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MAY 2018

Hot SHEET

Us TOO INTERNATIONAL Prostate Cancer Education and Support Network

SURVIVAL WITH BRACHYTHERAPY-BASED RADIOThERAPY OR RADICAL PROSTATECTOMY IN HIGH-RISK LOCALIZED PROSTATE CANCER

In a study of National Cancer Database data reported in the Journal of Clinical Oncology, Ennis et al. found no significant survival differences between patients receiving brachytherapy-based radiotherapy (RT) vs. radical prostatectomy (RP) in men with high-risk localized prostate cancer. The study involved data from 42,765 men in the National Cancer Database diagnosed between 2004 and 2013 treated by RP (N=24,688); external beam radiotherapy (EBRT) combined with androgen deprivation therapy (ADT, N=15,435); or EBRT plus brachytherapy with or without ADT (N=2,642). Inverse probability of treatment weighting was used to adjust for covariate imbalance among treatment groups. A weighted time-dependent Cox proportional hazards model was used to estimate effects of treatment on survival, while accounting for differential treatment initiation times.

In weighted analysis adjusting for age, PSA score, clinical T stage, Charlson-Deyo score, biopsy Gleason score, and year of diagnosis, no significant difference in overall survival was observed for RP vs. EBRT plus brachytherapy with or without ADT (hazard

(Continued on page 4)

No Benefit in Outcomes with Higher Resource Use in Metastatic Prostate Cancer

Increases in monitoring of PSA levels and bone health were not associated with improved survival or quality of care at end of life (EOL) for men with metastatic prostate cancer, according to a new study. The higher resource use was associated with significantly increased healthcare costs.

“Although it is widely recognized that cancer and EOL care is responsible for a substantial proportion of healthcare expenditures, the appropriateness of that care is challenging to quantify objectively,” wrote study authors led by Jim C. Hu, MD, MPH, of Weill Cornell Medical College in New York. “Evaluating the cost-effectiveness of screening and treatment protocols and their impact on care remains important as more men with metastatic disease are being diagnosed and living longer.”

The new study used data from the Surveillance, Epidemiology, and End Results (SEER) database to examine treatment patterns and healthcare costs in metastatic prostate cancer patients. It included a total of 3,026 men. The results were published in Cancer.

Men were categorized based on use of healthcare resources. “Extreme” users were those who either received PSA testing more than once per month, or who underwent cross-sectional imaging or bone scanning more than every two months over a six-month period. A total of 791 (26%) men fit this category. The extreme users were younger (median age of 73 years) than the non-extreme users (77 years; P <0.001). They were also

(Continued on page 3)

FDA Approves Apalutamide for Nonmetastatic Castration-Resistant Prostate Cancer

The FDA has approved apalutamide (Erleada®) for the treatment of patients with nonmetastatic castration-resistant prostate cancer (nmCRPC). The drug is now the first FDA-approved treatment in this setting.

The approval is based on the phase III SPARTAN trial in which apalutamide reduced the risk of metastasis or death by 72% in men with nmCRPC. The median metastasis-free survival (MFS) was 40.5 months in the apalutamide vs. 16.2 months in the placebo arm (HR, 0.28; 95% Confidence Interval [CI], 0.23-0.35; P <0.0001).

“ ‘The FDA evaluates a variety of methods that measure a drug’s effect, called endpoints, in the approval of oncology drugs. This approval is the first to use the endpoint of metastasis-free survival, measuring the length of time that tumors did not spread to other parts of the body or that death occurred after starting treatment,’” Richard Pazdur, MD, acting director of the FDA’s Oncology Center of Excellence and acting director of the Office of Hematology and Oncology Products in the FDA’s Center for Drug Evaluation and Research, said in a statement.

“In the trial supporting approval, Erleada had a robust effect on this endpoint. This demonstrates the agency’s commitment to using novel endpoints to expedite important therapies to the American public.”

The SPARTAN trial evaluated the safety and efficacy of

(Continued on page 4)
Higher Radiation Dose May Not Improve Prostate Cancer Outcomes

Escalating a patient’s radiotherapy (RT) dose for localized prostate cancer may not improve overall survival (OS), although it may reduce the likelihood of distant metastases, according to research published 15 March 2018 online in *JAMA Oncology*.

While RT may be curative for men with intermediate-risk, localized prostate cancer, it was previously unknown if increasing RT dosage would improve clinical outcomes. For the randomized phase 3 NRG Oncology RT0126 study (ClinicalTrials.gov identifier: NCT00033631), researchers evaluated whether 79.2 Gy in 44 fractions would improve clinical outcomes over 70.2 Gy in 39 fractions. The primary endpoint was OS. Secondary outcomes included PSA level change, prostate cancer–related mortality, local and distant disease progression, and grade 2 or worse gastrointestinal/genitourinary adverse events (AEs). Of 1,499 men included in the study, the median age was 71 years, the median PSA at baseline was 7.6 ng/mL, and 83.9% of men had a Gleason score of 7 (all others had a Gleason score of 2–6). Seven hundred and fifty-one patients were assigned to the 70.2 Gy group and 748 were assigned to the 79.2 Gy group. The median follow-up was 8.4 years.

No difference in OS was found between treatment arms: the five-year OS rates were 89% in the 70.2 Gy arm and 88% in the escalation arm; the eight-year OS rates were 75% and 76%, respectively (hazard ratio [HR], 1.0; P=0.98, not a statistically significant difference). Rates of grade 2 or worse gastrointestinal/genitourinary AEs were, furthermore, higher in the 79.2 Gy arm. The cumulative eight-year rates of distant metastases were, 6% and 4% in the 70.2 Gy and 79.2 Gy arms, respectively (HR, 0.65; P=0.05, *not a statistically significant difference*). Biochemical (PSA) failure rates were also better, but not significantly so, in the 79.2 Gy arm.

The authors concluded that dose “escalation has several clinical advantages including improved rates of biochemical and clinical cancer control. These benefits do not translate into improved OS. The decision to deliver high RT dose must be balanced against the risk of morbidity in the individual patient.”

*Prostate Cancer Advisor* 15 March 2018

Digital Rectal Examination for Prostate Cancer Screening in Primary Care: A Systematic Review and Meta-Analysis


*Ann Fam Med* 16: 149-154, 2018

**Purpose:** Although the digital rectal examination (DRE) is commonly performed to screen for prostate cancer, there is limited data to support its use in primary care. This review and meta-analysis aims to evaluate the diagnostic accuracy of DRE in screening for prostate cancer in primary care settings.

**Methods:** We searched MEDLINE, Embase, DARE (Database of Abstracts of Reviews of Effects), Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and CINAHL (Cumulative Index to Nursing and Allied Health Literature) from their inception to June 2016. Six reviewers, in pairs, independently screened citations for eligibility and extracted data. Pooled estimates were calculated for sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of DRE in primary care settings using an inverse-variance meta-analysis. We used QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies 2) and GRADE (Grades of Recommendation Assessment, Development, and Evaluation) guidelines to assess study risk of bias and quality.

**Results:** Our search yielded 8,217 studies, of which 7 studies with 9,241 patients were included after the screening process. All patients analyzed underwent both DRE and biopsy. Pooled sensitivity of DRE performed by primary care clinicians was 0.51 (95% CI, 0.36–0.67; I² = 98.4%) and pooled specificity was 0.59 (95% CI, 0.41–0.76; I² = 99.4%). Pooled PPV was 0.41 (95% CI, 0.31–0.52; I² = 97.2%), and pooled NPV was 0.64 (95% CI, 0.58–0.70; I² = 95.0%). The quality of evidence as assessed with GRADE was very low.

**Conclusion:** Given the considerable lack of evidence supporting its efficacy, we recommend against routine performance of DRE to screen for prostate cancer in the primary care setting.
Doc Moyad’s What Works & What is Worthless Column – Also Known as “No Bogus Science” Column

“Okay, Curcumin is Having a Good 2018... So Far?”

Mark A. Moyad, MD, MPH, University 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.

What makes turmeric look yellow, or how about what makes mustard look yellow even though it is not naturally yellow? The answer is “curcumin” and in the area of neurology it just hit a single (I love baseball analogies), so it is time to watch it more closely in cancer and other fields of medicine. However, perhaps the type of curcumin matters?

How many “experts” over my 33 years of working in nutrition and supplements have been wrong in their bold predictions? Well, if I had a penny for every “expert” wrong prediction I witnessed, I would own enough pennies to make a few dollars! Selenium? Wrong! Vitamin E? Wrong! Exotic elixirs? Sorry, and thanks for playing! Now, some folks are hot on “curcumin.” I have not been impressed with it yet for a few reasons. Nonetheless, one reason I take pride in my prediction record of what might work and what might not work is that I try and keep a constant eye on what is going on outside of prostate cancer. Recently, UCLA researchers completed a small 18-month randomized trial of 40 “non-demented” adults (age 51-84 years) to evaluate a more bioavailable (better absorbed) form of curcumin known as “Theracurmin.” (FYI – I never worked with this company in my life). Theracurmin dosed at 90 mg twice a day (total 180 mg daily) was compared against placebo. Study results demonstrated significantly improved memory and attention span in the Theracurmin group. Not only that, PET scans of the brain performed before and after randomized treatment suggested a reduction in plaque and tangle accumulations in areas that can impact memory and mood. Thus, the researchers suggested that curcumin could have anti-inflammatory effects and/or anti-amyloid brain impacts. Wow! Does this mean Theracurmin also prevents or treats Alzheimer’s disease? I have no idea. Does this mean it has anti-cancer effects? I have no idea (and neither does anyone else as of yet). However, it means that perhaps the first big obstacle with curcumin has been overcome, which is finding a way to increase its absorption and bioavailability. Now, more positive studies in neurology and cancer using these lower, more bioavailable doses are needed.

Regardless, this was an interesting preliminary study that got my attention. It does not mean I am inviting curcumin to the “Moyad Successful Dinner Research Table” (aka MSDRT). Would I take this form of curcumin based on this study? I would not, but show me several more positive studies and things would get a bit more interesting. In the meantime, I love my mustard even more now and I might even throw in a little more turmeric into my next meal. What the heck! And, I do hope that Theracurmin or another form of curcumin will hit a home run soon! We need more homeruns!

Reference:


Higher Resource Use in Metastatic CRPC (Continued from page 1)

more likely to be white (78.4% vs. 71.8%; P <0.001), and had a higher education level and higher median income; there were some regional differences as well.

There were no differences, however, with regard to the quality of care at EOL. Among the extreme users, 20.1% had more than one hospital admission, compared with 16.7% of non-extreme users (P=0.07, a statistically significant difference); 18.2% and 15.7%, respectively, had more than one emergency department visit (P=0.16, not a statistically significant difference).

There was also no statistically significant difference in the number of men who entered the intensive care unit within one month of death (26.2% vs. 22.7%; P=0.09), or in the proportion of men who had a length of stay of 14 days or longer (13.8% vs. 12.3%; P=0.36).

The same was true for proportions of men who entered hospice care within seven days of death (4.5% of extreme users vs. 3.3% of non-extreme users; P=0.20, not a statistically significant difference), within 30 days of death (15.0% vs. 12.8%; P=0.19), and within six months of death (21.5% vs. 20.3%; P=0.53). The adjusted rate of deaths per 100 person-years was 29.22 among extreme users; P=0.20, not a statistically significant difference).

In men diagnosed with metastatic prostate cancer, more frequent PSA testing and imaging were associated with substantially higher costs without an observed benefit, neither in survival nor in quality of care at EOL, the authors concluded.

“Physicians are encouraged to discuss treatment goals with patients and to devise appropriate monitoring plans based on these goals.”

CancerNetwork
30 March 2018
apalutamide vs. placebo in 1,207 men with nmCRPC and a rapidly rising PSA level despite receiving continuous androgen deprivation therapy (ADT). Nonmetastatic status was determined by a negative bone scan, as well as a negative CT of the pelvis, abdomen, chest, and brain. Patients were required to have a PSA doubling time (PSADT) of ≤10 months, since “prior data has shown that these are the patients most at risk for developing metastases and death,” said Dr. Eric Small, primary author of the abstract for the SPARTAN trial.

Men were randomized in a 2:1 ratio to 240 mg of apalutamide daily (N=806) or placebo (N=401). The average baseline PSADT was less than five months in both arms. Men who developed metastases were allowed to receive abiraterone acetate (Zytiga®) plus prednisone, which, Small noted, is the standard of care in patients with metastatic CRPC.

Beyond the primary MFS endpoint, secondary endpoints included time to metastasis, progression-free survival, time to symptomatic progression, and overall survival (OS). For patients who developed metastases, the researchers also evaluated the time between randomization to first treatment for metastatic CRPC and subsequent progression (PFS2). At a median follow-up of 20.3 months, 61% of the apalutamide arm remained on treatment compared with 30% of the placebo group. An interim OS analysis (24% of events) revealed a trend favoring apalutamide.

“The SPARTAN trial results demonstrated impressive clinical benefits in patients with nmCRPC,” Matthew Smith, MD, PhD, co-principal investigator of the SPARTAN study, director of the Genitourinary Malignancies Program at the Massachusetts General Hospital Cancer Center, and Professor of Medicine at Harvard Medical School, said in statement. “As an oncologist and clinical investigator, I know how devastating it can be for patients and their families to hear that the cancer has spread. With this approval, doctors now have the chance to offer hope for delaying metastases in patients with CRPC.”

Adverse events led to discontinuation in 10.7% and 6.3% of the apalutamide and control arms, respectively. Neither group had a reduction in mean baseline health-related quality-of-life scores as the trial progressed, and there was no difference over time in the scores between the groups. Eighty percent of placebo patients who progressed and 56% of apalutamide patients were treated for metastatic CRPC. The researchers noted that PFS2 was longer for patients who were initially randomized to apalutamide.

“There is a population of men with prostate cancer who have no visible evidence of spread but who have a rise in their blood markers. These patients can have a poor prognosis and, until now, the optimal management of their cancer remained an enigma. These findings suggest there may finally be a treatment that holds real promise for extending their health and their lives,” ASCO expert Sumanta K. Pal, MD, a medical oncologist and assistant clinical professor in the Department of Medical Oncology and Therapeutics Research at City of Hope, said in a statement when the SPARTAN data were presented at the 2018 Genitourinary Cancers Symposium (GUCC).

*Presented at the 2018 GUCC, abstract 161.*

Onclive, 14 February 2018

Quality of Life with Chemohormonal Treatment in Prostate Cancer

In the E3805 trial reported in the *Journal of Clinical Oncology*, Morgans et al. found that chemohormonal therapy with docetaxel and androgen-deprivation therapy (ADT) was associated with poorer quality-of-life (QOL) at three months but better QOL at 12 months vs. ADT alone in metastatic hormone-sensitive prostate cancer. Chemohormonal therapy has been shown to improve overall survival vs. ADT alone in this setting.

In the trial, 790 men were randomized between July 2006 and December 2012 to receive docetaxel for six cycles plus ADT (N=397) or ADT alone (N=393). QOL was assessed with the Functional Assessment of Cancer Therapy-Prostate (FACT-P) instrument at three, six, nine, and 12 months. Completion rates were 90% at baseline, 86% at three months, 83% at six months, 78% at nine months, and 77% at 12 months.

Compared with baseline, men in the chemohormonal therapy group had a significant decline in FACT-P at three months (P <0.001) but not at 12 months (P=0.38). Compared with patients in the ADT alone group, those in the chemohormonal therapy group had significantly worse FACT-P scores at three months (P=0.02) but significantly better scores at 12 months (P=0.04). Differences between groups in FACT-P never exceeded the prespecified minimal clinically important difference. Patients in 2:1 ratio [HR] 1.17, 95% confidence interval [CI] 0.88-1.55). EBRT plus AD was associated with greater mortality risk vs. RP (HR 1.53, 95% CI 1.22-1.92). Adjustment of models for predicted pathologic nodal status did not result in statistically different results. Sensitivity analysis indicated that the HR for mortality in the EBRT plus AD subgroup receiving total RT dose ≥7,920 cGy was 1.33 (95% CI 1.05-1.68), lower than that in the subgroup receiving <7,920 cGy (HR 1.68, 95% CI 1.37-2.06). The investigators concluded, “After comprehensively adjusting for imbalances in prostate cancer prognostic factors, other medical conditions, and socioeconomic factors, this analysis showed no statistical survival difference between men treated with RP vs. EBRT plus brachytherapy with or without AD. EBRT plus AD was associated with lower survival.”

*The ASCO Post 13 March 2018*

Brachytherapy vs. Radical Prostatectomy in High-Risk Localized Prostate Cancer

*Continued from page 1*
More High-Risk Prostate Cancer Now in the US Than Before

More men are now presenting with higher-grade, more invasive prostate cancer in the wake of 2012 recommendations from the US Preventive Services Task Force (USPSTF) not to routinely screen asymptomatic patients to detect early disease, more epidemiologic evidence indicates.

As predicted by urologists in 2012 after the recommendations were released, there has been a consistent, stepwise increase in cancers of higher Gleason score, as well as a stepwise increase in the median level of PSA, in the four years after the USPSTF recommendations were released, compared to the four years before the recommendations were issued.

At the same time, both surgical volume and the proportion of low-grade cancers have been dropping, as reported by Thomas Ahlering, MD, University of California, Irvine, and colleagues during a poster session of the European Association of Urology (EAU) 2018 Congress.

“Treating high-risk disease has its limitations, because you are not going to cure the majority of men no matter what you do, so the better answer is to diagnose prostate cancer earlier,” Ahlering stated. “If our data are correct, the most important thing to do is to start screening more intensely again,” he reaffirmed.

In one of two related studies, Ahlering and colleagues carried out a retrospective analysis of nine high-volume referral centers throughout the United States to compare men who presented with prostate cancer of Gleason grade 8 or higher and who had seminal vesicle and lymph node involvement before the 2012 USPSTF recommendations were issued with such men after the recommendations were issued. A total of 19,602 men were analyzed; four-year average diagnoses were compared between October 2008 and September 2012, and between October 2012 and September 2016, before and after the recommendations had been released. Researchers observed a 22.6% reduction in radical prostatectomy (RP) volume in the post-recommendation period compared to the pre-recommendation period. They also noted the median PSA level increased from 5.1 ng/mL prior to the recommendations to a median of 5.8 ng/mL after their release (P <0.001, a statistically significant difference).

Mean age at the time of diagnosis also increased, from 60.8 years before the recommendations to 62 years after the recommendations (P <0.001, a statistically significant difference).

“Expectedly, the proportion of low-grade Gleason 3+3 cancers decreased from 30.2% to 17.1% (P <0.001, a statistically significant difference),” the investigators write.

In contrast, the incidence of high-grade Gleason 8+ prostate cancers increased from 8.4% prior to the recommendations to 13.5% after the recommendations (P <0.001, a statistically significant difference). “In this Gleason 8+ group, we saw a 24% increase in absolute numbers [of prostate cancer diagnoses]. One-year biochemical recurrence (BCR) rose from 6.2% to 17.5% (P <0.0001, a statistically significant difference),” they report.

Ahlering and colleagues also performed a propensity score-matched analysis to rule out the possibility that the increase in high-risk disease was not due to referral patterns. “For any given age and PSA, propensity matching showed that there is now more aggressive disease in the post-recommendation era,” the researchers report.

“So these centers dispersed throughout the US have witnessed a tripling of BCR and a quadrupling of nodal metastasis,” the team concludes.

“A potential epidemiological shift towards high-risk disease raises concern for increased PCSM [prostate cancer-specific mortality], secondary interventions, and associated side effects.”

In a separate but related study, Linda Huynh, BS, clinical research assistant, University of California, Irvine, assessed the effect of the 2012 USPSTF recommendation in a population-based cohort. Huynh also assessed national diagnostic patterns during three eras: 2004 to 2007 (era one), 2008 to 2011 (era two), and 2012 to 2015 (era three). In total, the researchers analyzed data from 1,380,219 men who had undergone RP in one of the three eras assessed.

“Pathological endpoints of p-stage, lymph node metastasis, and surgical margins were compared between screening eras,” the researchers note. The investigators observed a 15.8% drop in surgical volume from both era one and era two. Importantly, the age at which men had undergone a RP dropped in the period 2008 to 2012 after an earlier USPSTF recommendation not to screen men aged 75 years and older (P <0.001).

“In contrast, preoperative PSA experienced an upward trend from 69 to 67 and 73 ng/mL (P <0.001),” the researchers observe. The risk in absolute numbers of high-risk prostate tumors of Gleason score 8 to 10 also increased in a stepwise fashion — “meaning that as we get further and further away from the 2012 recommendations, each year we are seeing more high-grade disease. Therefore, it does not look as if we are plateauing,” Huynh explained.

The investigators also reported a steady increase in diagnoses of prostate cancer with lymph node involvement across the three eras, from 1% in era one, to 2% in era two, to 3% in era three (P <0.001). Similarly, the incidence of high-stage disease (pT3/T4) increased from 6% in era one, to 10% in era two, to 19% in era three (P <0.001). After adjusting for age and PSA levels in a propensity score-matched analysis, the researchers also observed significant increases in positive surgical margin rates, tumor volume, and lymph node involvement.

Since era one, the USPSTF has made two recommendations against the use of PSA screening, first with respect to men aged 75 years and older, and in 2012, against PSA screening in men of all ages. The USPSTF recently changed its recommendation on PSA screening. In 2017, an updated recommendation emphasized that the decision to undergo PSA screening must be individualized for men aged 55 to 69 years. For men aged 70 years and older, the USPSTF still does not recommend PSA-based screening.

Despite this backtracking, it appears the fallout from the 2012 null recommendation remains unchecked. As previously reported, a new (Continued on page 8)
After Cancer, Accelerated Aging?

Even decades after treatment, cancer survivors tire more easily than people with no history of the disease, according to new research. The findings hint at a pattern of “accelerated aging” for people with a cancer history. Results were published recently in the journal Cancer.

“The main goal of cancer treatment has been survival, but studies like this suggest that we need also to examine the longer-term effects on health and quality of life,” said senior author, Jennifer Schrack, assistant professor at the Johns Hopkins School of Public Health.

The researchers analyzed data from a long-term study on normal aging. More than 300 were cancer survivors, with an average age of 74. About 1,330 of those studied, average age 69, had not had the disease. Researchers compared results of cancer survivors with results of adults who never had cancer.

Participants completed periodic treadmill tests and 400-meter walks (two-tenths of a mile) to assess their endurance, beginning in 2007. Afterward, they were asked to rate their level of fatigue. “We were surprised by the magnitude of the differences we found,” Schrack said in a university news release.

On average, those with a history of cancer treatment tired more easily on the treadmill tests and took longer to finish the walking tests, the study found. It showed cancer treatment was linked to a 1.6 times greater risk of a high level of fatigue. Being older than 65 was associated with a 5.7 higher risk for this decline in endurance. The cancer survivors walked, on average, 14 seconds slower and got tired more quickly, the study found.

Previous studies have shown that cancer treatment – often including chemotherapy and radiation – appears to speed up the aging process, leading to fatigue, a decline in brain function, heart disease and return of cancer. These new findings “support the idea that a history of cancer is associated with higher fatigability and that this effect worsens with advancing age,” Schrack said.

“The long-term goal is that doctors and patients will be able to take those specific long-term effects into account when they decide how to treat different cancers,” she added.

HealthDay News
2 April 2018

Diet, Exercise with Behavioral Counseling Can Reduce ADT Side Effects

Personalized exercise and diet intervention can lead to clinical improvement in mobility, body composition and strength in sedentary men receiving androgen-deprivation therapy (ADT) for prostate cancer, researchers reported in the Annals of Behavioral Medicine on 6 March 2018.

“As they gain fat and lose muscle during hormone therapy, these men are at significant risk for chronic health problems including metabolic disorder, a precursor to diabetes and heart disease,” lead investigator Brian C. Focht, PhD, of Ohio State University in Columbus, OH, stated in a university news release.

In the single-blind IDEA-P trial, Dr. Focht and his colleagues assigned 32 sedentary patients from their cancer center (mean age 66 years) to a group-based, cognitive-behavioral exercise and dietary intervention program or to a 12 weeks of standard care that involved exercise education.

“We think the group approach is important, because it creates social support for a group of men who have experienced shared challenges, and that can increase the chances of long-term behavior change,” he stated.

The intervention group received exercise and dietary prescriptions along with cognitive-behavioral counseling (GMCB) to promote independent improvement in behavior. The men received supervised resistance and aerobic exercise, tailored to each participant’s baseline function, for one hour twice a week. Dietary advice was based on guidelines that promoted increased fruit and vegetable intake.

The intervention group experienced significantly greater improvements in mobility performance, muscular strength, body fat percentage, and fat mass over three months compared with the standard care group. The team adjusted for ADT duration and patient status at baseline. “No patients experienced a serious intervention-related adverse event, and the program had favorable adherence and retention rates,” the researchers added.

“Taken collectively, these findings provide initial evidence supporting the value of lifestyle interventions combining GMCB counseling with personalized exercise and diet prescription in offsetting androgen-deprivation-induced toxicities upon body composition,” Dr. Focht stated.

Renal & Urology News
6 April 2018

QOL in Chemohormonal Treatment in PCa

(Continued from page 4)

the chemohormonal therapy group had significantly poorer Functional Assessment of Chronic Illness Therapy-Fatigue scores at three months vs. the ADT alone group (P <0.001), with similar scores between groups at all other time points. Compared with baseline, both groups had significantly poorer FACT-Taxane scores over time (P <0.001). There were no significant between-group differences in Brief Pain Inventory scores over time.

Both arms reported a similar minimally changed QOL over time, suggesting that ADT + [docetaxel] is not associated with a greater long-term negative impact on QOL.

The ASCO Post
29 March 2018

Resources Address Anxiety, Depression and Prostate Cancer

Many men who are diagnosed with prostate cancer, or are managing the disease, experience some level of anxiety and/or depression. Caregivers may also be affected. The psychosocial challenges surrounding treatment choices and side effect management can have a negative impact on the prostate cancer journey. Anxiety and depression aren’t always effectively treated, in part because the symptoms may not be recognized.

We encourage you to visit the Us TOO web page for information on recognizing and managing anxiety, depression and prostate cancer.

www.ustoo.org/anxiety-and-depression
P1, “Survival with...” Which treatment is best for men with high-risk localized disease: RP, EBRT with ADT or EBRT with brachytherapy +/- ADT? A non-randomized study was performed with information from the National Cancer Database. The authors found that survival with surgery was comparable to radiation plus brachytherapy but superior to radiation with or without ADT. The authors made efforts to control for as many variables as possible but, once again, without a randomized study these findings are not definitive proof and, therefore, the conclusions must be interpreted with care.

The Bottom Line: Despite the findings from this study, it is not possible to determine the relative effectiveness of RP, RT with ADT or RT plus brachytherapy without a randomized trial.

P1, “No Benefit in...” What is an appropriate amount of medical intervention for men who are approaching their death from metastatic prostate cancer? This certainly is not an easy answer, nor is it an easy topic to discuss, but it is important. The study by Hu, et al. looks at this question and found that higher resource use did not translate into better outcomes, but it did result in significantly higher costs. Given the finding that greater use of resources occurred more often in Caucasian vs. African-American men, in better educated, and in those with a higher median income, raises questions about whether different criteria are being used to influence who receives greater use of resources. Regardless, results showed that more intensive care does not lead to better outcome. Clinicians should become aware of these findings as they manage men near the end of their lives.

The Bottom Line: More intensive interventions during the last months of a man’s life when he is dying from prostate cancer do not translate into better outcomes.

P1, “FDA Approves...” Until recently, men with a rising PSA while on androgen deprivation therapy (ADT, also called castration resistant prostate cancer [CRPC]) have had no good treatment option unless the disease metastasized. Now one, and probably other, options are becoming available. The SPARTAN Trial tested a new androgen, apalutamide, in a large double-blinded study. Men were enrolled if they had a fast PSA doubling time on ADT and no evidence of metastases. The study end-point was development of metastatic disease and it occurred significantly less often in men randomized to the study drug vs. placebo. Interestingly, the FDA approved apalutamide even though it is not clear whether the drug will improve survival. More time will be needed to make that assessment. Fortunately, this is not the only drug capable of delaying metastatic disease in men with a rising PSA on ADT. Another study using enzalutamide has also been shown to delay development of metastatic disease and is likely to be approved for this new indication soon.

With the availability of two drugs to treat the same group of patients, the question becomes “which one should men receive first?” Since a head-to-head comparison has not been, and will probably not be done, how will doctors decide? One factor that may influence the decision is the fact that enzalutamide has been shown to improve survival in men treated for advanced disease and apalutamide lacks similar data. So, it seems logical that enzalutamide should work well for nonmetastatic CRPC.

The Bottom Line: Apalutamide is a new treatment for nonmetastatic CRPC, but if enzalutamide gets approved, apalutamide may not be the drug of first choice.

P2, “Higher RT Dose...” The significance of approving apalutamide without an improvement in survival is also important because of the study comparing dose escalation of external beam radiotherapy (EBRT) for men with intermediate-risk disease. This large randomized study compared RT doses of 79.2 Gy or 70.2 Gy. Study results showed that the higher RT dose led to a significantly better biochemical recurrence (BCR) free survival rate and a 2% lower incidence of metastases at eight years. However, it did not translate into an improved survival. The higher dose also led to a higher rate of late toxic effects. The authors appear to conclude that the higher dose did not offer a sufficient benefit. Surprisingly, the study did not give men some form of ADT, even though randomized studies have shown improved survival when it is combined with RT for patients with intermediate-risk disease. It is unclear why this was not done. The second point is this is another example of a disconnect between the impact of a treatment on BCR and the impact on survival. It shows that improving the first outcome will not necessarily translate into improving the second outcome. Returning to the first study above, one wonders why the FDA accepted this outcome without an improvement in survival.

The Bottom Line: An RT dose of 79.2 Gy does not improve survival in intermediate-risk prostate cancer.

P2, “Digital Rectal...” Is a digital rectal exam worthwhile for screening for prostate cancer? Apparently not, according to a study by Naji, et al. who conducted a review and meta-analysis of published studies on the subject. Based on their findings, they recommend against doing a routine exam to check for prostate cancer. Of course, the question remains, what about testing for rectal cancer? Unless doctors are advised not to check for this disease, a rectal will still be performed and one has to ask whether it is worth checking the prostate for 10 seconds while the rectal exam is being performed.

The Bottom Line: There is little evidence in the literature supporting the value of doing a rectal exam to check for prostate cancer during a routine exam by primary care doctors.

P4, “Quality of Life (QOL)...” The management of newly diagnosed metastatic disease is undergoing a significant change based on the results of several randomized studies.

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The Bottom Line (Continued from page 7)

ies. They have found that combining docetaxel or abiraterone with ADT significantly improved survival. Another trial in the issue reported the impact of chemotherapy on QOL and found that QOL was worse in the first three months, but significantly better at 12 months than the men receiving only ADT. Based on these trials, all men should be told about these findings when deciding what to do.

The next challenge will be to determine which patients should get the abiraterone and which ones should get docetaxel. Some of the data suggest that the best results with docetaxel occur in men with more advanced disease. Nevertheless, patients with a new diagnosis of metastases with more advanced disease. The study by Ahlering and co-workers suggests that this has happened. They looked at the proportions of men with Gleason 6, >7 disease and those having RP, and the mean PSA at diagnosis and found all were worse in the group diagnosed after 2012.

However, one must interpret these findings very carefully before concluding that reduced screening led to worse outcomes for men. First, simply reducing Gleason 6 cancers will naturally result in a higher proportion with higher Gleason scores. That does not mean worse disease has become more common. Second, the fact that RP volume has declined could be partly due to greater selection of one of the many other options available, including greater use of active surveillance. Ultimately, whether reduced screening harmed men will depend on the long-term effect on prostate cancer mortality and so far, no data are available. Perhaps with longer follow-up, there will be a change in mortality but, until that happens, it is still too early to argue for more aggressive screening.

The Bottom Line: Although RP numbers appear to have dropped and the proportion of men diagnosed with Gleason >7 cancers has increased, more data are needed to know if reduced screening is causing more harm to men.

More High-Risk PCa
(Continued from page 5)

analysis of data from the European Randomized Study of Screening for Prostate Cancer (ERSPC) and the PLCO trial now indicates that both studies support a prostate-cancer mortality benefit with PSA screening. The new analysis showed a 25% to 31% lower risk for prostate cancer mortality in the ERSPC and a 27% to 32% lower risk in the PLCO among men who were screened compared to men who were not screened.

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