Urinary Assay Improves Prostate Ca Detection

BY SUSAN LONDON

VITALS

Major Finding: A new urinary assay had high specificity for distinguishing between patients with and without cancer (88%-93%).

Data Source: Two cohort studies in men who were scheduled for prostatectomy or prostate biopsy.

Disclosures: Dr. Wei and Dr. Amberson reported receiving research funding from Gen-Probe Inc. Some coauthors of both studies disclosed employment or leadership roles and stock ownership in Gen-Probe.

SAN FRANCISCO — A new urinary assay for a common gene rearrangement in prostate cancer improves the detection of this disease and the differentiation of its more aggressive forms, according to two cohort studies reported at a symposium on genitourinary cancers.

The studies, conducted among men who were scheduled for prostate biopsy or prostatectomy, found that the assay supplemented conventional risk factors for accurately identifying those having prostate cancer. In addition, higher assay scores correlated with the presence of adverse tumor features.

"This new … urinary assay has the ability to not only detect prostate cancer, but may help move us forward in our paradigm to also detect clinically significant prostate cancer," said Dr. John T. Wei, who presented results of the first study on behalf of first author Sheila M.J. Aubin, Ph.D., of Gen-Probe Inc., the company that is developing the assay.

Prostate-specific antigen (PSA) level and digital rectal examination both have poor specificity for detecting prostate cancer, Dr. Wei observed. "Because of this, many patients will go on to have false-positive PSA tests and unnecessary prostate biopsies, and suffer a significant amount of distress."

Moreover, these tests are unable to differentiate indolent from aggressive cancer, which becomes more important given current efforts to tailor management to disease characteristics, according to Dr. Wei, professor of urology at the University of Michigan in Ann Arbor. "Taken together, there is a significant unmet need, and that is to develop a highly specific test that can tell us if a patient has clinically significant cancer or not," he said.

About half of prostate cancers exhibit fusion of the androgen-regulated TMPRSS2 gene and the ERG oncogene, Dr. Wei told attendees of the symposium, which was sponsored by the American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Urologic Oncology. Cancers that harbor this fusion gene (abbreviated T2:ERG) have increased cell growth, invasion, and metastasis, and decreased apoptosis.

In the first study, the investigators assessed the performance of the novel assay, which measures levels of T2:ERG messenger RNA in urine, using urine specimens collected after digital rectal examination and before either prostate biopsy (623 men) or prostatectomy (142 men).

Analyses of biopsy-based indicators showed that the T2:ERG score was correlated with the number of cores that were positive, the percentage of cores that were positive, and the greatest percentage involvement of any core by cancer, according to Dr. Wei. Also, the median score was higher among patients with biopsy-significant cancer as defined by Epstein criteria.

Analyses of prostatectomy-based indicators showed that the T2:ERG score was correlated with the maximum tumor dimension. In addition, the median score was higher among patients who had an upgrade of the Gleason score between biopsy and prostatectomy, a prostatectomy Gleason score of greater than 6, and prostatectomy-significant cancer as defined from tumor characteristics.

Compared with the PCPT (Prostate Cancer Prevention Trial) risk score alone, the combination of this score with the T2:ERG score more accurately identified men who had prostate cancer.

Dr. Wei noted that at cutoff scores of 100 and 200, the T2:ERG assay had high specificity for distinguishing between patients with and without cancer (88%-93%), with biopsy-significant and -insignificant cancer (85%-95%), and with prostatectomy-significant and -insignificant cancer (95%-100%).

Independent trials of the assay are needed, Dr. Wei acknowledged. He said that ongoing discussions are looking at the possibility of incorporating the assay into trials of the Early Detection Research Network.

In the second study, investigators tested the same T2:ERG assay using urine specimens that were collected after digital rectal examination from 471 men who were scheduled for prostate cancer biopsy at community clinics, according to presenting author Dr. James B. Amberson.

Some 44% of patients had positive biopsies, he reported. The median age was 66 years in the patients with cancer and 63 years in the patients without it. The median serum PSA level was 5.0 and 4.3 ng/mL, respectively.

When used alone, the T2:ERG score had a high specificity (87%) for detection of biopsy-proven cancer, reported Dr. Amberson, divisional medical director of Dianon Systems, which performs diagnostic and prognostic testing. Sensitivity was 39%, "in line with the expected gene fusion prevalence in this population of about 50%."

The median T2:ERG score was higher in patients who had a Gleason score of 7 or greater, involvement of more than 50% of positive cores by cancer, and three or more positive cores.

"The T2:ERG assay significantly improved the diagnostic accuracy of a logistic regression model" for prostate cancer detection, Dr. Amberson said.

The area under the curve was 0.597 for serum PSA level alone, 0.715 for a model using multiple risk factors (serum PSA level, percentage of free PSA, age, prostate volume, family history, race, digital rectal examination result, prior biopsy history, and urine prostate cancer gene 3 level), and 0.754 when the T2:ERG score was added to the model. ■

Cystoscopy Alone Excels for Bladder Cancer Surveillance

BY SUSAN LONDON

VITALS

Major Finding: Cystoscopy alone, the least expensive of five surveillance strategies, picked up two invasive bladder cancers that were missed by urine testing.

Data Source: A study in 200 consecutive patients.

Disclosures: Dr. Karam reported having no conflicts of interest related to the study. A coauthor received honoraria from Abbott Molecular.

SAN FRANCISCO — Cystoscopy alone offers the best combination of cost and sensitivity for surveillance after treatment of superficial bladder cancer, new data show.

In a prospective study comparing five surveillance strategies in 200 patients, the addition of various urine tests to cystoscopy increased the cost per cancer detected, but did not find more invasive tumors, researchers reported at a symposium on genitourinary cancers.

"Our data suggest that cystoscopy alone is the most cost-effective strategy, and that the addition of urinary markers adds to cost without improved detection of invasive disease," said first author Dr. Jose A. Karam, a urologic oncology fellow at the University of Texas M.D. Anderson Cancer Center in Houston.

Evidence-based data are lacking on the outcomes of surveillance strategies among patients who have been treated for superficial (non–muscle invasive) bladder cancer. Many urinary-based markers are now available for use, but cystoscopy remains the standard of care, he said.

In the study, consecutive patients needing surveillance after treatment of superficial bladder cancer underwent these tests at study entry: cystoscopy, urine cytology, NMP22 BladderChek test (a urine test marketed by Inverness Medical Innovations that measures a protein associated with bladder cancer), and FISH (fluorescence in situ hybridization) UroVysion test (a urine test marketed by Abbott Molecular that detects chromosomal abnormalities associated with bladder cancer).

The bladder cancers for which they had been treated were mainly of Ta stage (71%) and low grade (58%). In 25 patients, new tumors were found at study entry or by the first follow-up assessment, a median of 4.1 months later, Dr. Karam reported at the symposium, sponsored by the American Society of Clinical Oncology, the American Society for Radiation Oncology, and the Society of Urologic Oncology.

Based on 2009 Medicare reimbursement rates, the cost per cancer detected was lowest with cystoscopy alone ($7,692), and highest with cystoscopy plus FISH ($19,111). Values were intermediate for cystoscopy plus cytology ($10,267), cystoscopy plus NMP ($11,143), and cystoscopy plus NMP with FISH confirmation in the event of a positive NMP result ($9,557).

The cancer detection rate was lowest with cystoscopy alone (52%) and highest with cystoscopy plus FISH (72%). Values were intermediate for cystoscopy plus cytology (60%), cystoscopy plus NMP (56%), and cystoscopy plus NMP with FISH confirmation (56%). Subsequent analyses showed that cystoscopy plus FISH picked up more early, noninvasive (carcinoma in situ and Ta) tumors than did cystoscopy alone. But it similarly missed the two more advanced (T1 and T2) tumors that were found, "which arguably are the ones that matter the most," Dr. Karam commented.

Urinary-based markers 'should be used carefully and judiciously in patients with bladder cancer.'

DR. KARAM

Cystoscopy alone appears to be the most cost-effective approach, he concluded, cautioning that "these [urinary-based] markers should be used carefully and judiciously in patients with bladder cancer." Because all patients received care from bladder specialists, the findings may not be generalizable to community practices, he added.

Dr. Nicholas J. Vogelzang, one of the developers of the NMP22 assay, chaired a press briefing at which the study was discussed. Dr. Vogelzang, chair and medical director of the developmental therapeutics committee of U.S. Oncology, said he found the results "very chagrining but nonetheless very important." ■