Limited clinical significance of tissue calprotectin levels in bowel mucosa for the prediction of complicated course of the disease in children with ulcerative colitis

Ondřej Fabián¹², Ondřej Hradský³, Tereza Lerchová³, Filip Mikuš¹, Josef Zámečník¹, Jiří Bronský³

1 - Department of Pathology and Molecular Medicine, Motol University Hospital, Second Faculty of Medicine, Prague
2 - Department of Pathology, Royal Vinohrady Teaching Hospital, Third Faculty of Medicine, Prague
3 - Department of Paediatrics, Motol University Hospital, Second Faculty of Medicine, Prague
Conflict of interest

• None
Background

- Microscopy plays a fundamental role in diagnostic of the ulcerative colitis.
- However, its contribution to the monitoring of the disease activity is unclear.
- Endoscopy remains a gold standard in the assessment of the luminal activity of the inflammation.
- But it is invasive and requires a general anesthesia.
Background

• Search for non-invasive markers of the inflammation activity.

Fecal calprotektin (F-CPT)
F-CPT
Limitations of F-CPT

- False positivity in patients with IBS or even with normal findings.
- False negativity due to a bowel cleansing.
- Ill-defined normal values in pediatric population.
- Fluctuating day-to-day values.
What if we measured CPT directly in the tissue?
Methods

Revised Porto criteria from 2014

- Previous treatment
- Incomplete clinical data
- Missing endoscopic findings
- Missing bioptic material

n = 81

6/2010 - 1/2018
n = 130

Revised Porto criteria from 2014

n = 49
Methods

n = 49
Methods

n = 49

Geboes score
Nancy score
Nancy score

- **Ulcereation**
  - Yes = Grade 4 (severely active disease)
  - No
    - Acute inflammatory cells infiltrate
      - No
        - Chronic inflammatory infiltrate
          - No or mild increase = Grade 0 (no histological significant disease)
          - Moderate or marked increase = Grade 1 (chronic inflammatory infiltrate with no acute inflammatory infiltrate)
      - Yes
        - Moderate or = Grade 3 (Moderately active disease)
        - Mild = Grade 2 (Mildly active disease)
Methods

n = 49
Methods

n = 49

Ulcerative Colitis Endoscopic Index of Severity (UCEIS)
## UC Endoscopic Index of Severity (UCEIS)

<table>
<thead>
<tr>
<th>Most Severely Affected Area on Endoscopy</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vascular pattern</strong></td>
<td></td>
</tr>
<tr>
<td>0 = Normal</td>
<td></td>
</tr>
<tr>
<td>1 = Patchy obliteration</td>
<td></td>
</tr>
<tr>
<td>2 = Obliterated</td>
<td></td>
</tr>
<tr>
<td><strong>Bleeding</strong></td>
<td></td>
</tr>
<tr>
<td>0 = None</td>
<td></td>
</tr>
<tr>
<td>1 = Mucosal</td>
<td></td>
</tr>
<tr>
<td>2 = Luminal, mild</td>
<td></td>
</tr>
<tr>
<td>3 = Luminal, moderate or severe</td>
<td></td>
</tr>
<tr>
<td><strong>Erosions and Ulcers</strong></td>
<td></td>
</tr>
<tr>
<td>0 = None</td>
<td></td>
</tr>
<tr>
<td>1 = Erosions</td>
<td></td>
</tr>
<tr>
<td>2 = Superficial ulcer</td>
<td></td>
</tr>
<tr>
<td>3 = Deep Ulcer</td>
<td></td>
</tr>
</tbody>
</table>

| **Sum**                                 |       |
Methods

n = 49
Methods

n = 49

Pediatric Ulcerative Colitis Activity Index (PUCAI)
• Terminal ileum
• Caecum
• Ascending colon
• Transverse colon
• Descending colon
• Rectum

n / 1 HPF
Methods

n = 49

min. 12 months

Incomplete clinical data at the end of the minimal follow-up
n = 8

complications
Complications

A
• Acute Severe Colitis (PUCAI > 65)
• Colectomy
• anti-TNF treatment

B
• Systemic corticotherapy

C
• Systemic 5ASA therapy
Aims

• Correlation of levels of T-CPT (number of CPT+ cells in the bowel mucosa) and F-CPT at the time of the diagnosis.

• Correlation of T-CPT and F-CPT with microscopic, endoscopic and clinical activity of the inflammation.

• Predictive value of T-CPT, F-CPT and given scoring systems for complicated course of the disease.
Correlation of T-CPT with the scoring systems

- Geboes score (k=0.65)
- Nancy score (k=0.62)

+/-

- UCEIS (k=0.38)
- PUCAI (k=0.42)
- F-CPT (k=0.44)
What does it mean?

- T-CPT adequately reflects actual histopathological activity of the inflammation.
- Microscopy itself poorly correlates with the endoscopic and clinical disease activity.
Correlation of F-CPT with the scoring systems

Geboes (k=0.39)
Nancy (k=0.38)
UCEIS (k=0.36)

+/-

PUCAI (k=0.36, p=0.06)
What does it mean?

- According to some studies, F-CPT correlates well with the endoscopy in adults. There is a lack of data and inconsistent results in pediatric population.

Fecal calprotectin levels in children is more tightly associated with histological than with macroscopic endoscopy findings.

(PMID:25651733)


Clinical Laboratory [01 Jan 2014, 60(12):1993-2000]
Neither Geboes score nor Nancy score nor UCEIS predicted any complications.
Predictors of the complications

T-CPT values were not predictive as well.

F-CPT and PUCAI > 40 (moderate clinical disease activity) were associated with the time to development B and C complications (systemic corticotherapy and systemic 5ASA).
Conclusions

• First study that evaluated a benefit of the tissue calprotectin in pediatric population.

• T-CPT correlated with microscopic activity of the inflammation, but didn’t improve its exactness and had no predictive value.

• F-CPT and PUCAI are better predictors of complicate course of the disease.