

# Multicenter Validation of Screening Tool for diagnosing Non-Alcoholic Fatty Liver Disease in patients with Crohn's Disease

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## Background

- Crohn's Disease (CD) patients are twice as likely compared to controls to develop nonalcoholic fatty liver disease (NAFLD)<sup>1</sup>.
- NAFLD is associated with increased risk of cardiometabolic complications.
- We developed the first clinical screening tool for NAFLD in CD: Clinical Predictor for NAFLD in Crohn's Disease (CPN-CD)<sup>2</sup>.
- We have demonstrated CPN-CD outperforms the Hepatic Steatosis Index in detecting NAFLD in CD but it has not yet been externally validated.

## Research Goals

1. Externally validate CPN-CD against transient elastography and establish its diagnostic accuracy to detect NAFLD in CD at two different controlled attenuation parameters (CAP).
2. Measure prevalence of NAFLD in CD across four institutions.

## Methods

- 454 patients with CD across four prospective cohorts from tertiary IBD centers in United States, Canada, and India were reviewed.
- All patients were screened for NAFLD with transient elastography. 42 were screened with an additional MRI-PDFF.
- CPN-CD was derived from the standard algorithm combining; duration of CD, ethnicity, gender, age, dyslipidemia, hypertension, diabetes mellitus, current use of azathioprine or 6 mercaptopurine, ALT, and BMI.
- To evaluate discriminative ability of CPN-CD to screen for NAFLD, patients were split into two CAP categories;  $\geq 248$  dB/m or  $\geq 300$  dB/m.
- Analysis was performed using logistic regression.

## Results

- The C-statistic of CPN-CD to CAP at two thresholds were:
  - 0.80 (0.75 – 0.84) at  $\geq 248$  dB/m
  - 0.79 (0.73 – 0.85) at  $\geq 300$  dB/m

## Results, continued

- At the higher CAP level of  $\geq 300$  dB/m, CPN-CD had increased specificity (74%) and NPV (80%) compared to CAP  $\geq 248$  dB/m (**Table 1**).
- Prevalence of NAFLD in CD varied across cohorts; 31%, 39%, 57%, and 76%.

**Table 1.** Diagnostic accuracy of CPN-CD in detecting NAFLD in CD patients using Transient Elastography as reference standard

|             | CAP $\geq 248$ dB/m | CAP $\geq 300$ dB/m |
|-------------|---------------------|---------------------|
| Sensitivity | 36%                 | 29%                 |
| Specificity | 17%                 | 74%                 |
| PPV         | 21%                 | 22%                 |
| NPV         | 30%                 | 80%                 |

## Legend

CAP, controlled attenuation parameter; CD, Crohn's disease; CPN-CD, clinical prediction tool for NAFLD in Crohn's disease; dB/m, decibels per meter; MRI-PDFF, magnetic resonance imaging proton density fat fraction; NPV, negative predictive value; PPV, positive predictive value; TE, transient elastography.

## Implications and Future Directions

- We found CPN-CD provides fair discrimination to detect NAFLD determined on TE at CAP  $\geq 300$  dB/m in an external validation study conducted in four multinational cohorts.
- For the group who first underwent screening MRI-PDFF followed by TE, the yield of finding NAFLD was 2- to 6-fold higher compared to TE alone.
- Further research is needed to:
  - Use synchronous MRI-PDFF and transient elastography to recalibrate the score to improve specificity.
  - Test generalizability in ulcerative colitis.

## References

1. McHenry S, Sharma Y, Tirath A, et al. Crohn's Disease Is Associated With an Increased Prevalence of Nonalcoholic Fatty Liver Disease: A Cross-Sectional Study Using Magnetic Resonance Proton Density Fat Fraction Mapping. Clin Gastroenterol Hepatol 2019.
2. McHenry S, Tirath A, Tsai R, et al. Derivation and Internal Validation of a Clinical Prediction Tool to Predict Nonalcoholic Fatty Liver Disease in Patients With Crohn's Disease. Inflammatory Bowel Disease 2020.

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