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Gender and menopause impact severity of fibrosis among patients with nonalcoholic steatohepatitis.

Yang JD, Abdelmalek MF, Pang H, Guy CD, Smith AD, Diehl AM, Suzuki A.
Department of Internal Medicine, University of Arkansas for Medical Science.

Abstract

Estrogens inhibit stellate cell activation and fibrogenesis. Thus, gender and reproductive states may influence the degree of fibrosis in patients withnonalcoholic steatohepatitis (NASH). To investigate the association between gender, menopause, and the severity of liver fibrosis in patients with NASH, we analyzed 541 adult patients enrolled from our Duke Liver Clinics (n=338) and the Duke Metabolic and Weight Loss Surgery Program (n=203) who had a histologic diagnosis of NASH. Multiple ordinal logistic regression models were used to assess the association between gender,menopause and severity of liver fibrosis. Overall, men, pre-menopausal and post-menopausal women composed 35.1%, 28.4%, and 36.5% of the population, respectively. The mean age was 48 years and 22% had advanced fibrosis. After adjusting for covariates (enrolling site, grades of portal inflammation, and hepatocyte ballooning) and potential confounders (race, body mass index, diabetes/prediabetes, hypertension), adjusted cumulative odd ratio (ACOR) and 95% confidence interval (CI) for greater fibrosis severity was 1.4 [0.9, 2.1] (p=0.17) for post-menopausal women and 1.6 [1.0, 2.5] (p=0.03) for men, having pre-menopausal women as a reference. There was borderline interaction between gender and age group divided by age 50, the average age at menopause in the US (p=0.08): ACOR and 95% CI of having greater fibrosis severity in men compared to women was 1.8 [1.1, 2.9] for patients with age <50 years (p=0.02) and 1.2 [0.7, 2.1] for patients with age ≥ 50 years (p=0.59). Conclusion: **Men are at a higher risk of having more severe fibrosis compared to women before menopause, while post-menopausal women have a similar severity of liver fibrosiscompared to men**. **These findings may be explained by the protective effects of estrogen against fibrogenesis**. (Hepatology 2013;).