EDITORIAL

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Fecal Immunochemical Test and Fecal Calprotectin Measurement Are Noninvasive Monitoring Tools for Predicting Endoscopic Activity in Patients with Ulcerative Colitis

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See "Fecal Immunochemical Test and Fecal Calprotectin Results Show Different Profiles in Disease Monitoring for Ulcerative Colitis" by Sakiko Hiraoka, et al. on page 142, Vol. 12. No. 2, 2018

Mucosal healing (MH) has been considered as the target in the treatment of inflammatory bowel disease (IBD) based on the observation that MH is associated with improved clinical outcomes reducing the risk of surgery, hospitalization, and steroid dependency.[1,2] However, endoscopic assessment, the gold standard for evaluating MH has several limitations in its clinical use because of its inconvenience, invasiveness, and high-cost, while symptom-based disease activity score has a quite discordance with MH.[3] Thus, need for reliable, noninvasive, surrogate markers precisely reflecting the mucosal status has fuelled interests in the use of fecal immunochemical test (FIT) and fecal calprotectin (Fcal) measurement. Although several IBD clinicians have used these markers as assistant tools for diagnosis, monitoring, and decision making for further invasive tests for years, there still remain controversies regarding "how to use fecal markers" in routine clinical practice.

In this issue of *Gut and Liver*, the article entitled "Fecal immunochemical test and fecal calprotectin results show different profiles in disease monitoring for ulcerative colitis"[4] sought to determine the best choice of fecal markers in real clinical practice by evaluating changes in the values of each marker based on the findings of consecutive colonoscopies in patients with ulcerative colitis (UC). A total of 110 colonoscopy intervals from 84 patients were identified and the data of fecal samples which were collected within 2 days before colonoscopy were evaluated. This study adopted cutoff values of FIT and Fcal as 100 ng/mL, and 180 μg/g, respectively, and defined MH as Mayo endoscopic subscore of 0 throughout the entire colon. Interestingly, changes of fecal marker levels were found to have different patterns according to the presence or absence of mucosal inflammation in the precedent colonoscopy. FIT had an advantage in predicting the results of subsequent colonoscopic examinations in patients with MH and a negative FIT result at the precedent examination showed 93% of the overall accuracy compared with Fcal showing 79% of accuracy. On the other hand, Fcal measurement was superior in terms of reflecting the change in endoscopic activity than FIT ($r=0.59$, $p<0.0001$ vs $r=0.30$, $p=0.054$) in patients with a persistent high endoscopic activity. In addition, FIT was useful in predicting the achievement of MH after therapy in patients with active endoscopic inflammation at the precedent colonoscopy. The ratios of negative conversion of Fcal and FIT in these patients were 92% and 62%, respectively.

Fecal markers have been shown to be associated with endoscopic disease activity, treatment response, and prediction for relapse. Ma *et al*.[5] reported similar performance of FIT and Fcal in identifying MH in IBD patients by showing that positive predictive value (PPV) for FIT <100 ng/mL and Fcal ≤250 μg/g were 0.78 and 0.77, respectively, but better performance were observed in patients with UC, particularly for FIT (area under the curve, 0.88 vs 0.69, $p=0.05$). Ryu *et al*.[6] reported a positively correlation of FIT with endoscopic activity ($r=0.626$, $p<0.01$) and clinical activity ($r=0.496$, $p<0.01$) in patients with UC. Furthermore, Mooiweer *et al*.[7] confirmed the added value of Fcal over MH for predicting clinical relapse and Molander *et al*.[8] found a precedent increase of Fcal 6 months before clinical relapse in patients who discontinued anti-tumor necrosis factor

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therapy after achieving deep remission.

In accordance with previous studies, this study[4] enlarged our knowledge about the appropriate choice of fecal markers for disease monitoring at specific clinical situations of UC, and confirmed different values of the two markers, namely FIT as a surrogate measure of bleeding from mucosal ulceration, and Fcal as a surrogate measure of mucosal inflammation per se.[5] Based on these results, the authors proposed an algorithm for using fecal markers in specific situations. Fcal was recommended for the monitoring of treatment efficacy after induction therapy. On the other hand, FIT was recommended to monitor endoscopic disease activity after symptom improvement following induction therapy, and repetitively after achieving MH confirmed by colonoscopy due to its higher PPV for MH and low cost. A positive conversion of FIT during monitoring of stable patients aids in deciding further colonoscopy or additional treatment.

However, there are several limitations in using fecal markers in real practice. One of the major concerns regarding Fcal is its large variations in day-to-day, by time of day, and within the same bowel movement. Moreover, the ideal cutoff value has not yet been determined[9] and discrepancies between different Fcal kits are another problems.[10] Finally, high false positive rates of FIT require caution in the interpretation of results. Examinations of multiple samples in a serial manner are thought to reduce possible errors and could be more beneficial for monitoring disease activity.[6]

Now, it is clear that repeated measurements of FIT and Fcal are well correlated with endoscopic activity in UC, and they are able to predict the changes of mucosa in disease course. Therefore, this study is meaningful in terms of suggesting typical fecal markers in specific situations in real clinical practice. Further studies are required to demonstrate whether modifications in medical treatments according to the results of fecal markers ultimately could alter the long-term disease outcomes.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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