

Fecal Occult Blood Tests for Colorectal Cancer Screening

Background Information

In the United States, colorectal cancer is the third most common cancer diagnosed among men and women and the second leading cause of death from cancer. Colorectal cancer can largely be prevented by the detection and removal of adenomatous polyps. Five-year survival is 90% if the disease is diagnosed while still localized, but only 68% for regional disease (disease with lymph node involvement) and only 10% if distant metastases are present.¹ In spite of this, a majority of U.S. adults are not receiving regular age- and risk-appropriate screening or have never been screened at all.² There is a range of options for colorectal cancer screening that includes stool testing for the presence of occult blood or exfoliated DNA, or structural examinations that include flexible sigmoidoscopy, colonoscopy, double contrast barium enema and CR-colonography. Beginning in 1980, the American Cancer Society first issued formal guidelines for colorectal cancer screening in average-risk individuals and these have been periodically updated, along with additional guidelines for high-risk individuals.³ Other organizations such as the American College of Radiology, U.S. Preventive Services Task Force and the U.S. Multi-Society Task Force on Colorectal Cancer have also issued recommendations. Collaborative efforts among these groups took place in 2008 to come to consensus and provide joint guidelines and recommendations.¹

Occult gastrointestinal bleeding refers to bleeding that is not apparent to the patient. It has traditionally been identified by tests that detect fecal blood or, if bleeding is sufficient, as iron deficiency anemia. A variety of fecal occult-blood (FOB) tests have been designed primarily to screen for colon cancer, including both guaiac-based (gFOB) and immunochemical-based stool tests (iFOBT or FIT). The likelihood that FOB tests will detect gastrointestinal blood is affected by the type of test utilized, anatomical level of bleeding (upper GI vs. colonic), stool transit time, stool mixing, intra-luminal hemoglobin degradation, and features intrinsic to bleeding lesions (i.e. irregular bleeding).⁴

Clinical Indications

There are two major reasons to detect occult blood in the stool, i.e., as a screen for colorectal cancer (as mentioned) or to detect upper or lower GI bleeding. In the outpatient settings, an immunochemical-based assay (iFOBT or FIT) will be used to detect fecal occult blood for colorectal cancer screenings. The three-part guaiac-based fecal occult blood test will no longer be available for screening. The single guaiac card (SENSA) will continue to be used for detection of bleeding (upper or lower GI bleeding). The iFOBT (FIT) cannot be used for detection of upper GI bleeding and should only be used as a colon cancer screen test. The HemaPrompt card (a guaiac-based POCT assay) was introduced in October 2009 for use as a point-of-care test for detection of upper and lower GI bleeding. It can be used in the Emergency Department and a few other clinical areas that have been granted POCT testing privileges; if colorectal cancer screening is the intended use of the occult blood test, though, even in these settings, the iFOBT is the preferred method because it is the more sensitive screen and only a single sample collection is required.

One of the main reasons for the change to iFOBT for colorectal cancer screening is due to the fact that the guaiac-based tests lack the sensitivity and specificity that can be seen with the iFOBT assays. In an early study of iFOBT assays, specimens obtained from 107 colorectal cancer subjects showed that the iFOB test had a 97% sensitivity for detection of colorectal cancer, as compared to a very sensitive guaiac-based test (Hemoccult Sensa) in which the sensitivity was 94%. The iFOBT also demonstrated greater sensitivity (76%) in detecting large adenomas as compared with guaiac-based tests in which the sensitivity was 42%. The specificity of the iFOBT was 97.8% as compared to 96.1% for the gFOB when 1,355 screening tests were performed. The authors concluded that the iFOBT provided the best combination of specificity and sensitivity.⁵ In a more recent study of performance characteristics for detecting cancer, the sensitivity of the iFOBT test was 81.8% vs. 64.3% with gFOB test.

Specificity for iFOBT was 96.9% and 97.3%, respectively, for detecting cancer and adenomas vs. 90% and 90.6% with gFOB. For the detection of large polyps, the sensitivity of the gFOB was actually higher than that with iFOBT in this study.⁶ In a recent study out of Seoul, Korea, a population of average risk individuals (770 patients from four centers) undergoing colorectal cancer screening were assayed for occult blood comparing a gFOB to an iFOB. The iFOBT provided a higher sensitivity for detecting cancer and advanced colorectal neoplasia than the gFOB and had an acceptable specificity that could significantly reduce the need for colonoscopic evaluation of the screened population.⁷ An editorial in the same issue of the journal from Seoul suggested that the data supported an effort to increase use of iFOBT assays in the U.S. and publishing of studies in average-risk individuals here as well.⁸

Secondly, various foods and exogenous substances can yield false positive guaiac-based FOB test results. Vitamin C in excess of 250 mg/day from all sources (dietary and supplemental) can oxidize guaiac. False positive guaiac-based test results can also occur with excess dietary red meat (beef, lamb, processed meat, liver) or plant peroxidases contained in raw fruits and vegetables (especially radishes, turnips, horseradish, cantaloupes and other melons.) Such foods should be avoided for 72 hours prior to testing. GI bleeding can be induced by alcohol, and also has well-known iatrogenic causes, such as steroids and NSAIDs.⁹ The iFOBT assays detect human globin, a protein that along with heme constitutes human hemoglobin. It is more specific for human blood as compared to the guaiac-based tests and is not subject to the false negative results seen in the guaiac-based tests in the presence of high dose vitamin C supplements. It is important to remember that the iFOBT assays are specific to bleeding in the lower GI tract.

Thirdly, because of the increased sensitivity of these assays, only one sample is usually required for screening as compared to the three samples needed when guaiac-based tests are used. The ease of use of these screening assays should enhance patient compliance.

Interpretation

Results of the iFOBT assays will be:

- *Positive:* samples with a hemoglobin concentration ≥ 100 ng/ml.
- *Negative:* samples with a hemoglobin concentration of < 100 ng/ml.

Because gastrointestinal lesions may bleed intermittently and blood in feces is not distributed uniformly, a negative result may not assure absence of a lesion.

Limitations

Patients with the following conditions should not be tested due to a potential for false positive results: bleeding hemorrhoids, menstrual bleeding, constipation bleeding and urinary bleeding.

Certain medications such as aspirin and non-steroidal anti-inflammatory drugs may cause gastrointestinal irritation and subsequent bleeding in some patients and cause false positive results. Contamination of the sample with urine or toilet water also may cause erroneous results.

The OC-Sensor Diana iFOBT should not be used for testing urine, gastric or other body fluids.

Because iFOB (FIT) tests are dependent on the intact antigenic structure of heme molecules, its use is limited to screening for FOB that is not gastric or upper GI in origin.

Bulk stool samples should not be sent to the lab for occult blood testing, as hemoglobin present in stool begins to degrade within hours of passage.

Methodology

The OC-Sensor Diana iFOB test is an immunoassay-based test that uses rabbit polyclonal antibodies to detect hemoglobin in stool. The test is a turbidimetric latex agglutination test. Hemoglobin present in the patient sample will combine with latex-coated antibody to cause a change in absorbance. A light beam is passed through the reaction cells and measures changes in the intensity of light beam. Testing is performed on an automated analyzer and qualitative results are generated.

Patients for whom a colorectal cancer screening test is ordered will be given a collection “kit,” which is composed of a “labeled collection vial,” instructions on how to collect the stool sample and inoculate the vial, and an envelope into which the vial can be placed and sent back to Cleveland Clinic Laboratories for testing on the OC-Sensor Diana. Testing is performed on a daily basis, Monday through Friday.

References

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Test Overview

Test Name	Immunoassay Fecal Occult Blood Test
Reference Range	Negative for hemoglobin at < 100 ng/ml
Specimen Requirements	Collection kits should be submitted to the laboratory containing the vial with inoculated stool sample. Specimens should be received in the laboratory within 15 days.
Test Ordering Information	iFOBT
Billing Code	88086
CPT Code	82274

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