Endoscopic and Histological Grading in IBD

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BELGIUM
Inflammatory Bowel Diseases 2008
3rd Congress of ECCO – the European Crohn’s and Colitis Organization

Cité – Centre de Congrés Lyon, France
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ECCO website: www.ecco-ibd.eu
Typical Lesions in Active Crohn’s Disease

- Aphthous ulcerations
- Deep irregular ulcerations
- ‘punched-out’ ulcers
- Longitudinal ulcerations
- Cobblestoning
- Discontinuous involvement (86%)
- Rectal sparing (25%)
- Luminal narrowing
- Fistulas
Typical lesions in Upper GI Crohn’s Disease

• Invariably accompanied by small bowel / colonic disease
• Prospective studies: 17 – 75 % (sympt and asympt)
• Retrospective studies: 0.5 – 13 %
• Oral (6-9%) > gastroduodenal (1.8-4.5%) > oesophageal (1.8%)
• Oesophageal CD: aphthous ulcers, punched-out ulcers, erosions, strictures
Measurement of Endoscopic Disease Activity in Crohn’s Disease

- The Crohn’s Disease Endoscopic Index of Severity (CDEIS)
- The Simple Endoscopic Index for Crohn’s Disease (SES-CD)
- The Rutgeerts’ score for postoperative recurrence
Endoscopic endpoints

Ileocolonic segments
<table>
<thead>
<tr>
<th>Deep ulcerations</th>
<th>Rectum</th>
<th>Sigmoid and left colon</th>
<th>Transverse colon</th>
<th>Right colon</th>
<th>Ileum</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>(12 if present, 0 if absent in the segment)</td>
<td>_____+</td>
<td>_________+</td>
<td>_______+</td>
<td>_____+</td>
<td>____+</td>
<td>Total 1+</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Superficial ulcerations</th>
<th>Rectum</th>
<th>Sigmoid and left colon</th>
<th>Transverse colon</th>
<th>Right colon</th>
<th>Ileum</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>(6 if present, 0 if absent in the segment)</td>
<td>_____+</td>
<td>_________+</td>
<td>_______+</td>
<td>_____+</td>
<td>____+</td>
<td>Total 2+</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Surface involved by disease (cm)</th>
<th>Rectum</th>
<th>Sigmoid and left colon</th>
<th>Transverse colon</th>
<th>Right colon</th>
<th>Ileum</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>_____+</td>
<td>_________+</td>
<td>_______+</td>
<td>_____+</td>
<td>____+</td>
<td>Total 3+</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Surface involved by ulcerations (cm)</th>
<th>Rectum</th>
<th>Sigmoid and left colon</th>
<th>Transverse colon</th>
<th>Right colon</th>
<th>Ileum</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>_____+</td>
<td>_________+</td>
<td>_______+</td>
<td>_____+</td>
<td>____+</td>
<td>Total 4=</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total A</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Number of segments totally or partially explored (1-5)</th>
<th>n</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Total A/ n = Total B</th>
</tr>
</thead>
</table>

If **ulcerated stenosis** is present anywhere add 3= C

If **non-ulcerated stenosis** is present anywhere add 3= D

TOTAL B + C + D = CDEIS
Endoscopic endpoints

CDEIS

Scores range from 0-44 (higher=more severe)

Mary JY et al. Gut 1989
### Simple endoscopy index : SES-CD

<table>
<thead>
<tr>
<th>SEVERITY</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence and size of ulcers</td>
<td>None</td>
<td>Aphtous</td>
<td>Large,</td>
<td>&gt;2 cm</td>
</tr>
<tr>
<td></td>
<td>&lt;0.5 cm</td>
<td>0.5-2 cm</td>
<td>&gt;2 cm</td>
<td></td>
</tr>
<tr>
<td>Extent of ulcerated surface</td>
<td>0%</td>
<td>&lt;10%</td>
<td>10-30%</td>
<td>&gt;30%</td>
</tr>
<tr>
<td>Extent of affected surface</td>
<td>0%</td>
<td>&lt;50%</td>
<td>50-75%</td>
<td>&gt;75%</td>
</tr>
<tr>
<td>Presence and type of narrowings</td>
<td>None</td>
<td>Single,</td>
<td>Multiple,</td>
<td>Cannot</td>
</tr>
<tr>
<td></td>
<td>can be</td>
<td>can be</td>
<td>can be</td>
<td>be</td>
</tr>
<tr>
<td></td>
<td>passed</td>
<td>passed</td>
<td>passed</td>
<td>passed</td>
</tr>
</tbody>
</table>
### SES-CD

<table>
<thead>
<tr>
<th>Presence and size of ulcers (0-3)</th>
<th>Ileum</th>
<th>Right colon</th>
<th>Transverse colon</th>
<th>Left colon</th>
<th>Rectum</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Extent of ulcerated surface (0-3)</th>
<th>Ileum</th>
<th>Right colon</th>
<th>Transverse colon</th>
<th>Left colon</th>
<th>Rectum</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>+++</td>
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<td>+++</td>
<td>+++</td>
<td>+</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Extent of affected surface (0-3)</th>
<th>Ileum</th>
<th>Right colon</th>
<th>Transverse colon</th>
<th>Left colon</th>
<th>Rectum</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+++</td>
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<td>+++</td>
<td>+++</td>
<td>+</td>
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</tbody>
</table>

<table>
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<th>Ileum</th>
<th>Right colon</th>
<th>Transverse colon</th>
<th>Left colon</th>
<th>Rectum</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>=</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>RAW SUM OF VARIABLES</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of affected segments</td>
<td>n</td>
</tr>
</tbody>
</table>

\[ \text{Total} - 1.4 \times n = \text{SES-CD} \]
Correlation between SES-CD and CDEIS (191 examinations)

Daperno et al, 2004
### Clinical-endoscopic Correlations

<table>
<thead>
<tr>
<th></th>
<th>SES-CD</th>
<th>CDEIS</th>
<th>GELS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CDAI</strong></td>
<td>0.371</td>
<td>0.321</td>
<td>0.250</td>
</tr>
<tr>
<td></td>
<td>(p&lt;0.0001)</td>
<td>(p=0.0003)</td>
<td>(p=0.005)</td>
</tr>
<tr>
<td><strong>IBDQ</strong></td>
<td>-0.231</td>
<td>-0.240</td>
<td>-0.203</td>
</tr>
<tr>
<td></td>
<td>(p=0.019)</td>
<td>(p=0.015)</td>
<td>(p=0.039)</td>
</tr>
<tr>
<td><strong>CRP</strong></td>
<td><strong>0.453</strong></td>
<td>0.422</td>
<td>0.400</td>
</tr>
<tr>
<td></td>
<td>(p&lt;0.0001)</td>
<td>(p&lt;0.0001)</td>
<td>(p&lt;0.0001)</td>
</tr>
</tbody>
</table>

- Correlations to clinical variables were significant

Daperno et al, GI Endoscopy 2004
Endoscopic Assessment following surgery: Rutgeerts’ score

- Developed for lesions in the neoterminal ileum and at the ileocolonic anastomosis
- i0 – i4
- Correlates with clinical behavior in the future

Rutgeerts P et al. Gastroenterology 1990
Effect of steroids (1 mg/kg/d) on endoscopic lesions in CD after 3-7 weeks

- Before CS: 144
- Responders: 133
- Non responders: 11

Endoscopic remission:
- Responders: 27%
- Non responders: 0%

Modigliani et al, Gastroenterology, 1990
Symptom Improvement with Mucosal Healing

D’Haens G et al. Gastroenterology 1999
## Treatment of CD: Mucosal Healing

<table>
<thead>
<tr>
<th></th>
<th>No or only Limited Healing</th>
<th>Important but Slow Healing</th>
<th>Important and Rapid Healing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminosalicylates</td>
<td>Aminosalicylates</td>
<td>Azathioprine</td>
<td>Infliximab</td>
</tr>
<tr>
<td>Steroids</td>
<td>Steroids</td>
<td>6-MP</td>
<td>Adalimumab?</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>Antibiotics</td>
<td>Methotrexate (?)</td>
<td>Certolizumab?</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
IOIBD CONSENSUS

- CDEIS to be used as a secondary endpoint in studies looking at inflammatory activity
- Rutgeerts’ score to be used in studies for postoperative recurrence
- Significant recurrence = i3 or i4

Typical lesions in Active Ulcerative Colitis

- Continuous involvement (caution: treatment effects)
- Erythema
- Friability
- Granularity
- Micro-ulcerations
- Shallow ulcerations
- Cecal patch
Typical lesions in Quiescent Colitis

- Attenuated vascular pattern/loss of vascular pattern
- Mucosal bridging
- Pseudopolyps
- Stricture formation: pylorus, ileocecal valve, rectosigmoid junction

(CD >> UC)
UC: Location and Extent

- 30% Proctitis
- 40% Distal/Left-sided colitis
- 30% Extensive/Pancolitis

Percentages based on extent of disease at diagnosis.
Natural Course of UC: Proctosigmoiditis

*Based on a multivariate analysis

Endoscopic changes in UC

Normal mucosa
↓
Edema (obscuring normal vessels)
↓
Erythema (capillary dilatation)
↓
Granularity and friability
↓
Pinpoint ulceration
↓
Larger ulcers

? ➔
distorted vasc pattern
peudopolyps

mucopus ➔

Larger ulcers ➔
Endoscopy in Active Ulcerative Colitis

- Full ileocolonoscopy recommended at diagnosis
- Flexible sigmoidoscopy sufficient for F/U
- No bowel prep needed in pts with active symptoms
- Continuous involvement (caution: treatment effects)
- Caution in fulminant colitis!
- Deep ulcers in spite of therapy: poor prognostic sign
- Biopsies to be taken in relapse! (CMV, C Diff, …)
Endoscopic scores for UC

- Useful since endoscopic improvement lags behind symptom improvement and endoscopic healing is an endpoint that is aimed at
- Problematic ‘inter-observer variability’
- Problem of definitions: friability ? granularity ? Ulcers ?
Baron Endoscopic score for UC: ‘Activity variables’

- 0= Normal: mat mucosa, ramifying vascular pattern clearly visible throughout, no bleeding spontaneous or to light touch
- 1= Abnormal but not hemorrhagic (between 0-2)
- 2= moderately hemorrhagic: bleeding to light touch but no spontaneous bleeding
- 3= severely hemorrhagic= spontaneous bleeding

*Problem: no description of ‘ulcers’*

Baron et al, BMJ 1964
Endoscopic score for UC: Baron

• Interobserver variation highest for ‘graded’ variables (eg ‘redness’)

• Score developed in mild/moderate cases (no ulcers !)

• Best agreement: friability (bleeding to light touch) spontaneous bleeding

• Lowest agreement: granularity

Baron et al, BMJ 1964
## Endoscopic Indices for UC

<table>
<thead>
<tr>
<th>Indexed by</th>
<th>Scale 0</th>
<th>Scale 1</th>
<th>Scale 2</th>
<th>Scale 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Powell-Tuck</td>
<td>no bleeding</td>
<td>bleeding on light touch</td>
<td>spontaneous bleeding</td>
<td></td>
</tr>
<tr>
<td>Sutherland</td>
<td>normal</td>
<td>mild friability</td>
<td>moderate friability</td>
<td>exsudation</td>
</tr>
<tr>
<td>Schroeder</td>
<td>normal</td>
<td>disturbed vessels</td>
<td>loss of vasc pattern</td>
<td>ulcers</td>
</tr>
</tbody>
</table>
Daclizumab in UC: Pilot Study

Endoscopy Scores

<table>
<thead>
<tr>
<th>Time, weeks</th>
<th>Mean score ± SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>8</td>
<td>4</td>
</tr>
</tbody>
</table>

Endoscopic score
- Granularity
- Vascular pattern
- Vulnerability
- Mucosal damage

min 0, max 12

Daclizumab in UC: Pilot Study Results
Mucosal Improvement After Treatment With Daclizumab

Week 0
Week 1
Week 8

Healing in UC: points to consider

• Active UC is associated with a higher likelihood of dysplasia/cancer

• Endoscopy correlates well with histology and ‘histological healing’ predicts longer ‘time to relapse’ (Riley at al.)

• In ACT, if healing at w8 (score 0): 4 x higher likelihood of clinical remission at w 30 (43.8 % vs 9.5 %)
Differential diagnosis CD/UC

CROHN’S

- Discontinuous involvement
- Cobblestoning
- Aphthous ulcers
- Deep serpiginous ulcers
- Rectal sparing
- Anal lesions
- Ileocecal valve stenotic/ulcerated

UC

- Continuous involvement
- Erosions/microulcerations
- Loss of vascular pattern
- Rectal involvement
- Ileocecal valve patulous and free of ulceration

Indeterminate: 10%
Crohn’s disease histology: general features

• CD can affect the entire GI tract
• CD is a segmental disease
• CD is a transmural disease
  – Mucosal lesions > endoscopic samples
  – Deeply situated lesions > surgical samples
Crohn’s disease microscopic features: early lesions

- Early lesions occur in a background of normal mucosa (focal lesions)
- Types
  - Summit lesions: damage of small capillaries and loss of epithelial cells
  - Epithelial patchy necrosis
  - Mucosal microulcerations (loss of up to 6 cells)
  - Aphthoid ulcer
  - Mountain peak ulcer: ulcers at the base of crypts
Crohn’s disease: Aphthoid ulcer
Crohn’s disease: Mountain peak ulcer
Crohn’s disease microscopic features & diagnosis

- Epithelial alterations
  - Cytological changes > damage & repair
  - Architectural changes
  - Metaplastic changes

- Inflammatory response
  - Intensity
  - Composition
  - Distribution
Histologic Disease Activity in CD

- Epithelial damage 0-2
- Architectural changes 0-2
- Mononuclear infiltrate in LP 0-2
- PMN infiltrate in LP 0-2
- PMN infiltrate in epithelium 1-3
- Erosion/ulcers 0-1
- Granulomas 0-1
- Proportion of biopsies affected 0-3

D’Haens et al. Gastroenterology 1998
Histologic Disease Activity in CD

- Correlation between histological changes and clinical improvement is poor
- Score not validated prospectively
- Histology recommended for exploratory studies
Crohn’s disease : 4w after IFX
Geboes Index: different grades used for evaluation of histologic disease severity in UC

**Geboes Index:**

Grade 0: Structural (architectural) changes
   0= No abnormality, 1= Mild abnormality, 2= Mild or moderate diffuse or multifocal abnormalities, 3= Severe diffuse or multifocal abnormalities

Grade 1: Chronic inflammatory infiltrate
   0= No increase, 1= Mild but unequivocal increase, 2= Moderate increase, 3= Marked increase

Grade 2: Lamina propria neutrophils and eosinophils
   2A Eosinophils
   0= No increase, 1= Mild but unequivocal increase, 2= Moderate increase, 3= Marked increase

   2B Neutrophils
   0= No increase, 1= Mild but unequivocal increase, 2= Moderate increase, 3= Marked increase

Grade 3: Neutrophils in epithelium
   0= None, 1= < 5% crypts involved, 2=< 50% crypts involved, 3=> 50% crypts involved

Grade 4: Crypt destruction
   0=None, 1=Probable – local excess of neutrophils in part of crypt, 2=Probable – marked attenuation, 3=Unequivocal crypt destruction

Grade 5: Erosion or ulceration
   0=No erosion, ulceration, or granulation tissue, 1= Recovering epithelium + adjacent inflammation, 2= Probable erosion – focally stripped, 3= Unequivocal erosion, 4= Ulcer or granulation tissue
Conclusions

• In UC endoscopic (and histological) scores are absolutely recommended in the assessment of disease activity and effects of drug therapy

• In Crohn’s disease endoscopic endpoints are gradually entering routine clinical practice and should be part of the evaluation of drug effects

• More research is needed to ascertain if ‘healing of the mucosa’ should be the ultimate goal of treatment in CD
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In collaboration with GETAID – Groupe d’Étude Thérapeutique des Affections Inflammatoires du Tube Digestif

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