of this study further exploit the potential clinical relevance of SS measurement by pSWE in cirrhotic patients. The SS may play a crucial role as a non-invasive screening test for predicting the risk of varices

P.04.4

NUCLEAR ORPHAN RECEPTOR COUP-TF2 INCREASED THE RESISTANCE TO ANIKOISIS AND THE METASTATIC POTENTIAL IN HEPATOCELLULAR CARCINOMA

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Background and aim: Hepatocellular carcinoma (HCC) is the second cause of cancer-related death worldwide. In the last few years, the role of nuclear receptors in hepatocarcinogenesis has received great attention. The orphan nuclear receptor COUP-TF2 regulates important biological processes such as glucose and lipid metabolic homeostasis. Recent studies indicate that COUP-TF2 is a pro-oncogenic factor but its role in HCC is still controversial. Aim of this study was to evaluate the role of COUP-TF2 in hepatocarcinogenesis and in HCC progression.
Material and methods: COUP-TFII expression on primary HCC samples was evaluated by immunohistochemistry. Overexpressing COUP-TFII HCC cells lines were created through stable transfection with pcR3.1/COUP-TF2 (Hepa1–6/COUP-TF2, HuH7/COUP-TF2, HepG2/COUP-TF2). The migration and the ability to colonize sites at a distance from the growth front were evaluated by Time-Laps microscopy. Finally, we studied the role of COUP-TFII in an in vivo model of mouse carcinogenesis (TgN(Alb1HBV)44Bri) realizing a triple transgenic animal where the liver-specific Cre expression deletes COUP-TF2 in hepatocytes.
Results: COUP-TFII was over-expressed in primary HCC samples and Kaplan-Meier and Cox regression analysis showed that it may be an independent prognostic factor of worse outcome. Overexpression of COUP-TF2 has no significant effect on cell proliferation, but induces a pro-metastatic phenotype characterized by an increased resistance to anikoisis. Live cell imaging experiments showed that COUP-TF2 over-expressing cells had increased cell motility, higher shape plasticity and increase tendency to form colonies distant from the cellular growth front. Moreover, we found that several proteins involved in the organization of the cytoskeleton, cell-cell or cell-substrate adhesion (i.e. FAK, P-FAK, T-cadherin, β-catenin, αV-integrin, VCAM and α-tubulin), were differently modulated in COUP-TF2 overexpressing vs control cells. Finally, COUP-TF2 deletion in hepatocytes of HBV-transgenic mice (Tg[HBV]COUP-TF2-KO) reduced tumor growth and pulmonary metastasis compared to control animals.
Conclusions: In the light of our data, COUP-TFII appears to play a role in the metastatic progression of HCC. Ongoing research will help clarifying the molecular mechanisms regulated by and the clinical significance of COUP-TF2 expression in HCC cancer cells.

P.04.5

EFFECT OF BISPHENOL A EXPOSURE ON HEP-G2 CELLS AND ITS INTERFERENCE IN CELL PROLIFERATION, OXIDATIVE STRESS AND OXIDATIVE METABOLISM OF STEROID HORMONES

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Background and aim: Human liver is known as one of the target organs for estrogens, with mitogenic activity. Bisphenol A (BPA), is an artificial environmental endocrine disrupting chemicals (EDCs) that leaches from polycarbonate plastics that consequently leads