CALIFORNIA Prostate Cancer COALITION

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NEWS

Volume 16, Issue 2

August 2014

PRESIDENT'S MESSAGE

Summer is here and CPCC is busily working on our Laminate Pilot Project. For those of you unfamiliar with this project, we have developed an educational tool in the form of a Laminate on Informed Decision Making, with one side for Men 40 and Over, and the flip side for Primary Care Physicians, namely internists, GP's and Family Practice physicians. This is frankly the only way to get around the "D" Recommendation of the United States Preventive Services Task Force, which has relieved the physician of any obligation to even raise the issue of PSA testing with men, UNLESS the patient brings up the topic, at which point informed discussion should take place. We are hopeful that men will understand the information contained in the Laminate and will take it with them to their physician's office to discuss at their next appointment.

For our Pilot Project, we distribute the Laminate, an attached cover letter and a postcard with 5 questions for you to answer and mail back to CPCC. We want to see what language, if any, needs to be tweaked, and also what distribution points and locales are the most effective for distributing this educational tool. If any of you would like to help us distribute the Laminate, please contact me at mgrey@ucsd.edu or Stan Rosenfeld, one of our Board Members, at Vegstan2@ix.netcom.com.

Great news in prostate cancer came out at the Annual Meeting of ASCO (American Society of Clinical Oncology) held in Chicago in June. To summarize, the results of the phase III E3805 trial funded by the National Institutes of Health and pre-

(Continued on page 4)

UROLOGIST MOST INFLUENTIAL IN PROSTATE CANCER TREATMENT DECISIONS

For older men with low-risk prostate cancer, the urologist who diagnoses the disease could play a pivotal part in whether they are actively treated and, if so, the type of treatment they receive. "The diagnosing urologist plays an important role in treatment selection" for prostate cancer, because he or she is the first to convey the diagnosis to the patient and discuss disease severity and management options, the investigators conclude.

The study was published online July 14 in JAMA Internal Medicine. The findings "strongly suggest that physicians substantially influence not only decision making regarding up-front treatment vs observation but also the type of up-front treatment when treatment is selected," write Karen E. Hoffman, M.D, MPH, assistant professor in radiation oncology at the University of Texas M.D. Anderson Cancer Center in Houston, and colleagues.

In the study, 2145 urologists diagnosed low-risk prostate cancer in 12,068 men, 80.1% of whom received treatment and 19.9% of whom were followed with active surveillance (AS). However, the urologists varied widely in their use of observation (range, 4.5% to 64.2% of patients), the investigators note. The 870 radiation oncologists who met with study participants also varied widely in their use of observation (range, 2.2% to 46.8%).

"What's striking was just how much variation exists in managing prostate cancer, with the diagnosing physician playing as much a role, if not more of a role, than accepted patient factors that impact AS use," said Dr. Hoffman in a release. In addition, urologists who treat non-low-risk prostate cancer and graduated less recently from medical school were less likely to manage low-risk disease with AS.

Patients were more likely to undergo medical interventions, including radical prostatectomy (RP) and external-beam radiotherapy (EBRT), if their urologist performed that procedure. The phenomenon of using RT if there is equipment in-house has been reported previously, and has led to allegations that urologists "follow the money." According to 2 reports, financial incentives were the likely driver of the dramatic increase in the use of intensity-modulated RT, which has the highest reimbursement from Medicare of all the definitive treatments for early prostate cancer.

In the current study, the diagnosing urologist was the most influential factor measured. They were responsible for 16.1% of the variance in management choice, whereas only 7.9% of the variance was attributable to measured patient characteristics, the investigators report. "The variance in treatment selection attributable to physicians was

(Continued on page 3)

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NO EVIDENCE, YET ANDROGEN DEPRIVATION THERAPY OFTEN USED IN LOCALIZED PROSTATE CANCER

Androgen-deprivation therapy (ADT) is widely used as a primary therapy in localized prostate cancer, despite a lack of solid data supporting its use. Now, long-term results provide further evidence that ADT does not improve overall or disease-specific survival in this population.

The large population-based cohort study of more than 66,000 men 66 years and older was conducted by Grace L. Lu-Yao, MPH, PhD, from the Rutgers Cancer Institute of New Jersey and Robert Wood Johnson Medical School in New Brunswick, and colleagues. The results were published online July 14 in *JAMA Internal Medicine*.

Rates were similar in areas with high use of ADT and in areas with low use for 15-year prostate-cancer-specific survival (85.4% vs 85.4%; hazard ratio [HR], 1.01) and for 15-year overall survival rate (15.9% vs 16.8%; HR, 1.04).

Previous research has shown that ADT is appropriate for use in high-risk patients and in combination with other treatments, but ADT alone, especially in an older population, should be carefully considered. "Because of the potential side effects of osteoporosis, diabetes, and decreased muscle tone, clinicians must carefully consider the rationale behind ADT treatment if used as the primary therapy for older patients," Dr. Lu-Yao said in a statement. Results could be different for younger men, she added, who were not part of this study.

On the basis of "randomized trials and observational data from [Surveillance, Epidemiology and End Results] SEER–Medicare and from integrated healthcare networks, there is no compelling evidence to prescribe ADT alone for men with localized prostate cancer," write Quoc-Dien Trinh, MD, and Deborah Schrag, MD, MPH, from the Dana-Farber Cancer Institute, in an accompanying commentary.

Perhaps the most important contribution made by this study is that it demonstrates as recently as 2009 that use of primary ADT in the setting of localized prostate cancer is "alarmingly high." This is regardless of the "evidence indicating the potential for harm and discouraging its use," they note. In addition, these drugs place a large economic burden on the Medicare system. Fifteen years ago, leuprolide and goserelin accounted for 23% ($4 billion) of all Medicare Part B drug expenditures, Drs. Trinh and Schrag report.

The inappropriate prescribing to Medicare recipients of outpatient drugs, such as the luteinizing-hormone-releasing hormone agonists, declined after the 2003 Medicare Modernization Act decreased reimbursement for such drugs. However, the "estimated annual direct cost of guideline-discordant ADT in the Medicare population was recently estimated to be $42 million," they write.

"Given persistent high use rates, primary ADT for localized prostate cancer is a prime candidate for inclusion in the American Board of Internal Medicine Foundation and the American Urological Association 'Choosing Wisely' campaign to encourage clinicians to avoid use of therapeutic interventions with marginal benefits," Drs. Trinh and Schrag conclude.

In a previous study by Dr. Lu-Yao's team, ADT was associated with a possible borderline survival benefit for patients with poorly differentiated prostate cancer during the 10-year period after diagnosis. The research team also previously reported that ADT does not delay the use of secondary cancer therapies and is associated with an increased risk for fracture and subsequent mortality. Earlier this year, a retrospective cohort study of more than 15,000 men newly diagnosed with clinically localized prostate cancer also found no survival benefit with primary ADT.

Expanded Results Show No Benefit

Dr. Lu-Yao and colleagues note that one of the major limitations of their previous studies was the limited length of follow-up. In the current study, they added SEER regions and extended the follow-up by 6 years to see if there were long-term benefits with primary ADT.

The researchers conducted an instrumental variable analysis on 66,717 Medicare patients 66 years and older who were diagnosed with prostate cancer from 1992 to 2009. The patients received no definitive local therapy within 180 days of their diagnosis, and the study was conducted in predefined geographic areas in the United States covered by the SEER program.

For overall survival, median follow-up was 110 months. Patients who received primary ADT were slightly older than those who did not (79 vs 77 years), and were sicker, as indicated by a Charlson score of at least 2 (15.2% vs 12.5%). The ADT patients were also more likely to have high-risk disease (47.7% vs 23.0%) and a higher mean prostate-specific antigen level (19.5 vs 11.1 ng/mL).

There were 5275 deaths from prostate cancer in the cohort, and 39,801 deaths from any cause. In the preplanned instrumental variable analysis, low-risk and high-risk disease had similar outcome patterns.

(Continued on page 3)

15-Year Survival	High-Use Areas of ADT (%)	Low-Use Areas of ADT (%)
Moderately Differentiated Cancers		
Overall	20.0	20.8
Disease-specific	90.6	90.6
Poorly Differentiated Cancers		
Overall	8.6	9.2
Disease-specific	78.6	78.5

UROLOGIST MOST INFLUENTIAL IN PROSTATE CANCER TREATMENT DECISIONS *(Continued from page 1)*

at least double the variance attributable to measured patient-level characteristics such as age, comorbidity, clinical stage category, and PSA level," they write.

"Patients who received their diagnoses from urologists who treated non-low-risk prostate cancer were more likely to receive up-front treatment and, when treated, more likely to receive a treatment that their diagnosing urologist used for men with non-low-risk disease," Dr. Hoffman and colleagues add.

Investigators examined the impact of physicians on disease management in 12,068 men, 66 years of age and older, who were diagnosed with low-risk prostate cancer from 2006 to 2009. Patient and tumor characteristics were obtained from Surveillance, Epidemiology, and End Results cancer registries. The diagnosing urologist, consulting radiation oncologist, cancer-directed therapy, and comorbid medical conditions were determined from linked Medicare claims.

Urologists who treat non-low-risk prostate cancer were less likely to manage low-risk disease with AS (adjusted odds ratio, 0.71; P = 0.01), as were urologists who graduated "in earlier decades" (P = 0.004). Management with observation was not associated with the diagnosis volume of the urologist (P >0.10), and older men who received a more recent diagnoses were more likely to be monitored with AS (P <0.001). However, 55.1% of men older than 80 years still received up-front treatment.

Observation was more common in men seen only by urologists than in men seen by a radiation oncologist and a urologist (43.8% vs 8.6%; P <0.001). Overall, 70.8% of men who underwent observation saw only a urologist.

For patients who received active therapy, the investigators evaluated whether the type of treatment performed by the diagnosing urologist affected the type of treatment that the patient actually received. If the urologist performed treatment for non-low-risk disease, patients were more likely to undergo RP (23.8% vs 12.4%; P <0.001), cryotherapy (22.0% vs 1.0%; P <0.001), and brachytherapy (47.5% vs 21.0%; P <0.001). If the diagnosing urologist billed for EBRT, men were more likely to receive that therapy (52.7% vs 42.9%; P = 0.005). In addition, 78.1% of men who underwent RP had the procedure performed by the diagnosing urologist.

Impact of Radiation Oncologist

Of the 7554 men who met with a radiation oncologist, 91.5% received up-front treatment and 8.5% were observed. On multivariable analysis, radiation oncologists with a DO degree were less likely to manage disease with observation (P = 0.02), but there was no association between observation and physician treatment volume or date of graduation (P >0.10). On multilevel analyses, 19.0% of the variance in the choice of management was attributed to the radiation oncologist, and only 3.2% was attributed to measured patient characteristics.

"Public reporting of physicians' cancer management profiles would enable primary care physicians and patients to make more informed decisions when selecting a physician to diagnose and manage prostate cancer," the investigators explain. Dr. Hoffman pointed out that primary care physicians play a key role, because they are the ones who refer patients to urologists. "Increasing transparency could lead to selecting physicians more open to surveillance," she said.

The investigators note that there were several limitations to the study. Shifting practice patterns, for example, could have influenced treatment decisions. In addition, the inability to measure certain factors that could impact treatment choice, such as family history and patient anxiety, were not accounted for.

Follow-up work in this area will evaluate whether patient counseling in a multidisciplinary setting, along with patient decision aids, will increase the acceptance of AS.

Medscape Medical News, 16 July 2014

NO EVIDENCE, YET ANDROGEN DEPRIVATION THERAPY USED IN LOCALIZED PROSTATE CANCER *(Continued from page 2)*

When the researchers excluded cancers with Gleason scores of 7 from the poorly differentiated cancer group, the results were still similar. The HR for disease-specific mortality decreased from 0.99 (95% CI, 0.84 - 1.17) to 0.96 (95% CI, 0.81 - 1.13) and for overall mortality decreased from 1.03 (95% CI, 0.96-1.10) to 1.01 (95% CI, 0.93-1.09).

"For low-risk patients, neither our previous study nor the updated analysis showed any improvement in survival associated with primary ADT use," the researchers write. "In high-risk patients, our earlier publication showed a borderline survival benefit, which was not confirmed in the updated study."

The study was supported by the National Cancer Institute and the Cancer Institute of New Jersey. Dr. Lu-Yao reports financial relationships with Merck Research Laboratories and Schering-Plough. Coauthor Weichung Shih, PhD, from Rutgers Cancer Institute of New Jersey, reports financial relationships with Myriad.

Medscape Medical News, 14 July 2014

IMPACT OF NADIA PROSVUE PSA SLOPE ON SECONDARY TREATMENT DECISIONS AFTER RADICAL PROSTATECTOMY

Moul JW, Chen DYT, Trabulsi EJ, et al, on behalf of the investigators for the NADiA ProsVue Field Experience Trial

Prostate Cancer Prostatic Dis 15 July 2014; Epub

Background: Selecting appropriate candidates for postprostatectomy radiotherapy is challenging because adverse pathologic features cannot accurately predict clinical recurrence. Biomarkers that identify residual disease activity may assist clinicians when counseling patients on the risks, benefits and costs of secondary treatment. NADiA® ProsVue™ PSA slope results ≤2.0 pg/mL/mo are predictive of a reduced risk of clinical recurrence, however, its clinical utility has not yet been studied.

Methods: We prospectively enrolled men treated by radical prostatectomy in a multicenter, IRB-approved clinical trial. At post-surgical followup, investigators (N=17) stratified men into low-, intermediate- or high-risk groups for prostate cancer recurrence based on clinicopathologic findings and other factors. Investigators documented their initial treatment plan for each subject and serially collected three serum samples for ProsVue testing. After the ProsVue result was reported, investigators recorded whether or not the initial treatment plan was changed. The proportion of cases referred for secondary treatment before and after ProsVue was reported and the significance of the difference determined.

Results: Complete assessments were reported for 225 men, 128 (56.9%) of whom were stratified into intermediate and high risk groups. Investigators reported that they would have referred 41/128 (32.0%) at-risk men for secondary treatment. However, after results were known, they referred only 15/128 (11.7%) men. The difference in proportions (-20.3%, 95% confidence interval [CI] -29.9 to -10.3%) is significant (p <0.0001). Odds of a referral was significantly reduced after results were reported (Odds Ratio 0.28, 95% CI 0.15–0.54, p <0.0001).

Conclusion: Knowledge of a ProsVue result had significant impact on the final treatment plan. A ProsVue result ≤2.0 pg/mL/mo significantly reduced the proportion of men at risk of recurrence that would otherwise have been referred for secondary treatment.

PRESIDENT'S MESSAGE

(Continued from page 1)

sented at ASCO found an "unprecedented" survival benefit (more than one year) in men with newly diagnosed metastatic hormone-sensitive prostate cancer by adding docetaxel to standard androgen ablation therapy (testosterone suppression). What was observed was a greater benefit in those men with more extensive metastatic disease. Thus the study aimed to see whether adding docetaxel when men were still hormone-sensitive would make a difference in survival, which it did. Extensive disease involved either a high burden of bone metastases or liver or lung metastases. In those men, adding docetaxel early as described meant a 40% reduction in the risk of death. This may truly be a practice-changer and is obviously very dramatic and exciting news.

I wish you all a wonderful, enjoyable summer!

Merel Grey Nissenberg

CPCC PHONE NUMBER & E-MAIL ADDRESS

For more information concerning CPCC or its programs and services, please call Stan Rosenfeld at (415) 459-4668 or send an E-mail to 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

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CPCC publishes all major events in bi-monthly newsletter (February, April, June, August, October and December). If you have any newsworthy events you would like us to report, please E-mail CPCC at cpcc@prostatecalif.org.

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