Blood Test for CD24 Detects Colon Neoplasms

BY SUSAN BIRK

CHICAGO — A blood test for a protein associated with colorectal cancer can detect adenomas and colorectal cancer, according to two studies of a total of 370 patients.

The test, the first of its kind, holds promise for early disease detection and surveillance, said Dr. Nadir Arber of Tel Aviv Medical Center, Israel, at the annual Digestive Disease Week.

"This is a simple blood test measuring the levels of CD24 protein [a cell surface protein and P-selectin ligand] in peripheral blood lymphocytes (PBLs), and we can successfully distinguish healthy subjects from patients with colorectal neoplasm," Dr. Arber reported at a research forum that was sponsored by the AGA Institute.

The findings provide further substantiation that CD24 levels are significantly elevated in the majority of patients with adenomas and colorectal cancer (CRC), he said.

Previous research by Dr. Arber and his colleagues with both animal and human cancer cell lines confirmed the overexpression of CD24 in the colonic mucosa as an early event in CRC carcinogenesis, and identified the protein as a potential biomarker for early CRC detection and a target for therapy (Gastroenterology 2006;131:630-9).

The low level of public compliance with current CRC screening techniques underscores the need for a noninvasive test, Dr. Arber said.

Analyses of PBLs for expression of CD24 detected CRC in a pilot study of 203 consecutive subjects with a sensitivity and specificity of 70.5% and 83.3%, respectively. The test also distinguished patients with adenomas from normal patients with a sensitivity and specificity of 84.2% and 73.5%, respectively (confidence interval 95%).

An external third-party evaluation of 143 blood samples from this population yielded a lower specificity of 65% for normal versus CRC patients and a specificity of 76.7% for normal versus adenoma patients. Dr. Arber noted in an interview that the somewhat lower specificity could be attributed to potential degradation of the protein during storage and transportation.

Patients completed a detailed questionnaire, provided a blood sample, and underwent a colonoscopy. PBLs were isolated and analyzed with Western blot, a technique that detects levels of a protein using antibodies specific to the target protein. Sensitivity and specificity for CD24 were calculated using receiver operating characteristic curves.

COURTESY DR. NADIR ARBER

The test can be performed in any hospital, Dr. Nadir Arber said.

In a second validation study of an independent sample of 167 subjects, the blood test yielded improved values for the detection of CRC (sensitivity 92.3%; specificity 83.8%). The values for the detection of normal versus CRC and adenoma patients were 77.1% and 86.8%, respectively.

Dr. Arber said that a goal of further research is to collect data on CD24 levels and polyp size.

When asked what additional research would be needed before the test could be widely offered for CRC detection and surveillance, Dr. Arber said he is focusing on increasing the test's negative predictive values and is exploring whether there are certain subpopulations for whom the test is not predictive.

In its current form, the test, based on Western blot analysis, can be performed in any hospital, Dr. Arber said. He added that he and his colleagues are developing an ELISA (enzyme-linked immunosorbent assay) kit designed to facilitate use of the test in any laboratory worldwide.

Dr. Arber disclosed that he is chief scientist at Micromedic Technologies Ltd., which supported this research. Dr. Arber also is on the review panel for GI View Ltd., which develops gastrointestinal diagnostic devices, and has received research support from Pfizer. ■

Neoplasia Detection Rate Higher With Five-Year Interval Between Sigmoidoscopies

BY MICHELE G. SULLIVAN

CHICAGO — Repeating a flexible sigmoidoscopy at 5 years instead of 3 years after an initial negative exam increases the risk of finding a cancer or advanced adenoma by 70%.

Men are particularly at risk when they delay the follow-up, Dr. Robert Schoen said at the annual Digestive Disease Week.

Men were significantly more likely than women to have a neoplasm identified.

DR. SCHOEN

"Not only did men have more neoplasias than women at the 5-year exam, but, when we compared the 3- and 5-year exams, the increase in yield was significantly greater in men than in women."

The findings were seen in a subanalysis of the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. Initially, the trial protocol called for repeat flexible sigmoidoscopy 3 years after an initial negative exam. In 1998, the protocol changed to a 5-year follow-up period, said Dr. Schoen of the University of Pittsburgh.

The analysis included two cohorts: those whose repeat screenings took place after 3 years (9,000) and those whose repeat screenings took place after 5 years (24,000). None of the subjects had a polyp identified on their initial exam.

Overall, he said, significantly more 5-year exams were positive for a neoplasm (21% vs. 14%) than were 3-year exams. The crude number of cancers identified was not significantly different between the cohorts, but the number of cancers or advanced adenomas was (12/1,000 vs. 9/1,000 subjects). The crude rate of cancer or any adenoma also was significantly higher in the 5-year group (49/1,000 vs. 34/1,000).

In both cohorts, men were significantly more likely than women to have a neoplasm identified. But in a comparison of the 3- and 5-year exams, men also had a significantly higher change in the yield with the different follow-up times. (See chart.)

After controlling for age, gender, and history of a colon procedure at least 3 years before enrollment, the investigators found delaying the repeat exam to 5 years significantly increased the yield of a cancer or any adenoma by 70% and of cancer or an advanced adenoma by 47%.

Dr. Schoen had no financial disclosures relevant to the study. ■

Neoplasia Yield for Repeat Flexible Sigmoidoscopy (Age Adjusted)

	3-year interval (n = 9,000)	5-year interval (n = 24,000)
Total cancer/ advanced adenoma per 1,000		
Men	16	27
Women	8	12
Total cancer/ any adenoma		
Men	53	93
Women	31	51
Distal cancer/ advanced adenoma		
Men	10	16
Women	7	8
Distal cancer/ any adenoma		
Men	39	61
Women	26	36

Note: Data are from the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial.
Source: Dr. Schoen

ELSEVIER GLOBAL MEDICAL NEWS

Immunochemical Test Beats Guaiac Test for Screening

CHICAGO — Although it is more expensive to administer, colorectal cancer screening with a fecal immunochemical test is less expensive in the long run than a guaiac-based test because it detects more high-risk lesions and thus prevents more cancers, a cost-analysis study has concluded.

The fecal immunochemical test (FIT) had better adherence rates and detected more high-risk adenomas than did the guaiac-based test, making it a much better option overall, Dr. Rodrigo Jover said at the annual Digestive Disease Week.

Positivity rates were 9.5% with the FIT and 2% with the guaiac test. "This provoked a huge difference in the detection rate of high-risk adenoma and cancer: 34 per 1,000 screened, compared with just 5 per 1,000," said Dr. Jover of the Hospital General Universitario de Alicante, Spain.

Dr. Jover and his colleagues compared the first-round results of two regional colorectal cancer screening programs. The County of Valencia program invited 98,600 residents aged 50-69 years to be screened by mailing them a guaiac-based fecal occult blood test. The Region of Murcia program invited 35,700 residents of the same age to complete a FIT screen.

Dr. Jover had no relevant financial disclosures.

—Michele G. Sullivan