UvA-DARE (Digital Academic Repository)

Nuclear gastroenterology: novel techniques in clinical and experimental gastrointestinal mobility, IBD and hepatology
Bennink, R.J.

Link to publication

Citation for published version (APA):

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.
Chapter 10

Evaluation of early treatment response and predicting the need for colectomy in active ulcerative colitis with $^{99m}$Tc-HMPAO WBC scintigraphy

Roelof Bennink¹, Marc Peeters², Paul Rutgeerts¹, Luc Mortelmans¹

Departments of ¹Nuclear Medicine and ²Gastroenterology
(UZ KU Leuven, Leuven, Belgium)

Submitted for publication
Chapter 10

Abstract

The rate of treatment failure in acute exacerbation of ulcerative colitis (UC) still reaches 20-30%. Early identification of nonresponders to therapy is important, since intensified or other medical treatment or ultimately colectomy should be considered to reduce morbidity. Since $^{99m}$Tc labeled HMPAO white blood cell (WBC) scintigraphy is accurate in determination of the severity and extent of UC lesions, the aim of the current study was to assess if WBC scintigraphy can predict early treatment failure in patients with an acute attack of UC.

Methods. We included 20 consecutive patients (7F, 13M, age 36.8 ± 10.9 yr) with a history of UC who were hospitalized with severe exacerbations. All patients underwent scintigraphy the day of admission and one wk after start of treatment. WBC’s were labeled with 200 MBq $^{99m}$Tc-HMPAO. SPECT of the abdomen was performed 60 min after WBC reinjection. Maximum tracer uptake in the different colon segments was defined and expressed as a ratio of lumbar bone marrow uptake. The scintigraphic activity score (SAS) was expressed as the sum of segmental colon uptake ratios. Scintigraphic evolution was considered favorable when the SAS decreased with ≥ 50% and post therapeutic SPECT uptake ratio’s were ≤ 1.5 per segment. Rectosigmoidoscopy with biopsy was performed within 24 h after scintigraphy.

Results. Outcome analysis after 3 mo showed 6/20 patients in clinical and endoscopic/histologic (rectosigmoid) remission, without alteration of treatment (responders). Of the other patients (nonresponders), 5/14 were colectomized, 5/14 received prolonged or intensified treatment, and 4/14 received other treatment. In the responders group, SAS (determined 1 wk after start of therapy) significantly decreased in all patients. In the group of nonresponders, 10 patients had an increase of SAS of more than 10%, 2 patients had an unchanged SAS and 2 patients had a decreased SAS of > 10% but had a residual mean segmental WBC uptake ratio > 1.5. There was a statistical significant difference between the responders and nonresponders ($P < 0.01$).

Conclusion. Repeated $^{99m}$Tc-HMPAO WBC scintigraphy seems able to predict therapy resistance in UC within 1 week after start of treatment.
Predicting outcome in ulcerative colitis

Introduction

Ulcerative colitis (UC) is a chronic inflammatory bowel disease characterized by periods of acute attacks and remission. Treatment is mainly based on corticosteroids, administered orally, parenterally or rectally. A rapid and sustained response is usually seen within a few days following initiation of treatment. However, the overall rate of steroid treatment failure in acute exacerbations of UC remains high, and 20-30% of patients ultimately require surgery. The introduction of cyclosporine as a potent immunosuppressive drug for treatment of corticosteroid-refractory UC benefits the short-term management in 60-80% of patients. However, several questions remain regarding the long-term maintenance strategies, since long-term prognosis is not overall impressive and cyclosporine treatment is known for its possible important side effects.

Prediction of the long-term prognosis of UC at the time of diagnosis and early identification of which patients with a severe exacerbation will not respond to therapy remains difficult. However, it is of great clinical importance to be able to predict a need for step-up medical treatment or colectomy at an early stage of the acute attack.

Multiple clinical and laboratory parameters have been suggested as valuable predictors of outcome with respect to colectomy for assessment of glucocorticoid response. Recent trials identified persisting high stool frequency, bloody diarrhea, continued CRP elevation and sustained elevation of body temperature as strongly predictive parameters of clinical steroid resistance in acute attacks of ulcerative colitis, with high chance of ultimate need for colectomy. Clinical and laboratory indices, however, seem relatively inaccurate in assessment of disease severity at tissue level.

White blood cell (WBC) scintigraphy has been shown to be a reliable and accurate determinator of the extent and intensity of UC lesions, combining imaging of the affected colon with a semi-quantitative scoring of disease activity. WBC scintigraphy has been shown to be superior to the activity index and the gastroenterologist's clinical opinion for diagnosing active inflammation in IBD patients.

Influx of neutrophils and other acute inflammatory cells in inflamed intestinal mucosa is a prominent feature in acute attacks of UC. Neutrophils are the predominant effector cell within the active lesions of UC and probably mediate most of the tissue damage.
Chapter 10

Therapeutic action is based on reduction of inappropriate gut inflammation, by means of glucocorticoids, immunomodulators like cyclosporine or biological therapeutic intervention in mucosal homing. Since scintigraphy and histology correlate very well in this particular field, WBC scintigraphy could become a reliable, noninvasive prognostic tool in prediction of therapeutic response and the follow-up of treatment for CU.

The aim of the current study was to determine if WBC scintigraphy can predict early treatment failure in patients with acute attacks of UC.

Materials and Methods

Subjects

We included 20 consecutive patients (13 men, 7 women, mean age 36.8 ± 10.9 yr) with a history of ulcerative colitis who were hospitalized with severe exacerbations. A severe episode was defined as an acute attack of UC with an activity score of ≥ 10. Exclusion criteria were toxic megacolon or perforation evident on plain abdominal radiographs, infectious disease and use of intravenous steroids for more than 12 h before admission. Patients with a history of bowel surgery were not included. All patients gave written informed consent to participate in the study, which was approved by the medical ethics committee of the Leuven University Hospital.

The clinical activity score was determined upon admission and daily after initiation of therapy. For this study, only the activity scores on admission and one wk after initiation of therapy were recorded. A rectosigmoidoscopy with biopsy was performed within 24 h of inclusion. The macroscopic appearance of the mucosa was classified using a 4-grade scoring system. Mucosal biopsy specimens obtained in the most severely affected areas were also graded on a 4-point scale. All patients underwent scintigraphy within 24 h after endoscopy. Rectosigmoidoscopy with biopsy and scintigraphy were repeated 1 wk after initiation of therapy. All scores (endoscopic, histologic and scintigraphic) were interpreted as grade 0 meaning normal bowel mucosa and grade 1-3 meaning mild, moderate and severe disease, respectively.
Predicting outcome in ulcerative colitis

TABLE I. Patient characteristics

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Cyclosporine</th>
<th>Methylprednisolone</th>
</tr>
</thead>
<tbody>
<tr>
<td>( n )</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Age (range)</td>
<td>37.10 ± 3.01 (20-50)</td>
<td>39.6 ± 5.19 (21-67)</td>
</tr>
<tr>
<td>Sex M/F</td>
<td>6/4</td>
<td>8/2</td>
</tr>
<tr>
<td>Clin (_t)</td>
<td>12.60 ± 0.78</td>
<td>13.10 ± 1.15</td>
</tr>
<tr>
<td>Endo (_t)</td>
<td>2.20 ± 0.25</td>
<td>2.60 ± 0.16</td>
</tr>
<tr>
<td>Hist (_t)</td>
<td>2.60 ± 0.16</td>
<td>2.40 ± 0.22</td>
</tr>
<tr>
<td>Scint (_t)</td>
<td>10.32 ± 2.66</td>
<td>11.53 ± 4.08</td>
</tr>
<tr>
<td>Segm</td>
<td>4.30 ± 0.30</td>
<td>4.30 ± 0.18</td>
</tr>
</tbody>
</table>

Clin\(_t\): clinical -; Endo\(_t\): endoscopic -; Hist\(_t\): histologic – and Scint\(_t\): scintigraphic disease activity score upon inclusion; Segm: number of affected segments on scintigraphy

**Scintigraphic test procedure**

The technique of labeling granulocytes in mixed leukocyte suspension using \(^{99m}\text{Tc}-\text{HMPAO} \) (Amersham Health) has been performed according to the consensus protocol for leukocyte labeling.\(^{18}\) An average of 200 ± 10 MBq of \(^{99m}\text{Tc}\)-HMPAO labeled granulocytes was reinjected into the patient.

Planar anterior and posterior 3-min images of the abdomen and pelvis were obtained at 45 min post reinjection using a large-field-of-view gamma camera (Bodyscan; Siemens Medical Solutions) fitted with a low-energy general-purpose collimator. Just before scintigraphy, the patient was asked to void. The 45-min image was used for localization and determination of the extent of bowel activity.

At 60 min postreinjection SPECT was performed (BIAD; Trionix). A 360° circular orbit was used acquiring 90 views of 40 seconds in a 30 min duration study. An image matrix of 64 x 64 pixels was used. After data acquisition, images were processed on a Trionix workstation using filtered backprojection using a Ramp reconstruction filter with Hamming window. Correction for attenuation was made using the Chang technique with an attenuation coefficient of 0.12 cm\(^{-1}\).\(^{19}\) Transaxial abdominal slices of 8.4 mm thickness were reconstructed. After reconstruction, a 9-point smoothing was applied.
Chapter 10

Data analysis

The planar scintigrams were evaluated by 2 physicians without knowledge of the endoscopic, histologic, or clinical findings.

On SPECT images, the colon was divided into 5 segments: ascending colon, transverse colon, descending colon, sigmoid and rectum. Tracer uptake was determined as described by Weldon et al.\textsuperscript{20, 21} Therefore, the maximum counts per pixel in each of these segment was measured using region of interest analysis of serial transaxial slices to obtain the maximal value for each colon segment. The SPECT segment uptake ratio was expressed as a fraction of bone marrow activity, obtained by averaging the maximum counts in five transaxial slices of lumbar spine. All processing was carried out by the same observer.

The SPECT segment uptake ratio was converted into a segmental SPECT severity score with grade 0 (no uptake), grade 1 (uptake ratio 0.326 ± 0.19 SD), grade 2 (uptake ratio 1.11 ± 0.36), and grade 3 (uptake ratio 3.33 ± 1.84).\textsuperscript{20, 21} This severity score was used for comparison of scintigraphy and histology. For comparison of total colon uptake before and after therapy, the pathologic segmental uptake ratios were summed and expressed as the scintigraphic activity score (SAS). The difference of SAS before and 1 wk after start of treatment (ΔSAS) was expressed as percentage post therapeutic change in SAS compared to the baseline scintigraphy.

Dosimetry

The radiation dose received by target organs – spleen, liver and bone marrow – were 0.21 mGy/MBq, 0.025 mGy/MBq and 0.023 mGy/MBq, respectively.\textsuperscript{22} The effective dose equivalent was 0.011 mSv/MBq (ICRP-62).

Management

Patients were double blind randomized as part of another pharmacotherapeutical trial and treated either with i.v. corticosteroids 40 mg/d continuous infusion or i.v. cyclosporine 4 mg/kg body weight. Cyclosporine was administered by continuous infusion adjusted to blood levels between 200 and 300 by a physician not taking part in the direct patient management. Treatment was continued for 8 d and subsequently
Predicting outcome in ulcerative colitis

adjusted if necessary. Patients who had a clinical response in the cyclosporine group were switched to oral cyclosporine started in a dose of 8 mg/kg in 2 equally divided doses per day and adjusted to serum levels between 200 and 350 ng/mL. Patients in the corticosteroid group who had a clinical response were switched to oral methylprednisolone 32 mg/d for the first 3 wk and tapered by 4 mg/wk until discontinuation.

Outcome

After seven days treatment patient were classified according to the clinical activity score. Immediate clinical response to intensive medical therapy was defined as improvement of the clinical activity score to a score < 10 with a drop of at least 3 points, with the ability to discharge the patient. Immediate scintigraphic response was defined as decrease of SAS of more than 50% and had a residual mean segmental WBC uptake ratio < 1.5. The scintigraphic response was not used for immediate patient management decisions. After 3 mo all patients were reviewed. For this study, patients were considered responders when the initial treatment strategy led to remission without alteration or intensifying of the regimen. Patients were considered nonresponders when the initial treatment strategy needed to be intensified or changed to yield remission or when patients required a colectomy.

Statistical analysis

All results are expressed as mean ± SEM values. The paired samples / test was used to compare differences between activity scores. Spearman’s rank correlation was used for statistical analysis of results. All statistical tests were 2-tailed and differences were evaluated at the 5% level of significance.
**Chapter 10**

**Table 2. Patient data**

<table>
<thead>
<tr>
<th>No</th>
<th>Clin&lt;sub&gt;1&lt;/sub&gt;</th>
<th>Clin&lt;sub&gt;2&lt;/sub&gt;</th>
<th>Clin&lt;sub&gt;0&lt;/sub&gt;</th>
<th>D&lt;sub&gt;C&lt;/sub&gt;</th>
<th>Seg&lt;sup&gt;1&lt;/sup&gt;</th>
<th>S&lt;sub&gt;1&lt;/sub&gt;</th>
<th>S&lt;sub&gt;2&lt;/sub&gt;</th>
<th>ΔSAS&lt;sup&gt;1&lt;/sup&gt;</th>
<th>D&lt;sub&gt;S&lt;/sub&gt;</th>
<th>Outc&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13</td>
<td>1</td>
<td>-12</td>
<td>R</td>
<td>2</td>
<td>5.96</td>
<td>2.83</td>
<td>-53</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>2</td>
<td>15</td>
<td>4</td>
<td>-11</td>
<td>R</td>
<td>4</td>
<td>27.52</td>
<td>24.61</td>
<td>-11</td>
<td>N</td>
<td>F&lt;sub&gt;C&lt;/sub&gt;</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>5</td>
<td>-5</td>
<td>R</td>
<td>5</td>
<td>7.51</td>
<td>11.66</td>
<td>55</td>
<td>N</td>
<td>F&lt;sub&gt;A&lt;/sub&gt;</td>
</tr>
<tr>
<td>4</td>
<td>15</td>
<td>11</td>
<td>-4</td>
<td>N</td>
<td>5</td>
<td>2.39</td>
<td>3.41</td>
<td>43</td>
<td>N</td>
<td>F&lt;sub&gt;A&lt;/sub&gt;</td>
</tr>
<tr>
<td>5</td>
<td>11</td>
<td>10</td>
<td>-1</td>
<td>N</td>
<td>4</td>
<td>21.50</td>
<td>3.53</td>
<td>-84</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td>9</td>
<td>-1</td>
<td>N</td>
<td>4</td>
<td>7.33</td>
<td>3.01</td>
<td>-59</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>7</td>
<td>16</td>
<td>9</td>
<td>-7</td>
<td>R</td>
<td>4</td>
<td>4.21</td>
<td>5.19</td>
<td>23</td>
<td>N</td>
<td>F&lt;sub&gt;A&lt;/sub&gt;</td>
</tr>
<tr>
<td>8</td>
<td>11</td>
<td>12</td>
<td>1</td>
<td>N</td>
<td>5</td>
<td>12.31</td>
<td>11.86</td>
<td>-4</td>
<td>N</td>
<td>F&lt;sub&gt;C&lt;/sub&gt;</td>
</tr>
<tr>
<td>9</td>
<td>10</td>
<td>7</td>
<td>-3</td>
<td>R</td>
<td>5</td>
<td>1.89</td>
<td>2.98</td>
<td>58</td>
<td>N</td>
<td>F&lt;sub&gt;A&lt;/sub&gt;</td>
</tr>
<tr>
<td>10</td>
<td>15</td>
<td>7</td>
<td>-8</td>
<td>R</td>
<td>5</td>
<td>12.61</td>
<td>4.39</td>
<td>-65</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>11</td>
<td>10</td>
<td>2</td>
<td>-8</td>
<td>R</td>
<td>4</td>
<td>7.82</td>
<td>22.60</td>
<td>189</td>
<td>N</td>
<td>F&lt;sub&gt;A&lt;/sub&gt;</td>
</tr>
<tr>
<td>12</td>
<td>10</td>
<td>11</td>
<td>1</td>
<td>N</td>
<td>4</td>
<td>3.54</td>
<td>14.50</td>
<td>310</td>
<td>N</td>
<td>F&lt;sub&gt;C&lt;/sub&gt;</td>
</tr>
<tr>
<td>13</td>
<td>11</td>
<td>6</td>
<td>-5</td>
<td>R</td>
<td>4</td>
<td>4.46</td>
<td>12.83</td>
<td>188</td>
<td>N</td>
<td>F&lt;sub&gt;A&lt;/sub&gt;</td>
</tr>
<tr>
<td>14</td>
<td>16</td>
<td>11</td>
<td>-4</td>
<td>N</td>
<td>5</td>
<td>7.51</td>
<td>19.28</td>
<td>157</td>
<td>N</td>
<td>F&lt;sub&gt;A&lt;/sub&gt;</td>
</tr>
<tr>
<td>15</td>
<td>20</td>
<td>12</td>
<td>-8</td>
<td>N</td>
<td>4</td>
<td>44.87</td>
<td>22.08</td>
<td>-51</td>
<td>N</td>
<td>F&lt;sub&gt;C&lt;/sub&gt;</td>
</tr>
<tr>
<td>16</td>
<td>11</td>
<td>3</td>
<td>-7</td>
<td>R</td>
<td>5</td>
<td>4.11</td>
<td>8.10</td>
<td>97</td>
<td>N</td>
<td>F&lt;sub&gt;C&lt;/sub&gt;</td>
</tr>
<tr>
<td>17</td>
<td>18</td>
<td>16</td>
<td>-2</td>
<td>N</td>
<td>4</td>
<td>11.09</td>
<td>12.02</td>
<td>8</td>
<td>N</td>
<td>F&lt;sub&gt;A&lt;/sub&gt;</td>
</tr>
<tr>
<td>18</td>
<td>13</td>
<td>5</td>
<td>-8</td>
<td>R</td>
<td>5</td>
<td>9.28</td>
<td>1.78</td>
<td>-81</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>19</td>
<td>12</td>
<td>7</td>
<td>-5</td>
<td>R</td>
<td>5</td>
<td>20.91</td>
<td>4.61</td>
<td>-78</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>20</td>
<td>10</td>
<td>6</td>
<td>-4</td>
<td>R</td>
<td>3</td>
<td>1.69</td>
<td>4.79</td>
<td>183</td>
<td>N</td>
<td>F&lt;sub&gt;A&lt;/sub&gt;</td>
</tr>
</tbody>
</table>

<sup>*</sup> Clinical activity score upon inclusion (Clin<sub>1</sub>); 1 wk after start of therapy (Clin<sub>2</sub>); Difference in clinical activity score before and after treatment (Clin<sub>0</sub>); Early response assessment based on clinical score (D<sub>C</sub>)

<sup>†</sup> Number of colon segments affected on scintigraphy (Seg); SAS upon inclusion (S<sub>1</sub>); SAS 1 wk after start of therapy (SAS<sub>2</sub>); Percentage difference in SAS before and after treatment (ΔSAS); Early response assessment based on SAS (D<sub>S</sub>)

<sup>‡</sup> Clinical outcome at 3 mo. Remission without changed management (R); Remission with changed management (F<sub>A</sub>); Colectomy (F<sub>C</sub>)
Correlation of activity score assessment by histologic analysis and SPECT of the rectosigmoid upon inclusion (A) and 1 wk after start of treatment (B). There is a good correlation of scintigraphic and histologic assessment of disease activity before and after therapy ($r = 0.80$, $P < 0.01$ and $r = 0.88$, $P < 0.01$, respectively).
Chapter 10

Results

Patient data are illustrated in Table 1 and 2. Before treatment, 10 patients had a left-sided colitis and 10 patients had pancolitis. The mean inflammatory activity, determined clinically using the numeric symptom score, was 12.85 ± 0.68 (mean ± SEM). Upon inclusion, there was a significant correlation between planar scintigraphic (data not shown) and histologic indices of disease intensity of the rectosigmoid (r = 0.64, P < 0.01) before treatment. There was an even better correlation between SPECT derived scintigraphic and histologic indices of disease intensity of the rectosigmoid (r = 0.80, P < 0.01). One week after therapy, there was an excellent correlation between SPECT derived scintigraphic and histologic indices of disease intensity of the rectosigmoid (r = 0.88, P < 0.01, Fig. 1).

After 3 mo, 6/20 patients (30%) were responders and achieved a complete response without changing the therapeutic strategy (R). 14/20 (70%) patients were nonresponders to initial therapy. In this group 9/14 patients finally achieved a complete response but required a change of therapeutic strategy (RA) and 5/14 patients were treatment failures and required colectomy (FC).

In the group of responders, all patients had a decrease of SAS ≥ 50% and had a residual mean segmental WBC SPECT uptake ratio < 1.5 (Fig. 2 and 3). The mean decrease of SAS in this group was significant (P < 0.05). The mean decrease percentage (ΔSAS) in this group was 70% (range 53 - 84%).

In the group of nonresponders, 10 patients had an increase of SAS > 10%, 2 patients had an unchanged SAS and 2 patients had a decreased SAS >10% (Fig. 4) but had a residual mean segmental WBC SPECT uptake ratio > 1.5. There was a statistical significant difference in ΔSAS between the responders and nonresponders (P < 0.01, Fig. 5A). There was no significant difference in ΔSAS between nonresponders requiring altered management or colectomy (data not shown). There was no significant difference in response between treatment groups.

For clinical assessment by means of the clinical activity score, there was no significant difference between responders and nonresponders (Fig. 5B, mean ± SEM clinical activity score −5.83 ± 1.78 and −4.71 ± 0.93, respectively).
Predicting outcome in ulcerative colitis

Figure 2. Left sided ulcerative colitis

$^{99m}$Tc-HMPAO WBC Whole Body scintigraphy (pt. 6) in anterior (A) and posterior (B) view before therapy and 1 week after start of therapy (C and D; anterior and posterior, respectively). Scintigraphy before treatment (A, B) shows severe colitis in 4 segments. Scintigraphy 1 wk after treatment shows markedly decreased uptake with mild to moderate colitis in 4 segments.
Figure 3. $^{99m}$Tc-HMPAO WBC SPECT of left-sided ulcerative colitis

$^{99m}$Tc-HMPAO WBC SPECT (pt. 6). Transaxial slices at different levels in the abdomen from cranial to caudal before therapy (A to D) with the corresponding slices 1 wk after start of therapy (E to H). Colon activity before therapy (arrow) is manifestly increased (SAS 7.33) in transverse colon (A), descending colon (B), sigmoid (C) and rectum (D) as compared to bone marrow (▲). Colon activity 1 wk after start of therapy has decreased (SAS 3.01) in transverse colon (E), descending colon (F), sigmoid (G) and rectum (H) as compared to bone marrow (▲).
**Figure 4. Pancolitis**

$^{99m}$Tc-HMPAO WBC Whole Body scintigraphy (pt. 14) in anterior (A) and posterior (B) view before therapy and 1 wk after start of therapy (C and D; anterior and posterior, respectively). Scintigraphy before treatment (A, B) shows mild to severe colitis in 5 segments. Scintigraphy 1 wk after treatment shows markedly increased uptake with severe colitis in 5 segments.
Figure 5. Box plots

Panel A shows box plots (median and interquartile range) of the percentual difference between the SAS before and 1 wk after start of therapy (ΔSAS). There is a significant difference in ΔSAS between responders and nonresponders (*P < 0.01). Panel B shows box plots of the difference between the clinical activity score before and 1 wk after start of therapy. There is no significant difference in clinical score evolution between responders and nonresponders.
Predicting outcome in ulcerative colitis

Discussion

White blood cell scintigraphy has been used for several decades as a diagnostic tool for inflammatory bowel disease.\textsuperscript{23,25,111} In-labeled granulocytes have been replaced by \textsuperscript{99m}Tc-HMPAO-labeled granulocytes to yield a rapid, simple, nontraumatic and effective technique with an acceptable radiation dose.\textsuperscript{11,26-28} It has been shown that \textsuperscript{99m}Tc-HMPAO WBC scintigraphy is superior to the activity index of van Hees and the gastroenterologist’s clinical opinion for diagnosing active inflammation in patients with IBD.\textsuperscript{12} The sensitivity and specificity of \textsuperscript{99m}Tc-HMPAO WBC scintigraphy are very high (94 to 100\%) for active disease.\textsuperscript{12,29,30} Furthermore, it was recently published that disease severity can be determined adequately by planar scintigraphy in patients with a severe attack of ulcerative colitis and that WBC scintigraphy is able to assess disease activity and extent without the need for colonoscopy.\textsuperscript{11} Unlike \textsuperscript{99m}Tc-HMPAO WBC scintigraphy, \textsuperscript{99m}Tc-Leucoscan lacks sensitivity and has no place in the assessment of gastrointestinal inflammation in IBD.\textsuperscript{31,32}

Where planar \textsuperscript{99m}Tc-HMPAO WBC scintigraphy has proven to be reliable to assess disease extent when compared to histological findings,\textsuperscript{33,34} we have recently shown that the disease activity in the rectum can also be assessed with accuracy by scintigraphy.\textsuperscript{11} However, planar scintigraphy has inherent inaccuracies due to variable depth and overlapping activities. SPECT has the advantage to overcome these problems and the use of \textsuperscript{99m}Tc-HMPAO SPECT for detection and quantification of acute bowel inflammation has been extensively described by Weldon et al.\textsuperscript{21} The determination of maximum segmental bowel uptake and calculating an uptake ratio to bone marrow yields a noninvasive, objective and accurate approach to the assessment of disease activity.

We used histological findings from biopsy specimens obtained in the most severely affected areas in the rectosigmoid before and 1 wk after therapy as gold standard for disease activity. The sensitivity of WBC scintigraphy for identifying rectosigmoid involvement of ulcerative colitis in this series of selected patients was 100\%, which is in accordance with our previous observations.\textsuperscript{11} However, it has to be mentioned that the study population is a selected one with severe colitis and that it is known that WBC scintigraphy can be false negative in patients with only slight macroscopic changes.\textsuperscript{35,36}
Chapter 10

No controls were included in this study to assess the sensitivity of WBC scintigraphy in the full spectrum of clinical activity of IBD. There was a good correlation between disease activity in the rectosigmoid determined on histology and planar scintigraphy. There was an even better correlation for disease activity determined on SPECT.

Several attempts have been made to predict the responsiveness of UC exacerbations to initial therapy. These techniques are based on clinical and laboratory observations to identify patients likely to require intensified or altered therapy or ultimately colectomy. The correlation of a clinical index with other variables such as CRP, the erythrocyte sedimentation rate (ESR), or endoscopic, histologic or scintigraphic scores for the extent and severity of disease is not always reported as significant. Clinical indices have an inherent subjectivity, resulting in a less reliable activity score. Laboratory parameters such as CRP and ESR reflect inflammation in general, and conflicting results concerning the predictive value have been reported.

Scintigraphic assessment of disease activity correlates very well with histologic disease activity assessment. This was reconfirmed in this study, both before and after treatment. The summed scintigraphic activity score (SAS) represents the maximum inflammatory activity detected in each segment of the entire colon reflecting histological assessment, which is based on biopsies obtained from the most macroscopically severely affected areas of each segment. Since the correlation between histologic and scintigraphic disease activity assessment is that good, it seems appropriate to use scintigraphy for disease activity assessment.

The difference between SAS before and 1 wk after treatment was predictive for remission up to 3 mo after start of therapy without change of therapy. This would not have been possible with the clinical activity score alone. In our series, a decrease of SAS of ≥ 50% of the initial value and a SPECT uptake ratio of ≤ 1.5 per segment (representing not more than moderate disease) is predictive of remission without the need for altering therapeutic management. In our series, nonresponders have a 36% chance of colectomy in the following weeks, which is not different from other observations.
Predicting outcome in ulcerative colitis

Conclusion

Repeated $^{99m}$Tc-HMPAO WBC scintigraphy seems able to predict therapy resistance in UC within 1 wk after start of treatment. This technique provides a noninvasive and reliable tool to monitor therapy in ulcerative colitis and depict nonresponders in an early stage where intensifying therapy or changing management or ultimately colectomy is possible without losing valuable time and increasing risk of dangerous complications.

References


Predicting outcome in ulcerative colitis


