Type I collagen degradation fragments (C1M) and human neutrophil elastase-derived fragments of calprotectin (CPa9-HNE) reflect biochemical and endoscopic disease activity in patients with Inflammatory Bowel Disease

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Methods: Patients' records were collected from 3 tertiary hospitals (Seoul national university hospital, Seoul national university Bundang hospital, and Seoul metropolitan government Seoul national university Boramae medical center) from October 2004 to June 2021. Patients with IBD and concomitant AS (IBD-AS group) were identified and propensity score matching (PSM) was applied to match the IBD-AS group and IBD patients without AS (only IBD group).
Results: After PSM, significantly more patients in IBD-AS group had colectomies ($p = .017$) or were prescribed biologics ($p < .001$), immunosuppressive agents ($p = .021$), and steroid ($p = .017$) than in only IBD group. The number of patients treated with biologics ($p < .001$) or immunosuppressive agents ($p = .032$) were significantly greater in UC-AS group than in only UC group. There was no significant difference in outcomes between only CD group and CD-AS group. In logistic regression analyses, identified that concomitant AS was a significant factor associated with biologics treatment in patients with IBD. Kaplan-Meier analyses demonstrated that there was a significant difference in the probability of starting biologics treatment between IBD patients with and without concomitant AS ($p = 0.002$). In UC patients, the probability of starting biologics was also significantly different according to concomitance of AS ($p < 0.001$). Concomitant AS was a risk factor for predicting biologics treatment in patients with UC in Cox regression analysis after adjustment UC (adjusted hazard ratio, 6.296; confidence interval, 2.243 to 17.668; $p < 0.001$)
Conclusion: Patients with IBD-AS group were more likely to have a higher severity than in only IBD group. The current study result can help IBD specialists understand and treat patients with IBD and concomitant AS better.

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The predictive value of the modified Rutgeerts score at index endoscopy after primary ileocolic resection in patients with Crohn's disease for the risk of re-resection and severe endoscopic inflammation after long-term follow-up

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Background: The modified Rutgeerts score (mRS) differentiates i2 into lesions confined to the anastomosis (i2a) vs. ileal lesions (i2b), and is considered appropriate to assess postoperative recurrence in Crohn's disease (CD) patients. This study aimed to assess the predictive value of mRS at index endoscopy after primary ileocolic resection for the risk of re-resection and severe endoscopic inflammation after long-term follow-up. In addition, we aimed to predict the association of i2a and i2b for both outcomes.
Methods: Data of CD patients who underwent a ICR, between 2000 – 2019, were retrospectively collected from a national, multicenter database. Patients were eligible for inclusion if ≥1 postoperative endoscopy assessed with the mRS was available. Primary outcome was re-resection per mRS (i0-i4) at index (i.e. first postoperative) endoscopy. Secondary outcome was severe endoscopic inflammation (defined as i3-i4) for a subset of patients (mRS i0-i2b). Rates for both outcomes were compared in subgroups (i0-i1, i2a-i2b, i3-i4) by Kaplan-Meier analyses. Multivariable analysis was conducted to identify risk factors for both outcomes.
Results: In total, 638 patients were included. Index endoscopy was performed at median 8.5 months (IQR: 5.9 – 22.8) after ICR(Table 1), with a mRS of i0(30.4%), i1(17.7%), i2a(15.8%), i2b(19.6%), i3(9.6%) and i4(6.9%). After a mean follow up of 6.5 years (SD: 4.7), re-resection rate (Figure 1) was 7.2% for patients with a mRS of i0, 6.2%(i1), 14.9%(i2a), 18.4%(i2b), 22.9%(i3) and 47.7%(i4). Re-resection rates in the subgroups were significantly higher in the group with a mRS i2a-i2b (16.8%) vs. i0-i1 (6.8%) (log-rank test, p<0.001) and in i3-i4 (33.3%) vs. i2a-i2b (16.8%)(log-rank test, p=0.006). Follow-up endoscopy was performed in 54.0% of the patients with mRS i0-i2b at median interval of 20.4 months (IQR: 10.9 – 37.7). Progression to severe endoscopic recurrence was observed in 19.8% of patients with i0, 33.9%(i1), 25.4%(i2a) and 33.8%(i2b) (Figure 2), but no significant difference was observed between subgroups i0-i1 vs. i2a-i2b (respectively 24.7% vs. 30.2%)(log-rank test, p=0.134). In multivariable analysis, anastomotic lesions (i2a) are not statistically significant associated with re-resection and progression to i3-i4 (Table 2).
Conclusion: After primary ICR, the ascending order of the mRS corresponds with an increasing long-term risk of re-resection. In multivariable analysis, anastomotic lesions (i2a) are not significantly associated with the risk of re-resection and progression to severe endoscopic inflammation, in contrast to i2b lesions. The influence of therapeutic decisions on these associations requires further investigation.

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Type I collagen degradation fragments (C1M) and human neutrophil elastase-derived fragments of calprotectin (CPa9-HNE) reflect biochemical and endoscopic disease activity in patients with Inflammatory Bowel Disease

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Background: Crohn's disease (CD) and ulcerative colitis (UC) are characterized by intestinal inflammation and increased extracellular matrix (ECM) remodeling, which are key pathophysiological mechanisms in patients with IBD and highly related to mucosal damage. Alterations in intestinal ECM turnover as well as macrophage and neutrophil activity may be reflected by secreted products that are released into the systemic circulation. In this study, we aimed to investigate associations between serum biomarkers of neutrophil activity (serum calprotectin)

and collagen degradation (mucosal damage), and disease activity in patients with IBD.

Methods: Serological biomarkers of collagen formation (PRO-C3, PRO-C4, PRO-C6), matrix metalloproteinase (MMP)-mediated collagen degradation (C1M, C3M, C4M, C4G, C6Ma3) and intestinal inflammation (VICM [macrophage activity], human neutrophil elastase-derived fragment of calprotectin (CPa9-HNE [serum calprotectin, neutrophil activity]) were measured using Protein FingerPrint assay (PFA) technology in 100 patients with IBD (CD: *n*=44; UC: *n*=56). Biochemical disease activity was assessed using C-reactive protein (CRP) levels and available faecal calprotectin (FCal) levels. Endoscopic disease activity was determined using the Simple Endoscopic Score for CD (SES-CD) and Mayo endoscopic subscore for UC.

Results: C1M strongly associated with elevated CRP levels (defined as >5mg/L, $P<0.001$) in patients with IBD and significantly associated with faecal calprotectin levels in patients with UC (Spearman's $\rho=0.75$, $P<0.001$). In patients with CD, C1M reasonably discriminated between patients with mild and moderate-to-severe endoscopic disease activity (AUC=0.73, $P=0.01$), whereas this discrimination was more subtle in patients with UC (AUC=0.68, $P=0.08$). CPa9-HNE levels were significantly increased in patients with elevated CRP levels ($P=0.002$ for both CD and UC) and associated best with faecal calprotectin levels in patients with CD compared with UC (CD: $\rho=0.43$, $P=0.06$; UC: $\rho=0.20$, $P=0.45$). Finally, CPa9-HNE levels were able to discriminate between mild and moderate-to-severe endoscopic disease activity in patients with CD (AUC=0.75, $P<0.01$).

Conclusion: C1M and CPa9-HNE levels associate with biochemical (CRP, FCal) and endoscopic disease activity in patients IBD, where C1M demonstrated higher accuracy in UC and CPa9-HNE appeared to be more useful in CD in this cohort. Therefore, C1M and CPa9-HNE could serve as surrogate biomarkers for the assessment of disease activity in patients with UC and CD, respectively. Our results should be validated in additional prospective, larger patient cohorts to corroborate these findings.

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Accuracy of the combination of transabdominal and transperineal ultrasound for the evaluation of Ulcerative Colitis activity

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Background: Transabdominal Bowel Ultrasound (TBUS) is useful technique to assess disease activity and extent in patients with ulcerative colitis (UC); however, the evaluation of the rectum by TBUS is difficult. Recently, transperineal ultrasound (TPUS) has been proposed as a useful diagnostic tool in the evaluation of rectal disease. The aim of the study is to to assess the concordance between the combination of TPUS/TBUS and endoscopy in adult patients with UC.

Methods: Fifteen consecutive adult patients with UC were prospectively enrolled from June to November 2021. Disease activity was determined using Partial Mayo Score (PMS) and Mayo Endoscopic Subscore (MES). TBUS and TPUS were performed within a week from endoscopy. MES ≤ 1, bowel wall thickness ≤ 3mm in the colon and ≤ 4mm in the rectum were defined as remission. A concordance analysis comparing endoscopy and US was performed by kappa statistics

Results: Ten patients were male (66%) and 8 female (34%), with a median age of 39± 13,9. Two patients had a pancolitis, 6 a distal colitis, and 3 a proctitis. 4 patients were in remission. The agreement between endoscopy and rectal evaluation with TBUS was fair (k =0.40), while the agreement with TPUS was excellent (k =0.86). The evaluation of the colon with TBUS showed good concordance in the right colon (k= 0.63), left colon (k=0.65), and sigmoid colon (k=0.72), and excellent agreement in the transverse colon (k= 1).

Conclusion: These preliminary data showed that the combination of TBUS and TPUS allows to easily and accurately study all the segments of the large intestine in patients with UC, overcoming the limitation related to the reduced accessibility to the rectum with only trans abdominal approach.

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Hepcidin and ferritin index can help to differentiate between different types of anaemia: an exploratory study

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Background: Anaemia is frequent in patients with IBD. Iron deficiency anaemia [IDA] and anaemia of chronic disease [ACD] are the most common subtypes and warrant a different treatment approach.

The ESPGHAN/ NASHGAN position paper on Anaemia in Children with IBD describes cut-off values on ferritin, transferrin saturation [TSAT] and ferritin index (soluble transferrin receptor/log10(ferritin)) [sTfR-F], to distinguish between IDA and ACD. However, cut-off values for sTfR-F and hepcidin are based on adult data.

In this exploratory study we used a data driven approach to define different anaemia groups, using hepcidin and sTfR-F and studied differences between groups and their response to iron suppletion therapy. Insights contribute to a better description of ACD and IDA in a pediatric population.

Methods: Data from the multi-centre prospective POPEYE study (NTR4487) consisting of a paediatric IBD population was used. Subjects with anaemia (haemoglobin [Hb] < 2 standard deviations [SD] below the mean of a healthy age reference group) with baseline ferritin, TSAT, hepcidin, sTfR-F and erythrocyte sedimentation rate [ESR] values were selected. Summary statistics of these biomarkers were generated for the data-driven groups and compared with existing characteristics for IDA and ACD groups. At baseline subjects received oral or intravenous iron repletion therapy, Hb was determined at baseline and 1 month after iron therapy. Kmeans was used, an unsupervised clustering algorithm using Euclidean distance, to divide data points into k clusters based on sTfR-F and hepcidin.