Fecal Occult Blood Testing in Hospitalized Patients with Upper Gastrointestinal Bleeding

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The "Things We Do for No Reason" (TWDFNR) series reviews practices which have become common parts of hospital care but which may provide little value to our patients. Practices reviewed in the TWDFNR series do not represent "black and white" conclusions or clinical practice standards, but are meant as a starting place for research and active discussions among hospitalists and patients. We invite you to be part of that discussion.

CASE REPORT

A 47-year-old man with a history of alcohol abuse, cirrhosis, and grade II esophageal varices is admitted for treatment of alcohol withdrawal. He reports having some dark-colored stools a week prior to admission, but his stools since then have been normal in color. A repeat hemoglobin is stable, but a fecal occult blood test is positive. What should be done next?

BACKGROUND

The US Preventive Services Task Force and the American College of Gastroenterology recommend fecal occult blood testing (FOBT) as one method for colorectal cancer (CRC) screening in average risk populations.[1,2] FOBTs can be divided into guaiac-based tests (gFOBTs), which measure heme, and fecal immunochemical tests (FITs), which measure the globin portion of human hemoglobin (Hb). In gFOBTs, heme present in the sample reacts with a hydrogen peroxide developer to oxidize guaiac, producing a blue color.[3] Screening gFOBT was shown to decrease mortality from CRC in several landmark studies in the 1990s, but its sensitivity is poor, ranging from 30% to 57%.[4] Because the guaiac-induced color change is determined visually, interpretation of gFOBT results are subject to error. In a survey of 173 medical providers, 12% did not accurately interpret gFOBT results.[5] In light of these limitations, recent guidelines support the use of newer FITs for CRC screening. FITs utilize antibodies directed against the human globin moiety and demonstrate an increased sensitivity when compared with gFOBTs (by 32% to 62%) for detecting neoplasm.[6] While evidence supports the use of FOBTs in CRC screening, providers use these tests for nonvalidated purposes, including the evaluation of suspected acute upper gastrointestinal bleeding (UGIB).

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Received: July 19, 2016; **Revised:** November 4, 2016; **Accepted:** November 10, 2016

2017 Society of Hospital Medicine DOI 10.12788/jhm.2773

WHY YOU MIGHT THINK FOBT IS HELPFUL FOR EVALUATION OF INPATIENTS WITH SUSPECTED ACUTE UGIB

Given the incidence (up to 100 per 100,000 persons per year) and high mortality of UGIB (up to 20,000 deaths annually in the United States),[7] there would ideally be a noninvasive test available to help guide management. In evaluating a patient with possible acute UGIB, FOBT affords several theoretical benefits. FOBT is quick, inexpensive, and can be performed by any health professional. In contrast, the primary diagnostic procedure for UGIB, esophagogastroduodenoscopy (EGD), carries procedural and sedation-related risks, can be costly and time-consuming, and requires consultation from subspecialty providers.

WHY FOBT IS NOT HELPFUL FOR EVALUATION OF INPATIENTS WITH SUSPECTED ACUTE UGIB

While FOBTs are valuable as screening tests for CRC in the outpatient setting, their use has been extended to diagnose gastrointestinal (GI) bleeding in the inpatient setting without supporting data. As is true for many screening tests, FOBT is associated with a high incidence of false-positive results, or type I errors.[8,9] False-positive FOBT results can occur from ingested blood via extra-intestinal sources (eg, epistaxis, gingival bleeding, pharyngitis, hemoptysis), or in medical conditions with intestinal mucosal inflammation (eg, esophagitis, gastritis, inflammatory bowel disease). False-positive results can also be due to clinically insignificant GI blood loss induced by medications (eg, aspirin, nonsteroidal anti-inflammatory drugs), alcohol,[10] or by ingestion of meats, fruits, or vegetables containing peroxidase (eg, broccoli, cauliflower).[11]

Outpatients using FOBTs for cancer screening are advised to hold medications and avoid foods that may lead to false-positive results. Despite institution of these restrictions, false-positive rates are still high, as 37% to 53% of CRC screening patients with a positive FOBT have a subsequent negative colonoscopy, and only 11% to 21% of these patients have a source of bleeding identified on subsequent EGD.[12] False-positive results might be even higher in the inpatient setting, where patients typically do not adhere to these restrictions. A review of FOBTs performed in 3 acute care hospitals revealed that 65% of patients tested were on

TABLE. Causes of Inaccurate Fecal Occult Blood Test Results

	gFOBT	FIT
False-Positive Results	Ingestion of nonhuman heme (eg, meat products) Ingestion of peroxidases (eg, broccoli) Ingestion of non-GI blood (eg, epistaxis) Use of aspirin, NSAIDs, or anticoagulant medication	Use of aspirin, NSAIDs, or anticoagulant medication
False-Negative Results	Ingestion of antioxidants (eg, Vitamin C)	Bleeding from the upper GI or proximal lower GI tracts
Additional Considerations	Potential for visual misinterpretation Low sensitivity (requires multiple samples)	Potential for visual misinterpretation (qualitative tests only) Varying test characteristics depending on manufacturer

NOTE: Abbreviations: FIT, fecal immunochemical test; FOBT, fecal occult blood testing; gFOBT, guaiac-based FOBT; GI, gastrointestinal; NSAIDs, nonsteroidal anti-inflammatory drugs.

at least one medication that impacted the validity of gFOBT results, and 98% had no evidence of dietary restriction prior to testing.[13]

The use of FOBTs (particularly FITs) is also subject to false-negative results, or type II errors. While FITs have increased specificity for lower GI bleeding, their ability to detect UGIB is limited, because most Hb is digested in the small intestine and not present in rectal stool.[14] In a study of more than 2,700 patients, FIT results were not correlated with the presence of upper GI pathology.[15] False-negative results are less common with gFOBTs, although these may occur with low volume, slow or intermittent bleeding,[16] or with ingestion of substances that inhibit oxidation, such as vitamin C.[17]

Beyond these test limitations, studies suggest that the majority of inpatient FOBT results do not impact immediate medical decision-making or management. In one study, only 34% of hospitalized patients with a positive FOBT underwent further GI studies, with the majority of those patients (60%) receiving endoscopy before the results of the FOBT were known.[18] In another study of 201 FOBTs performed on hospitalized patients, those with negative results underwent further GI evaluation at a higher rate than those with positive results (41% vs 38%).[8] This aligns with a study that revealed the majority of patients suspected of having a GI bleed underwent endoscopic evaluation regardless of the FOBT result.[9]

WHEN MIGHT FOBT BE HELPFUL?

FOBT currently has a role in CRC screening and may have a role in the evaluation of anemia of unknown etiology to evaluate for occult GIB, although the yield is likely low.[13] In one retrospective analysis of inpatients with unexplained anemia, 43.6% of FOBTs were positive, but a potential GI cause was found in only 6.8% of patients.[9] Patients with anemia from an unknown etiology should have a workup based on the history, physical, and complete blood count indices. While iron deficiency anemia warrants eventual evaluation for occult blood loss, noncritical anemia in an otherwise stable patient does not require an inpatient evaluation. When FOBT is used in the outpatient setting, patients can be counseled on proper dietary and medication modifications prior to testing.

WHAT WE SHOULD DO INSTEAD

A careful history, physical examination, and visual inspection of the stool remain the foundation of establishing UGIB as the etiology of anemia. Observed melena (either by passed stool or a rectal examination) has a likelihood ratio (LR) of 25 for UGIB; a patient's self-report of stools that sounds melenic (black or tarry) has an LR of 5-6.[19] An upper GI source may be further supported by an elevated blood urea nitrogen (BUN) to creatinine ratio, as blood is absorbed through the small bowel and patients may have concomitant decreased renal perfusion. A BUN to creatinine ratio of >30 is associated with a positive LR (LR+) of 7.5 for UGIB.[19] Recall that the higher the LR+, and the lower the negative LR (LR-), the better the test is at ruling in and out the diagnosis, respectively. LR+ of 2–10 and LR− of 0.1–0.5 represent a modestly helpful diagnostic test, whereas LR+ >10 and LR- <0.1 are considered robust. These are generalizations only, as value of LR+/LR- depends on pretest probability.

Clinical decision tools, such as the Glasgow-Blatchford and Rockall scores, utilize the history, physical examination, laboratory results, and pretest probability for high-grade peptic ulcer stigmata to estimate the severity of an UGIB and risk for adverse outcomes, respectively. Notably, these scoring systems do not include FOBT results. Despite the relatively inexpensive cost per FOBT ($3.03 per unit),[20] this test's poor specificity when used in the inpatient setting has the potential to lead to significant, unnecessary downstream expense (as well as the potential for procedural risk and anxiety for patients). Given that the incidence of acute UGIB is approximately 100 per 100,000 persons per year,[7] based on the United States population in 2016,[21] there were 323,936 patients with UGIB. If each patient underwent an FOBT, the direct expense would be nearly a million dollars. Nonetheless, the number of patients getting a FOBT in the inpatient setting for a suspected UGIB (or for other indications) is unknown, and the direct costs of the tests itself likely represent a fraction of the healthcare expenditures associated with this practice. Allowing that only a third of patients with positive

FOBTs in the inpatient setting typically undergo EGD,[22] overuse of this test would lead to a high number of unnecessary EGDs, and potentially colonoscopies or additional diagnostic procedures (eg, capsule endoscopy). In light of the false-positive results associated with FOBT, and lack of diagnostic utility, this brief cost analysis suggests FOBT is a low-value test for suspected UGIB in the inpatient setting, and there are potential significant cost savings if FOBTs are withheld.

Although Gastroccult[23] may be considered for the detection of occult blood in gastric juice, its package insert states: "As with any occult blood test, results with the Gastroccult test cannot be considered conclusive evidence of the presence or absence of upper gastrointestinal bleeding or pathology." As with any diagnostic evaluation, we would only recommend this test if it would change management.

RECOMMENDATIONS

- FOBT should not be performed to diagnose UGIB.
- When there is clinical suspicion of acute GI bleeding, the best diagnostic tools are a good history, physical examination, and visual inspection of the stool by the clinician to determine the presence of hematochezia or melena.
- Deferring FOBT to the ambulatory setting may improve test performance characteristics.

CONCLUSION

Revisiting our patient, for all of the reasons discussed above, there is no indication for FOBT as it would not affect management. Based on a careful history and physical examination, our patient would likely require upper endoscopy either as an inpatient or an outpatient depending on his clinical course.

FOBT is validated as an outpatient colon cancer screening tool in asymptomatic patients, not for inpatient evaluation of acute GIB. Given the poor positive predictive value for a positive FOBT in an acute GIB scenario, the potential risk for unnecessary treatments or procedures is real. Conversely, a negative FOBT (particularly FIT) does not rule out GI bleeding and risks a false sense of security that may result in under-treatment. In most scenarios in which FOBT is performed, clinicians can make decisions based on a composite of history, physical exam, visual inspection of the stool, and laboratory investigation. Until further research substantiates the utility of FOBT for this purpose, we would recommend against the routine use of FOBT for evaluating UGIB in hospitalized patients.

Acknowledgment

The authors would like to thank and acknowledge the team from Orlando Health for their review of this manuscript.

Disclosure: The authors do not have any relevant financial disclosures to report. The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs.

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