

Urine test boosts detection of recurrent bladder cancer

Addition of point-of-care test to cystoscopy increases cancer detection rate to 99%

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Rochester, NY—A point-of-care assay that measures the nuclear matrix protein NMP22 in urine significantly improves detection of recurrent bladder cancer when used with cystoscopy, according to a new study.

The study, published recently in *JAMA* (2006; 295:299-305), found that cystoscopy alone identified 91.3% of cancers, whereas the combination of cystoscopy and the NMP22 test (BladderChek, Matritech, Inc., Newton MA) detected 99% of cancers. The test is FDA-approved both as an aid in the initial diagnosis of bladder cancer and for surveillance.

The fifth most common malignancy, bladder cancer comes with a 50% to 90% chance of recur-

rence. The resulting need for frequent surveillance cystoscopies after the initial tumor resection tends to include supplemental cytology, which can pick up hidden or small tumors, according to Edward Messing, MD, a co-author of the *JAMA* study. However, the success of this traditional combination approach is hampered by inconsistencies.

“Not everyone does cystoscopy the same way. Different institutions do it differently, and there are problems in its reproducibility,” said Dr. Messing, WW Scott professor and chairman, department of urology, University

of Rochester (NY) School of Medicine.

In a study published last year (*JAMA* 2005; 293:810-6), researchers reported on 1,331 patients who had an elevated risk of bladder cancer, but who had not yet been diagnosed with it and found that the combination of cystoscopy and the NMP22 test detected 94% of bladder cancers compared with 89% detected by cystoscopy alone.

Anticipating recurrence

The new study looked at subjects with a history of bladder cancer. The study, conducted

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between 2001 and 2002, included 23 academic, private practice, and hospital facilities in nine states. Urine samples were collected from the 668 enrolled patients for analysis of the NMP22 protein and for cytology testing before they underwent follow-up cystoscopy.

Researchers reported that they found bladder cancer in 103 of the 668 patients. Cystoscopy alone identified 91.3% of the cancers (94/103; 95% CI, 84.1%-95.9%). The combination of cystoscopy with the NMP22 assay detected 99% of the cancers (102/103; CI, 94.7%-100%; $p=.005$), and the NMP22 assay detected eight of nine cancers missed by cystoscopy alone. Seven of those tumors were high grade.

Sensitivity of the NMP22 test alone was 49.5% (51/103; 95% CI, 39.5%-59.5%). Its specificity was 87.8% (493/565; 95% CI, 84.2%-89.9%).

Cytology based on voided urine detected only three malignancies missed during initial cystoscopy and did not significantly increase the sensitivity of cystoscopy (94.2%; 95% CI, 87.7%-97.8%; $p=.08$). The NMP22-cystoscopy combination missed one low-grade tumor, according to Dr. Messing.

"The critical part here, which surprised me, was that of the nine tumors that the NMP22 BladderChek picked up, almost all were very high-grade and aggressive cancers," he said. "They were the kind of cancers where a significant delay in diagnosis may have been very dangerous for the patient."

More aggressive tumors can escape cystoscopic detection, according to Dr. Messing,

because they might be flat tumors that do not grow into the lumen of the bladder.

A second recent trial of the NMP22 test also showed positive results.

Giora Katz, MD, a co-author on both *JAMA* studies, reported on the results of a new analysis of a large, multicenter clinical trial that included two Veterans Administration hospi-

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tals. The two hospitals represented 9% of sites in the multicenter study, but represented 16% of the total cancer cases. Eleven percent of the VA patients were diagnosed with bladder cancer compared with 5.7% at all other study sites, and most of the malignancies at the VA hospitals were in the invasive stage, while the cancers at other sites were predominantly early stage tumors.

Data indicated that the NMP22 assay detected three times more cases of bladder cancer in symptomatic patients than did cytology, according to Dr. Katz, a urologist at the Lake City, FL, VA Hospital. His findings were reported at the 2006 James C. Kimbrough

Urological Seminar in Savannah, GA.

Easy to administer

The NMP22 test involves placing four or five drops of urine in a paper well supplied by the manufacturer and waiting about 35 minutes for a line on the paper to change color.

"It is basically like a pregnancy test," Dr. Messing said.

Since performing the study in his clinic, Dr. Messing has begun to replace cytology with the NMP22 assay. While most patients are candidates for the NMP22 test, those with extremely bloody urine or active urinary tract infections might produce false-positive test readings. The false-positive rate is higher with the NMP22 (13%) than with cytology (5%), according to Dr. Messing.

"If there's a positive test, you probably have to re-cystoscope patients quickly," he said. "But I do not know that you have to take them to the OR and biopsy them unless you are afraid that it is an angry tumor.

"The high false positive rate is a drawback to the test."

The NMP22 is not a replacement for cystoscopy. In the study, the NMP22 picked up about 45% of all the tumors, while cystoscopy detected about 55%, according to Dr. Messing.

Matritech supplied the NMP22 test to investigators involved in the current study at no cost and reimbursed clinical sites for the time involved in data collection. **UT**

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