New Tests for Prostate Cancer

By Leslie Harris O’Hanlon

This last year has seen a surge of activity in researching and developing tests to help clinicians better diagnose and treat prostate cancer.

Better tests are needed, many say, to more accurately detect prostate cancer and to help men and their physicians decide what to do about it. A few such tests have become commercially available recently or are poised to do so. But researchers warn that the tests need to pass muster before being adopted for use in the clinic.

“They need to be proven,” said Scott A. Tomlins, M.D., Ph.D., assistant professor of pathology and urology at the University of Michigan at Ann Arbor. “This is an important consideration for clinicians to have: How much does this test improve their clinical decision making, and what will they do with the results of the test?”

Aggressive Disease

Many of the nearly 250,000 men diagnosed with prostate cancer in the United States annually don’t need treatment because their slow-growing, low-risk tumors are not likely to do them harm. But predicting which tumors will turn aggressive can be difficult with current clinical measures. As a result, many men will have radiation, surgery, or both to treat their prostate cancer. These treatments can cause uncomfortable side effects, including urinary incontinence, bowel function problems, and erectile dysfunction.

“The answer to the prostate cancer controversy is not to stop screening,” said Matthew Cooperberg, M.D., M.P.H., assistant professor of urology and epidemiology–biostatistics at the University of California, San Francisco. “But the answer is to fix overtreatment. We can’t stick our heads in the sand and stop looking for prostate cancer.”

The Oncotype DX prostate cancer test, developed by Genomic Health, analyzes the expression of 17 genes. On the basis of the expression of these genes, men can be categorized as having low-, intermediate-, or high-risk prostate cancer. Those in the low-risk group could opt for active surveillance, monitoring a patient’s condition through serial prostate-specific antigen (PSA) screening and prostate biopsies rather than for more radical treatment. The test went on sale after Cooperberg presented results of a UCSF validation study at the 2013 American Urological Association annual meeting in San Diego in May. The study involved nearly 400 men who could have gone on active surveillance but chose surgical removal of their prostate.

Researchers used the Oncotype test to analyze biopsy tissues from these men and then looked at the men’s medical records to see whether the test accurately predicted which men had prostate cancers showing evidence of aggressive disease. According to the UCSF researchers, the test added clinically meaningful prognostic information and identified more men with low-risk disease who could safely choose surveillance.

“Sixty percent of men diagnosed with prostate cancer have localized prostate...
cancer and should not be treated,” said Otis Brawley, M.D., chief medical officer at the American Cancer Society in Atlanta. “This test may help us better identify who those guys are.”

Diagnosing prostate cancer often starts with detecting a rising or elevated PSA level in the blood, which sometimes occurs in men with prostate cancer. But levels may also be high in men who have infections, inflammation, or an enlarged prostate. Conversely, a low PSA level doesn’t always mean that a man doesn’t have prostate cancer. On the basis of PSA levels, men often get a biopsy to determine whether cancer is present. Biopsies carry risks, including bleeding, infection, and discomfort. During this procedure, a doctor inserts a probe through a man’s rectum into the prostate, taking about 12 small samples of tissues from the prostate in areas considered safe to biopsy. Those samples are then analyzed under a microscope and given a Gleason score between 1 and 10. The score is a comparison between what normal prostate cells should look like and the appearance of a particular sample. The higher the score, the more likely the cancer will be aggressive. But interpreting biopsy results isn’t always straightforward because the samples may not represent what’s going on in the entire prostate.

“Because there may be multiple cancers in the prostate, the concern is that you may not have biopsied the more aggressive cancer,” said William Dahut, M.D., clinical director of the Center for Cancer Research at the National Cancer Institute. “That’s why when we put patients in the low-risk group, we do it based on a criterion that is not so great.”

Oncotype DX could give doctors more information to help decide who has low-risk or aggressive disease, he said.

“A test like this would potentially help one better determine the biology of the cancer beyond the somewhat crude Gleason score,” Dahut said.

Another company, Myriad Genetics, released a similar test last year called Prolaris, which measures expression of 46 cell cycle progression genes to determine whether a man’s cancer is aggressive. Five retrospective studies of the test have been published, all concluding that the test could predict disease outcome, according the company.

David Houchens, a prostate cancer survivor, and vice chairman of the board of the nonprofit Us TOO International Prostate Cancer Education & Support Network, said these tests could help men, but their cost may exclude some men from getting any benefit if insurance does not cover the tests. Both tests cost more than $3,000. Further, even if men learn that their cancer is slow growing, many may be reluctant to leave it be.

“The first thing men say when they hear that they’ve got cancer is, ‘Get it out of me at any cost,” said the 76-year-old Columbus, Ohio, resident. “The doctor may talk about potential side effects, but they don’t hear all that.”

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New Diagnostic Tests

Most men diagnosed with prostate cancer will not die from their disease. But amid all the debates about screening, remembering that prostate cancer can be deadly is important, said Ashley E. Ross, M.D., Ph.D., assistant professor of urology, oncology, and pathology at the Johns Hopkins Medical Institution in Baltimore. Almost 30,000 men will die from prostate cancer this year, according to the National Cancer Institute.

So tests must be able to accurately diagnose clinically meaningful prostate cancer. Some clinicians are using the new PCA3 test. The U.S. Food and Drug Administration approved the test in 2012 for use in men with an elevated PSA level but a negative biopsy. The test aims to help determine which men will need a repeat biopsy. When prostate cells become cancerous, their PCA3 genes produce large amounts of a cancer-specific nucleic acid. PCA3 is a prostate-specific gene that 95% of prostate cancer cells overexpress. After a digital rectal exam—a procedure that checks for irregularities in size, shape, and texture of the prostate—cancerous cells with high levels of PCA3 are shed into the urine. A urine sample is then collected and sent to a laboratory to determine PCA3 score. Unlike PSA, PCA3 levels don’t rise if a man has an inflamed or enlarged noncancerous prostate.

“It’s for a guy who comes in with an elevated PSA: He has a biopsy done, but there’s no cancer,” said James D. Brooks, M.D., chief of urologic oncology at the Stanford Cancer Institute at the Stanford University Medical Center. “We know that 10%–25% of biopsies are false negatives because they can miss things. So PCA3 can help predict which men may have something.”

University of Michigan researchers also have developed a urine test that they say can help determine when a man may need to have a biopsy. This test looks for two genetic fingerprints common in most prostate cancers and detectable in a urine test: TMPRSS2:ERG gene fusion—a combination that occurs in about half of prostate cancer patients—and PCA3. The test gives a percent risk assessment of a man having prostate cancer, anywhere from a 5% to 95% chance, explained Tomlins, who helped develop the test. Patients with low levels of TMPRSS2:ERG and PCA3 in their urine have a 20% chance of being diagnosed with prostate cancer, and their chances of having a high-risk cancer are less than 10%. Patients with high levels of TMPRSS2:ERG and PCA3 in their urine have an 80% chance of having cancer, with a 50% risk of having high-grade cancer, Tomlins said. Clinical trials run by NCI’s Early Detection Resource Network
are studying the test, and it will most likely be available at the University of Michigan this year.

Another test, the Prostate Health Index, measures three forms of PSA in the blood: total PSA, free PSA (a form that circulates in the bloodstream, unbound to other proteins), and a subcategory of free PSA called pro-PSA. Doctors can use the score to help decide whether a biopsy will find prostate cancer. FDA approved the test in 2012, and a study at this year’s American Urological Society annual meeting found that the Prostate Health Index more accurately diagnosed clinically meaningful prostate cancer than PSA alone.

Looking Ahead
Although these new tests may help better diagnose and treat prostate cancer, some researchers say all this information pouring out of universities and companies could confuse men and their doctors. These tests also need further study. UCSF is developing a comprehensive risk assessment for men that uses results from the Oncotype DX test, genetic information, lifestyle factors, and other clinical information, Cooperberg said. Twelve institutions, and 900 men, are involved in the Prostate Active Surveillance Study (PASS) designed to identify biomarkers that predict aggressive prostate cancer. (NCI’s Early Detection Resource Network coordinates PASS.) Brooks said that PASS is running various tests on blood, urine, and biopsy samples from these men on active surveillance to see whether the results agree with the original clinical information for these men. Ross would like to use one of the genomic tests for men with prostate cancer when they are first diagnosed and see whether the results predict the course of their disease.

“These tests are fairly new, and their use, to some extent, should be considered cautiously until validated prospectively,” Ross said. “That will take a while.”

© Oxford University Press 2013. DOI:10.1093/jnci/djt344
Advance Access publication November 6, 2013