CALIFORNIA Prostate Cancer COALITION

"Fighting Prostate Cancer in California!"

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NEWS

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PRESIDENT'S MESSAGE

It is summer and all is quiet – now that the AUA and ASCO Meetings are concluded. But men are still being diagnosed with prostate cancer at all stages, and we worry that with the current "D" Recommendation of the United States Preventive Services Task Force (USPSTF) recommending AGAINST PSA testing, we will see fewer men being referred to urologists, fewer early stage disease at diagnosis and an increasing number of men who will already have advanced disease when their disease is found. Then the AUA Guidelines suggesting that a man not even discuss prostate cancer testing until he's 55 didn't help. Their Guidelines are for men of "average" risk – but sometimes you need a baseline PSA to determine risk! It does seem like an endless battle but if we can save even one life it is worth it.

To that end, the California Prostate Cancer Coalition is already deep in work on a laminated one-pager that will have 10 important questions for a man to ask his primary care doctor (and not wait until the subject of screening of testing may or may not come up.) The reverse side of this laminated one-pager will be directed to primary care physicians who do not have the in-depth knowledge of the array of tests available to determine if a man has prostate cancer and whether, if so, it is low-risk disease or potentially lethal. They also lack the firsthand knowledge of various treatments for prostate cancer since primary care physicians usually refer the patient with suspected prostate cancer to the urologist. So their side of this laminated document will describe the newest tests as well as types of treatments including active surveillance. CPCC is excited to be working closely with our Board Member Family Practice physician on this project.

Just because prostate cancer is not currently all over the news doesn't mean that it is any less prevalent in the population or that it is never dangerous. Survival is often determined by how advanced the disease is once it is diagnosed. Therefore let's all keep vigilant and get our men tested!! If you know men over the age of 40 (or 35 if high-risk, including African-American men and men with a certain or an indeterminate family history of prostate cancer), PLEASE convince them to have a PSA and DRE for baseline assessment. Let's each save at least one life!

Respectfully submitted,
MEREL GREY NISSENBERG

'ACTIVE SURVEILLANCE' MAY MISS AGGRESSIVE PROSTATE CANCERS IN BLACK MEN

A Johns Hopkins study suggests that African-American (AA) men diagnosed with very-low-risk prostate cancers are much more likely than white men to actually have aggressive disease that goes unrecognized with current diagnostic approaches. Although prior studies have found it safe to delay treatment and monitor some presumably slow-growing or low-risk prostate cancers, such "active surveillance" (AS) does not appear to be a good idea for black men, the study concludes.

"This study offers the most conclusive evidence to date that broad application of AS recommendations may not be suitable for AA men," stated co-author Edward M. Schaeffer, MD, PhD, associate professor of urology, oncology and pathology at the Johns Hopkins University School of Medicine and director of global urologic services for Johns Hopkins Medicine International and co-director of the Prostate Cancer Multi-Disciplinary Clinic at The Johns Hopkins Hospital's James Buchanan Brady Urological Institute.

"This is critical information because if AA men do have more aggressive cancers, as statistics would suggest, then simply monitoring even small cancers that are very low risk would not be a good idea because aggressive cancers are less likely to be cured," he says. "We think we are following a small, nonaggressive cancer, but in reality, this study highlights that in black men, these tumors are sometimes more aggressive than previously thought.

The Johns Hopkins study also showed that the rate of increased pathologic risk, as measured by the Cancer of the Prostate Risk Assessment (CAPRA), was also significantly higher in AA men (14.8 percent vs. 6.9 percent). Schaeffer and his team say their data suggest that "very-low-risk" AA men have different regional distributions of their cancers and appear to also develop more high-grade cancers. Researchers added that these tumors hide in the anterior prostate – a region that is quite difficult to assess using current biopsy techniques.

All study participants, of whom 1,473 were white and 256 black, met current National Comprehensive Cancer Network (NCCN) criteria for very-low-risk prostate cancer, and were thus good candidates for AS. The study showed that preoperative characteristics were similar for very-low-risk whites and blacks, although black men had slightly worse Charlson comorbidity index scores, a commonly used scale for assessing life expectancy. Detailed

(Continued on page 4)

EXPANDED CRITERIA TO IDENTIFY MEN ELIGIBLE FOR ACTIVE SURVEILLANCE OF LOW-RISK PROSTATE CANCER AT JOHNS HOPKINS: A PRELIMINARY ANALYSIS

Reese AC, Landis P, Han M, Epstein JI, Carter HB

J Urol, 13 May 2013; Epub ahead of print

Purpose: The following eligibility criteria are used to enroll patients in active surveillance (AS) at Johns Hopkins: clinical stage T1, PSA density <0.15, biopsy Gleason score ≤6, ≤2 positive biopsy cores, and ≤50% involvement of any biopsy core. We hypothesized that these criteria may be excessively strict, thereby precluding many men from AS.

Materials and Methods: We studied pathological outcomes in men treated between 1995 and 2012 with radical prostatectomy (RP) who met ≥4 of five AS criteria. Outcomes included a definition of significant tumor (pathological Gleason ≥7 or non-organ confined). Rates of adverse pathology were compared between men meeting all vs four of five AS criteria.

Results: Of 8261 men, 1890 (22.9%) met all AS eligibility criteria and 2133 (25.8%) met four of five criteria. Men exceeding PSA density and biopsy Gleason criteria were at increased risk of adverse pathological outcomes. Clinical stage >T1 was not associated with adverse pathology. Men with clinical stage T2 lesions, ≤2 positive biopsy cores, and <60% core involvement were at comparable risk of significant tumors to men meeting all AS criteria.

Conclusions: PSA density >0.15 and biopsy Gleason score ≥7 are strongly associated with adverse pathology at RP. Our findings suggest expanding active AS criteria to include men with clinical stage T2 lesions and a greater number of positive biopsy cores of low grade. Based on these preliminary findings, we are in the process of reassessing AS eligibility criteria using more detailed pathological analysis.

SOY FAILS TO HALT PSA RISE IN PROSTATE CANCER

Soy supplementation had no effect on the risk of biochemical recurrence (BCR) after radical prostatectomy (RP) in high-risk patients, investigators in a randomized trial reported online in the *Journal of the American Medical Association* (JAMA). The study ended early after an interim analysis showed a BCR rate of 27.2% in men who took the soy supplement vs. 29.5% in men who received a calcium-derived control therapy. The results did not change in an analysis limited to adherent patients.

Many studies examined the effect of soy protein on PSA levels in various populations of healthy men, men on active surveillance for presumably indolent prostate cancer (PCa), men with high-grade prostatic intraepithelial neoplasia (HGPIN) , and men with untreated PCa. Collectively, the trials produced mixed and inconsistent results. None had evaluated soy's effect on BCR after RP.

In the study, Bosland and colleagues at 7 US centers enrolled men who had localized PCa (T1c or T2) and a PSA value <0.07 ng/mL after RP. Eligible men had one or more high-risk features: PSA >20 ng/mL, final Gleason score ≥8, positive surgical margins, extracapsular extension, seminal vesicle invasion, or micrometastases in pelvic lymph nodes. Men were randomized to a soy protein isolate or a caseinate-based product, both incorporated into a beverage powder and consumed daily.

The primary endpoint was the 2-year rate of BCR and time to BCR. The investigators defined BCR as a serum PSA value ≥0.07 ng/mL, confirmed by 2 subsequent tests at least 1 month apart. Adherence was self-reported and monitored by serial measurement of serum genistein. The groups had similar rates of adverse events, and the principal reasons for discontinuation related to the taste and palatability of assigned treatment.

Investigators randomized 177 men from July 1997 to May 2010. The trial design called for an interim analysis after 45 BCR events. At the interim analysis, 22 of 81 (27.2%) evaluable men in the soy arm had BCR compared with 23 of 78 (29.5%) in the control group. The authors reported that 11 adherent participants discontinued treatment before the interim analysis but remained in follow-up. Exclusion of those patients in a per-protocol analysis did not change the results, nor did censoring of 13 participants considered possibly non-adherent because of serum genistein levels.

Despite the negative outcome, the investigators emphasized that the results apply only to a specific patient population. "The lack of protective activity of soy against PCa recurrence observed in this study was limited to men at above-average risk of recurrence within the first 2 years after RP and to the soy protein dose tested," Maarten C. Bosland, DVSc, PhD, of the University of Illinois at Chicago, and co-authors concluded in the article. "The findings of this study may therefore not be generalizable to PCa patients at average risk of recurrence."

The trial had limitations that go beyond generalizability, said Derek Raghavan, MD, PhD, of Carolinas HealthCare System in Charlotte, NC, who was not involved in the trial. "This is a really disappointing study, because it was poorly designed and executed, and I don't think it tells us anything new," he added. The trial included men with various levels of risk, required 13 years to conduct, and enrolled relatively few men despite screening thousands of patients, he added.

"Half of the patients got what appears to be a poorly characterized soy product and the other half got a calcium caseinate product, which in other contexts is used as a source of energy in diet supplementation. It's really impossible to figure out whether those confounding factors would have made the study null and void," he stated.

MedPage Today, 10 July 2013

PET MR DETECTS PROSTATE CANCER RECURRENCE

An ^{11}C-choline Positron Emission Tomography (PET)/Magnetic Resonance (MR) protocol for the restaging of prostate cancer was well tolerated by patients and detected significantly more recurrences than PET/Computed Tomography (CT), according to new research. PET/MR was particularly good at detecting small local recurrences.

In theory, MR imaging is better than CT for prostate cancer restaging because it provides higher soft-tissue contrast. "In the analysis of recurrent disease, it would potentially have a higher detection rate," said lead investigator Matthias Eiber, MD, a radiologist from the Technical University Munich in Germany. Dr. Eiber presented the research here at the Society of Nuclear Medicine and Molecular Imaging (SNMMI) 2013 Annual Meeting.

To compare the techniques, investigators evaluated 31 men who underwent a single-injection, dual-imaging protocol with PET/CT (Siemens Biograph 64) 5 minutes after injection, followed by PET/MR (Siemens Biograph mMR) 51 minutes after injection.

DETECTION RATES FOR PET/MR

Detection Rate	# Regions	# Men	Mean Rating
Local recurrence	17	12	1.12
Lymph node metastases	42	—	1.38
Bone metastases	17	5	1.17

PET/MR involved 3 to 4 bed positions (4 minutes per position) covering the area from the chest to the pelvis. It involved a coronal Dixon-VIBE scan for attenuation correction, a coronal T1-weighted spin-echo sequence, and an axial fat-saturation T2-weighted sequence.

Investigators obtained axial diffusion-weighted images (b-values 0, 400, and 800 s/mm²) and axial T1-weighted dynamic contrast-enhanced sequences during an additional 20-minute PET scan over the pelvis for T2-weighted axial and coronal planes. They used axial contrast-enhanced fat-saturated T1-weighted gradient recalled-echo sequences for the trunk.

Researchers used a 3-point scale to classify suspicious lesions, with 1 = definite metastasis, 2 = probable metastasis, and 3 = indeterminate status. Imaging time was longer with PET/MR than with PET/CT (41 vs 23 minutes), but patients tolerated the longer procedure. PET/MR outperformed PET/CT, particularly with respect to local recurrences.

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Because PET/MR machines are expensive, they are currently very rare; there are about 20 installed worldwide, according to Dr. Eiber. It remains to be seen if clinical applications will justify the cost.

In the case of prostate cancer recurrence, PET/MR has clear value, he noted. Patients are monitored for levels of prostate-specific antigen, and when the levels rise, physicians suspect a recurrence. But the recurrence could be local, in the lymph nodes, or a bone metastasis.

"The site of recurrence tremendously influences the choice of therapy," said Dr. Eiber.

DETECTION RATES FOR PET/CT

Detection Rate	# Regions	# Men	Mean Rating
Local recurrence	12	8	1.40
Lymph node metastases	39	—	1.45
Bone metastases	14	4	1.15

Another advantage is that the radiation dose delivered by PET/MR is about 80% lower than that delivered by PET/CT, according to the researchers' calculations. This potential dose reduction could be relevant for patients who undergo many exams over several years, because radiation can accumulate, Dr. Eiber explained, although he noted that many prostate cancer patients are elderly.

These results clearly demonstrate the value of PET/MR, explained Sandi Kwee, MD, program director for PET research at The Queen's Medical Center in Honolulu, Hawaii. "MR provides better tissue contrast and some additional features that are beyond just the structural information that the CT portion provides," said he added.

Nevertheless, the expense of PET/MR demands a high bar for clinical utility. "It has to be looked at on a more global population scale to see whether the overall benefit is worthwhile for medical centers to adopt that technology," said Dr. Kwee.

He noted that most major medical centers have both PET and MRI scanners, and doing consecutive scans can often provide the same information, albeit with potential imaging artifacts because of position changes between scans.

Presented at the 2013 SNMMI meeting, abstract 343

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The blue ribbon is the universal symbol for *Prostate Cancer Awareness*

AS LESS EFFECTIVE IN AFRICAN-AMERICAN MEN

(Continued from page 1)

analysis showed that black men had a lower rate of organ-confined cancers (87.9 percent vs. 91.0 percent), a higher rate of Gleason score upgrading (27.3 percent vs. 14.4 percent) and a significantly higher hazard of PSA defined biochemical recurrence (BCR) of prostate cancer.

Schaeffer emphasizes that "the criteria physicians use to define very-low-risk prostate cancer works well in whites – this makes sense, since the studies used to validate the commonly used risk classification systems are largely based on white men." But, he adds, "Among the vast majority of AA males with very-low-risk cancer who underwent surgical removal of the prostate, we discovered that they face an entirely different set of risks."

"Alternate race-specific AS entry criteria should be developed and utilized for AA men to ensure oncologic parity with their white counterparts. Our research team, in collaboration with the internationally recognized Hopkins pathologist Dr. Jonathan Epstein, is currently developing new race-based risk tables that begin to solve this key issue," he adds.

Science Daily, 25 June 2013

CPCC PHONE NUMBER & E-MAIL ADDRESS

For more information concerning CPCC or its programs and services, you can call us at (707) 786-7009 or send us an E-mail at cpcc@prostatecalif.org.

CPCC HELPLINE

This service is available for families and significant others of men with newly diagnosed prostate cancer, are undergoing treatment or have suffered recurrent disease. Members of CPCC provide this service and are available to respond to your inquiries 7 days a week between 10:00 AM and 10:00 PM Pacific time. You may call:

Stan Rosenfeld	(415) 459-4668
Erlinda Patterson (Spanish)	(909) 754-8392

CPCC WEBSITE

Go to our website <www.prostatecalif.org> for our calendar of events, legislative page, support group meetings and lending library. You can also access copies of past issues of CPCC News in PDF or Word format. There are direct links to other websites including current NCI trials.

CPCC publishes all major events in bi-monthly newsletter (February, April, June, August, October and December). We need your notice by the 9th of the month before printing. E-mail Stan Mikkelsen at cpcc@prostatecalif.org.

"YOUR CONTRIBUTIONS MAKE OUR WORK POSSIBLE"

Enclosed is my gift of $_____. **Mail to:** CPCC, 6709 La Tijera Blvd, Suite 473 Los Angeles, CA 90045

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