

EFFECTIVE DATE: 10|01|2015

POLICY LAST UPDATED: 10|07|2016

OVERVIEW

Fecal calprotectin is a calcium and zinc-binding protein that is a potential marker of intestinal inflammation. Fecal calprotectin testing is proposed as a noninvasive test to diagnose inflammatory bowel disease (IBD). Other potential uses are to evaluate response to treatment for patients with IBD and as a marker of relapse.

MEDICAL CRITERIA

None

PRIOR AUTHORIZATION

Prior authorization is not required.

POLICY STATEMENT

Fecal calprotectin testing is considered not medically necessary in the diagnosis and management of intestinal conditions, including the diagnosis and management of inflammatory bowel disease as there is insufficient peer-reviewed literature that demonstrates that the procedure/service is effective.

COVERAGE

Benefits may vary between groups/contracts. Please refer to the appropriate Evidence of Coverage or Subscriber Agreement for limitations of benefits/coverage when services are not medically necessary.

BACKGROUND

IBD is a chronic inflammatory condition typically associated with the symptoms of diarrhea, defecation urgency, and sometimes rectal bleeding and abdominal pain. There are 2 main forms of the disorder, Crohn disease (CD) and ulcerative colitis (UC). Noninvasive diagnosis of inflammatory intestinal disease is difficult because the clinical manifestation of intestinal disorders and colon cancer are relatively nonspecific. For example, a patient presenting with diarrhea or abdominal pain has a wide range of diagnostic possibilities. Endoscopy with histology is the criterion standard method for diagnosing bowel inflammation. Limitations of this approach are that it is invasive, with an associated risk of adverse events, and not well tolerated by some patients.

Thus, there is the need for simple, accurate, noninvasive tests to detect intestinal inflammation. Potential noninvasive markers of inflammation fall into several categories including serologic and fecal. Serologic markers such as C-reactive protein and antineutrophil cytoplasmic antibodies tend to have low sensitivity and specificity for intestinal inflammation because they are affected by inflammation outside of the gastrointestinal (GI) tract. Fecal markers, in contrast, have the potential for being more specific to the diagnosis of GI tract disorders, because their levels are not elevated in extradigestive processes. Fecal leukocyte testing has been used to evaluate whether there is intestinal mucosal inflammation. The level of fecal leukocytes can be determined by the microscopic examination of fecal specimens; however, leukocytes are unstable and must be evaluated promptly by skilled personnel. There is interest in identifying stable proteins in stool specimens, which may be representative of the presence of leukocytes, rather than evaluating leukocyte levels directly.

Fecal calprotectin is 1 protein that could possibly be used as a marker of inflammation. It is a calcium- and zinc-binding protein that accounts for approximately 60% of the neutrophils' cytoplasmic proteins. It is released from neutrophils during activation or apoptosis/necrosis and has a role in regulating inflammatory

processes. In addition to potentially higher sensitivity and specificity than serologic markers, another advantage of fecal calprotectin as a marker is that it has been shown to be stable in feces at room temperature for up to 1 week, leaving enough time for patients to collect samples at home and send them to a distant laboratory for testing. In contrast, lactoferrin, also a potential fecal marker of intestinal inflammation, is stable at room temperature for only about 2 days.

Potential disadvantages of fecal calprotectin as a marker of inflammation include that fecal calprotectin levels increase after use of nonsteroidal anti-inflammatory drugs, that levels may change with age, and that bleeding (e.g., nasal, menstrual) may cause an elevated fecal calprotectin level. Moreover, there is uncertainty about the optimal cutoff to use to distinguish between IBD and noninflammatory disease.

Fecal calprotectin testing has been used to differentiate between organic and functional intestinal disease. Some authors consider fecal calprotectin to be a marker of neutrophilic intestinal inflammation rather than a marker of organic disease and believe the appropriate use of the marker is in its use to distinguish between IBD and non-IBD. In practice, the test might be suitable for selecting patients with IBD symptoms for endoscopy, i.e., deciding which patients do not require endoscopy. Fecal calprotectin testing has also been proposed to evaluate the response to IBD treatment and for predicting relapse. If found to be sufficiently accurate, results of calprotectin testing could potentially be used to change treatment, such as adjusting medication levels.

There is a commercially available enzyme-linked immunosorbent assay test measuring fecal calprotectin levels, the PhiCal™ (Genova Diagnostics). Recent literature from Europe and Canada has also discussed a rapid test for fecal calprotectin that could be used in the home or doctor's office. At least 1 product, the BÜHLMANN Quantum Blue® Calprotectin Rapid Test, is being marketed outside of the United States; rapid tests have not been U.S. Food and Drug Administration (FDA) approved for use in the U.S.

CODING

BlueCHiP for Medicare and Commercial Products

83993: Calprotectin, fecal

RELATED POLICIES

None

PUBLISHED

Provider Update, January 2017

Provider Update, August 2015

REFERENCES

1. FDA. PhiCal 510(k) Substantial Equivalence Determine Decision Summary. Available online at: http://www.accessdata.fda.gov/cdrh_docs/reviews/K050007.pdf. Last accessed March, 2014.
2. Waugh N, Cummins E, Royle P et al. Faecal calprotectin testing for differentiating amongst inflammatory and non-IBDs: systematic review and economic evaluation. *Health Technol Assess* 2013; 17(55):xv-xix, 1-211.
3. van Rheenen PF, Van de Vijver E, Fidler V. Faecal calprotectin for screening of patients with suspected IBD: diagnostic meta-analysis. *BMJ* 2010; 341:c3369.
4. von Roon A C., Karamountzos L., Purkayastha S. et al. Diagnostic precision of fecal calprotectin for IBD and colorectal malignancy. *Am J Gastroenterol* 2007; 102(4):803-13.
5. Henderson P, Anderson NH, Wilson DC. The Diagnostic Accuracy of Fecal Calprotectin During the Investigation of Suspected Pediatric IBD: A Systematic Review and Meta-Analysis. *Am J Gastroenterol* 2013.

6. Kostakis ID, Cholidou KG, Vaiopoulos AG et al. Fecal Calprotectin in Pediatric IBD: A Systematic Review. *Dig Dis Sci* 2012.
7. Manz M, Burri E, Rothen C et al. Value of fecal calprotectin in the evaluation of patients with abdominal discomfort: an observational study. *BMC Gastroenterol* 2012; 12:5.
8. Otten CM, Kok L, Witteman BJ et al. Diagnostic performance of rapid tests for detection of fecal calprotectin and lactoferrin and their ability to discriminate inflammatory from irritable bowel syndrome. *Clin Chem Lab Med* 2008; 46(9):1275-80.
9. Schroder O, Naumann M, Shastri Y et al. Prospective evaluation of faecal neutrophil-derived proteins in identifying intestinal inflammation: combination of parameters does not improve diagnostic accuracy of calprotectin. *Aliment Pharmacol Ther* 2007; 26(7):1035-42.
10. Sidler MA, Leach ST, Day AS. Fecal S100A12 and fecal calprotectin as noninvasive markers for IBD in children. *Inflamm Bowel Dis* 2008; 14(3):359-66.
11. Ashorn S, Honkanen T, Kolho KL et al. Fecal calprotectin levels and serological responses to microbial antigens among children and adolescents with IBD. *Inflamm Bowel Dis* 2009; 15(2):199-205.
12. Turner D, Leach ST, Mack D et al. Faecal calprotectin, lactoferrin, M2-pyruvate kinase and S100A12 in severe UC: a prospective multicentre comparison of predicting outcomes and monitoring response. *Gut* 2010; 59(9):1207-12.
13. Molander P, af Bjorkesten CG, Mustonen H et al. Fecal calprotectin concentration predicts outcome in IBD after induction therapy with TNFalpha blocking agents. *Inflamm Bowel Dis* 2012; 18(11):2011-7.
14. Wagner M, Peterson CG, Ridefelt P et al. Fecal markers of inflammation used as surrogate markers for treatment outcome in relapsing IBD. *World J Gastroenterol* 2008; 14(36):5584-9; discussion 88.
15. Mao R, Xiao YL, Gao X et al. Fecal calprotectin in predicting relapse of IBDs: a meta-analysis of prospective studies. *Inflamm Bowel Dis* 2012; 18(10):1894-9.
16. Yamamoto T, Shiraki M, Bamba T et al. Fecal calprotectin and lactoferrin as predictors of relapse in patients with quiescent UC during maintenance therapy. *Int J Colorectal Dis* 2013.
17. Lasson A, Simren M, Stotzer PO et al. Fecal Calprotectin Levels Predict the Clinical Course in Patients With New Onset of UC. *Inflamm Bowel Dis* 2013.
18. Gisbert JP, Bermejo F, Perez-Calle JL et al. Fecal calprotectin and lactoferrin for the prediction of IBD relapse. *Inflamm Bowel Dis* 2009; 15(8):1190-8

CLICK THE ENVELOPE ICON BELOW TO SUBMIT COMMENTS

