JUNE 2015

Hot SHEET

Us TOO INTERNATIONAL Prostate Cancer Education and Support Network

INSIDE

Affected by Prostate Cancer?

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SUPPORT - EDUCATION - ADVOCACY

Low Use of Adjuvant Radiotherapy after Radical Prostatectomy

Despite evidence from clinical trials and recommendations from professional organizations for the use of adjuvant radiotherapy (RT) after radical prostatectomy (RP) in men with localized prostate cancer with high-risk features, a new study finds little use of RT in this setting. The study, published online April 20 in *European Urology*, reports that fewer than 20% of men with prostate cancer at risk for recurrence received postoperative RT within six months of surgery.

Corresponding author Helmneh M. Sineshaw, MD, MPH, senior epidemiologist at the American Cancer Society, Atlanta, and colleagues garnered data from the National Cancer Data Base – a US hospital-based cancer registry that captures approximately 70% of men newly diagnosed with cancer. They found that 97,270 men aged 18 to 79 years with newly diagnosed invasive prostate cancer were treated with RP between 2005 and 2011. Of those, only 7,766 (8%) received RT +/- androgen deprivation therapy (ADT) post-RP.

The reported trends were:

- RT +/- ADT decreased from 9.1% in 2005 to 7.3% in 2011 (P <0.001 for trend).
- 8.5% of men aged 18-59 years received RT +/- ADT vs. 6.8% of men aged 70-79 (P <0.001 for trend).
- 14% of men treated at community centers received RT +/- ADT vs. 7.3% at academic centers.
- 17% of men with stage pT3/T4 disease and positive surgical margins (SMs) received RT +/- ADT vs. 3.9% of men with pT3/T4 disease and negative SMs.
- 17% of men with a Gleason score (GS) of 8-10 received RT +/- ADT vs. 4.2% for men with a GS of 2-6.
- 9.1% of men with positive SMs received RT vs. 5.8% for men with negative SMs.

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Prostate Cancer Treatment with New Injectable Gel

A device to lower side effects of radiation treatment (RT) for prostate cancer received FDA clearance on April 1. The device injects a temporary gel to create a space between the prostate and the rectum. Named the SpaceOAR System ("OAR" stands for "organ at risk"), FDA granted clearance after a US clinical trial showing that SpaceOAR hydrogel achieved a significant reduction in rectal radiation dose and late rectal toxicity.

Despite advancements in RT for prostate cancer, a common side effect is damage to the rectum, which is located just below the prostate. Unintended RT exposure to the rectum often results in complications including diarrhea, bleeding and pain.

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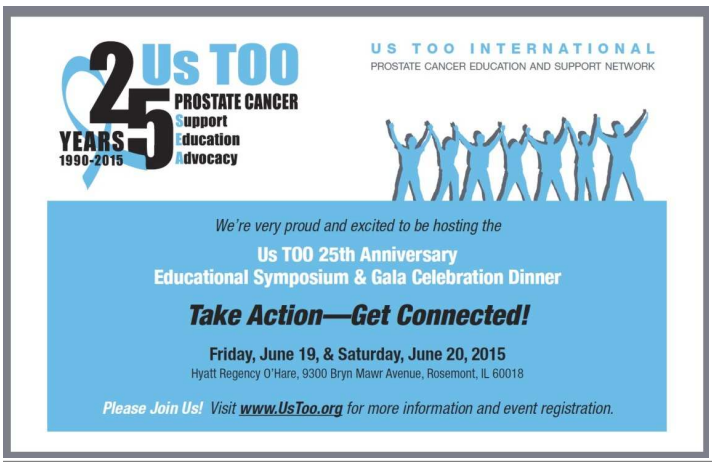

Aspirin Does Not Reduce Mortality in Prostate Cancer

The use of aspirin after newly diagnosed nonmetastatic prostate cancer does not lower disease-specific or overall mortality, according to a large population-based study conducted in the United Kingdom. In fact, the risk for prostate cancer mortality increased in men who started aspirin therapy after diagnosis. The study was published in the April issue of the *Journal of Urology*.

"It is likely that the observed risk is due to some confounding factors," said Laurent Azoulay, PhD, from the Department of Oncology at McGill University in Montreal. "It is possible that men who start aspirin after their prostate cancer diagnosis have other conditions that are associated with worse survival. As such, our results should not detract men from starting aspirin after their diagnosis," Dr. Azoulay told Medscape Medical News.

Several observational studies have assessed the association between aspirin use and prostate cancer outcomes, with mixed results. These studies, Dr. Azoulay said, had "important methodological limitations that exaggerated the potential effects of aspirin in men with prostate cancer. Using the appropriate

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Update of the Results of the Spanish Branch of the European Randomized Study on Screening for Prostate Cancer (ERSPC)

Luján M, Páez Á, Angulo JC, et al

Actas Urol Esp 13 March 2015; Epub

Objective: The role of prostate cancer (PC) screening is currently being questioned. The objective of the European Randomized Study of Screening for Prostate Cancer (ERSPC) was to demonstrate whether PC screening reduced mortality from this disease. The results from the Spanish branch of this study are presented: all-cause and cancer-specific mortality, the characteristics of the detected tumors, primary treatments and progression to advanced disease.

Material and methods: A total of 18,612 men, between the ages of 45 and 70, were invited to participate in the study, excluding those with a life expectancy of less than 10 years. The men were randomized to the screening arm (serum PSA reading) or the control arm (no diagnostic tests). Randomized transrectal ultrasound-guided sextant prostate biopsies were indicated for the men in the screening arm with PSA levels ≥ 3ng/ml. The detected PCs were identified (stage and primary treatment), as well as the deaths that occurred (date and cause of death).

Results: The study was performed with 4,276 men (2,415 in the screening arm and 1,861 in the control arm). The median age and serum PSA level were 57 years and 0.90 ng/mL, respectively. The median follow-up time was 15.8 years. A total of 242 PCs were diagnosed, 162 (6.7%) in the screening arm and 80 (4.3%) in the control arm (P < 0.001). Of these, 214 (88.4%) had an organ-confined clinical stage at onset (91.4% in the screening arm vs. 82.5% in the control arm; P = 0.024). A total of 112 men (46.3%) underwent radical prostatectomy, 53 (21.9%) radiation therapy, 24 (9.9%) hormone therapy and 47 (19.4%) were kept under observation. A total of 18 PCs progressed to advanced disease (M+ or PSA levels >100 ng/mL), with no differences between the study arms (P = 0.938). A total of 618 (14.5%) patients died during follow-up: 340 (14.1%) in the screening arm and 278 (14.9%) in the control arm, with no differences between the arms in terms of cancer-specific (P = 0.907) or all-cause (P = 0.399) mortality. The main causes of death were neoplasia (54.0%), cardiovascular (17.6%), respiratory (8.7%) and gastrointestinal (4.0%), with no difference between study arms. Of the 334 patients who died from neoplasia, only 12 (3.6%) died from PC.

Conclusions: PC screening results in a shifting of the diagnosis towards earlier stages. Nevertheless, we have not demonstrated a benefit in terms of overall or cancer-specific survival after more than 15 years of follow-up. The low mortality from this disease in our community could be one of the main factors that explain these results.

New Tool for Guiding Therapy in Prostate Cancer Patients

Researchers at the University of Central Florida say they have now come up with a $1 test using gold nanoparticles that can outperform PSA (prostate specific antigen) screening for prostate cancer. The researchers report that cancer biomarkers cling to gold nanoparticles, and may provide more accurate early-stage detection for a number of tumor types. This type of technology may usher in a new era in determining which patients should receive targeted therapies.

Test developer Qun "Treen" Huo, PhD, who is a research scientist at University of Central Florida, said this new technique could reduce the number of unnecessary and invasive biopsies due to PSA screening. Huo's test detects this immune response using gold nanoparticles, and it is rather simple. When a few drops of serum are mixed with the gold nanoparticles, certain cancer biomarkers cling to the surface of the tiny particles, increasing their size and causing them to clump together.

Urologic oncologist Inoel Rivera, MD, who collaborated with Huo on the recent pilot studies, said this is a rather simple test and it's cost-effective. Gold nanoparticles are known for their extraordinary efficiency at absorbing and scattering light. Huo and her team at UCF's NanoScience Technology Center developed a nanoparticle-enabled dynamic light scattering assay (NanoDLSay) to measure the size of the particles by analyzing the light they throw off. The size of the particles reveals whether a patient has prostate cancer and how advanced it may be.

The researchers noted that this technology is very appealing for a number of reasons, including cost. They report that even though the test uses gold, it is inexpen-

(Continued on page 5)

Docetaxel and Prednisone with or without Lenalidomide in Chemotherapy-Naive Patients with Metastatic Castration-Resistant Prostate Cancer (MAINSAIL): A Randomised, Double-Blind, Placebo-Controlled Phase 3 Trial

Petrylak DP, Vogelzang NJ, Budnik N, et al

Lancet Oncol 2015;16:417-25

Background: Men with metastatic castration-resistant prostate cancer (CRPC) have few treatment options. We investigated the safety and efficacy of lenalidomide, an immunomodulatory agent with anti-angiogenic properties, combined with docetaxel and prednisone in chemotherapy-naive men with metastatic CRPC (mCRPC).

Methods: In this randomised, double-blind, placebo-controlled, phase 3 study, we randomly assigned chemotherapy-naive men with progressive mCRPC in a 1:1 ratio to receive docetaxel (75 mg/m^2) on day 1 and prednisone (5 mg twice daily) on days 1-21 and either lenalidomide (25 mg) or placebo once daily on days 1-14 of each 21 day treatment cycle. Permuted block randomisation was done with an interactive voice response system and stratified by Eastern Cooperative Oncology Group performance status, geographic region, and type of disease progression. Clinicians, patients, and investigators were masked to treatment allocation. The primary endpoint was overall survival. Efficacy analysis was by intention to treat. Men who received at least one dose of study drug were included in safety analyses. This study is registered with ClinicalTrials.gov, number NCT00988208.

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Doc Moyad's What Works & What is Worthless Column, Also Known as "No Bogus Science" Column –

"Adult vaccines like the pneumonia shot and tetanus shot are also anti-heart disease and/or anti-cancer?! What "

Mark A. Moyad, MD, MPH, Univ. of Michigan Medical Center, Department of Urology

Editor's Note: Us TOO invites certain physicians and others to provide information and commentary for the *Hot SHEET* to enrich its content to empower the reader. This column contains the opinions and thoughts of its author and are not necessarily those of Us TOO International.

Bottom Line:

If you qualify for any adult vaccine right now please go get it right now. Well, not now but after you read this. It may not only reduce your risk of cardiovascular disease (CVD), but it might also enhance the effects of your cancer treatment. This is preliminary but darn interesting![1,2]

I apologize for being redundant, and I apologize for being redundant (get it!). However, I have explained in the past how many adult vaccines like the flu vaccine are heart-healthy and you need to get these vaccines for all the side benefits! And now the latest data show that preventing pneumonia may fight heart disease and other vaccines could enhance the effects of cancer treatment! Okay, this is preliminary stuff but it is quite amazing! A recent well-done study of over 5,800 adults found that pneumonia might be an independent risk factor for cardiovascular disease (CVD)! Hospitalization for pneumonia was associated with an increased short- and long-term risk of CVD! Why? Infections can cause pro-inflammatory changes in the composition of plaques in the coronary arteries (heart disease) and render them more vulnerable to cause sudden cardiac events (heart attack, stroke…).

Additionally, there were somewhat stunning (this is preliminary but stunning-like my wife in the dress she will wear at the US TOO 25th anniversary celebration dinner on June 19th) result reported in a randomized human study in patients with brain tumors. Researchers gave a small number a tetanus/Td shot (actually tetanus/diphtheria toxoid) to enhance their immune response to an experimental dendritic cell immune therapy. For some of the patients, it appeared to provide a "boost" or enhanced treatment effect! In fact, it appeared to significantly enhance survival in patients with glioblastoma (a very, very tough tumor to treat). Among the six patients who received the Td shot, three lived between 20 and 24 months from diagnosis, and three lived longer than three years – including one patient who is still alive after nine years. And if you are not yet impressed, the control group of this study only had a median survival of 18.5 months.

Researchers thought the Td shot would work by causing an immune response locally at the vaccine site, but were surprised that it appeared to cause a systemic (body wide) immune response. I do not want anyone reading this to get too excited because it is a small human study of brain cancer. However, I do think it is time to get excited about getting both pneumonia vaccines if you qualify (PCV13 = Prevnar® and PPSV23 = Pneumovax®; since September 2014, both are recommended, just not at the same time). So I recommend you speak with your doctor, because if you are 65 years or older or in many other special cases, you may qualify ASAP. Also, for all those adults who have let too much time go by since they had their tetanus shot or never had one – it is time to go and get it ASAP if you qualify! Incredible and exciting stuff! And, you only thought vaccines prevent or mitigate the one disease it is advertised to prevent or mitigate?! Silly boys and girls (sarcasm alert #2384) – vaccines are not just for kids anymore!

References:

1. Corrales-Medina VF, Alvarez KN, Weissfeld LA, et al. Association between hospitalization for pneumonia and subsequent risk of cardiovascular disease. *JAMA* 313: 264-274, 2015.
2. Mitchell DA, Batich KA, Gunn MD, et al. Tetanus toxoid and CCL3 improve dendritic cell vaccines in mice and glioblastoma patients. *Nature* 519 (7543): 366-369, 2015.

SpaceOAR

(Continued from page 1)

SpaceOAR (pronounced "space oar"), developed by Augmenix, Inc., temporarily positions the front portion of the rectum away from the prostate during RT, creating space for protection. The device uses hydrogel. The gel is injected in liquid form through a needle and quickly solidifies into a soft gel to separate the two organs.

Evidence suggests that by reducing RT side effects, this method will bring two additional benefits: it opens the way to dose escalation (more RT for improved cancer kill rates) and hypofractionation (fewer RT sessions). All around, these potential benefits should improve patient experience, improve therapy outcomes, and help reduce healthcare costs.

"Shielding the rectum from radiation allows us to increase the RT dose used to kill cancerous cells in the prostate," said Rodney Ellis, MD, radiation oncologist at UH Seidman Cancer Center.

"The SpaceOAR System represents a significant development in advancing the safety, precision and flexibility with which prostate cancer RT can be delivered," he said. "The procedure is performed on an outpatient basis and patients are able to return home and resume their normal activities right away."

According to the FDA approval letter, the gel expands the space between prostate and rectal wall, normally about 3.8 mm, to almost 12 mm. The gel maintains this space for "about three months." After six months, all the gel has been absorbed and the space returns to normal.

PSA Rising
23 April 2015

Low Use of Adjuvant RT after Radical Prostatectomy

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"Although receipt of such therapy [RT] was higher in younger men and in those at highest risk for recurrence, overall rates of use remain low, with <20% of men receiving RT, even in subgroups most likely to benefit from such therapy," write Dr. Sineshaw and colleagues in their discussion.

"Despite category 1 evidence, the trend for providing adjuvant RT (ART) to men with localized prostate cancer and adverse pathological features (APFs) is not as one would expect," she said. Senior author Jason A. Efstathiou, MD, DPhil, who is associate professor at Harvard Medical School and is with the Department of Radiation Oncology at Massachusetts General Hospital in Boston added, "The broad adoption of ART has been low. Indeed, usage is decreasing since the availability of high-level evidence."

The evidence comes from three randomized clinical trials, two in Europe and one in the US, which have shown significant progression-free survival (PFS) benefits and decreased risk for biochemical recurrence (BCR) when men with prostate cancer and APFs are provided ART post-RP. The American Society for Radiation Oncology (ASTRO) and the American Urological Association (AUA) endorsed these studies with a guideline in 2013.

Medscape Medical News reached out to several radiation oncologists not associated with the study. The opinions were conflicting, varying from disappointment with current practice to lack of wholehearted support that advances ART for all men with prostate cancer post-RP.

"It is extremely disappointing to see that the urologic oncology community has not embraced the consistent results of three prospective randomized trials that have provided class 1 evidence of benefit from ART for men with APFs following RP," stated Jeffrey M. Michalski, MD, vice chairman of radiation oncology and chief of the genitourinary service at the Washington University School of Medicine in St. Louis. "Despite data demonstrating the low rate of toxicity from ART, men are being denied the opportunity to receive this important and highly effective treatment," he added.

Anthony V. D'Amico, MD, PhD, FASTRO, professor in the Department of Radiation Oncology and chief of genitourinary radiation oncology at the Dana-Farber and the Brigham and Women's Hospital in Boston indicated that "some clinicians are not entirely convinced about the three randomized trials that support ART for men undergoing RP because while all three show a benefit in PFS, only one showed a decrease in metastasis-free survival (MFS) and prolongation in overall survival (OS). Some have interpreted this to suggest that only men with multiple indications [APFs] for ART after surgery, and not a single indication, may be best treated," Dr. D'Amico told Medscape Medical News.

Michael J. Zelefsky, MD, professor of radiation oncology in the Department of Radiation Oncology at Memorial Sloan Kettering Cancer Center, New York City, stated "These findings are not surprising and reflect current practice patterns and trends. While one study has demonstrated a survival benefit for the use of ART in high-risk patients, it remains unclear that the outcomes are compromised if one waits until the PSA becomes detectable. If the PSA is watched carefully and RT is administered when it [PSA] becomes a detectable and rising value, the disease is likely being picked up in an early state, and the survival outcome is not likely compromised," he said.

According to Dr. Sineshaw and colleagues, "The pattern of declining use [of RT] could be due to multiple factors, including patient preference, physician and referral bias, concern about toxicity, lack of a consistent survival benefit seen in the updated randomized trials, or a growing preference for salvage RT at time of BCR."

But according to Dr. Zelefsky, "Not every high-risk patient will fail after surgery," and he suggested that men should not be exposed to RT if they do not need it. Dr. D'Amico agreed, explaining that data from a Duke University study suggest that a man with a GS of 7, extracapsular extension, and negative SM may be watched, whereas a man with a GS of 8, extracapsular extension, and a positive margin would be referred for adjuvant RT, given their relatively higher risk for subsequent failure.

"The results of the current study suggest that this is what is happening," he added.

Medscape Medical News
29 April 2015

New Tool for Guiding Therapy in Prostate Cancer Patients

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sive. A small bottle of nanoparticles suspended in water costs about $250 and contains enough for about 2,500 tests. Huo said the test should be available for clinicians to use in their offices within the next 24 to 36 months. Early detection can help lead to improved outcomes by helping to better guide treatment decisions. After lung cancer, prostate cancer is the second-leading killer cancer among men, with more than 240,000 new diagnoses and 28,000 deaths every year.

Pilot studies have demonstrated this technique is significantly more exact than PSA screening. The test determines with 90% to 95% confidence that the result is not a false-positive, according to the researchers. The results of the pilot studies were published in the March 2015 issue of ACS Applied Materials & Interfaces.

Dr. Huo is scheduled to present her findings in June at the TechConnect World Innovation Summit & Expo in suburban Washington, DC. Huo said she and her team hope to develop an array of assays for early detection and diagnosis of all major cancer types.

Oncotherapy Network
8 April 2015

Aspirin Does Not Reduce Mortality in Prostate Cancer

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methods, we found that aspirin was not associated with a protective effect. This does cast some doubt on the potential antitumor effects of this drug in this population," he explained.

Using the National Cancer Data Repository, the Clinical Practice Research Datalink, and other databases, the researchers identified 11,779 men with nonmetastatic prostate cancer diagnosed from 1998 to 2009. The mean age at diagnosis was 71.3 years. During a mean follow-up of 5.4 years, 1,793 men died of prostate cancer and 3,502 died from any cause.

Overall, the use of aspirin after diagnosis was associated with a 46% increased risk for prostate cancer mortality (Hazard Ratio [HR], 1.46; 95% confidence interval [CI], 1.29 - 1.65) and a 37% increased risk for all-cause mortality (HR, 1.37; 95% CI, 1.26-1.50). There was no evidence of a duration-response relation between aspirin use and prostate or all-cause mortality.

However, the increased risks for prostate cancer mortality (HR, 1.84: 95% CI, 1.59-2.12) and all-cause mortality (HR, 1.70; 95% CI, 1.53-1.88) were restricted to men who initiated aspirin after diagnosis. No increased risk was observed in men who started aspirin before diagnosis, a finding consistent with three other observational studies, the researchers note.

In light of a recent study that reported decreased prostate cancer mortality in high-risk patients (HR, 0.60; 95% CI, 0.37-0.99), Dr. Azoulay's team performed a similar analysis but was unable to replicate the finding (HR, 1.85; 95% CI, 1.51-2.30). "Taken together, these results argue against a protective association between the use of aspirin and the risk of prostate cancer mortality and all-cause mortality," the researchers say.

Dr. Azoulay noted, "These drugs are commonly used in patients with cardiovascular conditions, where benefits have been observed. Our null results should not change this practice."

"It's possible that the use of aspirin after prostate cancer diagnosis is related to prostate cancer disease progression," the researchers explain. They note that certain prostate cancer treatments, such as androgen-deprivation therapy, are associated with an increased risk for cardiovascular events and, "thus, it is possible that the prescribing of aspirin was the result of treatment-related adverse events, which themselves are associated with worse disease progression."

Although the researchers adjusted for more than 30 potential confounders, residual confounding remains a possibility, they point out.

There are "several shortcomings" in this study, said Kevin Choe, MD, PhD, radiation oncologist at University of Texas Southwestern Medical School in Dallas, who has studied aspirin use in prostate cancer but was not involved in this study.

"For example, there are clinical factors known to be most powerful prognostic factors in prostate cancer outcomes, including Gleason grade and PSA value," he observed. "In this registry study, they were missing these critical values in more than 50% of their patients, and therefore they were not accounted for in their analysis."

Researchers acknowledge these limitations and others, including the relatively short follow-up period (5.4 years) and the mean advanced age of the men at study entry (71.3 years). "Additional well-conducted studies are needed," said Dr. Azoulay, to "shed more light on the effects of aspirin in men with prostate cancer."

Medscape Medical News
14 April 2015

Does Obesity Explain the High Risk for Prostate Cancer in Black Men?

Black men who are obese are at higher risk for prostate cancer than non-Hispanic white men, according to a study published online April 16 in *JAMA Oncology*. In fact, results suggest that, for black men, risk of prostate cancer nearly quadruples as body mass index (BMI) increases.

"The relation between obesity and prostate cancer risk is different in black men than in non-Hispanic white men," said Wendy Barrington, PhD, MPH, from the University of Washington School of Nursing and the Fred Hutchinson Cancer Research Center in Seattle, WA.

In black men, "obesity substantially increases the risks of both low- and high-grade prostate cancer," she explained. In contrast, in white men, obesity "modestly decreases the risk of low-grade and increases the risk of high-grade cancer."

Black men develop and die from prostate cancer at higher rates than white men. Obesity, which disproportionately affects black men, influences physiologic processes

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Obesity & Prostate Cancer in Black Men

(Continued from page 5)

involved in the development of cancer, such as inflammation and insulin sensitivity, and could affect black men differently, the researchers note. Obesity could also affect levels of PSA and genetic risk alleles, which are also more prevalent in black men.

For their study, Dr. Barrington and her colleagues analyzed data on 3,398 black men and 22,673 white men who participated in the Selenium and Vitamin E Cancer Prevention Trial (SELECT), which was conducted in Canada, the US, and Puerto Rico from 2001 to 2011. The men took either vitamin E or selenium, and were followed for the development of prostate cancer. The trial ended early because of the lack of evidence that these supplements lowered the risk for prostate cancer.

The researchers defined a Gleason score below 7 as low-grade cancer and a Gleason score above 7 as high-grade cancer. During a follow-up of 5.6 years, the proportion of men who developed prostate cancer was higher in black men than white men (7.9% vs. 6.4%). The same pattern was observed for high-grade disease (2.6% vs. 1.9%).

For men with a BMI of at least 35 kg/m² , the risk for prostate cancer was 103% higher in black men than white men (HR, 2.03; 95% CI, 1.38-2.98; P for trend = 0.03).

For black men, the risk for prostate cancer was higher for those with a BMI of at least 35 kg/m² than for those with a BMI below 25 kg/m² (hazard ratio [HR], 1.49; 95% confidence interval [CI], 0.95 - 2.34; P for trend = 0.03). In contrast, for white men, the risk for prostate cancer was lower for those with a BMI of at least 35 kg/m² (HR, 0.80; 95% CI, 0.58-1.09; P for trend = 0.02). For black men, the risk for low-grade disease was a significant 122% higher for those with a BMI of at least 35 kg/m² than for those with a BMI below 25 kg/m² (HR, 2.22; 95% CI,1.36-3.65; P for trend = 0.005).

For black men, the risk for high-grade disease was 81% higher for those with a BMI of at least 35 kg/m² than for those with a BMI below 25 kg/m² (HR, 1.81; 95% CI, 0.79 -4.11; P for trend = 0.02). For white men, the risk was only 33% for those with a BMI of at least 35 kg/m² (HR, 1.33; 95% CI, 0.90-1.97; P for trend = 0.01). For black men, a BMI of at least 30 kg/m², compared with a BMI below 25 kg/m², meant 414.2 additional cases of prostate cancer per 100,000 person-years.

This study's results "provide a rationale for weight reduction and a target BMI for clinicians" who treat black men, Charles R. Thomas Jr, MD, deputy editor of *JAMA Oncology*, writes in an accompanying editor's note. However, he told Medscape Medical News, "The results might not be generalizable to the larger population of the United States. Moreover, the trial was not designed to provide recommendations about a specific target BMI that could help reduce prostate cancer risk in black men," he noted.

"For now, it would be reasonable to recommend a healthy lifestyle, such as a balanced diet that includes regular servings of fruit and vegetables along with regular exercise," Dr. Thomas emphasized.

Medscape Medical News
16 April 2015

Normal Erection after Prostatectomy is Rare

After radical prostatectomy (RP), it is highly uncommon for a man to have erections like the ones he normally had before RP, according to a study presented at the European Association of Urology (EAU) 30th Annual Congress in Madrid. The researchers reached that conclusion because < 10% of the 14 men in the reported that their erections were the same before and after surgery.

There is "controversy" about the incidence of erectile dysfunction (ED) after surgery for prostate cancer. This stems, in part, from the fact that the International Index of Erectile Function (IIEF), has not been validated in prostate cancer patients and is vague, the team notes.

To clarify this issue, Dr. Fode and colleagues added their own question to the IIEF-5, which is an abbreviated version of the longer questionnaire: "Is your [EF] as good as before the surgery (yes/no)?" They mailed their version of the IIEF-5 to 210 men treated at the Herlev Hospital who completed it an average of about 23 months post-RP.

Even without the extra question, IIEF-5 scores showed that the men (mean age, 65 years) were struggling. For men completing the IIEF-5 questionnaire before RP, the mean score was 21.7 (95% confidence interval [CI], 20.6-22.9). Post-RP, the mean score dropped to 9.9, with a lower score indicating more ED (95% CI, 8.6-11.3).

The researchers also collected information on the use of erectile aids. Of the 189 men who did not use aids before RP, 83 started to do so after surgery. Specifically, 58 men began using PDE5-Is, 17 began using penile injections, five began using urethral suppository alprostadil (MUSE), one began using a vacuum erection device, and two received a penile implant.

Notably, the 49 men (23.3%; 95% CI 18.9-28.5%) who did not use erectile aids showed no decline in IIEF-5 score. But an unchanged IIEF-5 does not necessarily mean that all is completely well, erection-wise, suggest Dr. Fode and colleagues. That's because only 14/210 (6.7%) men reported that their erections were unaffected by RP according to the extra question.

"The IIEF-5 questionnaire may not adequately reflect patients' experience," the researchers conclude.

"The study results are not entirely surprising," stated Alexander Kutikov, MD, an attending surgeon in urologic oncology at the Fox Chase Cancer Center in Philadelphia, PA. who was not involved in the study. "Prostate cancer treatment, whether RP or radiation, definitely hits below the belt," he said.

Return to normal sexual functioning might be regularly "overestimated" by clinicians, researchers suggested. Dr. Fode explained why: The IIEF-5 tool focuses on performance over a 6-month period, and asks questions about a man's "confidence" in his erection, "satisfaction" with intercourse, and ability to "complete" intercourse. There are no specific questions about the impact of treatment on erections.

Dr. Kutikov said that some variables help predict who will suffer the most. "We know very well that EF post-prostatectomy often suffers, and very much depends on the degree of nerve sparing, patient age at surgery, and level of potency prior to surgery," he explained.

EAU abstract 1629

Medscape Medical News
14 April 2015

Doctor Chodak's Bottom Line *(Ref Key: article #, page #, column #)*

Gerald Chodak, MD, Author, *Winning the Battle Against Prostate Cancer*, Second Edition http://www.prostatevideos.com/

Editor's Note: Us TOO has invited certain physicians and others to provide information and commentary for the *Hot SHEET* to enrich its content to empower the reader. This column contains the opinions and thoughts of its author and are not necessarily those of Us TOO International.

a1p1c1 Encouraging news was reported in a study involving a spacing gel (SpaceOAR) that is injected between the prostate and rectum prior to RT. Separating the two organs can reduce the amount of RT exposure to the rectal tissue. The study results have not yet been presented, but the FDA has given its approval. Details will be forthcoming when the study is published.

The Bottom Line: SpaceOAR appears beneficial in men about to receive RT.

a2p1c2 The most important article in this *Hot SHEET* deals with adjuvant radiotherapy (RT) after radical prostatectomy (RP). Sineshaw, et al, reported that fewer than 20% of eligible patients received post-RP RT despite three randomized studies showing some benefit. The AUA and ASTRO endorse a recommendation in support of adjuvant RT (ART) and several of the doctors interviewed were surprised or disappointed that more people have not received it. Unfortunately, no one really discussed some of the fundamental issues.

Let's begin with the actual randomized study results that have been reported. Only one showed an improvement in survival, but by no means was it very big. At a median follow-up of 12.6 years, only one out of every 12 men treated avoided metastatic disease and only one of every nine men had better survival. Although side effects were low, that is NOT a very big improvement and when presented with the data many men may have decided not to undergo ART. The other two studies did not show improved survival even though fewer men had a rise in PSA, again demonstrating the importance of NOT using PSA as a surrogate for survival. Should all men in this risk category be informed of the results with ART? The answer is absolutely YES. Unfortunately, we have no information about how often that information is being provided to these men. But, as I have often written, this means real absolute numbers should be presented rather than simply telling patients that ART improves survival or only gives relative benefits. None of the doctors interviewed emphasized that point. A study showing some treatment is beneficial does not mean all men need to receive it; they simply have to be appropriately informed so they can decide if the risk is worth a benefit. Finally, this study does not tell us how immediate RT would compare to delayed (salvage) RT that begins at some predefined PSA increase post-RP. In this study, only one-third of the men did get salvage RT and perhaps the benefit of ART would have been even smaller if the other two-thirds also received it when their PSA increased. A new study is needed to make that determination. The advantage of the delayed approach is many men would avoid ART, but some might be worse off for delaying RT. Without this information, the acceptance of immediate ART is likely to remain low.

The Bottom Line: ART for men with T3 disease benefits only about 10% of patients. Nevertheless, all men should be adequately counseled about the results of the three randomized trials. We also need to determine whether or not immediate RT is comparable to delayed RT.

a3p1c3 Keep the above comments in mind as you read the study about aspirin and prostate cancer. This *observational* study looked at the potential impact of aspirin intake in men with newly diagnosed non-metastatic prostate cancer. The authors analyzed a large database and found that overall mortality and prostate cancer-specific mortality were higher in men starting aspirin after their diagnosis but not before. First of all, this makes no sense scientifically because the timing of the diagnosis is not the timing of the development of the cancer. Secondly, if aspirin was really bad, why should it be that taking it before cancer diagnosis is okay but continuing on it thereafter is bad? As mentioned in the *Hot SHEET* article, important information was missing in more than 50% of men. That is just one of the problems with interpreting data from retrospective studies, and is yet another example of the hazards of making conclusions based on non-randomized controlled studies. The FDA would never use data from a retrospective study like this one to decide whether or not to approve a drug for commercial sale. Again, readers should avoid making treatment decision based on studies that are not properly designed.

The Bottom Line: The results of this study do not inform as to whether taking aspirin is good or bad for men with prostate cancer.

a6p3c1 The risk of conducting a randomized trial is that a new treatment may fail to show a benefit; however, this study design is the only valid way to determine drug efficacy. That is the finding of a randomized study in men with castrate resistant prostate cancer (CRPC) who received docetaxel plus prednisone plus lenalidomide or a placebo. The study drug, lenalidomide, is related to thalidomide, which has activity in prostate cancer and for which preliminary study data are encouraging. Unfortunately, in metastatic CRPC (mCRPC) patients, the study showed lenalidomide was inferior to placebo in overall survival and also in side effects. The importance of this study is that it highlights the importance of testing all therapies in a randomized setting. If men with CRPC relied on the findings from non-randomized trials, they would have falsely believed this drug would help them. Think about all the treatments we have available for which no randomized study has ever been done. One can't help wondering which of these drugs are inferior to other treatment options.

The Bottom Line: Lenalidomide has no activity against mCRPC when added to docetaxel and prednisone therapy.

a8p5c3 A study based on men participating in the SELECT TRIAL found that African American men have a greater risk of being diagnosed with low- and high-risk prostate cancer if they are severely overweight compared to non-Hispanic white men. Unfortunately, the study does not prove cause and effect, nor does it assess the impact of

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Lenalidomide in the MAINSAIL Trial

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Findings: 1,059 men were enrolled and randomly assigned between Nov 11, 2009, and Nov 23, 2011 (533 to the lenalidomide group and 526 to the control group), and 1,046 patients received study treatment (525 in the lenalidomide group and 521 in the placebo group). At data cutoff (Jan 13, 2012) after a median follow-up of 8 months (IQR 5-12), 221 men had died: 129 in the lenalidomide group and 92 in the placebo group. Median overall survival was 17.7 months (95% CI 14.8-18.8) in the lenalidomide group and not reached in the placebo group (Hazard Ratio [HR] 1.53, 95% CI 1.17-2.00, P = 0.0017). The trial was subsequently closed early due to futility. The number of deaths that occurred during treatment or less than 28 days since the last dose were similar in both groups (18/225 [3%] men in the lenalidomide group vs 13/521 [2%] men in the control group. 109 (21%) patients in the lenalidomide group and 78 (15%) in the placebo group died more than 28 days from last dose, mainly due to disease progression. At least one grade 3 or higher adverse event was reported in 381/525 (73%) men receiving lenalidomide and 303/521 (58%) men receiving placebo. Grade 3-4 toxicity including neutropenia, febrile neutropenia, diarrhoea, pneumonia, dyspnoea, asthenia, and pulmonary embolism occurred more frequently with lenalidomide than with placebo.

Interpretation: Overall survival with the combination of lenalidomide, docetaxel, and prednisone was significantly worse than with docetaxel and prednisone for chemotherapy-naive men with mCRPC. Further research with this treatment combination is not warranted.

The Bottom Line

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weight reduction on prostate cancer risk. This is an observational study, so confounding factors may have played a role in the results. Clearly, the health risks of obesity are well known and most primary doctors are no doubt counseling all their patients to reduce weight. But I doubt that adding prostate cancer risk to the other health risks will stimulate many more of those men to make the necessary changes, but an effort still should be made. One caution about the analysis is that the authors defined low- and high-risk disease as GS <7 and 7-10, respectively, thereby ignoring the intermediate-risk category. This is not a well-accepted approach and may have influenced their findings. A re-analysis may help.

The Bottom Line: Obesity is bad for health and may also have an adverse effect in African American men.

A9p6c3 Many surgeons place considerable emphasis on their results with erectile function following RP. They base their assessment on the IEFF questionnaire, but the study by Fode and co-workers suggests that the questionnaire does not ask all the right questions. They added one more question about how the erections after RP compared to those before RP and found only 7% were unchanged and the remainder said erections were worse. Now these results might be better for other surgeons, but the important message is that the question should be asked routinely and the results reported to all men considering surgery.

The Bottom Line: The IEFF survey does not provide men with a complete expectation of how their erections might be affected by RP. If more studies validate this, the IEFF survey may need to be modified for men treated by RP.

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