Single-fiber, high resolution, continuous fibrosis scoring is markedly superior to histology-based conventional staging in identifying fibrosis regression post-bariatric surgery

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INTRODUCTION

Metabolic dysfunction-associated steatohepatitis (MASH) is a progressive liver disease with no currently approved therapies, creating a significant gap in our ability to characterize and model its regression. Bariatric surgery, known for its significant clinical benefit in reducing liver fibrosis, presents a unique opportunity to serve as a surrogate model to quantify fibrotic regression in MASH.

AIM

This study leverages the novel digital pathology platform, FibroNestTM, to quantify fibrosis using the Phenotypic Fibrosis Composite Score (Ph-FCS) in patients undergoing bariatric surgery to quantify and characterize the reduction of fibrosis.

METHOD

Cohort

- 59 patients undergoing bariatric surgery (47 bypass, 11 sleeve, 1 band) had liver biopsies taken both pre-surgery (Baseline BL) and post-surgery (follow-up FU).
- FU samples were obtained over periods ranging from 1.2 to 10.9 years.

Sample Grading

- Samples were stained with PSR & imaged at 40X on an Aperio scanner.
- Each biopsy was graded by two pathologists (90% concordance) and graded along the NASH CRN fibrosis scale (F0-F4).
- Quantitative image analysis was performed to extract single-fiber quantitative traits (N=336) from the fibrosis, morpho and architectural histological phenotypes and combine into a continuous digital pathology biomarker for fibrosis severity (Ph-FCS, doi: 10.1111/liv.15788).

RESULTS

(a) Group Baseline vs Follow-Up

Phenotypic Fibrosis Composite Score

(b) Ph-FCS by Biopsy Interval

(c) Group Baseline vs Follow-Up

Paired Relative Change from Baseline

(d) Average Pair ± Ph-FCS by Num Stage

(e) Phenotypes of Regression

Volcano Plot Traits of Fibrosis Phenotypes of Regression

- A significant decrease in the severity of fibrosis was found in the post-surgery patients (Fig a) (mean pre-surgery: F-stage=2.4, Ph-FCS=7.11, mean post-surgery: F-stage=1.2, Ph-FCS=4.64).
- When grouped according to the time interval between the BL and FU biopsies, the Ph-FCS decreased as the interval increased (Fig b), but the paired relative change from BL did not (Fig c)
  - mean Ph-FCS: BL=7.11, 0-3years=5.52, 3-6years=4.68, >6years=4.28
  - mean paired R% Δ from BL: 0-3years=−36.1%, 3-6years=−30.3%, >6years=−31.9%
- Average changes in Ph-FCS corresponding to 0, 1, 2, and 3 stage improvements in fibrosis are similar (Fig d)
  - Of the 336 traits measured, 176 traits such as assembled-to-fine collagen area ratio and the mean entropy were found to change significantly between the BL and FU groups, indicating that these are phenotypes of regression (Fig e).

CONCLUSION

The Ph-FCS detects the reduction in fibrosis severity post-bariatric surgery with superior performance than histological stages, specifically by resolving reduction within categorical stages and within the cirrhosis continuum.

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