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Bladder cancer test boosts accuracy of cystoscopy

Mac Overmyer
UT CONTRIBUTING EDITOR

The NMP22® BladderChek® Test is the only FDA approved in-office test for diagnosing and monitoring bladder cancer.

Houston—Nuclear matrix protein 22 (NMP22) is to bladder cancer as PSA is to prostate cancer, perhaps better. That is the implication of a recently published, prospective, multi-institution study showing the point-of-care NMP22 assay (BladderChek, Matritech, Newton, MA) has a sensitivity of 55.7% and a specificity of 85.7%. In contrast, cytology was found to have lower sensitivity (15.8%) but higher specificity (99.2%).

When used in conjunction with cystoscopy, the office-based test detected 94% of bladder cancers, compared with 89% detected by cystoscopy alone, the authors reported. It also identified four invasive, life-threatening cancers missed during cystoscopy. The study appears in the Feb. 16 issue of JAMA (2005; 293:810-6).

Lead author H. Barton Grossman, MD, professor and deputy chairman of the department of urology at M.D. Anderson Cancer Center in Houston, said the study points out the value of the NMP22 test as a screening tool in high-risk patients.

"If someone is referred with hematuria or if there is a patient whom you suspect might have bladder cancer, the study shows that cystoscopy is still the best approach, although it is not perfect and can miss some tumors," Dr. Grossman said. "A combination of tests—a urine assay plus cystoscopy—is still the best way to go. The attractiveness of this [NMP22] test is that it is cheaper, it can be conducted right on the spot, and it has a higher sensitivity, albeit a somewhat lower specificity, than cytology. But it is still not an all-or-none answer."

Co-author Kevin Tomera, MD, a urologist in private practice with Alaska Clinical Research Center in Anchorage, noted that among the assay's virtues are convenience and speed.

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"The assay is three to four times [more sensitive] than cytology, and the specificity was impressive, greater than 80%. Everyone who visits a urologist offers a urine sample. If there is hematuria in the absence of infection or other known problems, this test offers a great deal of information while the patient is still in the office," said Dr. Tomera.

Sensitive to muscle-invasive Ca

The prospective study was conducted at 23 institutions and practices and included 1,331 patients who had risk factors for bladder cancer such as smoking history or symptoms, eg, hematuria and dysuria. Urine samples from those at risk were provided for cytology and NMP22 analysis prior to cystoscopy. Bladder cancer was diagnosed in 79 patients. The NMP22 assay detected cancer in 44 of these 79 patients, for a sensitivity of 55.7% (44.1% to 66.7% at the 95% confidence interval). In comparison, urine cytology diagnosed cancer in 12 of 76 patients, for a sensitivity of 15.8% (95% CI: 7.6% to 24.0%). The negative predictive value was 98.6% for the NMP22 test and 94.9% for cytology.

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The test's sensitivity varied according to the stage and grade of cancers present, not an uncommon finding in all tumor marker assays, Dr. Grossman said. For instance, the assay showed a 50% sensitivity to noninvasive Ta to T1 tumors and a 90% sensitivity to muscle-invasive T2 to T3 tumors. By comparison, cytology showed a 16.7% sensitivity to noninvasive Ta to T1 tumors and 22.2% sensitivity to invasive T2 to T3 tumors.

The NMP22 assay's sensitivity to well-differentiated tumors was 48.2%, and its sensitivity to poorly differentiated tumors was 72%. Initial cystoscopy, performed after urinalysis, detected 88.6% (70 of 79) cancers.

The NMP22 test picked up four potentially life-threatening tumors that were missed on initial cystoscopic examination of these patients. One of these was in the ureter and outside the viewing area of the cystoscope.

"Urologists often say that they do not miss on cystoscopy, but multiple rigorous studies show that cystoscopy can miss 10% to 20% of tumors," Dr. Tomera said. "A supplemental urine test is mandatory."

Significant cost savings

Although the authors had no hard data on the cost of the tests studied, which vary significantly around the country, they observed that the average Medicare reimbursement for voided cytology was approximately $56, compared with $24 for the NMP22 assay.

Both physicians feel the test should be incorporated in examinations as a screen, particularly in at-risk populations. These include individuals with gross or microscopic hematuria in the absence of infection or other known causes, those age 40 years or older, and those with a history of smoking.

"This [assay] allows a fairly simple initial screening for people who are at risk for bladder cancer. These people are generally not being screened. If we can increase screening and get these people to urologists, that would be a good thing," said Dr. Grossman.

"I think the test should be part of the AUA guidelines," Dr. Tomera said. "The guidelines recommend a CT IVP, which in our neck of the woods is about $3,800. This is a $30 test."

Matritech supplied the assay to the investigators who took part in this study. UT

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Matritech
330 Nevada Street
Newton, MA 02460
Tel: 800-320-2521
Fax: 617-928-9266
e-mail: nmp22@matritech.com