Is the fibrosis phenotype in pre- and post-menopausal F2/F3 women the same?

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Introduction

While several teams have hypothesized that the hepatic phenotype of pre- and post- menopausal women should be different, current histological methods (semi-quantitative categorical stages) do not have the analytical sensitivity to address the question. Here we use high-resolution, single-fiber digital pathology quantitative pathology and AI (FibroNest™) to distinguish different phenotypes of fibrosis between pre- and post-menopausal patients with moderate (F2/F3 stages) fibrosis.

Aim

The aim of this study is to find phenotypes of fibrosis to distinguish between pre- and post-menopausal patients with moderate fibrosis.

Method

This study was performed on a retrospective cohort of 28 biopsy-proven patients recruited between 2010 and 2018 at seven different Spanish hospitals. The overall cohort consisted of female patients with two different stages of fibrosis, 11 (39%) were F2 and 17 (61%) were F3, 16 (57%) had menopause and 12 (43%) didn't have it, a median age of 56 (±11) years. FFPE liver biopsies were stained with Masson Trichrome, scanned using 20X light microscopy and quantified using FibroNest™ for the Phenotypic Quantification of Fibrosis and its associated features. This method provides a continuous phenotypic Fibrosis Composite Severity (Ph-FCS) scores that ranges from 1 to 10 fibrosis severity observed in the liver. The Ph-FCS were evaluated at different groups: F2, F3, Menopause, No Menopause, F3-No menopause (N = 8), F3-Menopause (N = 9), F2-No menopause (N = 4), F2-Menopause (N = 7).

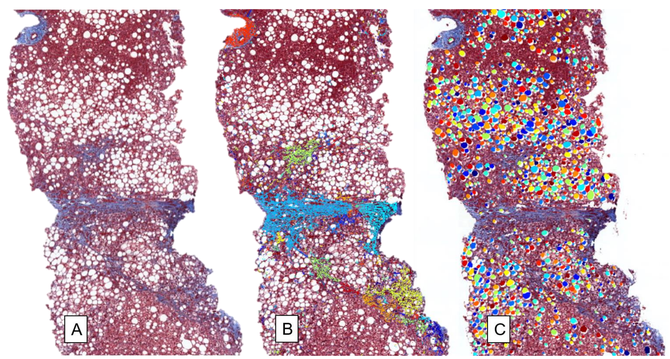

Figure 1: (A) Masson Trichrome liver biopsy, (B) Liver biopsy with detected fibers and (C) liver biopsy with detected vacuoles

Conclusions

Quantitative Digital Pathology analysis, using FibroNest™, was able to distinguish severity groups in concordance with NASH CRN stages in this limited cohort, as reported elsewhere. In each severity group and in aggregate we do not find statistically significant differences in fibrosis severity between pre- and post-menopausal women. It was also able to identify specific differences in the progression of fibrosis between pre- and post- menopausal women.

Results

F2 cases had lower Ph-FCS than F3 cases with a significant difference between them independently of the menopause state (Student's t-Test p = 0.0003)(Figure 2, A). When F2/F3 cases were compared considering the menopause stage, there was no significant difference between pre-/post-menopause (p = 0.15 for F2 and p = 0.38 for F3) (Figure 2, B). Yet, we found 55 phenotypes that changed significantly in both cases (pre-/post-menopause), among them perimeter and filled to area ratio of assembled collagen phenotypes. We found 16 phenotypes changed significantly for only post-menopause cases and 75 phenotypes changed significantly only for pre-menopause cases.

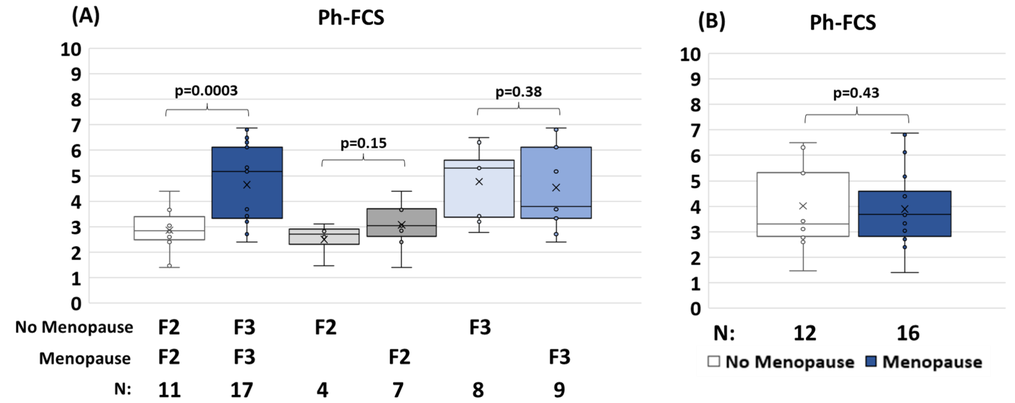

Figure 2: Phenotypic Fibrosis Severity Score (Ph-FCS) and qFTs of different groups under analysis

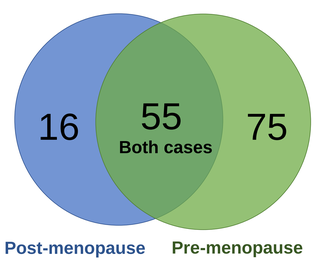

Figure 3: Groups of phenotypes that changed significantly in pre-menopause, post-menopause and both cases.

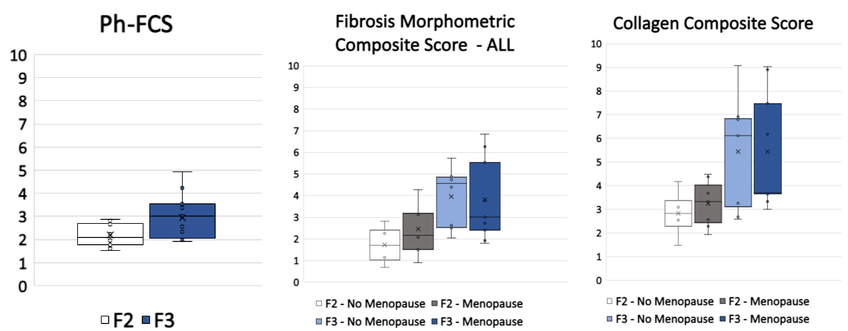

Figure 4: (A) Ph-FCS of F2/F3 patients with and without menopause. (B) Fibrosis Morphometric Composite Score of different groups under analysis. (C) Collagen Composite Score of different groups under analysis

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