children with IBD could predict the risk for myopenia in young adulthood.

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Association between histological indices and ulcerative colitis activity measures among patients in the HICKORY (etrolizumab) open-label induction cohort

L. Peyrin-Biroulet¹, B. Feagan², R. K. Pai³, U. Arulmani¹, A. Boruvka¹, Y. S. Oh¹, A. Scherl¹, A. Scalori¹, P. Arrisi¹, S. Tole¹, D. T. Rubin⁶
¹Université de Lorraine, Vandœuvre-lès-Nancy (Nancy University Hospital, Lorraine University), Nancy, France, ²University of Western Ontario, London, Canada, ³Mayo Clinic, Phoenix, USA, ⁴Genentech, South San Francisco, USA, ⁵Roche, Burgess Hill, UK, ⁶University of Chicago Medicine, Chicago, USA

Background: Cross-sectional studies in UC have shown an association between histological and clinical measures of disease activity, but few longitudinal studies have evaluated this relationship.¹,² Using data from the open-label induction (OLI) cohort of HICKORY,³ we evaluated the correlation between histological changes and established disease activity measures at end of induction (Week 14).

Methods: Baseline and Week 14 biopsies were scored by 4 central readers using the Robarts histopathology index (RHI) and the Nancy histological index (NHI) in patients who had active baseline histology (NHI > 1 and RHI > 3) and complete scoring at Week 14 (n = 97). Binary Week 14 histological outcomes were characterised by presence or absence of neutrophils (NHI ≤ 1 or RHI ≤ 3 and Geboes subgrades 2B.0/3.0). Pairwise associations were quantified by Spearman correlation (ρ; for correlation between change from baseline scores) and Cohen’s kappa coefficients (κ; for agreement among Week 14 outcomes). ARHI and ΔNHI were compared with determine the presence of a minimal clinically important difference (MCID) in Mayo Clinic score (MCS; ∆MCS ≥ 3). MCS endoscopic subscore (ES) was used to assess endoscopy.

Results: At Week 14, 22% (21/97), 23% (22/97) and 8% (8/97) of patients achieved resolution of neutrophilic inflammation, endoscopic improvement (ES ≤ 1) and endoscopic remission (ES=0), respectively; NHI ≤ 1 was achieved in 55% (12/22) of patients with ES ≤ 1 and 75% (6/8) of patients with ES=0. ΔNHI and ΔRHI were highly correlated (ρ = 0.91). There was little to no association between laboratory results and ΔNHI/ΔRHI/ΔES (Figure 1A). A weak correlation was seen between ΔNHI/ARHI and ΔES (ρ = 0.26–0.27) and between ΔNHI/ARHI and change in rectal bleeding and stool frequency. NHI, RHI and ES agreement with symptomatic outcomes were weak to moderate (κ = 0.28–0.45; Figure 1B). Difference in the mean grouped by achievement of AMCS ≥3 suggests MCIDs in ΔNHI and ΔRHI of 1 and 9, respectively (Table 1).

Figure 1. (A) Pairwise Spearman correlation coefficients between change from baseline scores at Week 14 and disease activity measures and (B) Pairwise Cohen’s kappa coefficients among Week 14 outcomes.
Serum biomarkers of degradation and formation of type III, IV and V collagen are associated with disease activity in patients with Crohn’s disease

V. Domislavic1, J. H. Mortensen2, M. A. Karsdal2, A. Barisic1, T. Manon-Jensen2, Z. Krznicar1,3,4
1Clinical Hospital Centre Zagreb, Department of Gastroenterology and Hepatology, Zagreb, Croatia, 2Nordic Bioscience A/S, Bimarkers and Research, Herlev, Denmark, 3Unit of Clinical Nutrition, University Hospital Zagreb, Zagreb, Croatia, 4University of Zagreb, School of Medicine, Zagreb, Croatia

Background: Crohn’s disease (CD) is characterised by episodes of relapse and remission and therefore requires continuous evaluation of disease activity. Extra Cellular Matrix (ECM) consists of basement membrane (BM) and interstitial matrix (IM). BM is positioned directly underneath the epithelial cells and consists mainly of type IV collagen, while IM consists mainly of type I, III and V collagen, and is produced by fibroblasts. Pathological environment, such as inflammation and fibrosis, leads to impaired remodelling, structure, quality and function of the collagen in the ECM. We investigated biomarkers of collagen degradation and formation and their association with disease activity and in patients with CD.

Methods: In this cross-sectional study we measured five biomarkers of ECM remodelling in 75 patients with CD (60% males, age 35 (IQR 26.5–43.5)), and 29 healthy controls matched by age and gender. Biomarkers of type III collagen degradation (C3M) and formation (PRO-C3), type IV collagen degradation (C4M) and formation (PRO-C4) and type V collagen formation (PRO-C5) were measured in serum by ELISA. Inflammatory activity was defined as combination of clinical or biochemical activity (CDAI ≥150 or CRP >5). One-way ANOVA (Tukey’s multiple comparisons test), and ROC analysis was applied in statistical analysis.

Results: Biomarkers of interstitial matrix remodelling showed that C3M was significantly elevated in active CD compared with inactive CD (p < 0.05) and HD (p < 0.05), whereas PRO-C3 and PRO-C5 were significantly elevated in active CD and inactive CD compared with HD (p < 0.001, p < 0.05)(Figure 1). Turnover type III collagen showed highest diagnostic accuracy for active disease (AUC=0.74). Area under curve was for C3M 0.63, PRO-C3 0.36 and PRO-C5 0.52. Biomarkers of BM remodelling showed significantly higher C4M in active CD compared inactive (p < 0.05) and HD (p < 0.001, p < 0.05) and (p < 0.01). Whereas PRO-C4 was significantly elevated in active and inactive CD compared with HD (p < 0.01). Area under curve was for C4M 0.64, C4M/PRO-C4 ratio 0.57 and PRO-C4 0.56.

Conclusions: The analysis showed no associations between changes in histological scores and changes in laboratory results, a weak correlation between changes in histological and endoscopic scores, and a weak to modest correlation between histological scores and symptoms at the end of induction.

References

Depiction of type III, IV, and V collagen remodelling in CD, and differences between healthy donors, CD in remission and active CD.

Conclusions: Both biomarkers of interstitial matrix (C3M) and basement membrane (C4M) were associated with disease activity. PRO-C3, PRO-C5 and PRO-C4 were associated with CD regardless of disease activity. Interstitial matrix biomarkers of turnover type III collagen C3M/PRO-C3 showed highest diagnostic accuracy for disease activity. In conclusion, these biomarkers may be used in monitoring and prediction of disease activity and in differentiation between patients with CD and healthy individuals.