Diagnostic Tests

What Physicians Need to Know

Fecal Calprotectin for the Evaluation of Inflammatory Bowel Disease

Carl Bryce, MD, FAAFP, and Merima Bucaj, DO, FAAFP

Abrazo Family Medicine Residency, Phoenix, Arizona

Calprotectin is a protein expressed by neutrophils. The presence of fecal calprotectin is a sensitive indicator of gastrointestinal inflammation, with higher levels representing more inflammation. The U.S. Food and Drug Administration has approved the use of fecal calprotectin testing to aid in the diagnosis of inflammatory bowel disease (IBD) in adults and children presenting with gastrointestinal symptoms, and differentiating IBD from irritable bowel syndrome.[1]

Test	Indication	Population	Cost*
Fecal calprotectin	Diagnosis of inflammatory bowel disease	Patients with symptoms suggestive of inflammatory bowel disease vs. irritable bowel syndrome	$19.63

*—Payment rate according to the 2021 Centers for Medicare and Medicaid Services clinical laboratory fee schedule.[5]

Accuracy

The manufacturer of the fecal calprotectin assay proposes a diagnostic threshold of greater than 50 mcg per g for the diagnosis of IBD. A systematic review of 19 diagnostic accuracy studies, which included 5,032 patients older than 16 years, examined the diagnostic performance of a fecal calprotectin assay compared with the reference standard of diagnostic colonoscopy. The pooled sensitivity and specificity for IBD were 0.88 (95% CI, 0.83 to 0.92) and 0.80 (95% CI, 0.69 to 0.88), respectively.[2]

In two prospective cohorts of children in the Netherlands with chronic diarrhea, recurring abdominal pain, or both, fecal calprotectin testing was compared with one of two reference standards: endoscopy or 12 months of clinical follow-up without an IBD diagnosis.[3] The standard of clinical follow-up was added by the authors of the study because of concerns that performing an invasive procedure in a large number of children with a low likelihood of organic gastrointestinal disease would be unethical. In a group of 114 patients initially seen in primary care, 13 tested positive using a calprotectin cutoff of greater than 50 mcg per g (although none of them had IBD), yielding a specificity of 0.87 (95% CI, 0.80 to 0.92). In 85 patients referred to a specialist, fecal calprotectin testing had a sensitivity of 1.00 (95% CI, 0.81 to 1.00) and a specificity of 0.84 (95% CI, 0.74 to 0.91).[3]

The diagnosis of IBD is unlikely in adults and children with a normal fecal calprotectin value of less than 50 mcg per g because of its high sensitivity and negative predictive value.[2,3] In children with symptoms suggestive of IBD, a combination of an increased fecal calprotectin threshold of greater than 250 mcg per g, C-reactive protein greater than 1 mg per dL (10 mg per L), and hemoglobin less than two standard deviations below the mean for age and sex increased the specificity to 0.97 (helping avoid unnecessary endoscopy), whereas sensitivity remained 100%.[4]

Benefit

A normal fecal calprotectin level could assist in the diagnostic evaluation of a patient who might otherwise have been referred for endoscopy because many of these patients will not have IBD.

This series is coordinated by Kenny Lin, MD, MPH, deputy editor.

A collection of Diagnostic Tests published in *AFP* is available at https://www.aafp.org/afp/diagnostic.

Author disclosure: No relevant financial affiliations.

Harms

A false-negative fecal calprotectin result in a patient with IBD could lead to a delay in diagnosis, persistence of symptoms, or additional complications of uncontrolled disease. This test is not appropriate for patients who are highly likely to have IBD based on the history and physical examination. A delayed diagnosis may be more harmful in children and adolescents than in adults.

The relatively low specificity of fecal calprotectin testing for IBD in adults means that false-positive results may be common, leading to potentially unnecessary colonoscopies. Other inflammatory diseases of the gastrointestinal tract that could cause false-positives include gastric or colorectal cancer, lymphoma, autoimmune enteropathy, diverticular disease, and microscopic or infectious colitis. However, endoscopic evaluation would likely be beneficial by improving appropriate diagnosis and treatment.

Cost

The reimbursement rate for a fecal calprotectin test is $19.63 according to the 2021 Centers for Medicare and Medicaid Services clinical laboratory fee schedule.[5] Because the direct and indirect costs of endoscopy are substantially higher, there is potential benefit to using fecal calprotectin testing for diagnostic triage before referring for endoscopy. With a high negative predictive value, fecal calprotectin testing can prevent the unnecessary use of endoscopy and is cost-effective when the pretest probability of IBD is less than 75% for adults and less than 65% for children, which is often the case in primary care.[6]

Bottom Line

Fecal calprotectin measurement is an accurate, simple, cost-effective test that can aid in selecting which patients presenting with possible IBD can be safely observed in the primary care setting. The threshold for an abnormal test is greater than 50 mcg per g in adults. A threshold greater than 250 mcg per g, combined with other blood tests, improves the specificity for diagnosing IBD in children.

Address correspondence to Carl Bryce, MD, FAAFP, at carl.bryce@abrazohealth.com. Reprints are not available from the authors.

References

1. U.S. Food and Drug Administration. Title 21, volume 8. Part 866—immunology and microbiology devices, subpart F—immunological test systems, sec. 866.5180 fecal calprotectin immunological test system. April 1, 2020. Accessed February 18, 2021. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=866.5180
2. Petryszyn P, Staniak A, Wolosianska A, et al. Faecal calprotectin as a diagnostic marker of inflammatory bowel disease in patients with gastrointestinal symptoms: meta-analysis. *Eur J Gastroenterol Hepatol*. 2019;31(11):1306-1312.
3. Holtman GA, Lisman-van Leeuwen Y, Kollen BJ, et al. Diagnostic accuracy of fecal calprotectin for pediatric inflammatory bowel disease in primary care: a prospective cohort study. *Ann Fam Med*. 2016;14(5):437-445.
4. Van de Vijver E, Heida A, Ioannou S, et al.; CACATU CONSORTIUM. Test strategies to predict inflammatory bowel disease among children with nonbloody diarrhea. *Pediatrics*. 2020;146(2):e20192235.
5. Centers for Medicare and Medicaid Services. 21CLABQ1. Item #83993. Accessed February 26, 2021. https://www.cms.gov/medicaremedicare-fee-service-paymentclinicallabfeeschedclinical-laboratory-fee-schedule-files/21clabq1
6. Yang Z, Clark N, Park KT. Effectiveness and cost-effectiveness of measuring fecal calprotectin in diagnosis of inflammatory bowel disease in adults and children. *Clin Gastroenterol Hepatol*. 2014;12(2):253-262.e2. ■