Current management of IBD: the ECCO Guidelines

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Overview

• Process
• Outpatient relapse
• Acute severe UC
• Biological therapy for CD
• Immunomodulators in CD
• Guidelines into practice
ECCO and Consensus

- **ECCO**
  - a forum for specialists in inflammatory bowel disease from 23 European countries

**Leading article**

157  Oral proteases: a new approach to managing coeliac disease  
N Cerf-Bensussan, T Matysiak-Budnik, C Cellier, M Heyman

**Editorial**

161  European evidence-based consensus on the diagnosis and management of Crohn’s disease  
S B Hanauer, W J Sandborn
Topics

Crohn’s disease
• Definitions and diagnosis
  – Clinical diagnosis
  – Histological diagnosis
  – Classification
• Current management
  – Active disease
  – Maintenance
  – Surgery
• Special situations
  – Post-operative
  – Fistulating disease
  – Children & adolescents
  – Pregnancy
  – Psychosomatics
  – Extraintestinal
  – CAM

Ulcerative colitis
• Definitions and diagnosis
  – Clinical diagnosis
  – Histological diagnosis
  – Classification
• Current management
  – Active disease
  – Maintenance
  – Surgery
• Special situations
  – Pouchitis
  – Surveillance
  – Pregnancy, Children & adolescents
  – Psychosomatics
  – Extraintestinal and anaemia
  – CAM
  – Patient perspective
Levels of evidence: OCEBM

<table>
<thead>
<tr>
<th>EL</th>
<th>Technique</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>Systematic review (SR) with homogeneity of randomized controlled trials</td>
</tr>
<tr>
<td>1b</td>
<td>Individual RCT</td>
</tr>
<tr>
<td>2</td>
<td>Cohort study</td>
</tr>
<tr>
<td>3</td>
<td>Case-Control Study</td>
</tr>
<tr>
<td>4</td>
<td>Case-series</td>
</tr>
<tr>
<td>5</td>
<td>Expert opinion</td>
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</tbody>
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For details see [http://www.cebm.net/levels_of_evidence.asp#refs](http://www.cebm.net/levels_of_evidence.asp#refs)
# Recommendation grades: OCEBM

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
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<tbody>
<tr>
<td>A</td>
<td>consistent level 1 studies</td>
</tr>
<tr>
<td>B</td>
<td>consistent level 2 or 3 studies <em>or</em> extrapolations from level 1 studies</td>
</tr>
<tr>
<td>C</td>
<td>level 4 studies <em>or</em> extrapolations from level 2 or 3 studies</td>
</tr>
<tr>
<td>D</td>
<td>level 5 evidence <em>or</em> troublingly inconsistent or inconclusive studies of any level</td>
</tr>
</tbody>
</table>

For details see [http://www.cebm.net/levels_of_evidence.asp#refs](http://www.cebm.net/levels_of_evidence.asp#refs)
Lessons from CD Consensus: recommendation grades

A: Consistent level 1 studies
B: Consistent EL2/3 or extrap.
C: Level 4, or extrap. from 2/3
D: Level 5, or inconsistency
RG cannot exceed EL

Knowledge gap

- Diagnosis (n = 37)
- Management (n = 64)
- Special situations (n = 133)
Ulcerative colitis

- **UC** - diffuse mucosal inflammation limited to the colon
  - Characterised by bloody diarrhoea, remission and relapse
  - Variable extent proctitis, distal, L sided, pancolitis
Outpatient assessment of the severity of active UC

<table>
<thead>
<tr>
<th></th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
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<tbody>
<tr>
<td>Bloody stools/day</td>
<td>&lt;4</td>
<td></td>
<td>≥6</td>
</tr>
<tr>
<td>Pulse</td>
<td>&lt;90 bpm</td>
<td></td>
<td>&gt;90 bpm</td>
</tr>
<tr>
<td>Temperature</td>
<td>&lt;37.5°C</td>
<td>In between</td>
<td>&gt;37.8°C</td>
</tr>
<tr>
<td>Hb</td>
<td>&gt;11.5 g/dL</td>
<td></td>
<td>&lt;10.5 g/dL</td>
</tr>
<tr>
<td>ESR</td>
<td>&lt;20 mm/hr</td>
<td></td>
<td>&gt;30 mm/hr</td>
</tr>
</tbody>
</table>

Easy to remember, easy to apply, defines severe attacks
Active UC

ECCO Statement: Left-sided UC

• Left-sided active ulcerative colitis of mild-moderate severity should initially be treated with topical aminosalicylates [EL1b, RG B] combined with oral mesalazine ≥2g/day [EL1a, RG A]....
SPD-476 (Mezavant) for mild-moderate UC data from MATRx 1

- Remission rates @ 8 weeks
- 280 patients, mild-mod UC
- Placebo vs 2.4g/d (1.2g bd) vs 4.8g od

Lichtenstein et al *CGH* 2007;5:95-102
### Conventional therapy UC - active disease

<table>
<thead>
<tr>
<th></th>
<th>Steroids</th>
<th>5ASA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NNT (95% CI)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Remission</td>
<td>2 (1.4-5)</td>
<td>10 (7-21)</td>
</tr>
<tr>
<td>Response</td>
<td>-</td>
<td>4 (3-6)</td>
</tr>
</tbody>
</table>

Bebb JR & Scott BB *APT* 2004;20:143-9
Active disease

ECCO Statement: Treatment of severe UC of any extent with signs of systemic toxicity

- Severe active ulcerative colitis with signs of systemic toxicity should be treated in hospital [EL5, RG D] with intravenous steroids (such as methylprednisolone 60 mg hydrocortisone 400 mg daily) [EL1b, RG B]. Monotherapy with intravenous ciclosporin (to achieve a minimum therapeutic concentration) [EL1b, RG C] is an option for patients intolerant of intravenous steroids. Patients are best cared for jointly by a gastroenterologist and colorectal surgeon [EL5, RG D]
Response of acute severe UC to iv steroids

Turner et al Clin Gastroenterol Hepatol 2007;5:103-10
National UK audit 2007: ASUC data
http://ibdaudit.rcplondon.ac.uk/2006/

- 2074 admitted as emergency for UC
- 71% response to steroids
- 150/2074 (7.2%) given CsA; 37 given IFX
- 318 colectomy (emergency: ?selection bias)
- Post-op mortality 15 patients
  - 15/318 = 4.7%
National UC audit snapshot:
2074 pts admitted with acute severe UC 2006

Leiper K, Mar 2007 unpublished
Active disease

ECCO Statement: Intravenous-steroid resistant ulcerative colitis of any extent

- The response to intravenous steroids is best assessed objectively (by stool frequency, CRP and abdominal radiography) on or about the third day \[EL2b, RGB\]. Surgical options should be considered and discussed at this stage or earlier...
Predicting outcome

If, on day 3 of intensive treatment, stool frequency >8/day, or CRP >45mg/L and stool frequency 3-8/d then 85% come to colectomy on that admission

Travis et al Gut 1996;38:905
**What is the long-term outcome of severe UC?**

**Complete response:** no visible blood, frequency $\leq 3$ on day 7 of intensive treatment  
**Incomplete:** visible blood or frequency $>3$/day on day 7

<table>
<thead>
<tr>
<th></th>
<th>Complete $n = 22$</th>
<th>Incomplete $n = 10$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colectomy in 12 mo</td>
<td>2/22 (9%)</td>
<td>6/10 (60%)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Colectomy over 15 yr</td>
<td>8/22 (36%)</td>
<td>8/10 (80%)</td>
<td>0.010</td>
</tr>
<tr>
<td>Median time index admission to colectomy (range, mo)</td>
<td>33.0 (3-99)</td>
<td>6.0 (3-29)</td>
<td>0.011</td>
</tr>
<tr>
<td>Median no. of relapses/yr (95% CI)</td>
<td>0.58 (0.50-1.73)</td>
<td>1.15 (0.74-2.96)</td>
<td>0.19</td>
</tr>
<tr>
<td>Longest period of remission (range, mo)</td>
<td>45.0 (0-120)</td>
<td>8.5 (1-35)</td>
<td>0.017</td>
</tr>
</tbody>
</table>

Bojic et al *Gut* 2005;54 Suppl VI:A155
Crohn’s disease

- **CD** - patchy transmural inflammation.
  - Characterised by pain, non-bloody diarrhoea and weight loss
  - **Distribution**: terminal ileal (30%), colonic (30%), ileocolic (30%), other
  - **Variable pattern**: inflammatory, fistulating, or stricturing
Biologics for CD

• Infliximab should be considered in addition for corticosteroid or immunomodulator-refractory disease or intolerance \([\text{EG}1b, \text{RGB}]\), although surgical options should also be considered and discussed…
Remission rates at 6 months in phase 3 trials of anti-TNF therapy for IBD
Indications for azathioprine

- After a severe relapse
- Two or more steroid courses within a year
- Relapse when prednisolone <15mg
- Relapse within 3 months of stopping steroids
- Post-operative prophylaxis of complex Crohn's

ECCO Guidelines Gut 2006;56 Suppl 1:i1-i58
Effectiveness of Aza/6-MP and MTX

• AZA for preventing relapse in CD
  – Overall OR 2.16 (CI 1.35-3.47) vs placebo, NNT = 5
  – 1 mg/Kg/day OR 1.20 (CI 0.60-2.41)
  – 2 mg/Kg/day OR 3.17 (CI 1.33-7.59)
  – 2.5mg/Kg/day OR 4.13 (CI 1.59-10.71)
  – Steroid sparing NNT = 3

  Pearson et al. Cochrane Review 2005

• MTX for steroid-free remission in CD
  – 9m 65% (vs 39% on placebo, p=0.04)
  – 24m 73% (case series)
  – 36m 51% (case series)

Implementing guidelines and improving standards of care
Conclusions

• Objective evaluation of disease activity
• Prednisolone for prompt response
• Azathioprine to maintain remission if relapse as steroids withdrawn
• Infliximab for active CD in spite of steroids or azathioprine
• Empathy, care and concern will always be central to the care of UC and CD
• Consider the direction of travel
Guidelines to IBD management: always consider the direction of travel
Theory vs practice: always consider the direction of travel
Theory vs practice: always consider the direction of travel

- Acute colitis
- Steroids
- 5ASA
- CsA
- Surgery
- IFX
- CAM
- Good health
Theory vs practice:
always consider the direction of travel
Inflammatory Bowel Diseases 2008
3rd Congress of ECCO – the European Crohn’s and Colitis Organization

Lyon, France
February 28 – March 1, 2008

ECCO website: www.ecco-ibd.eu