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Factors Affecting Liver Elastography In Community-based Young Adults In The Raine Study

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Background- Fibrosis, cholestasis, inflammation and hepatic congestion increase liver stiffness. There is paucity of data regarding factors influencing hepatic elastography in healthy populations. Aims- To determine the range and predictive factors of liver stiffness in healthy young adults without liver disease in the general population. Methods- Liver stiffness measurements (LSM) were assessed using transient elastography in 1241 participants in the Western Australian Pregnancy (Raine) Cohort between May 2010 and March 2012. Assessments included questionnaires, anthropometric examination and serum biochemical analysis. Subjects with nonalcoholic fatty liver disease (NAFLD) had been diagnosed previously with liver ultrasound. Study inclusion criteria were the absence of prior liver disease (including NAFLD), serum ALT < 40 U/L in males, <35 U/L in females and bilirubin <20 umol/L. LSM reliability was defined by interquartile range(IQR)/LSM≤0.3, ≥10 valid scans and success rate ≥60%. Results- Of the 1241 sub-

jects assessed, mean age 20 years, (634 [51%] males,), 337 (27.2%) did not fulfill our inclusion criteria and a further 46 (3.7%) were excluded due to an invalid liver stiffness assessment. Overall, the median (interquartile range) LSM was 4.8 kPa (4.0-5.7 kPa) and was significantly higher in males than females (5.2 vs 4.4 kPa, $p<2\times10^{-16}$). Other factors significantly (all $p<0.005$) associated with log transformed LSM on univariate analysis were height, ALT, ALP, AST, bilirubin, glucose, triglycerides, HDL and total cholesterol, SBP, heart rate, alcohol intake and measures of adiposity (BMI, skinfold thickness, waist circumference, waist-hip ratio). In multivariate analysis, male sex (beta=0.103, p=0.00002) and lower heart rate (HR beta=-0.445 and HR-squared beta=0.002 per 10 beats/min, $p=8\times10^{-7}$ and $p=6\times10^{-5}$, respectively) were the most significant factors predicting LSM. Other factors associated with log LSM in multivariate analysis included increased SBP (beta=0.014 per 5 mmHg p=0.005), serum triglyceride level (beta=-0.052 per 1 mmol/L; p=0.026), cholesterol (beta=-0.034 per 1 mmol/L,p=0.015) and alcohol intake (beta=-0.001 per 10gms p=0.001). These factors accounted for 28.4% of the variation in log LSM. Sex-specific analyses indicated similar associations in both males and females, although no triglyceride effect was observed in males and no SBP effect was observed in females. Conclusion- Male sex and low heart rate were significantly associated with higher liver stiffness measurements in a healthy adult population without liver disease. Normal values of liver stiffness should be stratified according to sex and heart rate.