pregnancy. LS was measured by Fibroscan either using the M or XL probe. Besides basic gynecological data, BMI and transaminases were obtained.
Results: LS could be measured in all 103 women using the M probe except one case where the XL probe was required for reliable interquartile range. 17 women (16.5%) had a pathological LS higher than 8 kPa, four of them higher than 12.5 kPa which is regarded as cut-off value for F4 fibrosis. All women with increased LS were in the third trimester starting with week 31 while all women within the second trimester had normal LS <6 kPa. LS correlated slightly with duration of pregnancy ($P < 0.05$), but not with gain of weight or BMI. Primary biliary or hepatic causes of increased LS were excluded by blood tests and ultrasound. No abnormal liver function tests were observed in this study population except one HELLP syndrome with elevated LS. Increased LS completely normalized after delivery in the three patients studied. Further studies on narcotized German landrace pigs suggest that not an elevated intraabdominal pressure alone but an impaired hepatic venous outflow seems to cause the increased LS during pregnancy.
Conclusion: LS is significantly increased in >20% of pregnant women in the third trimester probably due to hemodynamic reasons. Increased LS generally normalizes after delivery. Our data suggest that LS could be an important non-invasive predictor of hepatic complications during pregnancy.

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INVESTIGATING THE TISSUE TURNOVER PROFILE IN LIVER FIBROSIS BY NOVEL BIOCHEMICAL MARKERS OF EXTRACELLULAR MATRIX REMODELING

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Background and Aim: Liver fibrosis is an ECM related disease involving extensive connective tissue degradation and formation. This may result in end stage liver fibrosis, *i.e.* cirrhosis. Proteases such as matrix metalloproteinases (MMPs) are up regulated during fibrosis and are involved in the degradation of the excess connective tissue. Through this mechanism, small fragments of ECM proteins are produced, generating so-called neoepitopes. We investigated a range of novel ECM remodeling markers against collagen type I–VI formation and degradation marker as well as and biglycan fragments generated by MMPs, and correlated these to the extent of liver fibrosis Here we focused on the degradation markers of collagen type I (CO1–764) generated by MMP-2/9/13; collagen type III (CO3–610) generated by MMP-9 and biglycan (BGN-433) generated by MMP-2/12.
Methods: Liver fibrosis was induced in 52 male Wistar rats by inhalation twice weekly and phenobarbital (0.3 g/l) added to the drinking water. As controls, 20 rats received phenobarbital only. Rats were divided into groups: those treated for 8, 12, 16, or 20 weeks with CCL4 or vehicle. Liver sections 5 μm thick were stained with Sirius red for total collagen and quantified using Visiopharm technology. Serum CO1–764, CO3–610 and BGN-433 levels were measured in newly developed and technically robust competitive ELISAs.
Results: Sirius red stainings showed increased deposition of total collagen in the livers of CCL_4-treated rats. Total collagen was highly correlated to the markers ($p < 0.001$), while not in controls. Mean serum CO1–764 levels were statistically elevated in CCL_4-treated rats compared with vehicle-treated rats at week 12, 16 and 20 (1.2–1.5-fold; $p < 0.05$–0.001); CO3–610 and BGN-433 was statistically elevated at week 16 and 20 (1.6–1.9-fold; $p < 0.05$–0.01). When data was stratified by Sirius red into quartiles the CO1–764 was elevated in all quartiles expect Q2 ($p < 0.05$–0.001).
Conclusions: We demonstrated that these novel markers of ECM remodeling were related to extent of liver fibrosis induced by CCL_4. These data indicate that this biomarker may be valuable for diagnosis and progression of liver fibrosis. These markers combined may provide a tissue turnover profile enabling better diagnosis and allow earlier management of disease.

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STEATO-HEPATITIS HAS A STRONG IMPACT ON LIVER STIFFNESS MEASURED BY TRANSIENT ELASTOGRAPHY IN CHRONIC HEPATITIS C PATIENTS

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Liver stiffness assessed by transient elastography mainly reflects the amount of fibrosis present in liver. Other histological lesions such as congestion or inflammation could account for elasticity independently of fibrosis.
Objectives: To evaluate whether elementary liver lesions could contribute to liver stiffness, and to assess the impact of these lesions on the risk of misclassification using LSM for the diagnosis of significant fibrosis.
Methods: 417 CHC naive patients included in the Fibrostar ANRS study, who had the same day a liver biopsy, a valid transient elastography (TE) measurement (>10 valid shots, ratio >60%, IQR/LSM <20%) and a fibrotest (FT) were included. Biopsy samples were examined by two independent pathologists who graded METAVIR index, sinusoidal fibrosis, periportal and lobular necrosis, iron load, steatosis and steato-hepatitis.
Results: Characteristics of patients were: age 52±11 years, male 61%, ALT 88± 65 IU, biopsy length 25±8 mm, F0: 7%, F1: 45%, F2: 18.%, F3: 15.%, F4: 15%, METAVIR activity >2: 55%, steatosis >10%: 59%, sinusoidal fibrosis >0: 51%, iron overload: 23%, steato-hepatitis: 11%. By linear regression, METAVIR fibrosis (3.4, 95% CI 2.8–3.9, $p < 0.0001$), sinusoidal fibrosis (1.4, 95% CI 1.01–2.5, $p < 0.02$) and steatohepatitis (5.2, 95% CI 3.0–7.4) were significantly associated to liver stiffness. Using a cut-off of 7.6 kPa, 73% of patients were correctly classified. Among the 229 F0F1 patients, 20% had LSM above 7.6 and were classified as false positive (80% correctly classified by FT). No histological feature was associated to misclassification. Among the 187 F2F3F4 patients, 24% had LSM below 7.6 and were classified as false negative (78% correctly classified by FT). Absence of steato-hepatitis was associated to misclassification ($p < 0.0001$). By multivariate analysis low ALT (OR = 0.99, $p < 0.02$) and low GGT (OR = 0.99, $p < 0.02$) were associated to misclassification.
Conclusion: Beside fibrosis, steato-hepatitis and in a lesser extent sinusoidal fibrosis contribute to liver stiffness in CHC. Absence of steato-hepatitis, which is associated to lower ALT and GGT levels increases the risk of being false negative in patients with significant fibrosis. Cut-offs should be optimised according to metabolic factors.

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GENOMIC PROFILE AND FUNCTIONAL CHARACTERIZATION OF FIBROSIS IN PATIENTS WITH CHRONIC HEPATITIS B

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Background and Aims: A better understanding of HBV-induced fibrogenesis will ultimately aid in the identification of exact