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A Noninvasive Method to Assess Mucosal Healing in Patients* With Crohn's Disease

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Abstract: Ongoing inflammation in the gastrointestinal tract and loss of the mucosal barrier are key components of Crohn's disease. Current treatment paradigms, including treat-to-target, are based on improvement of both clinical and endoscopic symptoms. Endoscopy is an essential tool for the evaluation of mucosal healing, but patients may be reluctant to undergo repeated procedures. Surrogate markers of inflammation, such as C-reactive protein and fecal calprotectin, are being used, yet they have several limitations in the assessment of mucosal healing. A new strategy, known as the Monitr test, assesses mucosal healing status by evaluating serum levels of 13 biomarkers in patients with Crohn's disease. The 13 biomarkers are associated with cell adhesion, inflammation, angiogenesis, extracellular matrix remodeling, cell proliferation and repair, and immune cell recruitment. Monitr testing yields a mucosal healing index score that reflects disease severity. Validation of the test showed an overall accuracy of 90%, with a negative predictive value of 92% and a positive predictive value of 87% for identifying patients with endoscopic evidence of Crohn's disease. Use of this noninvasive test may aid in the monitoring and management of patients with Crohn's disease, while potentially reducing the need for repeated endoscopy.

*Validated in adult CD patients.

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The Role of Mucosal Healing in Patients With Crohn's Disease

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In Crohn's disease, mucosal healing is linked to the most important patient outcomes, namely, avoidance of surgery and hospitalization, and maintenance of a high quality of life.[1-3] Patients with Crohn's disease (as well as their unaffected first-degree relatives) have increased permeability within the intestine.[4-6] The origin of this increased permeability is uncertain.[5] One contributing factor may be inflammatory cytokines, such as tumor necrosis factor (TNF), that are produced locally.[7] In mouse models, TNF can disturb barrier function.[8] Anti-TNF therapy is one of the main modalities used to treat Crohn's disease.[1,7,8] It is assumed that local production of TNF-alpha in the intestines of patients with Crohn's disease contributes to a leaky mucosal barrier.[5,6,9] Some of the genetic defects that have been described in patients with Crohn's disease are closely linked to barrier function, particularly repair of the epithelium.[5]

One way to treat inflammatory bowel disease is to target the production of inflammatory cytokines, which can disrupt the barrier.[1,10] Research is also exploring methods that improve epithelial integrity, such as enhancing local levels of interleukin-22.[11] In patients with Crohn's disease, the inflammation is transmural,[8,12,13] which has repercussions for the structural damage that can occur in these patients, but is more rare in patients with ulcerative colitis.[12,13] In patients with Crohn's disease, even if the intestinal mucosa is eventually healed, there may be transmural structural damage that cannot be improved by medical therapy.[1,13]

Treatment Goals

There have been recent breakthroughs in the medical therapies available for patients with inflammatory bowel disease. Infliximab and other anti-TNF agents showed that it was possible to heal the intestinal lining.[1,3] Until the advent of infliximab, healing of the intestine was not even part of management goals. Currently, any new treatment under investigation for Crohn's disease or ulcerative colitis must be shown to improve ulcerations.[14-16]

Treatment goals have now evolved to consistently encompass mucosal healing. The strategy known as treat-to-target involves treating the target of inflammation until there is both symptomatic and endoscopic

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improvement.[15-17] This approach was highlighted by the phase 3 CALM study (Efficacy and Safety of Two Treatment Algorithms in Adults With Moderate to Severe Crohn's Disease).[15] In the control arm, changes in a patient's medication were based solely on clinical symptoms. In the treat-to-target arm, changes in medication were based on clinical symptoms, as well as biochemical markers of inflammation. These patients underwent testing for levels of fecal calprotectin and C-reactive protein. Therapy was escalated when patients showed objective evidence of inflammation. In both groups, treatment was escalated from no treatment, to adalimumab induction followed by adalimumab every other week, to adalimumab every week, to weekly adalimumab and daily azathioprine.

The study found that patients in the treat-to-target group had much better outcomes than the control patients.[15] Therapy was optimized quickly for patients in the treat-to-target arm, which led to higher rates of mucosal healing, deep remission, and reduced prednisone use compared with patients in the clinical management group. Post hoc exploratory analyses showed that the decision to escalate treatment was based on increased fecal calprotectin concentration in 62% of patients at 11 weeks after randomization and in 56% of patients at 23 weeks after randomization. Escalation based on increased C-reactive protein concentration, which is a less sensitive marker of inflammation,[18] was less common, occurring among 46% of patients at 11 weeks postrandomization and in 46% of patients at 23 weeks postrandomization. At week 35, fecal calprotectin and C-reactive protein concentrations contributed equally to the decision to escalate in 45% of patients. Overall, the CALM study proved that treat-to-target is an effective strategy.

The Role of Mucosal Healing

Mucosal healing can be defined in various ways.[3] One measure of mucosal healing is the absence of ulcerations or inflammation during colonoscopy or capsule endoscopy.[1,2,16] With histologic assessment, a pathologist confirms the absence of inflammatory cells in an area of previous involvement.[2] With the advances in medical therapy, the expectation is not only for patients to feel better, with fewer clinical symptoms, but also for endoscopy to show improvement.[2,3,16]

Endoscopy has been the primary method to evaluate mucosal healing.[1] Endoscopy enables the gastroenterologist to examine the mucosa and to obtain biopsies that can be evaluated microscopically for inflammation. However, patients with inflammatory bowel disease undergo many endoscopies, which can be a source of dissatisfaction, particularly because of the bowel prep.[19] Endoscopy is expensive, and, on rare occasions, it can be associated with perforation and bleeding. The risk of perforation is higher among patients with Crohn's disease compared with the general population.[20]

Data suggest that the severity of endoscopic lesions does not correspond to clinical symptoms. A multicenter, prospective study evaluated the connection between the Crohn's Disease Activity Index (CDAI) and the Crohn's Disease Endoscopic Index of Severity (CDEIS) among patients with active colonic or ileocolonic Crohn's disease. Only 29% of patients in clinical remission were also in endoscopic remission.[21]

Ideally, use of endoscopy to assess mucosal healing should follow a standardized method to capture data.[2] Various instruments are validated to assess the severity of inflammation endoscopically.[2] The CDEIS and the short version of the CDEIS (simple endoscopic score for Crohn's disease [SES-CD]) have both been validated.[2,22,23] The intestine is rated in segments. The ratings describe how much of the segment is involved, how much of it is ulcerated, the size of the ulcerations, and whether there are strictures.[2] This method highlights the importance of structural damage in Crohn's disease, which is difficult to manage once it has occurred.

The scoring systems are considered by many to be too complex for clinical use.[2,24] Many (if not most) gastroenterologists do not use these validated instruments to rate the severity of inflammation.[2,24] The lack of a standardized measurement has several implications. It can be difficult to measure changes without knowing the baseline levels. In many cases, there are no accurate assessments before or after an intervention. Endoscopy can be a sensitive method of detecting ulcerations, but the benefit is diminished if the gastroenterologist has not properly identified and quantified the severity of the disease. In addition, inter-observer variability in the interpretation of involvement can lead to inconsistency in scoring.[24]

Markers of Inflammation

Researchers are trying to develop noninvasive ways to identify whether a patient has active inflammation or disease. One approach is the use of fecal calprotectin as a marker of inflammation.[1,25] Fecal calprotectin is a reasonably sensitive marker of inflammation in the intestine. Calprotectin is more accurate in patients with colonic inflammation, and less accurate in patients with small-intestinal disease.[26] A recent systematic review of 19 studies (N=2499) on the value of calprotectin for the detection of endoscopic activity in symptomatic IBD patients concluded that calprotectin was more sensitive than C-reactive protein.[27] The study also showed that calprotectin was more sensitive in ulcerative colitis than

in Crohn's disease. Furthermore, in an earlier study, calprotectin levels showed a better association with disease activity in ulcerative colitis than in Crohn's disease.[28]

As a stool-based marker, fecal calprotectin is more accurate for assessing distal inflammation.[25] Inflammation that is higher in the small intestine may not be reflected in the fecal calprotectin test. In patients with colonic inflammation, the fecal calprotectin level can be much higher, even if the inflammation is limited.[29] In general, however, patients with a normal level of fecal calprotectin do not have active inflammation.[30] A limitation to the fecal calprotectin test is that patients are reluctant to collect stool samples. Another potential limitation of fecal calprotectin is that, although it measures a neutrophil protein, it does not help to determine if the bowel is in the repair phase. It is best when used in the same patient over time to determine if the value is decreasing or increasing.

Conclusion

It is necessary to find other ways to measure healing of the intestinal lining. Some patients may show some existing inflammation that is close to healing. A noninvasive method of monitoring mucosal healing would be a tremendous benefit to patients. It would be helpful to have a quantifiable measurement to provide a number that indicates the state of tissue injury and repair. Although stool testing is noninvasive, many patients are reluctant to collect stool samples.

Disclosure

Dr Abreu is a member of the scientific advisory boards of AbbVie Laboratories, Celgene Corporation, Shire Pharmaceuticals, Roche Pharmaceuticals, Boehringer Ingelheim Pharmaceuticals, AMGEN ABP 710 Biosimilar Infliximab, and MedStar Health. She is on the advisory boards of Allergan Brazikumab and SERES. She is a consultant for Prometheus Laboratories Inc; Takeda; UCB, Inc.; Pfizer; Janssen; Eli Lilly Pharmaceuticals; and Theravance Biopharma US, Inc. She has performed training/consulting for Focus Medical Communications. She has performed lecturing/teaching for Imedex, Inc. She has lectured for CME Outfitters.

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Emerging Modalities to Assess Mucosal Healing in Crohn's Disease

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As previously discussed, new modalities are needed to assess mucosal healing in Crohn's disease. The Monitr test (Prometheus) analyzes biomarkers in a patient's peripheral blood to assess mucosal healing.[1,2] Mucosal alterations involve particular pathways that mediate cell adhesion, inflammation, angiogenesis, matrix remodeling, growth factors, and immune recruitment modulation.[1-3] These pathways are associated with mucosal damage and/or repair in patients with Crohn's disease, and they were used to identify 13 biomarkers that are analyzed by the Monitr test. These biomarkers are CEACAM and VCAM (cell adhesion); C-reactive protein and serum amyloid A (inflammation); angiopoietin-1 and -2 (angiogenesis); matrix metalloproteases (MMP)1, MMP2, MMP3, MMP9, and extracellular matrix metalloproteinase inducer (matrix remodeling); transforming growth factor alpha (growth factor); and interleukin-7 (immune recruitment modulation; Figure 1).[1]

Matrix remodeling is most likely one of the more important pathways contributing to the formation of scar tissue or collagen.[4] The development of damage to the bowel wall involves matrix remodeling in addition to ongoing inflammation.[3,5] Therefore, in patients with Crohn's disease, we would expect to see increasing expression of biomarkers associated with matrix remodeling and inflammation.[1,4] The idea behind the Monitr test is that assessment of these biomarkers in the peripheral blood will reflect changes in the gut mucosa.[1] Until now, it was necessary to rely mainly on ileocolonoscopy and

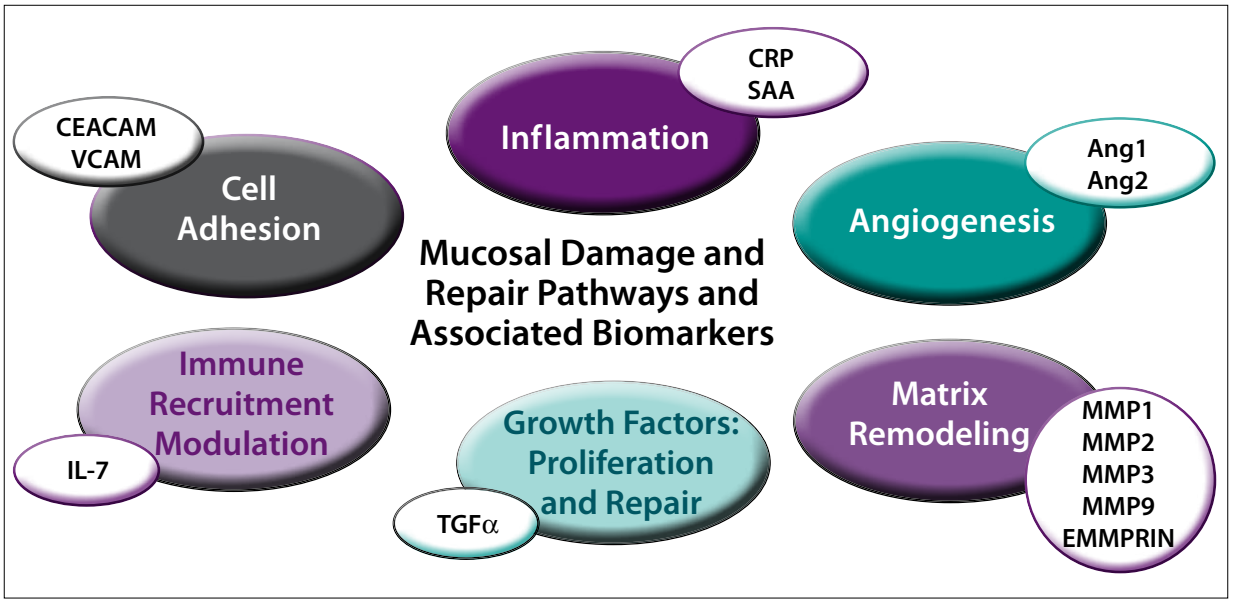

Figure 1. Biomarkers included in the Monitr test. Ang, angiopoietin; CEACAM, carcinoembryonic antigen-related cell adhesion molecule; CRP, C-reactive protein; EMMPRIN, extracellular matrix metalloproteinase inducer; IL, interleukin; MMP, matrix metalloproteinase; SAA, serum amyloid A; TGF, transforming growth factor; VCAM, vascular cell adhesion molecule. Adapted from Vermeire S et al. Abstract 74 presented at: the World Congress of Gastroenterology at ACG2017; October 13-18, 2017; Orlando, FL.[1]

Table 1. Patient Characteristics and Serum Samples

	Training Set (Cohorts 1-4)	Validation Set (Cohort 5: TAILORIX)	*P* Value
N, patients	**278**	**118**	
Age (mean in years [range])	34 (18-74)	34 (18-76)	.75
Male sex (n [%])	150 (54%)	45 (38%)	.02
Disease location			.14
Ileal only	43 (27.4%)	27 (22.9%)	
Colonic only	38 (24.2%)	20 (16.9%)	
Ileocolonic	76 (48.4%)	71 (60.2%)	
Endoscopic reading	Read at each center	Central read	
Therapy	All comers	IFX + IS	
N, samples	**335**	**413**	
Collection	Retrospective	Prospective	
Type	Cross-sectional	Longitudinal	
Time from nearest endoscopy			
0 days	147 (44%)	132 (32%)	
≤30 days	267 (80%)	376 (91%)	
"N" by endoscopic severity			
Severe (CDEIS >12)	39 (11.6%)	52 (12.6%)	
Moderate (CDEIS 9-12)	17 (5.1%)	40 (9.7%)	
Mild (CDEIS 3-8)	120 (35.8%)	146 (35.4%)	
Remission (CDEIS <3)	159 (47.5%)	175 (42.4%)	

CDEIS, Crohn's Disease Endoscopic Index of Severity; IFX, infliximab; IS, immunosuppressive therapy; TAILORIX, Study Investigating Tailored Treatment With Infliximab for Active Crohn's Disease.

Data from Vermeire S et al. Abstract 74 presented at: the World Congress of Gastroenterology at ACG2017; October 13-18, 2017; Orlando, FL.[1]

cross-sectional imaging to assess the extent of a patient's mucosal damage.[6]

The Mucosal Healing Index Score

The biomarkers that are assessed with the Monitr test are combined in an algorithm that results in the mucosal healing index (MHI) score, which ranges from 0 to 100.[2] Serum samples were taken from adult patients with Crohn's disease at or within 30 days of ileocolonoscopy.[1,2] There were 748 samples taken from 396 patients in separate training and validation phases. The clinical parameters of patients in the training and validation sets are listed in Table 1. A panel of serum biomarkers was used to train a logistic regression model against visualized endoscopic disease severity, with the latter determined by either CDEIS or SES-CD scores.[2] Expression of these serum protein markers was therefore compared with the endoscopic scoring of that subject at the time that was closest from the endoscopy to the collection of the serum. The training cohort included 278 patients and 335 samples from 4 sites, and the validation cohort included 118 patients and 413 samples from the TAILORIX trial (Study Investigating Tailored Treatment With Infliximab for Active Crohn's Disease). The validation cohort showed a 90% accuracy with endoscopically visualized mucosal inflammation. An MHI score of 0 to 40 is consistent with remission or mildly active Crohn's disease, and is similar to a CDEIS of less than 3 for patients in remission and a CDEIS of 3 to 8 for patients with mild disease activity (Figure 2). An MHI score of 41 to 49 is considered intermediate. In the validation study, 14% of the specimens fell within the intermediate zone, with an observed 78% probability of active disease.[2] An MHI score of 50 to 100 is consistent with active disease and is similar to a CDEIS score of 3 or greater.

Predictive Value

The performance of the Monitr test was determined using the validation cohort (Table 2). For the entire cohort the sensitivity and specificity were 82% and 94% respectively, indicating that the test has a 18% false negative rate but only a 6% false positive rate. The low false positive rate indicates that the test is good at ruling in active endoscopic disease. The predictive values were also assessed. In the validation cohort, 78% of the population was in remission/mild disease and 22% had moderate/severe disease as defined by endoscopy. In this specific population, the probability that a positive Monitr test result identified true active endoscopic disease was 87% (positive predictive value = PPV) and the probability that a negative Monitr result identified a patient with true mild endoscopic activity or remission was 92% (negative predictive value = NPV) (Table 2). In order to determine if disease location influenced test performance, the validation cohort was subdivided by the presence of ileal only, ileocolonic and colonic only disease. As shown in Table 2, sensitivity and specificity for the individual locations were similar to that for

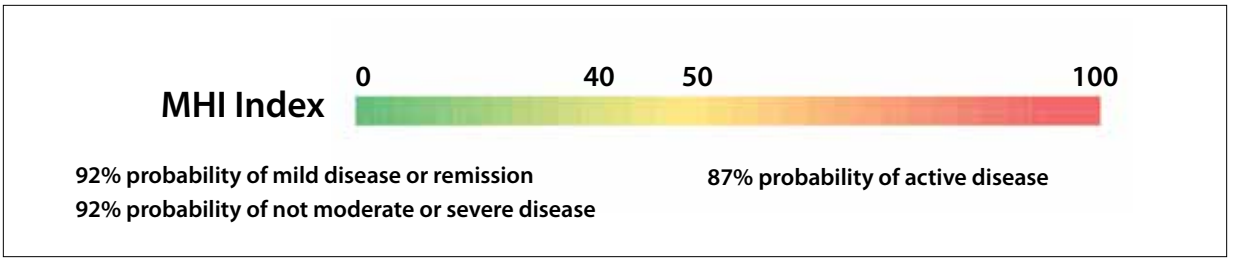

Figure 2. The Monitr test report includes a graphic representation of the patient's MHI score. A green zone indicates patients with no or mild disease, a gold zone indicates intermediate disease, and a red zone indicates moderate-to-severe disease activity. The biomarkers are combined in an algorithm to create an MHI score. MHI, mucosal healing index.

Adapted from Kelly OB et al. Abstract P2184 presented at: the World Congress of Gastroenterology at ACG2017; October 13-18, 2017; Orlando, FL.[2]

Table 2. Diagnostic Performance Is Comparable Across Anatomic Disease Locations

	All Patients (TAILORIX) (N=412[a])	Ileal Only (n=96)	Ileocolonic (n=244)	Colonic Only (n=72)
Patients (n [%])	118 (100%)	27 (22.9%)	71 (60.2%)	20 (16.9%)
Accuracy	90% (95% CI, 87%-93%)	95% (95% CI, 88%-99%)	90% (95% CI, 85%-94%)	87% (95% CI, 77%-94%)
Sensitivity	82% (95% CI, 75%-89%)	86% (95% CI, 65%-97%)	80% (95% CI, 69%-89%)	89% (95% CI, 67%-99%)
Specificity	94% (95% CI, 91%-97%)	98% (95% CI, 91%-100%)	95% (95% CI, 90%-98%)	86% (95% CI, 73%-95%)
PPV	87% (95% CI, 80%-93%)	95% (95% CI, 73%-99%)	89% (95% CI, 80%-94%)	74% (95% CI, 57%-86%)
NPV	92% (95% CI, 88%-95%)	95% (95% CI, 87%-98%)	90% (95% CI, 85%-94%)	95% (95% CI, 84%-99%)

[a]The numbers in this row represent blood samples. NPV, negative predictive value; PPV, positive predictive value; TAILORIX, Study Investigating Tailored Treatment With Infliximab for Active Crohn's Disease. Adapted from Vermeire S et al. Abstract 74 presented at: the World Congress of Gastroenterology at ACG2017; October 13-18, 2017; Orlando, FL.[1]

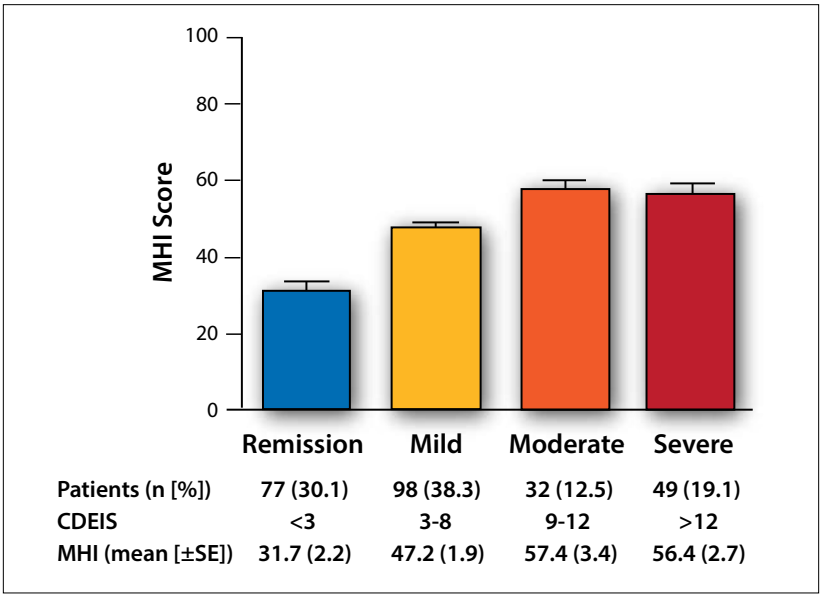

Figure 3. MHI scores correlate with the severity of endoscopic disease. CDEIS, Crohn's Disease Endoscopic Index of Severity; MHI, mucosal healing index; SE, standard error. Adapted from Dulai PS et al. Abstract P2142 presented at: the World Congress of Gastroenterology at ACG2017; October 13-18, 2017; Orlando, FL.[7]

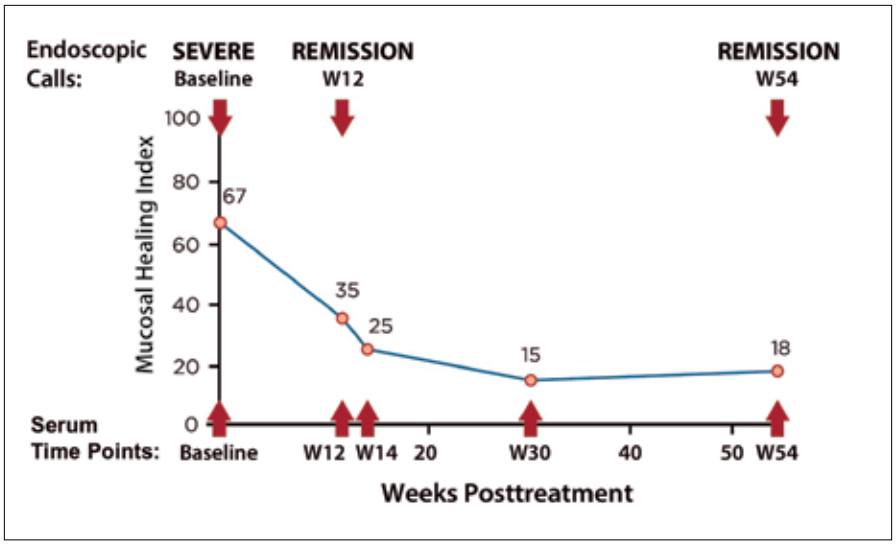

Figure 4. The MHI can be used to monitor a CD patient's response to treatment over time. CD, Crohn's disease; MHI, mucosal healing index; W, week. Adapted from Vermeire S et al. Abstract 74 presented at: the World Congress of Gastroenterology at ACG2017; October 13-18, 2017; Orlando, FL.[1]

the population overall, indicating that the test is not influenced by disease location.

MHI scores have been shown to correlate with endoscopic disease severity (Figure 3). In an analysis of the Monitr test that focused on the efficacy of biologic and nonbiologic therapies, the mean MHI values demonstrated a positive correlation with increasing endoscopic disease severity ($P<.0001$).[7] The mean MHI values were 31.7 among patients in remission, 47.2 in those with mild disease, 57.4 in those with moderate disease, and 56.4 in those with severe disease, and there was no significant difference between biologic exposed or nonexposed individuals.[7]

The study evaluating the predictive value of Monitr showed that the patients' MHI score changed throughout the weeks after treatment (Figure 4). The test can therefore be used to monitor patients with Crohn's disease over time.[6] Changes in the MHI score can offer insight into the patient's disease severity.

Conclusion

Monitr offers a noninvasive, comprehensive evaluation of biomarkers measured in the serum. The test can be used to assess baseline disease activity and response to therapy over time by following a patient with repeated measurements. Monitr could potentially be an adjunct to endoscopy, with testing at the same time as endoscopy, to provide a benchmark, and as a monitoring method thereafter.[8] Monitr test results are easily conveyed among physicians and to the patient.

Until now, the only biomarkers in inflammatory bowel disease were fecal calprotectin and C-reactive protein, both of which displayed limitations when used to assess mucosal healing.[6,7] The test appears to be especially beneficial for small bowel disease because it can be difficult to access the ileum.[9] In addition, Monitr minimizes the need for repeated endoscopic and radiologic procedures.[9,10] This test is a welcome addition and merits further exploration in the clinical space to optimize use.

Disclosure

Dr Dubinsky is a consultant for Prometheus Laboratories Inc.

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Clinical Use of a Noninvasive Test to Assess Mucosal Healing in Crohn's Disease

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As a newly launched test, the best use of Monitr in clinical practice is still under investigation.[1] However, the test will likely be ordered initially alongside an endoscopy, to see if results from both tests are confirmatory.[1-3] The validation of this test showed a 90% concordance rate with endoscopy. Monitr can then be used to monitor the effect of therapy between endoscopic procedures.[1] For example, a baseline value can be compared with results from 2 or 3 months later. The Monitr test can provide an indication of how the disease is changing. This monitoring could be used in the context of several types of therapies, such as corticosteroids, immunosuppressive agents, and biologic agents.[2]

Monitr is not meant to completely replace endoscopy.[2,3] It will likely be ordered with colonoscopy, in patients about to undergo a change in therapy or another intervention.[2] The test can be used for periodic monitoring, perhaps every 3 to 6 months at the discretion of the physician, or until another colonoscopy is performed 6 to 12 months later.[1] Decreasing the amount of colonoscopy procedures is appealing to patients.

The test offers a clear assessment for patients in mild remission and those with active disease.[1,4] Test results in the intermediate zone—with an MHI score between 40 and 50—still have an observed 78% probability of active disease, as compared with an 87% probability of active disease among patients with an MHI score in the high zone (from 50 to 100).

Assessment of Mucosal Healing Over Time

An important question in the field is how to assess mucosal healing status over time, and how monitoring should impact the decision to continue anti-TNF alpha agents and other therapies.[2,5] In addition, there is the question of when to withdraw anti-TNF therapy in patients who appear to be in remission.[5] Patients who are in clinical remission may still have endoscopic disease.[3,6] If the patient has endoscopic remission and clinical disease remission, some physicians believe that it is reasonable to withdraw anti-TNF therapy. Other physicians, however, believe that anti-TNF therapy should not be stopped, even in the case of a deep remission.[5]

It appears that the Monitr test reflects endoscopic healing.[1] If a patient receiving anti-TNF therapy achieves clinical remission, then the Monitr test should be used. If the test indicates that the patient likely has mucosal healing, then anti-TNF therapy may no longer be needed.[5] This approach makes sense for physicians who believe it is reasonable to withdraw anti-TNF therapy in the context of endoscopic remission. In this setting, monitoring for relapse is important, and regular colonoscopies can be replaced with Monitr testing.

In contrast, some physicians continue anti-TNF therapy in patients who are responding well, unless toxicity occurs.[7-9] In this setting, the Monitr test can verify that the treatment goal—endoscopic remission—was met.[3,10] The patient would continue with anti-TNF therapy, in the absence of toxicity.[7]

Use of Therapeutic Drug Monitoring

Therapeutic drug monitoring and Monitr testing are complementary tests that could be ordered together to identify a need to change therapy and to inform other management decisions. Therapeutic drug monitoring shows the level of drug in a patient's blood, and, in the case of biologics, it can also assess the levels of anti-drug antibodies.[8] Therapeutic drug monitoring is used for patients treated with any immunosuppressive or biologic agent, such as azathioprine, mercaptopurine, anti-TNF therapy, vedolizumab, and ustekinumab.[8,11-13] If the drug

concentration is subtherapeutic, and there are antibodies present, a new therapy could be considered.[8] If the drug concentration is therapeutic, it will then be necessary to switch the patient to a new class of medication. It will then be necessary to know whether the symptoms are caused by active inflammatory disease or other causes, a common scenario in patients with Crohn's disease. The Monitr test can indicate whether the patient has active disease in the context of his or her symptoms.[1]

Conclusion

Monitr will likely be used to evaluate patients at certain time points in between colonoscopy procedures. Patients appear to appreciate use of this test to decrease the number of colonoscopies they must undergo. Given the many possible uses for Monitr, it will be interesting to see how it will be employed across different clinical settings.

Disclosure

Dr Sandborn has received consulting fees from or performed contracted research for Janssen, AbbVie, UCB Pharma, Takeda, Pfizer, Amgen, Genentech, Receptos, Actavis, Shire, Salix, and Prometheus Laboratories Inc.

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Mucosal Healing in Crohn's Disease

In Crohn's disease, mucosal healing is linked to the most important patient outcomes:

- Avoidance of surgery
- Avoidance of hospitalization
- Maintenance of a high quality of life

How to Define Mucosal Healing

Mucosal healing can be defined in various ways:

- Endoscopy enables the gastroenterologist to examine the mucosa and to obtain biopsies that can be evaluated microscopically for inflammation
- Histologic assessment can confirm the absence of inflammatory cells in an area of previous involvement
- Serum testing of biomarkers

Treat-to-Target

- The phase 3 CALM study[1]
  - In the control arm, changes in a patient's medication were based solely on clinical symptoms
  - In the treat-to-target arm, changes in medication were based on clinical symptoms, as well as biochemical markers of inflammation. These patients underwent testing for levels of fecal calprotectin and C-reactive protein
  - The study found that patients in the treat-to-target group had better outcomes than the control patients

1. Colombel JF et al. Lancet. 2018;390(10114):2779-2789.

The Monitr Test

- The Monitr test analyzes biomarkers in a patient's peripheral blood to assess mucosal healing[1,2]
- Mucosal alterations involve particular pathways that mediate cell adhesion, inflammation, angiogenesis, matrix remodeling, growth factors, and immune recruitment modulation[1-3]
- These pathways are associated with mucosal damage in patients with Crohn's disease, and they were used to identify 13 biomarkers that are analyzed by the Monitr test[2]

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The Mucosal Healing Index Score

- The biomarkers that are assessed with the Monitr test are combined in an algorithm that results in the mucosal healing index score, which ranges from 0 to 100[1]
- A panel of serum biomarkers was used to train a logistic regression model against visualized endoscopic disease severity, with the latter determined by either CDEIS or SES-CD scores
- A validation cohort showed a 90% concordance rate between the mucosal healing index and endoscopically visualized mucosal inflammation

CDEIS, Crohn's Disease Endoscopic Index of Severity; SES-CD, simple endoscopic score for Crohn's disease.
1. Kelly OB et al. WCOG abstract P2186. Paper presented at: World Congress of Gastroenterology at ACG2017. Orlando, FL; October 13-18, 2017.

Therapeutic Drug Monitoring and Monitr Testing

- Therapeutic drug monitoring and Monitr testing are complementary tests that could be ordered together to identify a need to change therapy and to inform other management decisions
- Therapeutic drug monitoring shows the level of drug in a patient's blood, and, in the case of biologics, it can also assess the levels of anti-drug antibodies
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