

Evaluation of Fecal Lactoferrin, CRP and Clinical Activity Indices for Assessing the Presence of Intestinal Inflammation in IBD and IBS Patients Classified by Ileocolonoscopy

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Introduction

Identifying active disease in patients with inflammatory bowel disease (IBD) is essential for optimal medical therapy. The differentiation of noninflammatory functional illnesses like irritable bowel syndrome (IBS) from IBD can prove difficult. Clinical indices have proven too complex and unreliable for daily routine practice. Serologic parameters such as C-reactive protein (CRP) and sedimentation rate are hampered by a low sensitivity and specificity for intestinal inflammation. Lactoferrin, a neutrophil-derived protein, has been shown to be a sensitive marker for discriminating inflammatory conditions like active ulcerative colitis (UC) and Crohn's disease (CD) from cases of IBS.

Subjects and Methods

Test Population: A total of 120 adult patients, 42 Crohn's disease (CD), 36 ulcerative colitis (UC) and 42 IBS were enrolled following informed consent at an adult IBD clinic over a 24 month period. A total of 64 (84%) patients was scored as active IBD by endoscopy. The mean age was 42 years and the male:female ratio was 1:2.5. Receiver operator curve analysis (ROC) was performed and the area under the curve (AUC) for accuracy was calculated.

Lab Parameters: Fecal lactoferrin was determined using ELISA (IBD-SCAN®, TECHLAB®) with a cut-off for elevated levels of $\geq 7 \mu\text{g/mL}$. Serum CRP was determined using an ELISA (CRPLX, Tina-quant, Roche/Hitachi) with a positive cut-off of $\geq 0.5 \text{ mg/dL}$.

Activity Indices: A Colitis Activity Index (CAI) was used to assess subjects with UC using an adjusted cut-off of > 4 calculated score for indicating active disease. The Crohn's Disease Activity Index (CDAI) was calculated for CD and considered active at > 150 calculated score. In the analysis for correlation, the CAI and CDAI indices were combined.

Endoscopic Score: Endoscopically obtained histopathology specimens in addition to macroscopic colonoscopy results were used as the standard reference. Each endoscopy was scored regarding inflammation: 0 = "no acute inflammation", 1 = "mild acute inflammation", 2 = "moderate acute inflammation" and 3 = "high acute inflammation". "No inflammation" was defined as the appearance of a healthy mucosa with no ulcerations. "Mild inflammation" was defined by erythema, decreased or absent vascular pattern, friability of mucosa and single aphthous lesions. "Moderate inflammation" was defined as additional multiple aphthous lesions and small ulcers. "High inflammation" was characterized by additional presence of spontaneous bleeding, large ulcerous lesions, nodules and/or narrowing. Tissue biopsies were retrieved from areas of disease involvement as determined visually. Slides were prepared using conventional hematoxylin eosin (HE) stain and the magnification ranged from 50x to 400x.

References:

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Results

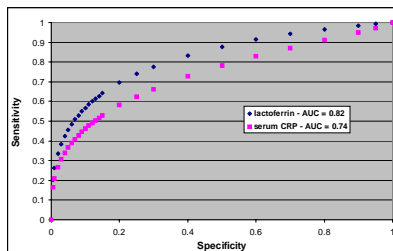
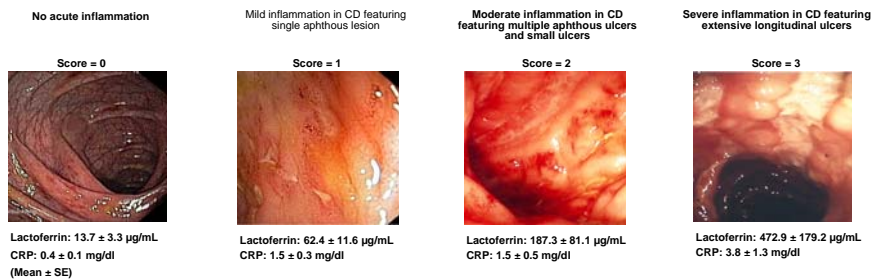


Figure 1. Receiver Operator Curve for Lactoferrin versus CRP compared to Endoscopy

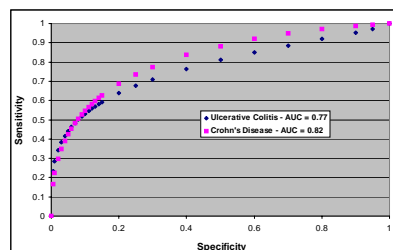


Figure 2. Receiver Operator Curve for Lactoferrin versus Endoscopy for UC and CD

Table 1: Sensitivity, Specificity and Diagnostic Accuracy

Parameter	Sensitivity	Specificity	Diag. Acc.	N
Lactoferrin	83 %	75 %	79 %	120
CRP	56 %	75 %	65 %	120
Clinic Indices	47 %	93 %	55 %	78
CAI	77 %	83 %	78 %	36
CDAI	21 %	100 %	36 %	42

Table 2: Levels of Fecal Lactoferrin and CRP in CD Patients

Crohn's Disease	mild to moderate		high
	LF (µg/ml)	CRP (mg/dl)	
Ileal	16±32	0.2±0.1	234±303
(median±S.E.)			3.2±4.8
Ileal/Colonic	90±68	1.3±0.8	810±1125
Colonic	52±67	2.2±2.9	107±775
			2.5±0.5

Table 3: Levels of Fecal Lactoferrin and CRP in UC Patients

Ulcerative Colitis	mild to moderate		high
	LF (µg/ml)	CRP (mg/dl)	
Proctitis	428±785	0.5±1.4	missing data
(median±S.E.)			missing data
Left sided	40±301	1.2±1.2	52±1
Pancolitis	71±45	1.1±1.7	518±699
			2.4±0.1

Conclusions

- Based on the ROC analysis, lactoferrin showed a higher accuracy than CRP for detecting intestinal inflammation
- Lactoferrin measurements showed acceptable sensitivity and specificity to endoscopy score for intestinal inflammation in patients assessed for active IBD and IBS
- The CAI index showed a higher sensitivity than the CDAI for assessing intestinal inflammation when compared to endoscopic and histologic results
- Lactoferrin is useful as a complementary tool for assessing intestinal inflammation in UC and CD