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CPa9-HNE: A NEUTROPHIL-DERIVED FRAGMENT OF CALPROTECTIN MEASURED IN SERUM CAN MONITOR ENDOSCOPIC AND CLINICAL DISEASE ACTIVITY IN ULCERATIVE COLITIS

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1) BACKGROUND

- Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) presenting in remitting ulcerations of the colonic mucosa and submucosa
- Mucosal healing is therefore an important treatment target for optimal disease management
- Fecal calprotectin is commonly used to monitor mucosal healing – however, patient compliance is low due to a preference for serological markers

2) AIM

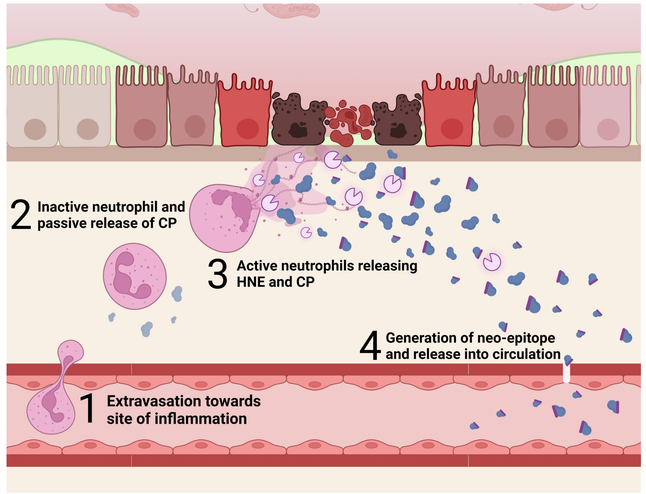
This study aimed at investigating the association of serum calprotectin [CPa9-HNE], a non-invasive neo-epitope biomarker of true neutrophil activity, with both clinical and endoscopic disease activity in UC.

Patient demographics

Patients, n	49
Age, years (range)	36 (20-73)
Female, n (%)	21 (43)
Male, n (%)	28 (57)
BMI kg/m2 (range)	23.6 (17.4-34.9)
Fecal calprotectin µg/g (range)	1202 (30-3000)
CRP, mg/L (range)	11 (1-108)
Total Mayo score	
Remission	0 (0)
Mild	8 (16.3)
Moderate	31 (63.3)
Severe	10 (20.4)
UCEIS, n (%)	
Remission	0 (0)
Mild	5 (10.2)
Moderate	34 (69.4)
Severe	9 (18.4)

3) METHODS

- The study included 49 patients with active UC and 50 healthy controls (HC) obtained from Bispebjerg Hospital, Denmark.
- Endoscopic and clinical disease activity was assessed using the Ulcerative Colitis Endoscopic Index of Severity (UCEIS) and the full Mayo score.
- A competitive enzyme-linked immunosorbent assay quantifying a human neutrophil elastase (HNE) generated neo-epitope of calprotectin [CPa9-HNE] was measured in serum, reflecting neutrophil activity.
- Group differences were evaluated using Kruskal-Wallis with Dunn's test, Bonferroni corrected for MCP.
- Diagnostic and discriminative capabilities were assessed using receiver operating characteristic (ROC) statistics with area under the curve (AUC).



Generation of the CPa9-HNE fragment *in vivo*. 1) Neutrophils are recruited to the site of inflammation. **2)** Calprotectin is released passively by inactive neutrophils en route to the site of injury. **3)** Upon neutrophil activation and subsequent release of intragranular components, both calprotectin (CP) and human neutrophil elastase (HNE) are released into the extracellular space **4)** resulting in the generation of the CPa9-HNE neo-epitope and its release into circulation, where it can be measured as a biomarker of true neutrophil activity.

4) RESULTS

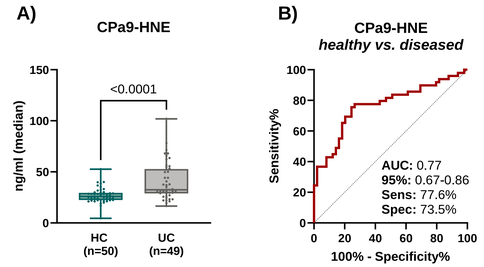


Figure 1. A) CPa9-HNE was significantly elevated in patients with UC compared to HC (ng/ml [IQR]: 32.4 [29.0–52.3] vs. 26.0 [22.6–29.0], p<0.0001) **B)** and presented with acceptable discriminative capabilities (AUC [95% CI]: 0.77 [0.67–0.86], p<0.0001).

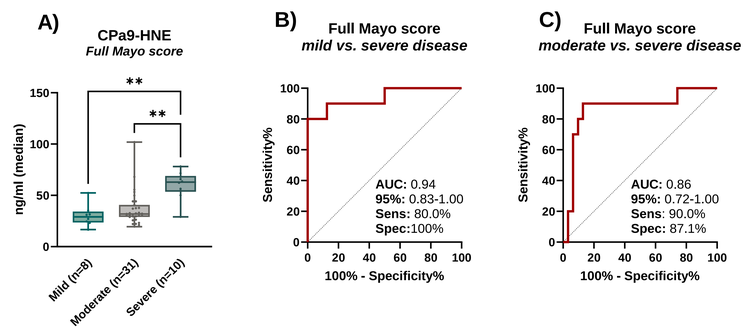


Figure 2. A) When patients were grouped according to the full Mayo score, CPa9-HNE was significantly elevated in patients with mild vs. severe disease (29.1 [24.3–32.4] vs. 62.9 [55.2–67.5], p<0.01) and moderate vs. severe disease (32.0 [29.2–39.2] vs. 62.9 [55.2–67.5], p<0.01), **B,C)** and could accurately discriminate between patients with mild, moderate, and severe clinical disease activity according to the full Mayo score.

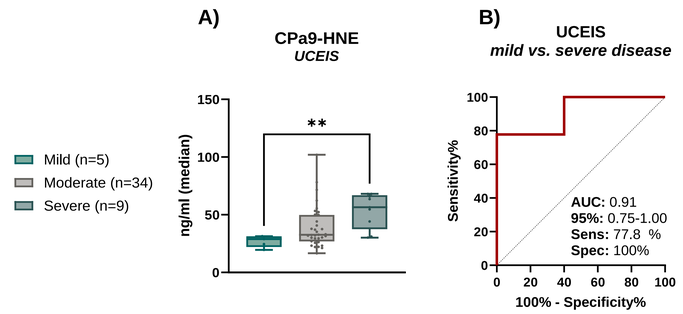


Figure 3. A) When patients were stratified according to endoscopic disease activity (UCEIS), CPa9-HNE was significantly elevated in patients with severe disease compared to those with mild disease (ng/ml [IQR]: 55.6 [40.9–66.4] vs. 28.9 [24.6–31.1], p<0.01) **B)** and could accurately discriminate between the two groups.

5) CONCLUSION

- **CPa9-HNE accurately reflected both clinical and endoscopic disease activity in ulcerative colitis, based on the UCEIS and full Mayo score.**
- **These findings highlight the potential use of CPa9-HNE as a non-invasive tool to monitor both endoscopic and clinical disease activity in UC, with the potential of guiding treatment decisions and better aligning with patient preferences.**

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